

## PARTE SECONDA

*Deliberazioni del Consiglio e della Giunta*

DELIBERAZIONE DELLA GIUNTA REGIONALE 3 maggio 2021, n. 713

**Min. Salute NET-2018-12368077 Progr. di Rete “Definition and testing of a new model of clinical governance based on the integration of tools such as HTA Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV” - Presa d’atto.**

L’Assessore, sulla base dell’istruttoria espletata dal Funzionario del Servizio Governo dell’Offerta (SGO), confermata dal Dirigente del Sezione Strategie e Governo dell’Offerta, riferisce quanto segue:

**PREMESSO CHE**

Con nota prot. 4460/SP del 10/11/2017 indirizzata alla Direzione generale della ricerca e dell’innovazione in sanità, il Presidente della Regione Puglia ha riscontrato la nota del Ministero della Salute GAB 0012261 –P-03/11/2017, ritenendo di interesse strategico per la Regione Puglia, la tematica Health Technology Assessment (HTA) a supporto del modello di governance dei sistemi sanitari.

in data 03/04/2018 è stato pubblicato sul sito del Ministero della Salute il “Bando della Ricerca Finalizzata anno 2018 (esercizi finanziari anni 2016-2017)”;

in risposta a detto Bando, sezione E “Programmi di Rete” - area tematica 4, l’Istituto Superiore di Sanità in qualità di Destinatario Istituzionale ha presentato al Ministero della Salute e agli Enti co-finanziatori (Regione Lombardia, Regione Marche, Regione Toscana, Regione Puglia e Regione Veneto), la proposta di Programma di Rete dal titolo “*Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV*” che vede il coinvolgimento dell’Istituto Tumori “G. Paolo II” IRCCS di Bari;

con decreto direttoriale del 26 luglio 2019, registrato dall’Ufficio centrale di bilancio presso il Ministero della Salute in data 3 settembre 2019 con visto n. 731 è stata approvata la graduatoria dei programmi di rete a seguito del bando della ricerca finalizzata 2018 - relativo agli anni finanziari 2016-2017 - nella quale è indicata, per ciascun programma, la somma destinata dal Ministero per la realizzazione del programma medesimo;

la suddetta graduatoria, per la tipologia Programmi di rete (NET) - area tematica 4, vede la presenza del progetto NET-2018-12368077 dal titolo “*Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings INTEGRATE-HEALTH-GOV*” con un finanziamento ministeriale assegnato complessivo di euro 1.594.238,00 ed un co-finanziamento di euro 150.000,00 dalla Regione Lombardia, di euro 300.000,00 dalla Regione Marche, di euro 299.998,00 dalla Regione Puglia, di euro 45.000,00 Regione Toscana, di euro 278.300,00 dalla Regione Veneto,

Con nota prot. 3526 del 11/10/2019 il Presidente della Regione Puglia ha delegato il Dott. Giovanni Campobasso nella qualità di Dirigente della Sezione SGO alla sottoscrizione della Convenzione attuativa con dell’Istituto Tumori “G. Paolo II” IRCCS di Bari.

**CONSIDERATO CHE**

con nota acquisita agli atti dell'Istituto Tumori "G. Paolo II" IRCCS di Bari prot. n. 18805 dell'8/10/2020, l'Istituto Superiore di Sanita ha trasmesso la convenzione stipulata con il Ministero della Salute, completo di:  
-piano esecutivo -corredato di cronoprogramma e schede finanziarie - in cui sono indicati i WP partecipanti al programma di rete:

- il documento Consortium Agreement;
- le convenzioni attuative;

i programmi di rete sono realizzati da consorzi di ricerca articolati in non meno di tre e non più di otto work package (WP) ed hanno per capofila un Ente del SSN che svolge le funzioni di coordinamento e, che nel caso di specie, relativamente al programma in oggetto, l'Ente capofila del programma è l'Istituto Superiore di Sanita, definito Work Package 1, ed il suo Principal Investigator e Coordinatore dell'intero programma è il Prof. Gualtiero Ricciardi e le Regioni partecipanti al Programma di Rete, per il tramite dei loro Enti di Ricerca, oltre all'ISS capofila sono: Regione Lombardia, Marche, Puglia, Toscana e Veneto;

come previsto dal bando, in data 18/10/2019 è stata stipulata la convenzione attuativa tra Regione Puglia e l'Istituto Tumori "G. Paolo II" che regola il rapporto tra Regione Puglia Dipartimento Promozione della Salute del Benessere Sociale e Sport per tutti – Sezione SGO e l'Istituto Tumori I.R.C.C.S. "Giovanni Paolo II", Regione, che è obbligata a concorrere con le modalità previste nel piano esecutivo del programma in oggetto; in base alla suddetta convenzione la Regione Puglia si impegnava a corrispondere all'Istituto Tumori "G. Paolo II IRCCS per il WP5 il finanziamento ministeriale ricevuto, secondo le seguenti modalità:

- la prima rata anticipata pari al 50% dell'importo del finanziamento ministeriale verrà corrisposta al momento della comunicazione da parte del responsabile Scientifico del WP5 Dr. Vito Lorusso dell'inizio dell'attività di ricerca;
- la seconda rata pari al 30% sarà erogata al diciottesimo mese anno di attività previa approvazione da parte del Ministero della Salute - Comitato Tecnico Sanitario - della relazione intermedia di cui all' art. 2 della convenzione;
- la terza rata pari al 20% sarà erogata a conclusione del progetto previa approvazione della relazione finale di cui all'art. 2 della convenzione;
- il co-finanziamento regionale complessivo da corrispondere di € 299.998,00 sarà erogato con le stesse modalità del Ministero e ripartito come da scheda finanziaria allegata al piano esecutivo;
- la Regione Puglia si impegna a trasferire all'Istituto Tumori IRCCS Giovanni Paolo II la prima rata del co-finanziamento regionale entro trenta giorni dalla comunicazione di inizio attività;

Successivamente in data 25/11/2019 è stato perfezionato il Consortium Agreement che regola i rapporti e le modalità di gestione attuazione del programma di rete in questione e disciplina il ruolo e compiti dei seguenti sottoscrittori (WP):

- Istituto Superiore di Sanita, sede del WP1
- Regione Lombardia e ASST - Grande Ospedale metropolitano Niguarda, sede del WP2;
- IRCCS Istituto Ortopedico Galeazzi, sede del WP3:
- Regione Marche e IRCCS Istituto Nazionale di Riposo e Cura per gli Anziani, sede del WP4:
- Regione Puglia e Istituto Tumori "G. Paolo II IRCCS, sede del WP5:
- Regione Toscana e Azienda Ospedaliera Universitaria Careggi Firenze, sede del WP6
- Regione Toscana e Scuola superiore di Studi universitari e di perfezionamento Sant'Anna, sede WP7
- Regione Veneto e Azienda Zero, sede del WP8

l'articolo 3 del richiamato Consortium prevede che il finanziamento messo a disposizione dal Ministero della salute, pari a complessivi euro € 1.594.238,00, sia distribuito tra i WP aventi sede presso enti del servizio sanitario nazionale, come di seguito riportato:

- Istituto superiore di sanità – WP1 - euro € 200.000,00;
- Regione Lombardia - WP2 - ASST - Grande Ospedale metropolitano Niguarda - euro € 140.000,00;
- Regione Lombardia - WP3 - IRCCS Istituto Ortopedico Galeazzi euro € 280.000,00;
- Regione Marche - WP4 - IRCCS Istituto Nazionale di Riposo e Cura per gli Anziani- euro € 280.000,00
- Regione Puglia- WPS-Istituto Tumori "G. Paolo II" IRCCS - euro 279.898,00;
- Regione Toscana- WP6 - Azienda Ospedaliera Universitaria Careggi Firenze- euro 280.000,00;
- Regione Veneto- WP8 - Azienda Zero- euro 274.340,00;

- il suddetto articolo 3 prevede altresì che il finanziamento di cui trattasi sia erogato dal Ministero della Salute all'Istituto Superiore di Sanità, capofila del programma di rete, ente co-finanziatore, destinatario istituzionale presso cui ha sede il WP1 del programma medesimo: il finanziamento ministeriale sarà trasferito dal Ministero della Salute, secondo le modalità indicate nella convenzione con esso stipulata, al Destinatario Istituzionale Capofila, il quale provvederà a liquidare direttamente negli Enti sede dei singoli WP le quote spettanti, compatibilmente con i vincoli temporali posti dalle procedure contabili in essere,

pertanto secondo il Consortium Agreement del 25/11/2019, diversamente da quanto previsto dalla Convenzione attuativa tra Regione Puglia e l'Istituto Tumori I.R.C.C.S. "Giovanni Paolo II" stipulata in data 18/10/2019, la Regione Puglia corrisponderà all' IRCCS soltanto la quota del co-finanziamento regionale pari a € 299.998,00 che sarà erogato con le stesse modalità del Ministero.

come da art 3 della Convenzione tra il Ministero della Salute e l'Istituto superiore di Sanità, il progetto avrà la durata di anni tre e che, come da art. 9, il termine della ricerca può essere prorogato dal Ministero per un periodo massimo di mesi 12 dalla data di scadenza solo a seguito di formale, motivata e documentata istanza firmata digitalmente dal legale rappresentante della richiamata Regione e del principal investigator del WP1 e che tale richiesta non può essere avanzata prima di 12 mesi dalla data di inizio della ricerca e non oltre novanta (90) giorni precedenti la data del termine della suddetta:

le attività relative al progetto hanno avuto inizio il 4 settembre 2020, come da nota del Direttore delle Risorse Umane ed Economiche del Ministero della Salute inviata a mezzo pec alla Presidenza della Regione Puglia in data 07/10/2020.

il Principal Investigator del progetto per la Regione Puglia WP 5 è il dott. Vito Lorusso, Direttore dell'U.O.C. di Oncologia Medica dell'Istituto Tumori I.R.C.C.S. "Giovanni Paolo II" e che i ricercatori collaboratori sono il dott. Francesco Giotta, la dott.ssa Raffaella Massafra e il dott. Alfredo Zito;

il finanziamento ministeriale concesso all'Istituto Tumori "G. Paolo II" IRCCS di Bari pari ad euro 279.898,00 e il co-finanziamento da parte della Regione Puglia pari ad euro 299.998,00, come da piano economico compreso nella convenzione, risultano suddivisi per voci di spesa come riportato nella Tabella sotto:

| COSTI   | Budget Totale | Co-finanziamento Istituto | Co-finanziamento Regione Puglia | Finanziamento Ministero della Salute |
|---|---------------|---------------------------|---------------------------------|--------------------------------------|
| Quote stipendiali personale di ruolo              | 230.000,00 €  | 230.000,00 €              | 0,00 €                          | 0,00 €                               |
| Contratti di lavoro subordinato o parasubordinato | 341.996.00 €  | 0,00 €                    | 220.998,00 €                    | 120.998.00 €                         |

|   |              |              |              |              |
|---|--------------|--------------|--------------|--------------|
| Apparecchiature strumentazioni (leasing noleggio) | 31.300,00 €  | 0,00 €       | 11.300,00 €  | 20.000,00 €  |
| Materiale di consumo                              | 105.000,00 € | 0,00 €       | 0,00 €       | 105.000,00 € |
| Costi per modelli animali                         | 0,00 €       | 0,00 €       | 0,00 €       | 0,00 €       |
| Subcontratti                                      | 30.000,00 €  | 0,00 €       | 30.000,00 €  | 0,00 €       |
| Costi per arruolamento pazienti                   | 0,00 €       | 0,00 €       | 0,00 €       | 0,00 €       |
| Servizi esterni statistici e/o informatici        | 0,00 €       | 0,00 €       | 0,00 €       | 0,00 €       |
| Spese per pubblicazioni                           | 10.500,00 €  | 0,00 €       | 5.100,00 €   | 5.400,00 €   |
| Convegni  | 5.000,00 €   | 0,00 €       | 2.600,00 €   | 2.400,00 €   |
| Missioni  | 10.100,00 €  | 0,00 €       | 5.000,00 €   | 5.100,00 €   |
| Spese generali                                    | 46.000,00 €  | 0,00 €       | 25.000,00 €  | 21.000,00 €  |
| Spese per le attività di coordinamento Totale     | 0,00 €       | 0,00 €       | 0,00 €       | 0,00 €       |
| TOTALE  | 809.896,00 € | 230.000,00 € | 299.998,00 € | 279.898,00 € |

## VISTA

La nota prot. 24464 del 28/12/2020, con cui il Coordinatore Scientifico del Progetto per il WP5 dell'Istituto Tumori "G. Paolo II" IRCCS di Bari, Dott. Vito Lorusso, ha comunicato alla Regione Puglia che le attività relative al WP5 hanno avuto inizio il 04/12/2020 ed ha richiesto l'erogazione del co-finanziamento regionale pari a € 299.998,00.

L'Assessore sulla base delle risultanze istruttorie come innanzi illustrate, ai sensi dell'art. 4, co.4 lett. K della L.R. n.7/1997, propone alla Giunta:

- 1 di prendere atto del Progetto di Ricerca Finalizzata - Ministero della Salute- NET-2018-12368077 - Programma di Rete dal titolo "Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV";
- 2 di demandare al Dirigente della Sezione Strategia e Governo dell'Offerta, l'adozione dei successivi provvedimenti ai fini dell'erogazione del co-finanziamento regionale secondo le modalità sopra riportate;
- 3 di notificare il presente provvedimento Segretario Generale della Presidenza ai fini della valutazione finale, ai sensi della D.G.R. 1626/2020;
- 4 di disporre la pubblicazione del presente provvedimento sul BURP.

## **VERIFICA AI SENSI DEL D.LGS. N. 196/2003 E DEL REGOLAMENTO (UE) 679/2016 GARANZIE DI RISERVATEZZA**

La pubblicazione sul BURP, nonché la pubblicazione all'Albo sul sito Istituzionale, salve le garanzie previste dalla legge 241/1990 in tema di accesso ai documenti amministrativi, avviene nel rispetto della tutela della riservatezza dei cittadini secondo quanto disposto dal Regolamento UE n. 679/2016 in materia di protezione dei dati personali, nonché dal D. Lgs. 196/2003 ss.mm.ii., ed ai sensi del vigente Regolamento regionale 5/2006 per il trattamento dei dati sensibili e giudiziari, in quanto applicabile. Ai fini della pubblicità legale,

il presente provvedimento è stato redatto da evitare la diffusione di dati personali identificativi non necessari ovvero il riferimento alle particolari categorie di dati previste dagli articoli 9 e 10 del succitato Regolamento UE.

**“COPERTURA FINANZIARIA DI CUI AL D.LGS. 118/2011 E SS.MM.II ”**

La spesa derivante dal presente provvedimento pari ad euro € 299.998,00 complessivi trova copertura sul capitolo U0721055 L.R. N. 45 DEL 28.12.2012, ART.17- ANNO 2013- IMPEGNO DI SPESA con gli impegni fatti con la d.d. 151/2013/177.

I sottoscritti attestano che il procedimento istruttorio affidato è stato espletato nel rispetto della normativa regionale, nazionale e comunitaria e che il presente schema di provvedimento, dagli stessi predisposto, ai fini dell'adozione dell'atto finale da parte della Giunta Regionale, è conforme alle risultanze istruttorie.

Il Funzionario: Roberto Carella

Il Dirigente della Sezione: Giovanni Campobasso

Il sottoscritto Direttore di Dipartimento non ravvisa la necessità di esprimere, sulla proposta di delibera, osservazioni, ai sensi del combinato disposto degli artt. 18 e 20 del DPGR n.443/2015.

IL DIRETTORE DEL DIPARTIMENTO POLITICHE DELLA  
SALUTE, BENESSERE SOCIALE E SPORT PER TUTTI  
(Vito Montanaro)

L'ASSESSORE ALLA SANITA' E BENESSERE ANIMALE  
(Pietro Luigi Lopalco)

**LA GIUNTA**

- Udita la relazione e la conseguente proposta dell'Assessore;
- Vista la sottoscrizione posta in calce al presente schema dal Dirigente della Sezione Strategia e Governo dell'Offerta;
- A voti unanimi espressi nei modi di legge

**DELIBERA**

per le motivazioni espresse in premessa, che quivi si intendono integralmente riportate,

- 1 di prendere atto del Progetto di Ricerca Finalizzata - Ministero della Salute- NET-2018-12368077 -Programma di Rete dal titolo "Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV";
- 2 di demandare al Dirigente della Sezione Strategia e Governo dell'Offerta, l'adozione dei successivi provvedimenti ai fini dell'erogazione del co-finanziamento regionale secondo le modalità sopra riportate;

- 3 di notificare il presente provvedimento Segretario Generale della Presidenza ai fini della valutazione finale, ai sensi della D.G.R. 1626/2020;
- 4 di disporre la pubblicazione del presente provvedimento sul BURP.

Il Segretario della Giunta  
GIOVANNI CAMPOBASSO

Il Presidente della Giunta  
MICHELE EMILIANO



DIPARTIMENTO PROMOZIONE DELLA SALUTE,  
DEL BENESSERE SOCIALE E DELLO SPORT PER TUTTI

SEZIONE STRATEGIE E GOVERNO DELL'OFFERTA

SERVIZIO STRATEGIE E GOVERNO DELL'ASSISTENZA ALLE  
PERSONE IN CONDIZIONI DI FRAGILITÀ – ASSISTENZA  
SOCIOSANITARIA

Codice CIFRA: SGO/DEL/2021/00025

**PARERE TECNICO**  
(Art. 7 co. 3 DGR n. 2100/2019)

**PROPOSTA DI DELIBERAZIONE DELLA GIUNTA REGIONALE AVENTE AD OGGETTO**

**Min. Salute NET-2018-12368077 Progr. di Rete "Definition and testing of a new model of clinical governance based on the integration of tools such as HTA Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV"- Presa d'atto.**

**VISTO CHE**

- con decreto direttoriale del 26 luglio 2019, registrato dall'Ufficio centrale di bilancio presso il Ministero della Salute in data 3 settembre 2019 con visto n. 731 è stata approvata la graduatoria dei programmi di rete a seguito del bando della ricerca finalizzata 2018 - relativo agli anni finanziari 2016-2017;
- la suddetta graduatoria, per la tipologia Programmi di rete (NET) - area tematica 4, vede la presenza del progetto NET-2018-12368077 dal titolo "*Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings INTEGRATE-HEALTH-GOV*" con un finanziamento ministeriale assegnato complessivo di euro 1.594.238,00 ed un co-finanziamento di euro 299.998,00 dalla Regione Puglia,

**CONSIDERATO CHE**

- Con nota prot. 4460/SP del 10/11/2017 indirizzata alla Direzione generale della ricerca e dell'innovazione in sanità, il Presidente della Regione Puglia ha riscontrato la nota del Ministero della Salute GAB 0012261 -P-03/11/2017, ritenendo di interesse strategico per la

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Codice CIFRA: SGO/DEL/2021/00025

**Oggetto:** : Min. Salute NET-2018-12368077 Progr. di Rete "*Definition and testing of a new model of clinical governance based on the integration of tools such as HTA Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV*"- Presa d'atto.

Regione Puglia, la tematica Health Technology Assessment (HTA) a supporto del modello di governance dei sistemi sanitari.

**RITENENDOSI CHE**

- La spesa derivante dal presente provvedimento per il co-finanziamento pari ad euro € 299.998,00 complessivi trova copertura sul capitolo U0721055 L.R. N. 45 DEL 28.12.2012, ART.17- ANNO 2013- IMPEGNO DI SPESA con gli impegni fatti con la d.d. 151/2013/177.

Il Dirigente di Sezione  
Giovanni Campobasso \_\_\_\_\_



CAMPOBASSO GIOVANNI  
15.04.2021 11:12:38 UTC

**Sottoscrizione ai fini della presa d'atto degli effetti finanziari della proposta di deliberazione sul Fondo Sanitario Regionale**

Il Dirigente della Sezione Amministrazione Finanza e Controllo nonché Responsabile della Gestione Sanitaria Accentrata  
Benedetto Pacifico \_\_\_\_\_

Firmato digitalmente da  
BENEDETTO GIOVANNI PACIFICO  
Regione Puglia  
Firmato il 15/04/2021 15:34  
Seriale certificato : 819214

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|---|--|
|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
| <p><b>Project Code:</b> NET-2018-12368077</p>   | <p><b>Principal Investigator:</b> ricciardi gualtiero</p>  |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto Superiore di Sanita'</p>   |
| <p><b>Project Type: Network Project/Progetti di Rete</b></p>  |  |

**Major Diagnostic Category\*:** Ortopedia

**Project Classification IRG:** Healthcare Delivery and Methodologies

**Project Classification SS:** Health Services Organization and Delivery - HSOD

**Project Keyword 1:** Healthcare organizations, programs, and delivery of services; including those delivered in non-traditional settings; integrated care delivery systems; disease management and modeling; continuous quality improvement; characteristics of the organization and patient outcomes; organizational performance and efficiency; cost-benefit analysis; economics of health care and pharmacoconomics.

**Project Keyword 2:** Health care governance and sustainability

**Project Keyword 3:** Health technology assessment and clinical practice guidelines

**Project duration (months):** 36

**Project Request:**      **Animals:**                       **Humans:**                       **Clinical trial:**

**The object/s of this application is/are under patent copyright Y/N:**

| Operative Units / WP |   |  |                     |
|----------------------|---|--|---------------------|
|                      | INSTITUTION                                     | Department/Division/Laboratory                 | Role in the project |
| 1                    | Istituto Superiore di Sanita'                   | Centro Nazionale HTA                           | WP1                 |
| 2                    | Regione Lombardia - Direzione Generale Sanità   | ASST GRANDE OSPEDALE METROPOLITANO NIGUARDA    | WP2                 |
| 3                    | Istituto Ortopedico Galeazzi                    | Scientific direction                           | WP3                 |
| 4                    | Istituto Nazionale di Riposo e Cura per Anziani | Department of Geriatric Medicine               | WP4                 |
| 5                    | Istituto tumori Giovanni Paolo II               | UOC Oncologia Medica                           | WP5                 |
| 6                    | Toscana   | AOUC Azienda Ospedaliero-Universitaria Careggi | WP6                 |
| 7                    | Toscana   | Scuola Superiore Sant'Anna di Pisa - SSSA      | WP7                 |
| 8                    | Veneto  | Azienda Zero                                   | WP8                 |

## Overall Summary

The present project aims to define a governance model for the introduction of health policies and programs into the Italian National Health Service (NHS) based on the integration of tools such as Health Technology Assessment (HTA), Clinical Practice Guidelines (CPGs) and Clinical Pathways (CPs), stressing the creation of partnerships between the various stakeholders, particularly citizens/patients and professionals. Specific objectives include i) testing of the model, and ii) performance measurement of the model.

Initially, the governance model as well as a tool for performance measurement will be proposed on the basis of previous experiences. Subsequently, the model will be tested on clinical areas of interest in the participating Regions.

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|--|--|
|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti</p> <p><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
| <p><b>Project Code:</b> NET-2018-12368077</p>  | <p><b>Principal Investigator:</b> ricciardi gualtiero</p>  |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                   | <p><b>Applicant Institution:</b> Istituto Superiore di Sanita'</p>   |
| <p><b>Project Type: Network Project/Progetti di Rete</b></p>   |  |

### Background / State of Art

Sustainability of the welfare system and in particular of the National Health Service (NHS) represents one of the main challenges for Italy. In order to continue guaranteeing the characterizing principles of universality and equity of the NHS, there is thus a necessary to implement a governance model for an appropriate, effective and efficient use of resources, able to rationalize organizational processes, manage the increasing costs for technological innovation and maintain quality of healthcare. There are several technical and scientific tools available to build such an approach, among which Health Technology Assessment (HTA), clinical practice guidelines, and clinical pathways. Currently, these tools are applied mainly in a separate way and without a systemic vision for integration into the Italian NHS. Sustainability of the system could be supported by creating a model of governance based on these elements, combined with a multi-dimensional performance measurement system.

**It's available a Systematic Review on this topic?** No

### Hypothesis and Specific AIMS

#### Hypothesis and Significance:

In recent years, medicine has undergone a very rapid transformation with the introduction of innovative health technologies into the market, which, on the one hand, allow the evolution towards increasingly accurate diagnostic and therapeutic procedures and, secondly, if not used correctly, they can lead to a global increase in healthcare system costs and patient risks.

A health technology is defined as an intervention that can be used to promote health, prevent, diagnose or treat acute or chronic diseases, or for rehabilitation. Health technologies include pharmaceuticals, devices, procedures and organizational systems used in health care. The use of a new health technology origins the modification of a health service delivery process and, consequently, of the clinical pathway for diagnosis, treatment and management of the health condition. Sustainability of the welfare system and in particular of the National Health Service (NHS) represents one of the main challenges for Italy. In order to continue guaranteeing the characterizing principles of universality and equity of the NHS, there is thus a necessary to implement a governance model for an appropriate, effective and efficient use of resources, able to rationalize organizational processes, manage the increasing costs for technological innovation and maintain quality of healthcare. There are several technical and scientific tools available to build such an approach, among which Health Technology Assessment (HTA), clinical practice guidelines, and clinical pathways. Currently, these tools are applied mainly in a separate way and without a systemic vision for integration into the Italian NHS. Sustainability of the system could be supported by creating an integrated model of governance based on these elements, combined with a multi-dimensional performance measurement system.

#### Preliminary Data:

There are several technical and scientific tools available to build a governance model for an appropriate, effective and efficient use of resources, able to rationalize organizational processes, manage the increasing costs for technological innovation and maintain quality of healthcare, such an approach, among which Health Technology Assessment (HTA), clinical practice guidelines, and clinical pathways. Currently, these tools are applied in a separate way and without a systemic vision for integration into the Italian NHS. Sustainability of the system could be supported by creating a model of governance based on these elements, combined with a multi-dimensional performance measurement system.

#### Picture to support preliminary data:

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| <p><b>Project Code:</b> NET-2018-12368077</p>   | <p><b>Principal Investigator:</b> ricciardi gualtiero</p>  |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto Superiore di Sanita'</p>   |
| <p><b>Project Type: Network Project/Progetti di Rete</b></p>  |  |

**Specific Aim 1:**

Define a governance model for the definition of health policies and the introduction of health programs and technologies into the Italian National Health System (NHS), Regional Health Systems or healthcare institutions based on the integration of tools such as health technology assessment (HTA), clinical practice guidelines (CPGs) and clinical pathways (CPs), stressing the creation of partnerships between the various stakeholders, particularly citizens/patients and professionals.

**Specific Aim 2:**

Testing the model on clinical areas of interest selected by participating institutions.

**Specific Aim 3:**

Identification of facilitating factors and barriers that could influence the dissemination and integration of such governance model into daily practice within different contexts of the Italian National Health System.

**Experimental Design Aim 1:**

In particular, the identification of needs for assessment of health technologies proposed for acquisition is entrusted to WP8, which is also entrusted with the task of modeling the process of updating Clinical Pathways and procurement processes. WP2 builds models for rapid responses and define an analysis model assembling several coordinated decision-making cycles.

Finally, WP7 defines performance measures related to the specific clinical areas identified by the other partners (WP2, WP3, WP4, WP5, and WP6), as well as methodologies for data collection (e.g. specific user-specific questionnaires, administrative data) and analysis in collaboration with partners, in order to verify the gap between expected results and those detected in the analyzed real life settings (system performance).

**Experimental Design Aim 2:**

Clinical units (WP2, WP3, WP4, WP5, and WP6) are specific WPs which develop, ex-novo or contextualizing to the local reality, Health Technology Assessments and / or Clinical Practice Guidelines and/or Clinical Pathways, in different clinical areas and settings and for different categories of health technologies:

WP2: cardiovascular (telecardiology for heart failure);

WP3: orthopedic (fast track orthopedic clinical pathway);

WP4: geriatric care (remote management of patients discharged to nursing homes);

WP5: oncology (personalized clinical pathways in Breast Units through machine learning);

WP6: trauma care (optimal management of acute traumatic coagulopathy).

**Experimental Design Aim 3:**

All WPs identify, according to their aims and activities, facilitating factors and barriers that could influence the implementation, integration and dissemination of such governance model into daily practice within different contexts of the Italian National Health System.

These aspects will be compiled in a database, and matched to identify common and specific issues.

**Methodologies and statistical analyses:**

The governance model is based on the following stages:

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| <p><b>Project Code:</b> NET-2018-12368077</p>   | <p><b>Principal Investigator:</b> ricciardi gualtiero</p>  |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto Superiore di Sanita'</p>   |
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1. Identification of needs for assessment of health technologies proposed for acquisition, according to methods and procedures that allow the launch of a specific information flow which can be integrated into regional government strategies;
2. Production of recommendations about health technologies of interest based on HTA reports and/or updated clinical practice guidelines, or rapid responses which can inform in a timely manner when these documents are lacking, considering the uncertainty of information sources;
3. Structuring coordinated decision-making processes informed by progressively available elements of knowledge, aimed at facilitating the transparent processing of responsible, articulated, revisable decisions for decision-makers at various levels;
4. A procurement process, which considers particularly the identification of needs in terms of comparative value that can actually be demonstrated for health technologies proposed for acquisition;
5. Measurement of performance in terms of clinical practice guidelines application and clinical outcomes deriving from the use of new health technologies introduced into the regional health system or into the healthcare institution, in order to compare real effects to those provided by scientific literature.

**Expected outcomes:**

These five stages will be implemented aiming to produce a common structure which can be tested and assessed in the context of research on those clinical areas selected by participating institutions, and, subsequently, be used on other clinical areas by any healthcare institution of the Italian National Health System.

**Risk analysis, possible problems and solutions:**

1. Insufficient coordination of the consortium for establishing synergies between WPs (likelihood: medium)  
WP leads will be in contact with other WP leads periodically to brief each other about progress and to seek for potential synergies. This will be prepared and coordinated by WP1 in order to keep overview. All partners meet every 12 months to discuss progress and potential synergies. Also, in between, bottom-up risk-mitigation is set in place: WPs have sufficient overlap in partners that they can alert in case of potential missed opportunities. WP1 will instruct to all partners to facilitate this.
2. Insufficient applicability of the proposed framework for future projects (likelihood: medium)  
Outputs will be of value if they a) are well-based in past experiences of partners and others, b) build sufficiently on existing literature and c) are not seen as academic exercise alone but always with applicability to settings of interest. Involvement of multiple partners avoid a narrow focus.
3. Insufficient linkage to existing initiatives in order to add value to what is being done (low)  
The consortium composition in itself is an important risk mitigating factor, as many partners are involved in multiple initiatives.

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| <p><b>Project Type: Network Project/Progetti di Rete</b></p>  |  |

### Significance and Innovation

Production of Health Technology Assessments, Clinical Practice Guidelines and Clinical Pathways represents the first element of the proposed process, providing useful elements for decision-making, purchase-planning and regulation, and definition of elements to be considered for healthcare performance analysis. Secondly, the development of elements such as rapid responses, healthcare performance measurement tools, clinical documentation of purchasing needs and decision models, produces information that can integrate, improve and extend the scope of application of Health Technology Assessment, Clinical Practice Guidelines and Clinical Pathways in a continuous and cyclic activity of processes management and improvement.

### Description of the complementary and synergy research team

The network involves multidisciplinary research teams with expertise in fields such as: research methodology, clinical areas (cardiovascular, orthopedics, geriatrics, oncology, trauma care), health technology assessment (methods for multidimensional analysis of clinical, social, organizational, economic, ethical and legal implications of a technology, through the evaluation of multiple dimensions such as effectiveness, safety, costs, and social and organizational impact), healthcare management, clinical engineering, data management, statistical analysis, project management, etc. Multidisciplinary and diversity of areas of expertise assures the know-how required for the proposed project. Detailed descriptions of team compositions can be found on each WP statement.

### Training and tutorial activities

See training and tutorial activities for each WP.

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| <p><b>Project Type: Network Project/Progetti di Rete</b></p>  |  |

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Frønsdal KB, Facey K, Klemp M, Norderhaug IN, Mørland B, Røttingen JA. Health technology assessment to optimize health technology utilization: using implementation initiatives and monitoring processes. *Int J Technol Assess Health Care*. 2010 Jul;26(3):309-16.

Gagnon MP, Desmartis M, Poder T, Witteman W. Effects and repercussions of local/hospital-based health technology assessment (HTA): a systematic review. *Syst Rev*. 2014 Oct 28;3:129.

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Philips Z, Ginnelly L, Sculpher M, Claxton K, Golder S, Riemsma R, Woolacoot N, Glanville J. Review of guidelines for good practice in decision-analytic modelling in health technology assessment. *Health Technol Assess*. 2004 Sep;8(36):iii-iv, ix-xi, 1-158.

Pyone T, Smith H, van der Broek N. Frameworks to assess health systems governance: a systematic review. *Health Policy and Planning*. 2017 Jun;32(5):710-722.

Rotter T, Kugler J, Koch R, Gothe H, Twork S, van Oostrum JM, Steyerberg EW. A systematic review and meta-analysis of the effects of clinical pathways on length of stay, hospital costs and patient outcomes. *BMC Health Serv Res*. 2008 Dec 19;8:265.

Schwarzer R, Siebert U. Methods, procedures, and contextual characteristics of health technology assessment and health policy decision making: comparison of health technology assessment agencies in Germany, United Kingdom, France, and Sweden. *Int J Technol Assess Health Care*. 2009 Jul;25(3):305-14.

### Timeline / Deliverables / Payable Milestones

1M Kick-off meeting.  
12M: Annual meeting.  
24M: Annual meeting.  
36M: Final conference.

12M: D01. Shared governance model.  
18M: D02. Protocols for model testing on clinical areas of interest in the participating Regions/Provinces.  
30M: D03. Report on identified facilitating factors and barriers that could influence the dissemination of the governance model.  
36M: D04. Final report.

### Milestones 18 month

1M Kick-off meeting.  
12M: Annual meeting.

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12M: D01. Shared governance model.

18M: D02. Protocols for model testing on clinical areas of interest in the participating Regions/Provinces.

### Milestones 36 month

24M: Annual meeting.

36M: Final conference.

30M: D03. Report on identified facilitating factors and barriers that could influence the dissemination of the governance model.

36M: D04. Final report.

### Gantt chart

WP Overall - Timeline.xlsx

### Equipment and resources available

See equipment and resources available for each WP.

### Translational relevance and impact for the National Health System (SSN)

Contextualization of the governance model is proposed for application on various clinical areas, healthcare settings and health technology categories in such a way that allows the identification of facilitating factors and barriers that could influence the dissemination and integration of such governance model into daily practice within different contexts of the Italian National Health System.

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| <p><b>Project Type: Network Project/Progetti di Rete</b></p>  |  |

### PRINCIPAL INVESTIGATOR PROFILE

|                                     |   |   |
|-------------------------------------|---|---|
| <p>Name<br/>ricciardi gualtiero</p> | <p>Institution<br/>Department/Unit<br/>Position Title</p> | <p>Istituto Superiore di Sanita'<br/>President's Office<br/>President</p> |
|-------------------------------------|---|---|

### Personal Statement

The project aims to define a governance model for the introduction of health policies and programs into the Italian National Health Service (NHS) based on the integration of tools such as health technology assessment (HTA), clinical practice guidelines (CPGs) and clinical pathways (CPs), stressing the creation of partnerships between the various stakeholders, particularly citizens/patients and professionals. Prof. Ricciardi will act as Principal Investigator of WP1 (Project Coordination) and therefore will supervise the management of the activities undertaken by ISS as well of within the whole project, will ensure the coordination of all WPs and will guarantee the coherence between the activities undertaken by WPs and the respective deliverables, and the objectives of the project.

| Education/Training - Institution and Location                       | Degree  | Year(s) | Field of study                                    |
|---|---|---------|---|
| Faculty of Medicine and Surgery of University Federico II of Naples | Postgraduate in Hygiene and Preventive medicine | 1990    | Specialization in Hygiene and Preventive Medicine |
| Faculty of Medicine and Surgery of University Federico II of Naples | MD  | 1986    | Medicine and Surgery                              |
| London School of Hygiene and Tropical Medicine, London              | Master of Science                               | 1989    | Community medicine                                |

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| Positions  |   |                     |  |           |         |
|--|---|---------------------|--|-----------|---------|
| Institution  | Division / Research group   | Location            | Position   | From year | To year |
| Istituto Superiore di Sanità - National Institute of Health                    | Presidenza  | Roma, Italy         | President  | 2015      | 2018    |
| Agenzia Italiana del Farmaco (Italian Medicine Agency) AIFA                    | Technical Scientific Committee and Pricing and Reimbursement Committee            | Rome, Italy         | Official member as President of the Istituto Superiore di Sanità   | 2015      | 2018    |
| Istituto Superiore di Sanità - National Institute of Health                    | Presidenza  | Rome, Italy         | Commissioner   | 2014      | 2015    |
| European Commission  | DG SANTE  | Brussels, Belgium   | Expert Panel Member on the Effective Ways of Investing in Health (EXPH)  | 2013      | 2018    |
| WHO  | European Advisory Committee on Health Research (EACHR)                            | Copenhagen, Denmark | Member   | 2012      | 2018    |
| Ministry of Health   | Directorate General of Health Planning  | Rome, Italy         | Member of the Scientific Committee   | 2012      | 2015    |
| Presidenza del Consiglio dei Ministri (Presidency of the Council of Ministers) | Joint State-Region Technical Monitoring Structure (STEM)                          | Rome, Italy         | Member representing the Minister of Health   | 2010      | 2015    |
| Università Cattolica del Sacro Cuore   | Faculty of Medicine and Surgery 'A. Gemelli'                                      | Rome, Italy         | Professor of General and Applied Hygiene (related scientific sector affine and competition sector inclusive of Medical Statistics) | 2002      | 2018    |
| Università Cattolica del Sacro Cuore   | School of Hygiene and Preventive Medicine of the Faculty of Medicine 'A. Gemelli' | Rome, Italy         | Director   | 2002      | 2015    |
| Università Cattolica del Sacro Cuore   | Institute of Hygiene of the Faculty of Medicine and Surgery 'A. Gemelli'          | Rome, Italy         | Director   | 2002      | 2012    |

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| <p><b>Project Type: Network Project/Progetti di Rete</b></p>  |  |

**Official H index:** 34.0 ( autocertificata )

**Source:** Scopus

**Scopus Author Id:** 22836118300

**ORCID ID:** 0000-0002-5655-688X

**RESEARCH ID:** K-3342-2018

**Awards and Honors:**

In 2010 he was elected President of the EUPHA and in 2011 he was re-elected for a second term up to 2014. He was member of the Higher Health Council of the Italian Ministry of Health in the years 2003-2006 and the Italian Minister of Health appointed him Chair of the Public Health Section of the Council itself (2010-2014). In December 2015 he was appointed Director of the WHO Collaborating Centre for Health Policy, Governance and Leadership at the Catholic University of the Sacred Heart, Rome.

**Other CV Informations:**

He manages several undergraduate and postgraduate teaching activities including a Master of Science programme and International Courses in Epidemiology. He is Editor of the European Journal of Public Health, of the Oxford Handbook of Public Health Practice and Founding Editor of the Italian Journal of Public Health and of Epidemiology, Biostatistics and Public Health.

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| <p><b>Project Type: Network Project/Progetti di Rete</b></p>  |  |

### Selected peer-reviewed publications of the PI

| Valid for PI minimum expertise level  |                                 |          |         |     |
|---|---------------------------------|----------|---------|-----|
| Title   | DOI                             | PMID     | Cit. ** | P.* |
| The future of best investing in vaccines: The Health Technology Assessment approach   | 10.1016/j.vaccine.2008.01.009   | 18289744 | 9       | L   |
| The effectiveness of computerized clinical guidelines in the process of care: A systematic review   | 10.1186/1472-6963-10-2          | 20047686 | 56      | L   |
| OPTIGOV - A new methodology for evaluating Clinical Governance implementation by health providers   | 10.1186/1472-6963-10-174        | 20565967 | 18      | L   |
| Guidance for future HTA applications to vaccines: The HPV lesson  | 10.4161/hv.7.9.16084            | 21865880 | 7       | L   |
| The current status of decision-making procedures and quality assurance in Europe: An overview   | 10.1007/s11019-011-9333-0       | 21647732 | 4       | L   |
| Health in Europe - Policies for progress  | 10.1016/S0140-6736(13)60356-6   | 23541051 | 2       | C   |
| A systematic review on the effectiveness of group versus single-handed practice   | 10.1016/j.healthpol.2013.07.008 | 23910731 | 12      | L   |
| Disinvestment in healthcare: An overview of HTA agencies and organizations activities at European level                                   | 10.1186/s12913-018-2941-0       | 29490647 | 0       | C   |
| The management of multiple sclerosis by reference centers in south of Italy: a 2011 survey on health demands and needs in Campania region | 10.1007/s10072-015-2389-5       | 26439919 | 3       | L   |
| Italy's response to vaccine hesitancy: An innovative and cost effective National Immunization Plan based on scientific evidence           | 10.1016/j.vaccine.2017.06.011   | 28651836 | 11      | L   |
| Effectiveness of nutritional interventions addressed to elderly persons: Umbrella systematic review with meta-analysis                    | 10.1093/eurpub/ckx199           | 29228152 | 1       | L   |
| Health technology assessment agencies: An international overview of organizational aspects.   | 10.1017/S026646230707064X       | 17937828 | 0       | L   |
| Health Technology Assessment in Italy   | 10.1017/S0266462309090539       | 19505352 | 18      | L   |
| Primary Care Efficiency Measurement Using Data Envelopment Analysis: A Systematic Review  | 10.1007/s10916-014-0156-4       | 25486892 | 13      | L   |
| Hospital efficiency: How to spend less maintaining quality?   | 10.4415/ANN_17_01_10            | 28361805 | 0       | L   |

\* Position: F=First L=Last C=Correspondent

\*\* Autocertificated

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
| <p><b>Project Code:</b> NET-2018-12368077</p>   | <p><b>Principal Investigator:</b> Ricciardi Gualtiero</p>  |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto Superiore di Sanita'</p>   |
| <p><b>Project Type: Network Project/Progetti di Rete</b></p>  |  |

| For evaluation CV   |                                 |          |        |
|---|---------------------------------|----------|--------|
| Title   | DOI                             | PMID     | Cit. * |
| CYP1A1, CYP2E1, GSTM1, GSTT1, EPHX1 exons 3 and 4, and NAT2 polymorphisms, smoking, consumption of alcohol and fruit and vegetables and risk of head and neck cancer                              | 10.1007/s00432-007-0254-5       | 17611777 | 59     |
| Smoking status and gastric cancer risk: An updated meta-analysis of case-control studies published in the past ten years  |                                 | 19366050 | 59     |
| The relationship between avoidable hospitalization and accessibility to primary care: A systematic review   | 10.1093/eurpub/cks053           | 22645236 | 62     |
| The financial crisis in Italy: Implications for the healthcare sector   | 10.1016/j.healthpol.2012.04.003 | 22551787 | 65     |
| Aldehyde dehydrogenase 2 and head and neck cancer: A meta-analysis implementing a mendelian randomization approach  | 10.1158/1055-9965.EPI-08-0462   | 19124505 | 69     |
| Overweight and obesity among secondary school children in Central Italy   | 10.1023/A:1007675005395         | 10543355 | 71     |
| Polymorphisms in metabolic genes, their combination and interaction with tobacco smoke and alcohol consumption and risk of gastric cancer: A case-control study in an Italian population          | 10.1186/1471-2407-7-206         | 17996038 | 74     |
| Meta- and pooled analyses of the methylenetetrahydrofolate reductase C677T and A1298C polymorphisms and gastric cancer risk: A Huge-GSEC review   | 10.1093/aje/kwm344              | 18162478 | 77     |
| Comparisons of American, Israeli, Italian and Mexican physicians and nurses on the total and factor scores of the Jefferson scale of attitudes toward physician-nurse collaborative relationships | 10.1016/S0020-7489(02)00108-6   | 12667519 | 90     |
| Evaluation of the endorsement of the preferred reporting items for systematic reviews and meta-analysis (PRISMA) statement on the quality of published systematic review and meta-analyses        | 10.1371/journal.pone.0083138    | 24386151 | 183    |

\* Autocertificated

| Grant                        |      |          |                      |
|------------------------------|------|----------|----------------------|
| Funded Institution / Country | Year | Title    | Position in Projects |
| Horizon 2020 - SC1           | 2016 | TO-REACH | Coordinator          |

**Employment contract extension:**

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
| <p><b>Project Code:</b> NET-2018-12368077</p>   | <p><b>Principal Investigator:</b> ricciardi gualtiero</p>  |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto Superiore di Sanita'</p>   |
| <p><b>Project Type: Network Project/Progetti di Rete</b></p>  |  |

| Total proposed budget ( Euro ) |                     |                     |   |   |   |
|--------------------------------|---------------------|---------------------|---|---|---|
| Costs                          | TOTAL BUDGET        | Co-Funding          | Project costs proposed to funding Organization (no moh request) | List of costs proposed for funding to the MOH | Percentage of total proposed to the MOH |
| 1a Staff Salary                | 1.033.684,00        | 1.033.684,00        | 0,00  | not permitted                                 | 0,00                                    |
| 1b Researchers' Contracts      | 1.846.996,00        | 0,00                | 1.085.998,00  | 760.998,00                                    | 47,73                                   |
| 2 Equipment (Leasing - Rent)   | 377.800,00          | 0,00                | 102.800,00  | 275.000,00                                    | 17,25                                   |
| 3a Supplies                    | 125.000,00          | 0,00                | 20.000,00   | 105.000,00                                    | 6,59                                    |
| 3b Model Costs                 | 0,00                | 0,00                | 0,00  | 0,00  | 0,00                                    |
| 3c Subcontracts                | 114.000,00          | 0,00                | 73.000,00   | 41.000,00                                     | 2,57                                    |
| 3d Patient Costs               | 0,00                | 0,00                | 0,00  | 0,00  | 0,00                                    |
| 4 IT Services and Data Bases   | 158.000,00          | 0,00                | 40.000,00   | 118.000,00                                    | 7,40                                    |
| 5 Publication Costs            | 49.200,00           | 0,00                | 22.100,00   | 27.100,00                                     | 1,70                                    |
| 6 Convegni                     | 26.000,00           | 0,00                | 14.100,00   | 11.900,00                                     | 0,75                                    |
| 7 Travels                      | 33.800,00           | 0,00                | 13.000,00   | 20.800,00                                     | 1,30                                    |
| 8 Overheads                    | 251.240,00          | 0,00                | 106.800,00  | 144.440,00                                    | 9,06                                    |
| 9 Coordination Costs           | 90.000,00           | 0,00                | 0,00  | 90.000,00                                     | 5,65                                    |
| <b>Total</b>                   | <b>4.105.720,00</b> | <b>1.033.684,00</b> | <b>1.477.798,00</b>   | <b>1.594.238,00</b>                           | <b>100,00</b>                           |

Report the Co-Funding Contributor:

WP 1 - Istituto Superiore di Sanita'  
Staff salary

WP 2 - Regione Lombardia - Direzione Generale Sanità  
3 man-month salary of PI, 5 man-month salary of Co-PI, 6 man-month salary of four research collaborators.

WP 3 - Istituto Ortopedico Galeazzi  
3 man-month salary of PI and 11 man-month salary of Co-PI

WP 4 - Istituto Nazionale di Riposo e Cura per Anziani  
for staff salary

WP 5 - Istituto tumori Giovanni Paolo II  
The personnel involved will dedicate from 5% to 20% of the work activity every year for this project. the staff salary budget has been defined on the basis of the salaries of the personnel involved.

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
| <p><b>Project Code:</b> NET-2018-12368077</p>   | <p><b>Principal Investigator:</b> ricciardi gualtiero</p>  |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto Superiore di Sanita'</p>   |
| <p><b>Project Type: Network Project/Progetti di Rete</b></p>  |  |

WP 6 - Toscana

Staff-salary dedicated to the project

WP 7 - Toscana

Staff Salary

WP 8 - Veneto

for staff salary

| Working Package summary budget ( Euro ) |   |  |                       |            |  |   |
|---|---|--|-----------------------|------------|--|---|
| WP                                      | Research Institution                            | Funding Institution  | TOTAL PROGRAMME COSTS | Co-Funding | Project costs proposed to funding Organization | List of costs proposed for funding to the MOH |
| WP-1                                    | Istituto Superiore di Sanita'                   | Staff salary   | 350.000,00            | 150.000,00 | 0,00   | 200.000,00                                    |
| WP-2                                    | Regione Lombardia - Direzione Generale Sanità   | 3 man-month salary of PI, 5 man-month salary of Co-PI, 6 man-month salary of four research collaborators.  | 402.142,00            | 112.142,00 | 150.000,00                                     | 140.000,00                                    |
| WP-3                                    | Istituto Ortopedico Galeazzi                    | 3 man-month salary of PI and 11 man-month salary of Co-PI  | 402.142,00            | 112.142,00 | 150.000,00                                     | 140.000,00                                    |
| WP-4                                    | Istituto Nazionale di Riposo e Cura per Anziani | for staff salary   | 730.000,00            | 150.000,00 | 300.000,00                                     | 280.000,00                                    |
| WP-5                                    | Istituto tumori Giovanni Paolo II               | The personnel involved will dedicate from 5% to 20% of the work activity every year for this project. the staff salary budget has been defined on the basis of the salaries of the personnel involved. | 809.896,00            | 230.000,00 | 299.998,00                                     | 279.898,00                                    |
| WP-6                                    | Toscana   | Staff-salary dedicated to the project  | 370.000,00            | 45.000,00  | 45.000,00                                      | 280.000,00                                    |
| WP-7                                    | Toscana   | Staff Salary   | 354.500,00            | 100.000,00 | 254.500,00                                     | 0,00  |
| WP-8                                    | Veneto  | for staff salary   | 687.040,00            | 134.400,00 | 278.300,00                                     | 274.340,00                                    |

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| <p><b>Project Code:</b> NET-2018-12368077</p>   | <p><b>Principal Investigator:</b> ricciardi gualtiero</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>  | <p><b>Applicant Institution:</b> Istituto Superiore di Sanita'</p>  |
| <p><b>Project Type: Network Project/Progetti di Rete</b></p>  |   |

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| <p><b>Project Code:</b> NET-2018-12368077-1</p>   | <p><b>Principal Investigator:</b> ricciardi gualtiero</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto Superiore di Sanita'</p>  |
| <p><b>Project Type: WP PROJECT - 1</b></p>  |   |

**Major Diagnostic Category\*:** Ortopedia

**Project Classification IRG:** Healthcare Delivery and Methodologies

**Project Classification SS:** Health Services Organization and Delivery - HSOD

**Project Keyword 1:** Healthcare organizations, programs, and delivery of services; including those delivered in non-traditional settings; integrated care delivery systems; disease management and modeling; continuous quality improvement; characteristics of the organization and patient outcomes; organizational performance and efficiency; cost-benefit analysis; economics of health care and pharmacoconomics.

**Project Keyword 2:** Health care governance and sustainability

**Project Keyword 3:** Health technology assessment and clinical practice guidelines

**Project duration (months):** 36

**Project Request:**      **Animals:**       **Humans:**       **Clinical trial:**

**The object/s of this application is/are under patent copyright Y/N:**

| Investigators, Institution and Role in the Project |       |                  |                              |                       |            |
|--|-------|------------------|------------------------------|-----------------------|------------|
|  | Co-PI | Key Personnel    | Institution/Org./Pos.        | Role in the project   | Birth Date |
| 1  |       | Roazzi Paolo     | Istituto Superiore di Sanità | Research Collaborator | 26/05/1960 |
| 2  | X     | Marchetti Marco  | Istituto Superiore di Sanità | Research Collaborator | 31/08/1965 |
| 3  |       | iannone primiano | Istituto Superiore di Sanità | Research Collaborator | 30/12/1960 |

## Overall Summary

The WP1 will be responsible for coordination, management and the good conduct of the research agenda and ensuring that the planned deliverables and milestones are achieved. The WP1 aims to ensure the execution of activities and timely progress of tasks, alignment and consistency of their implementation, and the effective communication between the project partners; guarantee the compliance with ethics and data management policies; in the case of requiring a deviation from the proposed work plan, the WP1 will ensure that specific actions are undertaken to amend tasks, responsibilities and timings and work as close as possible with the involved WP. This will be achieved by monitoring and controlling work plans and timelines of each WP, through project review activities; verifying the compliance of all WPs activities with ethics and data management policies; arranging a kick-off meeting, general meetings in an annual basis, and WP-specific periodic meetings; and issuing periodical reports.

## Background / State of Art

Sustainability of the welfare system and in particular of the National Health Service (NHS) represents one of the main challenges for Italy. In order to continue guaranteeing the characterizing principles of universality and equity of the NHS, there is thus a necessary to implement a governance model for an appropriate, effective and efficient use of resources, able to rationalize organizational processes, manage the increasing costs for technological innovation and maintain quality of

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| <p><b>Project Code:</b> NET-2018-12368077-1</p>   | <p><b>Principal Investigator:</b> ricciardi gualtiero</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto Superiore di Sanita'</p>  |
| <p><b>Project Type: WP PROJECT - 1</b></p>  |   |

healthcare. There are several technical and scientific tools available to build such an approach, among which Health Technology Assessment (HTA), clinical practice guidelines, and clinical pathways. Currently, these tools are applied in a separate way and without a systemic vision for integration into the Italian NHS. Sustainability of the system could be supported by creating a model of governance based on these elements, combined with a multi-dimensional performance measurement system.

### Hyphotesis and Specific AIMS

#### Hyphotesis and Significance:

The Wp1 will be responsible for coordination, management and the good conduct of the research agenda and ensuring that the planned deliverables and milestones are achieved.

#### Preliminary Data:

Not applicable

#### Specific Aim 1:

Ensure the execution of activities and timely progress of tasks, the alignment and consistency of their implementation, and the effective communication between the project partners.

#### Specific Aim 2:

Guarantee the compliance with ethics and data management policies.

#### Specific Aim 3:

In the case of requiring a deviation from the proposed work plan, the WP1 will ensure that specific actions are undertaken to amend tasks, responsibilities and timings and work as close as possible with the involved WP.

#### Experimental Design Aim 1:

Not applicable

#### Experimental Design Aim 2:

Not applicable

#### Experimental Design Aim 3:

Not applicable

#### Picture to support preliminary data:

#### Methodologies and statistical analyses:

Monitoring and control of work plan and timelines of each WP, through project review activities.  
Verifying the compliance of all WPs activities with ethics and data management policies.  
Arrangement of a kick-off meeting, general meetings in an annual basis, and WP-specific periodic meetings.

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| <p><b>Project Type: WP PROJECT - 1</b></p>   |   |

Issuing of periodical reports.

Coordination of communication between WPs.

**Expected outcomes:**

Effective monitoring and control of work plan and timelines of each WP.

Periodical reports at 12M, 24M and 36M.

**Risk analysis, possible problems and solutions:**

Difficulties with coordination of WP-specific meetings and availability of milestones of each WP. To mitigate this risk, timelines are flexible and modifiable according to agreements deriving from continuous communication.

**Significance and Innovation**

Not applicable

**Description of the complementary and synergy research team**

The WP1 team is a multidisciplinary group of professionals with expertise in different areas such as research methodology, project management, healthcare management, health technology assessment, epidemiology, etc. Such a team is able to meet the needs of WPs in terms of project administration and scientific direction.

**Training and tutorial activities**

Not applicable

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| <p><b>Project Type: WP PROJECT - 1</b></p>  |   |

## Bibliography

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Hailey D, Werkö S, Rosén M, Macpherson K, Myles S, Gallegos Rivero V, Hipólito-Olivares C, Sihvo S, Pwu J, Yang WW, Chen YC, Perez Galán A, Aleman A, Villamil E. Influence Of Health Technology Assessment And Its Measurement. *Int J Technol Assess Health Care*. 2016 Jan;32(6):376-384.

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Pyone T, Smith H, van der Broek N. Frameworks to assess health systems governance: a systematic review. *Health Policy and Planning*. 2017 Jun;32(5):710-722.

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Schwarzer R, Siebert U. Methods, procedures, and contextual characteristics of health technology assessment and health policy decision making: comparison of health technology assessment agencies in Germany, United Kingdom, France, and Sweden. *Int J Technol Assess Health Care*. 2009 Jul;25(3):305-14.

## Timeline / Deliverables / Payable Milestones

1M Kick-off meeting.  
12M: Annual meeting.  
24M: Annual meeting.  
36M: Final conference.

12M: D01. Report of all WPs activities.  
24M: D02. Report of all WPs activities.  
36M: D03. Final report of all WPs activities.

## Milestones 18 month

1M Kick-off meeting.  
12M: Annual meeting and report of all WPs activities.

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| <p><b>Project Code:</b> NET-2018-12368077-1</p>   | <p><b>Principal Investigator:</b> ricciardi gualtiero</p>   |
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| <p><b>Project Type: WP PROJECT - 1</b></p>  |   |

### Milestones 36 month

24M: Annual meeting and report of all WPs activities.

36M: Final meeting and report of all WPs activities.

### Gantt chart

GanttWP1.xlsx

### Equipment and resources available

The ISS has 6 conference rooms with a hosting capacity from 20 to 200 people. All conference rooms are equipped with audio and video system, Internet connection and WIFI connection.

The ISS manages a IT platform that can handle a large amount of data.

The ISS has a Training Office and can organize seminars, workshops and courses through different formulas (e-learning through its own platform, on-site, mixed).

### Translational relevance and impact for the National Health System (SSN)

Not applicable

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV - Project Coordination</p> |
| <p><b>Project Code:</b> NET-2018-12368077-1</p>   | <p><b>Principal Investigator:</b> ricciardi gualtiero</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto Superiore di Sanita'</p>  |
| <p><b>Project Type: WP PROJECT - 1</b></p>  |   |

### PRINCIPAL INVESTIGATOR PROFILE

|                                     |   |   |
|-------------------------------------|---|---|
| <p>Name<br/>ricciardi gualtiero</p> | <p>Institution<br/>Department/Unit<br/>Position Title</p> | <p>Istituto Superiore di Sanita'<br/>President's Office<br/>President</p> |
|-------------------------------------|---|---|

### Personal Statement

The project aims to define a governance model for the introduction of health policies and programs into the Italian National Health Service (NHS) based on the integration of tools such as health technology assessment (HTA), clinical practice guidelines (CPGs) and clinical pathways (CPs), stressing the creation of partnerships between the various stakeholders, particularly citizens/patients and professionals. Prof. Ricciardi will act as Principal Investigator of WP1 (Project Coordination) and therefore will supervise the management of the activities undertaken by ISS as well of within the whole project, will ensure the coordination of all WPs and will guarantee the coherence between the activities undertaken by WPs and the respective deliverables, and the objectives of the project.

| Education/Training - Institution and Location                       | Degree  | Year(s) | Field of study                                    |
|---|---|---------|---|
| Faculty of Medicine and Surgery of University Federico II of Naples | Postgraduate in Hygiene and Preventive medicine | 1990    | Specialization in Hygiene and Preventive Medicine |
| Faculty of Medicine and Surgery of University Federico II of Naples | MD  | 1986    | Medicine and Surgery                              |
| London School of Hygiene and Tropical Medicine, London              | Master of Science                               | 1989    | Community medicine                                |

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV - Project Coordination</p> |
| <p><b>Project Code:</b> NET-2018-12368077-1</p>   | <p><b>Principal Investigator:</b> ricciardi gualtiero</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto Superiore di Sanita'</p>  |
| <p><b>Project Type: WP PROJECT - 1</b></p>  |   |

| <b>Positions</b>   |   |                     |  |           |         |
|--|---|---------------------|--|-----------|---------|
| Institution  | Division / Research group   | Location            | Position   | From year | To year |
| Istituto Superiore di Sanità - National Institute of Health                    | Presidenza  | Roma, Italy         | President  | 2015      | 2018    |
| Agenzia Italiana del Farmaco (Italian Medicine Agency) AIFA                    | Technical Scientific Committee and Pricing and Reimbursement Committee            | Rome, Italy         | Official member as President of the Istituto Superiore di Sanità   | 2015      | 2018    |
| Istituto Superiore di Sanità - National Institute of Health                    | Presidenza  | Rome, Italy         | Commissioner   | 2014      | 2015    |
| European Commission  | DG SANTE  | Brussels, Belgium   | Expert Panel Member on the Effective Ways of Investing in Health (EXPH)  | 2013      | 2018    |
| WHO  | European Advisory Committee on Health Research (EACHR)                            | Copenhagen, Denmark | Member   | 2012      | 2018    |
| Ministry of Health   | Directorate General of Health Planning  | Rome, Italy         | Member of the Scientific Committee   | 2012      | 2015    |
| Presidenza del Consiglio dei Ministri (Presidency of the Council of Ministers) | Joint State-Region Technical Monitoring Structure (STEM)                          | Rome, Italy         | Member representing the Minister of Health   | 2010      | 2015    |
| Università Cattolica del Sacro Cuore   | Faculty of Medicine and Surgery 'A. Gemelli'                                      | Rome, Italy         | Professor of General and Applied Hygiene (related scientific sector affine and competition sector inclusive of Medical Statistics) | 2002      | 2018    |
| Università Cattolica del Sacro Cuore   | School of Hygiene and Preventive Medicine of the Faculty of Medicine 'A. Gemelli' | Rome, Italy         | Director   | 2002      | 2015    |
| Università Cattolica del Sacro Cuore   | Institute of Hygiene of the Faculty of Medicine and Surgery 'A. Gemelli'          | Rome, Italy         | Director   | 2002      | 2012    |

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV - Project Coordination</p> |
| <p><b>Project Code:</b> NET-2018-12368077-1</p>   | <p><b>Principal Investigator:</b> ricciardi gualtiero</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto Superiore di Sanita'</p>  |
| <p><b>Project Type: WP PROJECT - 1</b></p>  |   |

**Official H index:** 34.0 ( autocertificata )

**Source:** Scopus

**Scopus Author Id:** 22836118300

**ORCID ID:** 0000-0002-5655-688X

**RESEARCH ID:** K-3342-2018

**Awards and Honors:**

In 2010 he was elected President of the EUPHA and in 2011 he was re-elected for a second term up to 2014. He was member of the Higher Health Council of the Italian Ministry of Health in the years 2003-2006 and the Italian Minister of Health appointed him Chair of the Public Health Section of the Council itself (2010-2014). In December 2015 he was appointed Director of the WHO Collaborating Centre for Health Policy, Governance and Leadership at the Catholic University of the Sacred Heart, Rome.

**Other CV Informations:**

He manages several undergraduate and postgraduate teaching activities including a Master of Science programme and International Courses in Epidemiology. He is Editor of the European Journal of Public Health, of the Oxford Handbook of Public Health Practice and Founding Editor of the Italian Journal of Public Health and of Epidemiology, Biostatistics and Public Health.

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV - Project Coordination</p> |
| <p><b>Project Code:</b> NET-2018-12368077-1</p>   | <p><b>Principal Investigator:</b> ricciardi gualtiero</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto Superiore di Sanita'</p>  |
| <p><b>Project Type: WP PROJECT - 1</b></p>  |   |

### Selected peer-reviewed publications of the PI

| Valid for PI minimum expertise level  |                                 |          |         |     |
|---|---------------------------------|----------|---------|-----|
| Title   | DOI                             | PMID     | Cit. ** | P.* |
| The future of best investing in vaccines: The Health Technology Assessment approach   | 10.1016/j.vaccine.2008.01.009   | 18289744 | 9       | L   |
| The effectiveness of computerized clinical guidelines in the process of care: A systematic review   | 10.1186/1472-6963-10-2          | 20047686 | 56      | L   |
| OPTIGOV - A new methodology for evaluating Clinical Governance implementation by health providers   | 10.1186/1472-6963-10-174        | 20565967 | 18      | L   |
| Guidance for future HTA applications to vaccines: The HPV lesson  | 10.4161/hv.7.9.16084            | 21865880 | 7       | L   |
| The current status of decision-making procedures and quality assurance in Europe: An overview   | 10.1007/s11019-011-9333-0       | 21647732 | 4       | L   |
| Health in Europe - Policies for progress  | 10.1016/S0140-6736(13)60356-6   | 23541051 | 2       | C   |
| A systematic review on the effectiveness of group versus single-handed practice   | 10.1016/j.healthpol.2013.07.008 | 23910731 | 12      | L   |
| Disinvestment in healthcare: An overview of HTA agencies and organizations activities at European level                                   | 10.1186/s12913-018-2941-0       | 29490647 | 0       | C   |
| The management of multiple sclerosis by reference centers in south of Italy: a 2011 survey on health demands and needs in Campania region | 10.1007/s10072-015-2389-5       | 26439919 | 3       | L   |
| Italy's response to vaccine hesitancy: An innovative and cost effective National Immunization Plan based on scientific evidence           | 10.1016/j.vaccine.2017.06.011   | 28651836 | 11      | L   |
| Effectiveness of nutritional interventions addressed to elderly persons: Umbrella systematic review with meta-analysis                    | 10.1093/eurpub/ckx199           | 29228152 | 1       | L   |
| Health technology assessment agencies: An international overview of organizational aspects.   | 10.1017/S026646230707064X       | 17937828 | 0       | L   |
| Health Technology Assessment in Italy   | 10.1017/S0266462309090539       | 19505352 | 18      | L   |
| Primary Care Efficiency Measurement Using Data Envelopment Analysis: A Systematic Review  | 10.1007/s10916-014-0156-4       | 25486892 | 13      | L   |
| Hospital efficiency: How to spend less maintaining quality?   | 10.4415/ANN_17_01_10            | 28361805 | 0       | L   |

\* Position: F=First L=Last C=Correspondent

\*\* Autocertificated

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV - Project Coordination</p> |
| <p><b>Project Code:</b> NET-2018-12368077-1</p>   | <p><b>Principal Investigator:</b> ricciardi gualtiero</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto Superiore di Sanita'</p>  |
| <p><b>Project Type: WP PROJECT - 1</b></p>  |   |

| For evaluation CV   |                                 |          |        |
|---|---------------------------------|----------|--------|
| Title   | DOI                             | PMID     | Cit. * |
| CYP1A1, CYP2E1, GSTM1, GSTT1, EPHX1 exons 3 and 4, and NAT2 polymorphisms, smoking, consumption of alcohol and fruit and vegetables and risk of head and neck cancer                              | 10.1007/s00432-007-0254-5       | 17611777 | 59     |
| Smoking status and gastric cancer risk: An updated meta-analysis of case-control studies published in the past ten years  |                                 | 19366050 | 59     |
| The relationship between avoidable hospitalization and accessibility to primary care: A systematic review   | 10.1093/eurpub/cks053           | 22645236 | 62     |
| The financial crisis in Italy: Implications for the healthcare sector   | 10.1016/j.healthpol.2012.04.003 | 22551787 | 65     |
| Aldehyde dehydrogenase 2 and head and neck cancer: A meta-analysis implementing a mendelian randomization approach  | 10.1158/1055-9965.EPI-08-0462   | 19124505 | 69     |
| Overweight and obesity among secondary school children in Central Italy   | 10.1023/A:1007675005395         | 10543355 | 71     |
| Polymorphisms in metabolic genes, their combination and interaction with tobacco smoke and alcohol consumption and risk of gastric cancer: A case-control study in an Italian population          | 10.1186/1471-2407-7-206         | 17996038 | 74     |
| Meta- and pooled analyses of the methylenetetrahydrofolate reductase C677T and A1298C polymorphisms and gastric cancer risk: A Huge-GSEC review   | 10.1093/aje/kwm344              | 18162478 | 77     |
| Comparisons of American, Israeli, Italian and Mexican physicians and nurses on the total and factor scores of the Jefferson scale of attitudes toward physician-nurse collaborative relationships | 10.1016/S0020-7489(02)00108-6   | 12667519 | 90     |
| Evaluation of the endorsement of the preferred reporting items for systematic reviews and meta-analysis (PRISMA) statement on the quality of published systematic review and meta-analyses        | 10.1371/journal.pone.0083138    | 24386151 | 183    |

\* Autocertificated

| Grant                        |      |          |                      |
|------------------------------|------|----------|----------------------|
| Funded Institution / Country | Year | Title    | Position in Projects |
| Horizon 2020 - SC1           | 2016 | TO-REACH | Coordinator          |

**Employment contract extension:**

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV - Project Coordination</p> |
| <p><b>Project Code:</b> NET-2018-12368077-1</p>   | <p><b>Principal Investigator:</b> ricciardi gualtiero</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto Superiore di Sanita'</p>  |
| <p><b>Project Type: WP PROJECT - 1</b></p>  |   |

### Biographical Sketch Contributors 1

|                                      |  |
|--------------------------------------|--|
| <p><b>Name:</b><br/>Roazzi Paolo</p> | <p><b>Institution</b> Istituto Superiore di Sanità<br/><b>Department/Unit</b> Centro Nazionale HTA<br/><b>Position Title</b> research collaborator</p> |
|--------------------------------------|--|

| Education/Training - Institution and Location | Degree                      | Year(s) | Field of study   |
|---|-----------------------------|---------|--|
| Università Catt. Sacro Cuore- ALTEMS          | Master ( 1 year, on going)  | 2018    | Evaluation and management of health technologies (HTA) |
| Università LA SAPIENZA Roma                   | Specialist Degree (3 years) | 1996    | Health statistics, management                          |
| Università LA SAPIENZA Roma                   | MSc                         | 1993    | Political sciences - economy statistics address        |

#### Personal Statement:

The project aims to define a governance model for the introduction of health policies and programs into the Italian National Health Service (NHS) based on the integration of tools such as HTA, clinical practice guidelines (CPGs) and clinical pathways (CPs), stressing the creation of partnerships between the various stakeholders, particularly citizens/patients and professionals. Paolo Roazzi will contribute to the project as a scientist with his longstanding expertise in IT management, data management, clinical data registry, economy evaluation, healthcare management, statistics and performance evaluation for health systems.

| Institution                  | Division / Research group                     | Location | Position                     | From year | To year |
|------------------------------|---|----------|------------------------------|-----------|---------|
| Istituto Superiore di Sanità | Centro Nazionale Health Technology Assessment | Rome     | Senior Research Technologist | 2017      | 2018    |
| Istituto Superiore di Sanità | Information Technology Unit                   | Rome     | Director                     | 2004      | 2016    |
| Istituto Superiore di Sanità | Information Technology Unit                   | Rome     | Senior Research Technologist | 2000      | 2016    |
| Istituto Superiore di Sanità | Data Processing Center                        | Rome     | Analyst Programmer           | 1988      | 2000    |

#### Awards and Honors

**Official H index:** 24.0 ( autocertificated )

**Source:** Scopus

**Scopus Author Id:** 35313980400

**ORCID ID:** 0000-0001-7181-9513

**RESEARCH ID:** K-3326-2018

#### Awards and Honors:

N.A.

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV - Project Coordination</p> |
| <p><b>Project Code:</b> NET-2018-12368077-1</p>   | <p><b>Principal Investigator:</b> ricciardi gualtiero</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto Superiore di Sanita'</p>  |
| <p><b>Project Type: WP PROJECT - 1</b></p>  |   |

### Biographical Sketch Contributors 2

|   |  |
|---|--|
| <p><b>Name:</b><br/>Marchetti Marco</p> | <p><b>Institution</b> Istituto Superiore di Sanità<br/><b>Department/Unit</b> Centro nazionale HTA<br/><b>Position Title</b> research collaborator</p> |
|---|--|

| Education/Training - Institution and Location | Degree            | Year(s) | Field of study                        |
|---|-------------------|---------|---------------------------------------|
| Univ. Catt. Sacro Cuore Roma                  | Medical Doctor    | 1990    | Medicine                              |
| Univ. Catt. Sacro Cuore Roma                  | Specialist Degree | 1994    | Public Health and Preventive Medicine |
| Univ. Catt. Sacro Cuore Roma                  | Specialist Degree | 1999    | Legal and Forensic Medicine           |

#### Personal Statement:

The project aims to define a governance model for the introduction of health policies and programs into the Italian National Health Service (NHS) based on the integration of tools such as health technology assessment (HTA), clinical practice guidelines (CPGs) and clinical pathways (CPs), stressing the creation of partnerships between the various stakeholders, particularly citizens/patients and professionals. Dr. Marco Marchetti will act as CO-PI and Project Manager and will contribute to the project with his expertise in HTA and Health Management.

| Institution                                  | Division / Research group              | Location | Position            | From year | To year |
|--|--|----------|---------------------|-----------|---------|
| Istituto Superiore di Sanità                 | Centro Nazionale HTA                   | Rome     | Director            | 2017      | 2018    |
| Fond. Pol. Gemelli - Univ. Catt. Sacro Cuore | HTA Unit                               | Rome     | Director            | 2001      | 2016    |
| Università Cattolica Sacro Cuore             | School of Medicine-School of Economics | Rome     | Associate Professor | 2000      | 2018    |
| Pol. Gemelli - Univ. Catt. Sacro Cuore       | Office of the Medical Director         | Rome     | Health Manager      | 1995      | 2001    |

#### Awards and Honors

**Official H index:** 18.0 ( autocertificated )

**Source:** Scopus

**Scopus Author Id:** 55810978000

**ORCID ID:** 0000-0002-8367-8268

**RESEARCH ID:** K-3288-2018

#### Awards and Honors:

None.

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV - Project Coordination</p> |
| <p><b>Project Code:</b> NET-2018-12368077-1</p>   | <p><b>Principal Investigator:</b> ricciardi gualtiero</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto Superiore di Sanita'</p>  |
| <p><b>Project Type: WP PROJECT - 1</b></p>  |   |

### Biographical Sketch Contributors 3

|  |   |
|--|---|
| <p><b>Name:</b><br/>iannone primiano</p> | <p><b>Institution</b> Istituto Superiore di Sanità<br/><b>Department/Unit</b> Centro Nazionale Eccellenza Clinica, Qualità e Sicurezza delle Cure<br/><b>Position Title</b> research collaborator</p> |
|--|---|

| Education/Training - Institution and Location | Degree            | Year(s) | Field of study                 |
|---|-------------------|---------|--------------------------------|
| Università Modena e Reggio Emilia, Italy      | Master            | 2010    | Healthcare Research Management |
| Università di Bologna, Italy                  | Specialist Degree | 1994    | Gastroenterology               |
| Università di Bologna, Italy                  | Specialist Degree | 1990    | Internal Medicine              |
| Università di Bologna, Italy                  | MD                | 1985    | Medicine                       |

#### Personal Statement:

The project aims to define a governance model for the introduction of health policies and programs into the Italian National Health Service (NHS) based on the integration of tools such as HTA, clinical practice guidelines (CPGs) and clinical pathways (CPs), stressing the creation of partnerships between the various stakeholders, particularly citizens/patients and professionals. Dr. P. Iannone will contribute to the project with his expertise in Health Management, clinical practice guidelines, research methodology and experience in clinical practice.

| Institution                  | Division / Research group   | Location             | Position              | From year | To year |
|------------------------------|---|----------------------|-----------------------|-----------|---------|
| Istituto Superiore di Sanità | Centro Nazionale Eccellenza Clinica, Qualità e Sicurezza delle Cure | Rome, Italy          | Director              | 2017      | 2018    |
| ASL 4 Chiavarese             | Emergency Department  | Chiavari (GE), Italy | Department Director   | 2014      | 2016    |
| ASL 4 Chiavarese             | Emergency Unit  | Chiavari (GE)        | Director              | 2010      | 2016    |
| USL IMOLA                    | OBI Unit  | Imola, Italy         | Head of Unit Director | 2009      | 2010    |

#### Awards and Honors

**Official H index:** 12.0 ( autocertificated )

**Source:** Scopus

**Scopus Author Id:** 7005865064

**ORCID ID:** 0000-0001-7925-1168

**RESEARCH ID:** K-3792-2018

#### Awards and Honors:

None

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|  <p><i>Ministero della Salute</i><br/>         Direzione Generale della Ricerca Sanitaria<br/>         e Biomedica e della Vigilanza sugli Enti<br/> <b>BANDO RICERCA FINALIZZATA 2018</b><br/>         esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>         Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV - Project Coordination</p> |
| <p><b>Project Code:</b> NET-2018-12368077-1</p>   | <p><b>Principal Investigator:</b> ricciardi gualtiero</p>  |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>  | <p><b>Applicant Institution:</b> Istituto Superiore di Sanita'</p>   |
| <p><b>Project Type: WP PROJECT - 1</b></p>  |  |

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| <p><b>Project Code:</b> NET-2018-12368077-1</p>   | <p><b>Principal Investigator:</b> ricciardi gualtiero</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto Superiore di Sanita'</p>  |
| <p><b>Project Type: WP PROJECT - 1</b></p>  |   |

### Expertise Research Collaborators

| Selected peer-reviewed publications of the Research Group / Collaborators |   |                             |          |        |
|---|---|-----------------------------|----------|--------|
| Collaborator  | Title   | DOI                         | PMID     | Cit. * |
| iannone primiano  | [Recommendation for patient engagement promotion in care and cure for chronic conditions.]                    | 10.1701/2812.28441          | 29149163 | 0      |
| iannone primiano  | [Italian guidelines in accordance with the new National Guidelines System: critical issues and perspectives.] | 10.1701/2745.27986          | 28901343 | 0      |
| iannone primiano  | Wrong guidelines: how to detect them and what to do in the case of flawed recommendations                     | 10.1136/ebmed-2016-110607   | 27986816 | 1      |
| iannone primiano  | Wrong guidelines: why and how often they occur.   | 10.1136/ebmed-2016-110606   | 27986814 | 2      |
| Marchetti Marco   | Guiding Principles For Good Practices In Hospital-Based Health Technology Assessment Units.                   | 10.1017/S0266462315000732   | 26899230 | 7      |
| Marchetti Marco   | Organizational Models of Hospital Based HTA: Empirical Evidence from Adhophpta European Project.              | 10.1016/j.jval.2015.09.1823 | 26533143 | 3      |
| Roazzi Paolo  | Biobank networking: the European network initiative and the italian participation.                            | 10.1089/bio.2011.0004       | 24846264 | 2      |
| Roazzi Paolo  | The cure of cancer: A European perspective  | 10.1016/j.ejca.2008.11.034  | 19131242 | 60     |
| Marchetti Marco   | Testing the HTA core model: experiences from two pilot projects.  | 10.1017/S026646230999064X   | 20030887 | 14     |
| Marchetti Marco   | Health technology assessment in Italy.  | 10.1017/S0266462309090539   | 19505352 | 18     |

\* Auto-certificated

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| <p><b>Project Type: WP PROJECT - 1</b></p>  |   |

| <b>Grant</b>   |      |   |                      |                  |
|--|------|---|----------------------|------------------|
| Funded Institution / Country   | Year | Title   | Position in Projects | Collaborator     |
| European Commission - European Action Against Cancer, EPAAC  | 2013 | EUROCARE-5  | Collaborator         | Roazzi Paolo     |
| Presidenza del Consiglio dei Ministri  | 2011 | Progetto CRB-Net  | Coordinator          | Roazzi Paolo     |
| Ministero della Salute - Ricerca Finalizzata   | 2012 | Population-based comparison of cancer burden indicators.                                      | Collaborator         | Roazzi Paolo     |
| European Union's Seventh Framework Programme for research, technological development and demonstration | 2011 | European Multicentre Tics Study   | Collaborator         | Roazzi Paolo     |
| European Commission - Horizon 2020   | 2018 | Improved Methods and Actionable Tools for Enhancing Health Technology Assessment - IMPACT HTA | Collaborator         | iannone primiano |
| European Commission - Horizon 2020   | 2018 | Improved Methods and Actionable Tools for Enhancing Health Technology Assessment - IMPACT HTA | Collaborator         | Roazzi Paolo     |
| European Commission - Horizon 2020   | 2018 | Improved Methods and Actionable Tools for Enhancing Health Technology Assessment - IMPACT HTA | Collaborator         | Marchetti Marco  |

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| <p><b>Project Type: WP PROJECT - 1</b></p>  |   |

| Total proposed budget ( Euro ) |                   |                   |   |   |   |
|--------------------------------|-------------------|-------------------|---|---|---|
| Costs                          | TOTAL BUDGET      | Co-Funding        | Project costs proposed to funding Organization (no MOH request) | List of costs proposed for funding to the MOH | Percentage of total proposed to the MOH |
| 1a Staff Salary                | 150.000,00        | 150.000,00        | 0,00  | not permitted                                 | 0,00                                    |
| 1b Researchers' Contracts      | 90.000,00         | 0,00              | 0,00  | 90.000,00                                     | 45,00                                   |
| 2 Equipment (Leasing - Rent)   | 0,00              | 0,00              | 0,00  | 0,00  | 0,00                                    |
| 3a Supplies                    | 0,00              | 0,00              | 0,00  | 0,00  | 0,00                                    |
| 3b Model Costs                 | 0,00              | 0,00              | 0,00  | 0,00  | 0,00                                    |
| 3c Subcontracts                | 0,00              | 0,00              | 0,00  | 0,00  | 0,00                                    |
| 3d Patient Costs               | 0,00              | 0,00              | 0,00  | 0,00  | 0,00                                    |
| 4 IT Services and Data Bases   | 0,00              | 0,00              | 0,00  | 0,00  | 0,00                                    |
| 5 Publication Costs            | 0,00              | 0,00              | 0,00  | 0,00  | 0,00                                    |
| 6 Convegni                     | 0,00              | 0,00              | 0,00  | 0,00  | 0,00                                    |
| 7 Travels                      | 0,00              | 0,00              | 0,00  | 0,00  | 0,00                                    |
| 8 Overheads                    | 20.000,00         | 0,00              | 0,00  | 20.000,00                                     | 10,00                                   |
| 9 Coordination Costs           | 90.000,00         | 0,00              | 0,00  | 90.000,00                                     | 45,00                                   |
| <b>Total</b>                   | <b>350.000,00</b> | <b>150.000,00</b> | <b>0,00</b>   | <b>200.000,00</b>                             | <b>100,00</b>                           |

Report the Co-Funding Contributor:

Staff salary

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| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto Superiore di Sanita'</p>  |
| <p><b>Project Type: WP PROJECT - 1</b></p>  |   |

| <b>Budget Justification</b>  |  |
|------------------------------|--|
| 1a Staff Salary              | The personnel involved will dedicate from 5% to 20% of the work activity every year for this project. the staff salary budget has been defined on the basis of the salaries of the personnel involved. |
| 1b Researchers' Contracts    | We have estimated the need of research contract who will be dedicated to support the projects activities   |
| 2 Equipment (Leasing - Rent) | -  |
| 3a Supplies                  | -  |
| 3b Model Costs               | -  |
| 3c Subcontracts              | -  |
| 3d Patient Costs             | -  |
| 4 IT Services and Data Bases | -  |
| 5 Publication Costs          | -  |
| 6 Convegni                   | -  |
| 7 Travels                    | -  |
| 8 Overheads                  | -  |
| 9 Coordination Costs         | Organize annual assembly, travel and accommodation, periodical meeting   |

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| <p><b>Project Code:</b> NET-2018-12368077-2</p>   | <p><b>Principal Investigator:</b> Maria Frigerio</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Regione Lombardia - Direzione Generale Sanità</p>   |
| <p><b>Project Type: WP PROJECT - 2</b></p>  |  |

**Major Diagnostic Category\*:** Ortopedia

**Project Classification IRG:** Healthcare Delivery and Methodologies

**Project Classification SS:** Health Services Organization and Delivery - HSOD

**Project Keyword 1:** Healthcare organizations, programs, and delivery of services; including those delivered in non-traditional settings; integrated care delivery systems; disease management and modeling; continuous quality improvement; characteristics of the organization and patient outcomes; organizational performance and efficiency; cost-benefit analysis; economics of health care and pharmacoeconomics.

**Project Keyword 2:** Health care governance and sustainability

**Project Keyword 3:** Health technology assessment and clinical practice guidelines

**Project duration (months):** 36

**Project Request:**      **Animals:**                       **Humans:**                       **Clinical trial:**

**The object/s of this application is/are under patent copyright Y/N:**

| Investigators, Institution and Role in the Project |       |                  |   |                              |            |
|--|-------|------------------|---|------------------------------|------------|
|  | Co-PI | Key Personnel    | Institution/Org./Pos.                       | Role in the project          | Birth Date |
| 1  | X     | Tringali Michele | ASST Grande Ospedale Metropolitano Niguarda | Co-Principal Investigator    | 27/06/1959 |
| 2  |       | COLOMBO PAOLA    | ASST Grande Ospedale Metropolitano Niguarda | Expert Research Collaborator | 29/06/1971 |
| 3  |       | Mazzali Cristina | ASST Grande Ospedale Metropolitano Niguarda | Expert Research Collaborator | 23/04/1968 |

## Overall Summary

The impact of Heart Failure (HF) on life expectancy, quality of life, and resource utilization is well known. The effectiveness and cost-effectiveness of a whole range of Tele-Health (TH) solutions applied to HF patient populations have not been consistently assessed. Given the need for out-of-hospital management of chronic conditions, exploring current status, patients and providers knowledge, needs and expectations about TH tools and strategies may contribute to better identify the value of TH applications. The link between HTA reports and decision-making process is lacking. There is a need to streamline HTA procedures using rapid response services in the early phases of decision-making and methods, like Multiple Criteria Decision Analysis (MCDA), that take account of both measurable data and subjective judgements about the data, incorporating clinical judgement or patient preferences, in order to provide a systematic and transparent way of making health-care decisions (14).

## Background / State of Art

Chronic Heart Failure (HF) is a major healthcare problem in terms of mortality (with pump failure or sudden cardiac death as main modalities), reduced functional capacity, and epidemiological burden, resulting in huge resources utilization. HF patients experience periods of stable conditions or gradual decline punctuated by phases of decompensation, often

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| <p><b>Project Type: WP PROJECT - 2</b></p>   |  |

resulting in hospital admission. Optimal guideline-directed therapy, patient adherence, and surveillance for early indexes and hallmarks of decompensation are known to improve survival and reduce symptoms and hospitalizations, but there are not management strategies that can be universally effective for reaching these goals in all affected patients. Telemedicine is a growing field of interest in many settings and telemedicine strategies are applied to different patient categories, with various endpoints and different results in terms of effectiveness and cost-effectiveness (1). Three major types of telemonitoring of HF patients can be identified:

- 1) Scheduled, structured phone contacts between patient and medical personnel, mostly expert nurses. This may include or not transmission of ECG track, automated detection of basic parameters and unscheduled or emergency phone calls. These programmes are generally temporary (months) and aimed to medical therapy optimization, assessment of stability, flexible use of diuretics, and improvement in patient adherence and competences in self-assessment and self-care. The most relevant components for effectiveness appear to be the choice of the target population and personnel skills. Efficacy may decline after discontinuation (2).
- 2) Remote monitoring via electric devices (ICDs and pacemakers, cardiac resynchronization therapy CRT). Semi-automated detection of patient rhythm and device functioning are accompanied by expert review and phone contacts with the patients for simplifying follow-up. These devices provide information on patient activity and may be equipped with sensors for measuring bioimpedance as a proxy of fluid content, which is related to congestion (3). The effectiveness of these additional components is not universally recognized, and not all electrophysiology experts may be equally experienced in HF management.
- 3) Remote monitoring of pulmonary artery pressure (PAP) via a specifically designed, permanent, implanted device. Pulmonary artery pressure is strictly related to left ventricular filling pressure (LVFP), one of the most important hemodynamic indexes characterizing HF and its severity (4). The integration of this information with clinical and self-reported data for guiding therapy, according to pre-specified criteria, obtained a significant improvement of clinical outcomes. So far the device appears to be safe and durable, but its penetration in the European practice is low due to invasiveness, costs, and need for specific expertise for clinical decision making. Interestingly, both bioimpedance and especially hemodynamic monitoring demonstrated also that variations in these parameters precede weight increase and patient perception of worsening HF symptoms, motivating the limitations of self-reported changes for reducing episodes of worsening HF leading to re-hospitalizations (5). Foreign non-for-profit organization or agencies like ECRI Institute in the USA and CADTH in Canada developed a service of Rapid Responses in order to provide timely information in a context of uncertainty to support the decision-making process in health care (11,12). For properly justified decisions a robust process is needed which recognizes the multiplicity of involved factors, the imperfect status of available information and the stakeholder preferences (13). The MCDA provides support and structure to the decision-making process to overcome the challenges related to complex, and sometimes conflicting, criteria involved in the decision (14). A similar approach has been developed within a EU-funded research project (DECIDE).

## Hyphotesis and Specific AIMS

### Hyphotesis and Significance:

Different telemedicine strategies may be useful for specific scopes in specific subgroups of HF patients (6). Current uncertainties relate to unclear definition of requisites, responsibilities, staffing, monitored outcomes, and reimbursement for these services, which are often conducted as additional/ accessory services (7). In order to obtain reimbursement a clear picture of ongoing, desirable, and future programs should be obtained, taking into account all involved domains (8). In 2016, the two main Italian Scientific Associations of Cardiology, together with the Society of Information Technology,

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| <p><b>Project Type: WP PROJECT - 2</b></p>   |  |

released a consensus document on the future of telemedicine for HF management (9). This and other references will be used as a track for reviewing current status and perspectives of telecardiology services in our country and to explore new applications to help healthcare planners, providers, and beneficiaries in making the appropriate choices. A transverse task of this WP will address the development of a Rapid Responses (RRs) service tailored to telemedicine technologies and a related decision-making tool helpful in facing complex decisions and based on MCDA experience acquired in Lombardy region within the HTA program. RRs and MCDA tools are meant to help address the 'unmet-needs' of timeliness and robustness in making decisions. RRs are not replacement of the usual HTA reports, but rather as a information structured to identify the uncertainties which are unavoidable in the early phases of adoption and diffusion of technologies. MCDA provide several techniques to support decision makers to agree which assessment criteria are relevant, the importance attached to each and how to use this information to assess alternatives, ultimately helping to increase the consistency, transparency and legitimacy of decisions (14).

#### Preliminary Data:

Telecardiology's applications are extensive and can occur before, during and after hospitalization, giving it the power to increase access to cardiovascular care not only in rural regions but also within cities underserved areas. Somewhat ironically, this off-site care is aligned with a more patient-centric approach to care. It makes care more accessible, thereby increasing care overall and improving outcomes. The purpose of telecardiology is to make the necessary information available for the consulting cardiologist and other caregivers as quickly and reliably as possible about the current status and progress, thus alleviating the burden of clinical visits and unnecessary hospitalizations on the exhausted health system, and preventing worsening of patient's condition. On the other side, remote patient management systems provide a feedback to the patient in terms of appropriate information, education and coaching. International experience with RRs and MCDA methods to inform health care decision making are available (14) and have been introduced in health programming service practice in Lombardy region (regional act X/5671) but never applied to telemedicine services.

#### Specific Aim 1:

Since telemedicine services are not limited to specific geographical areas and given that patients and healthcare organization are different in culture, structure and performance levels and may differ greatly also within the same country (e.g. comparing urban vs rural settings), it will be interesting to verify if the standardization in the delivery of care that telecardiology can offer will be perceived as a value or as a limitation, or both. This appears of special importance when considering the room for future use of artificial intelligence and virtual assistants for decision-making and communication. Two innovative programs will be designed and tested in specific cohorts at the two end of the spectrum:

1. A Phone- and web-based service, offering educational programs and support to ambulatory patients undergoing medical therapy optimization, and to their family physicians. The program will target newly diagnosed patient, requiring titration of drugs or with recent or planned major change in therapy. The program will also serve as an aid for in-person contacts and for specialists consultation triggered by family physician.
2. An hemodynamic monitoring-based service, offered to special HF populations, such as for example patients receiving periodic inotropic treatment, and/or evaluated for advanced therapies (ventricular assist device implantation, heart transplantation). This service will be initially tested in special HF populations, such as HF patients receiving periodic inotropic treatment, in whom the small but real risk for complications related to the implantation procedure is justified. Subsequently, remote hemodynamic monitoring could provide a proof of concept for other complex management strategies of advanced HF such as periodic administration of Levosimendan (10).

MCDA takes account of measurable data and subjective judgements about the data, with the latter often representing

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| <p><b>Project Type: WP PROJECT - 2</b></p>  |  |

clinical judgement or patient preferences (14), that both can be acquired through TH applications. We plan to explore how MCDA methods and procedures can provide an opportunity to align decision-makers preferences with their choices and provide a systematic and transparent way of making health-care decisions in the setting of telemedicine applied for HF patients. A tailored version of the Rapid Response and MCDA support services developed for the HTA program in Lombardy region and managed by Niguarda Hospital will be modeled, tested and applied to explore the value of telemedicine solutions (from phone- and web-based educational program to hemodynamic monitoring based program) in the care pathways of HF patients. These services will be used at regional level as evidence-based guides for coverage and health care programming decisions in the area of telemedicine.

**Specific Aim 2:**

Not applicable.

**Specific Aim 3:**

Not applicable.

**Experimental Design Aim 1:**

Full HTA evaluation of the Specific Aim 1.

**Experimental Design Aim 2:**

Not applicable.

**Experimental Design Aim 3:**

Not applicable.

**Picture to support preliminary data:**

6\_RF\_2018\_Niguarda\_Picture\_eng.bmp

**Methodologies and statistical analyses:**

Identification, prioritization, assessment and appraisal of innovative telemedicine approaches for HF processes of care will be performed through Health Technology Assessment (HTA) procedures that Niguarda Hospital center of competence (regional act X/5671 of 2016) operates in Lombardy region, namely rapid responses and recommendations supported by MCDA methods. MCDA includes mixed quantitative and qualitative representations of decision-makers preferences and value judgements, expressed with indexes and texts. The preference value is evaluated through the collection of weights that experts, patients, committee's members attach to predefined criteria. HTA and guidelines information is then processed and performance of proposed technologies and processes is assessed through criteria-specific score scales. In order to compare the technology under investigation with the standard treatment, for all criteria. The assessment of uncertainty (structural, informational, judgmental) in the MCDA process is assured by proper sensitivity analyses carried on using suitable statistical and mathematical methodologies, which can vary from a deterministic approach to a probabilistic one (e.g. theoretical distribution of the parameters, application of Monte-Carlo methods, fuzzy set theory, etc.)

**Expected outcomes:**

Expected outcomes are:

1. A reduction in patient's days lost due to heart failure readmissions

Sent date: 20/05/2018 21.34

38 / 187

Sent date of moratorium changes: 01/06/2018 15.17

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| <p><b>Project Code:</b> NET-2018-12368077-2</p>   | <p><b>Principal Investigator:</b> Maria Frigerio</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Regione Lombardia - Direzione Generale Sanità</p>   |
| <p><b>Project Type: WP PROJECT - 2</b></p>  |  |

2. A reduction in healthcare costs related to hospital readmission and patient follow-up on site
3. The optimization of diagnostic and therapeutic process ok HF patients
4. The production of an integrated evidence-based guide to support National System of Guidelines for good clinical practice, and for accountable coverage and health care programming decisions in the area of telemedicine at regional level with contributions to the National Program of HTA for Medical Devices (L 190, L 208, Intesa Stato-Regioni 23.09.207).

**Risk analysis, possible problems and solutions:**

The Niguarda Cardiology, Heart Failure and Cardiac Transplant Unit assures high experience with respect to right heart catheterism, intravascular device implantation and management of all the steps of pathways of care (PDTA) for HF patients with any level of comorbidity. The regional Collaborative Center for HTA started in Niguarda Hospital with Lombardy Region contribution (DGR X/5671) assures the management of the full cycle of HTA procedures and methods: stakeholder contribution, management of conflicts of interests, identification, prioritization (with Rapid Responses and MCDA), assessment and appraisal (with MCDA) of technologies and processes. Diffusion of recommendations and implementation of regional acts is assured by Region Lombardy Government, which is the direct client of the regional Collaborative Center for HTA in Niguarda.

**Significance and Innovation**

The HTA evaluation of telemedicine services for HF patients in a hospital with a cardiac transplantation unit could supply valuable data for identifying the place in therapy of telecardiology solutions, helping to standardize procedures, advance guidelines, and propose innovative modalities of reimbursement ('bundled DRG'). This project is innovative for Italy since it could produce outcomes data on telecardiology which are scarce in Italy both on clinical, on patient-reported outcomes and preferences and on economical and organizational impact evaluation, and because MCDA methods have not been applied, since far, to identify and to measure the overall value of telecardiology in a broad spectrum of HF patients. The experience gained by Lombardy Region and ISS with MCDA in this area could also extend the capacity of industry to early identify and measure both barriers and drivers of innovation in the research and diffusion pipelines of drugs and medical devices for HF.

**Description of the complementary and synergy research team**

The management team for the project includes an expert of heart failure and cardiac transplants (FM) and an expert of HTA procedures and methods with specific expertise in RR and MCDA (TM), a hemodynamic cardiologist also expert HTA methods (CP) and a mathematician (MC) expert in data management and statistical analysis. Besides the proposants the team includes cardiology doctors and nurses applied to the HF management program. The background of the team is multi professional and complementary is assured by the wide spectrum of further expertise available for the project in Niguarda Hospital: a clinical engineer, two clinicians and a biomedical librarian, as collaborators. Greta Puleo, a clinical engineer, will collect and analyze technical information about medical devices, in particular from ECRI database which provides access to many evidence-based information tools on devices, drugs, biotechnologies, procedures, and healthcare services. Gloria Innocenti, a biomedical librarian, has experience in biomedical research methodology and will help with organization and management of the scientific literature. Pietro Barbieri and Giovanni Ceccarelli, medical doctors, will support the modeling of clinical pathways (PDTA) applied to telemedicine and with data interpretation. The whole team is assuring the complete evaluation of all aspects of the research program. The experience of proposants is assuring the correct scientific and practical approach to the process.

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### Training and tutorial activities

Tutorial activities will be developed directly by the cardiologist for young postgraduated MDs. Training of specialized personnel will be defined by single components of the whole team who manages the process. The expert on HTA and the mathematician will train the components of the team who did not have specific knowledge on the field about the different items needed to complete the HTA evaluation, specifically on RR and MCDA.

### Bibliography

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3. Perego GB et al. Correlation between pulmonary artery pressure and thoracic impedance: Insights from daily monitoring through an implanted device in chronic heart failure. *Int J Cardiol* 2017;245:196-200.
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### Timeline / Deliverables / Payable Milestones

See below

### Milestones 18 month

Release of Intermediate Data Analysis.

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### Milestones 36 month

Final evaluation and interpretation of data.

### Gantt chart

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### Equipment and resources available

Niguarda is a general hospital and offers all clinical and surgical specialties for adults and children, but its core identity that brings it to the highest levels of excellence is the ability to integrate care competences and technology, from diagnosis to rehabilitation. All medical disciplines and technologies are integrated on serving the best care even in situation of emergency or high complexity. In particular the Cardiovascular Department provides all medical interventional and surgical options for patients with any kind of disease at any age, i.e. from newborn and pediatric cardiac surgery, including pediatric transplantation, to transcatheter aortic valve implants. Multidisciplinary team case discussion, highly specialized cardiac and anesthesiology intensive care staff, intermediate facilities, active outpatient and tele- cardiology services, provide the full spectrum of care in both the emergency and long-term care settings. Niguarda is national referral Center for heart transplantation and assist device for advanced heart failure, complex arrhythmias, acute and chronic coronary artery disease. Clinical research and knowledge sharing are fully integrated in the hospital strategy. The presence of professional skills, technological competences, certified laboratories and high complexity patient cohorts make Niguarda a unique and interesting partner for future cooperation. The main strength point is the high volume of diagnostic/ therapeutic activities that allows an optimal integration between research and patient care. Niguarda recently was selected as scientific and management support center for the regional program of HTA (regional act X/5671). Updating of the technological park is driven by the development of professional skills of high profile. Diagnostic tests are shared in real time in safe and responsible way through our ICT system.

### Translational relevance and impact for the National Health System (SSN)

The project, innovative for Italy and even original for the EU considering RR and MCDA applied to a broad spectrum Telecardiology service, will supply data to model, prioritize and support health services programming and coverage decisions for advanced HF management processes supporting patients home care. The project has the characteristics of a Value Based Healthcare concept, supplying data and knowledge to define the needed requirements for engaging, preparing, treating and following the patient. Observed and interpreted data can supply useful process indicators, even to define "bundled reimbursements" for telecardiology services integrated with traditional hospital based and ambulatory based services to cut general costs, improve efficiency and efficacy of procedures, improve quality of life and outcomes of interest for the patient, and to integrate hospital with community healthcare. The project will supply data for defining economical models and enhance clinical guidelines on HF.

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| <p><b>Project Type: WP PROJECT - 2</b></p>  |  |

### PRINCIPAL INVESTIGATOR PROFILE

|                |                 |   |
|----------------|-----------------|---|
| Name           | Institution     | Regione Lombardia - Direzione Generale Sanità   |
| Maria Frigerio | Department/Unit | 2nd Section of Cardiology, Heart Failure and Cardiac Transplant Unit, ASST GOM Niguarda |
|                | Position Title  | Director  |

### Personal Statement

The responsibility of key person (FM) includes the management of the project, the training of different operators involved in the process for HTA model, the implementation of different items of HTA model on the process, the interrelationship with cooperators of the whole project, the definition of indicators, the interpretation of the results, and, finally, the proposal of conclusive data for healthcare experts and decision makers.

| Education/Training - Institution and Location | Degree                  | Year(s) | Field of study     |
|---|-------------------------|---------|--------------------|
| University of Milan                           | MD                      | 1979    | Degree in Medicine |
| University of Milan                           | Post graduate specialty | 1982    | Cardiology         |

### Positions

| Institution       | Division / Research group  | Location | Position | From year | To year |
|-------------------|--|----------|----------|-----------|---------|
| ASST GOM Niguarda | Cardiovascular Department  | Milan    | Staff    | 1982      | 2000    |
| ASST GOM Niguarda | "A. De Gasperis" Cardio-thoracic & Vascular Dept                     | Milan    | Director | 2011      | 2017    |
| ASST GOM Niguarda | 2nd Section of Cardiology, Heart Failure and Cardiac Transplant Unit | Milan    | Director | 2000      | 2018    |

**Official H index:** 22.0 ( autocerficated )

**Source:** Scopus

**Scopus Author Id:** 7005776572

**ORCID ID:** <https://orcid.org/0000-0001-9762-1222>

**RESEARCH ID:** Not available

### Awards and Honors:

None.

### Other CV Informations:

Experience in clinical cardiology, echocardiography, heart failure, heart transplantation, mechanical circulatory support (medical management).

Society affiliation ANMCO, ESC, ISHLT, NITp, member of the board for audit of Italian Heart Transplant Center on behalf of the National Transplant Center conducted in 2008.

Editor of GIC (Giornale Italiano di Cardiologia).

Participated to sponsored and publicly funded researches, including clinical research in the field of heart transplantation,

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| <p><b>Project Code:</b> NET-2018-12368077-2</p>   | <p><b>Principal Investigator:</b> Maria Frigerio</p>  |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>  | <p><b>Applicant Institution:</b> Regione Lombardia - Direzione Generale Sanità</p>  |
| <p><b>Project Type: WP PROJECT - 2</b></p>  |   |

chronic heart failure, ventricular assist devices.

Author or co-author of >150 publications on international peer reviewed journals.

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### Selected peer-reviewed publications of the PI

| Valid for PI minimum expertise level  |                                   |          |         |     |
|---|-----------------------------------|----------|---------|-----|
| Title   | DOI                               | PMID     | Cit. ** | P.* |
| Predicting short-term mortality in advanced decompensated heart failure - role of the updated acute decompensated heart failure/N-terminal pro-B-type natriuretic Peptide risk score. | 10.1253/circj.CJ-14-1219          | 25753469 | 4       | F   |
| A life-threatening presentation of eosinophilic granulomatosis with polyangiitis.   | 10.2459/JCM.00000000000330        | 26556445 | 2       | F   |
| Tricuspid Annular Plane Systolic Excursion in Acute Decompensated Heart Failure: Relevance for Risk Stratification  | 10.1016/j.cjca.2015.09.019        | 26860776 | 1       | L   |
| Incremental utility of prognostic variables at discharge for risk prediction in hospitalized patients with acutely decompensated chronic heart failure.                               | 10.1016/j.hrtlng.2016.03.004      | 27066878 | 1       | L   |
| A prospective comparison of mid-term outcomes in patients treated with heart transplantation with advanced age donors versus left ventricular assist device implantation              | 10.1093/icvts/ivw164              | 27245619 | 2       | L   |
| Prognostic impact of comorbidities in hospitalized patients with acute exacerbation of chronic heart failure  | 10.1016/j.ejim.2016.05.020        | 27263064 | 5       | L   |
| Getting approval for new therapeutic medical devices versus drugs: are the differences justified?   | 10.1183/16000617.0037-2016        | 27581821 | 1       | F   |
| Long-term prognostic implications of the ADHF/NT-proBNP risk score in patients admitted with advanced heart failure.  | 10.1016/j.healun.2016.07.007      | 27520779 | 1       | L   |
| The key clues to reach the diagnosis of Loeffler endomyocardial fibrosis associated with eosinophilic granulomatosis with polyangiitis.   | 10.2459/JCM.00000000000496        | 28072629 | 0       | L   |
| Trends in heart failure hospitalizations, patient characteristics, in-hospital and 1-year mortality: A population study, from 2000 to 2012 in Lombardy                                | 10.1016/j.ijcard.2017.02.052      | 28262349 | 1       | F   |
| Survival and Left Ventricular Function Changes in Fulminant Versus Nonfulminant Acute Myocarditis.  | 10.1161/CIRCULATIONAHA.117.026386 | 28576783 | 11      | L   |
| Optimal and Equitable Allocation of Donor Hearts: Which Principles Are We Translating Into Practices?   | 10.1097/TXD.0000000000000712      | 28795148 | 2       | F   |
| Female gender and mortality risk in decompensated heart failure   | 10.1016/j.ejim.2018.01.011        | 29317139 | 0       | L   |
| Single-center outbreak of Pneumocystis jirovecii pneumonia in heart transplant recipients.  | 10.1111/tid.12880                 | 29514393 | 0       | L   |
| Fulminant myocarditis: Characteristics, treatment, and outcomes   | 10.14744/AnatolJCardiol.2017.8170 | 29537977 | 0       | L   |

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| <p><b>Project Type: WP PROJECT - 2</b></p>  |  |

| Title  | DOI                         | PMID     | Cit. ** | P.* |
|--|-----------------------------|----------|---------|-----|
| A new life: motherhood after heart transplantation. A single center experience and review of literature. | 10.1097/TP.0000000000002281 | 29762460 | 0       | L   |

\* Position: F=First L=Last C=Correspondent

\*\* Autocertificated

| For evaluation CV  |                                   |          |        |  |
|--|-----------------------------------|----------|--------|--|
| Title  | DOI                               | PMID     | Cit. * |  |
| Ticagrelor for left ventricular assist device thrombosis: A new therapeutic option to be evaluated with caution  | 10.1016/j.ijcard.2016.06.304      | 27400299 | 1      |  |
| Prognostic impact of late gadolinium enhancement in the risk stratification of heart transplant patients   | 10.1093/ehjci/jew186              | 27625368 | 2      |  |
| Quantitative changes in late gadolinium enhancement at cardiac magnetic resonance in the early phase of acute myocarditis  | 10.1016/j.ijcard.2016.11.282      | 27913009 | 4      |  |
| Prognostic role of $\beta$ -blocker selectivity and dosage regimens in heart failure patients. Insights from the MECKI score database.                                       | 10.1002/ejhf.775                  | 28233458 | 4      |  |
| HeartWare-HVAD for end-stage heart failure: a review of clinical experiences with 50 patients  | 10.1080/17434440.2017.1325318     | 28467129 | 1      |  |
| An ISHLT consensus document for prevention and management strategies for mechanical circulatory support infection  | 10.1016/j.healun.2017.06.007      | 28949086 | 1      |  |
| Multiparametric prognostic scores in chronic heart failure with reduced ejection fraction: a long-term comparison  | 10.1002/ejhf.989                  | 28949086 | 6      |  |
| Refractory ventricular tachycardia caused by inflow cannula mechanical injury in a patient with left ventricular assist device: Catheter ablation and pathological findings. | 10.1016/j.joa.2017.04.007         | 29021856 | 0      |  |
| Mineralocorticoid receptor antagonists for heart failure: a real-life observational study  | 10.1002/ehf2.12244                | 29397584 | 0      |  |
| Clinical Presentation and Outcome in a Contemporary Cohort of Patients with Acute Myocarditis: The Multicenter Lombardy Registry.  | 10.1161/CIRCULATIONAHA.118.035319 | 29764898 | 0      |  |

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| <p><b>Project Type: WP PROJECT - 2</b></p>  |  |

| <b>Grant</b>                 |      |   |                      |
|------------------------------|------|---|----------------------|
| Funded Institution / Country | Year | Title   | Position in Projects |
| Ministry of Health, Italy    | 2009 | RF "HF DATA" (1483329) Utilization of regional health service databases for evaluating epidemiology, short and medium-term outcome, and process indexes in patients hospitalized for heart failure. | Coordinator          |

**Employment contract extension:**

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| <p><b>Project Type: WP PROJECT - 2</b></p>  |  |

### Biographical Sketch Contributors 1

|  |  |
|--|--|
| <p><b>Name:</b><br/>Tringali Michele</p> | <p>Institution ASST Grande Ospedale Metropolitano Niguarda<br/>Department/Unit SOC Qualità e Rischio Clinico<br/>Position Title Collaborator</p> |
|--|--|

| Education/Training - Institution and Location   | Degree   | Year(s) | Field of study                                  |
|---|--|---------|---|
| Lister Hill Center for Biomedical Communications at National Library of Medicine (Bethesda - MD, USA) | Visiting scholar   | 2001    | Biomedical information research center          |
| Ferrara University  | Gastroenterology and Gastrointestinal Endoscopy Postgraduate | 1994    | Gastroenterology and Gastrointestinal Endoscopy |
| Turin University  | Medical Doctor   | 1985    | Medicine and Surgery                            |

#### Personal Statement:

Michele Tringali is deputy officer for the Lombardy program of Health Technology Assessment in Milano, where he lead the implementation of a MCDA approach to appraisal of medical devices and other health care technologies. He is a member of the Steering Committee of the National Program for HTA of Medical Devices at MoH (2016-now). During 2008 he worked for a national committee in AIFA.

| Institution       | Division / Research group                  | Location | Position                  | From year | To year |
|-------------------|--|----------|---------------------------|-----------|---------|
| ASST GOM Niguarda | Quality and Risk Complex Structure         | Milan    | High Speciality           | 2018      | 2018    |
| AST Pavia         | HTA structure in Pharmaceutical Department | Pavia    | Director of HTA structure | 2009      | 2017    |
| AST Pavia         | Primary Care Department                    | Pavia    | High Speciality           | 2007      | 2009    |

#### Awards and Honors

**Official H index:** 2.0 ( autocertificated )

**Source:** Scopus

**Scopus Author Id:** 57198318247

**ORCID ID:** Not available

**RESEARCH ID:** Not available

#### Awards and Honors:

None.

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
|   | <p><b>Project Code:</b> NET-2018-12368077-2</p>  |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Regione Lombardia - Direzione Generale Sanità</p>   |
| <p><b>Project Type: WP PROJECT - 2</b></p>  |  |

### Biographical Sketch Contributors 2

|                                       |   |
|---------------------------------------|---|
| <p><b>Name:</b><br/>COLOMBO PAOLA</p> | <p><b>Institution</b> ASST Grande Ospedale Metropolitano Niguarda<br/><b>Department/Unit</b> Cardiovascular Department - Clinical Governance and quality<br/><b>Position Title</b> MD Staff</p> |
|---------------------------------------|---|

| Education/Training - Institution and Location | Degree                  | Year(s) | Field of study     |
|---|-------------------------|---------|--------------------|
| University of Milan                           | MD                      | 1996    | Medicine           |
| University of Milan                           | Post graduate specialty | 2002    | Cardiology         |
| University of Milan                           | PhD                     | 2004    | Cardiac physiology |
| LIUC University                               | Master                  | 2013    | Health management  |
| LIUC University                               | Master                  | 2018    | HTA                |

**Personal Statement:**

Given her expertise in the field of cardiovascular clinical research and patient management, she will participate to data collection and analysis within the present Network project. Given her collaboration with Clinical governance and quality She will also contribute to coordinate the work of clinical cardiologists about PDTA, GL and HTA analysis

| Institution       | Division / Research group       | Location | Position                          | From year | To year |
|-------------------|---------------------------------|----------|-----------------------------------|-----------|---------|
| ASST GOM Niguarda | Cardiovascular Departement      | Milan    | Interventional Cardiology - Staff | 2002      | 2018    |
| ASST GOM Niguarda | Clinical Governance and quality | Milan    | HTA- Staff                        | 2018      | 2018    |

**Awards and Honors**

**Official H index:** 11.0 ( autocertificated )

**Source:** Scopus

**Scopus Author Id:** 57201949569

**ORCID ID:** 0000-0003-1330-6191

**RESEARCH ID:** not available

**Awards and Honors:**

She wrote more than 80 papers about various cardiac topics on national and international journals. She wrote more than 200 abstracts. She attended at more than 200 national and international congress often as a speaker. GISE fellow.

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
| <p><b>Project Code:</b> NET-2018-12368077-2</p>   | <p><b>Principal Investigator:</b> Maria Frigerio</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Regione Lombardia - Direzione Generale Sanità</p>   |
| <p><b>Project Type: WP PROJECT - 2</b></p>  |  |

### Biographical Sketch Contributors 3

|  |  |
|--|--|
| <p><b>Name:</b><br/>Mazzali Cristina</p> | <p>Institution ASST Grande Ospedale Metropolitano Niguarda<br/>Department/Unit Procurement Dpt.<br/>Position Title HTA Staff</p> |
|--|--|

| Education/Training - Institution and Location | Degree               | Year(s) | Field of study                             |
|---|----------------------|---------|--|
| University of Milan, Italy                    | MS                   | 1996    | Mathematics                                |
| University of Milan, Italy                    | Postgraduate Diploma | 2003    | Medical Statistics post graduate specialty |
| University of Milan, Italy                    | PhD                  | 2007    | Biomedical Statistics                      |

**Personal Statement:**

Her expertise in statistical analysis varies from clinical observational studies to epidemiologic and clinical analysis based on the so-called administrative data. She will cooperate in the study-design of the research activities. She will contribute to the statistical and sensitivity analyses.

| Institution           | Division / Research group                | Location | Position            | From year | To year |
|-----------------------|--|----------|---------------------|-----------|---------|
| Ospedale Niguarda     | Quality and Safety Service               | Milan    | Staff               | 2001      | 2009    |
| University of Milan   | Dept. Biomedical and Clinical Sciences   | Milan    | postdoctoral fellow | 2009      | 2014    |
| Politecnico di Milano | Dept. Management, Economic and Ind. Eng. | Milan    | postdoctoral fellow | 2014      | 2017    |
| ASST GOM Niguarda     | HTA Procurement Dept.                    | Milan    | HTA-Staff           | 2017      | 2018    |

**Awards and Honors**

**Official H index:** 9.0 ( autocerficated )

**Source:** Scopus

**Scopus Author Id:** 6602818642

**ORCID ID:** 0000-0003-2645-9939

**RESEARCH ID:** not available

**Awards and Honors:**

None.

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
| <p><b>Project Code:</b> NET-2018-12368077-2</p>   | <p><b>Principal Investigator:</b> Maria Frigerio</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Regione Lombardia - Direzione Generale Sanità</p>   |
| <p><b>Project Type: WP PROJECT - 2</b></p>  |  |

### Expertise Research Collaborators

| Selected peer-reviewed publications of the Research Group / Collaborators |  |                               |                |        |
|---|--|-------------------------------|----------------|--------|
| Collaborator  | Title  | DOI                           | PMID           | Cit. * |
| Tringali Michele  | Embedding sustainable effectiveness in decision-making within an ecosystem: Lessons from the health technology assessment program at the Lombardy Region, Italy (Chapter of edited book)               | Not applicable                | Not applicable | 2      |
| Mazzali Cristina  | Eleven-year trends in gender differences of treatments and mortality in ST- elevation acute myocardial infarction in northern Italy, 2000 to 2010  | 10.1016/j.amjcard.2014.05.007 | 24925728       | 12     |
| Mazzali Cristina  | Use of administrative data in healthcare research  | 10.1007/s11739-015-1213-9     | 25711312       | 7      |
| Mazzali Cristina  | Methodological issues on the use of administrative data in healthcare research: The case of heart failure hospitalizations in Lombardy region, 2000 to 2012  | 10.1186/s12913-016-1489-0     | 27391599       | 2      |
| Mazzali Cristina  | Trends in heart failure hospitalizations, patient characteristics, in-hospital and 1-year mortality: A population study, from 2000 to 2012 in Lombardy   | 10.1016/j.ijcard.2017.02.052  | 28262349       | 1      |
| COLOMBO PAOLA   | Thrombus aspiration before primary angioplasty improves myocardial reperfusion in acute myocardial infarction: the DEAR-MI (Dethrombosis to Enhance Acute Reperfusion in Myocardial Infarction) study. | 10.1016/j.jacc.2016.03.068    | 17045887       | 320    |
| COLOMBO PAOLA   | A multidisciplinary consensus document on follow-up strategies for patients treated with percutaneous coronary intervention  | 10.1002/ccd.25724             | 25380511       | 4      |
| Tringali Michele  | Diffusion of biosimilar hemopoietic growth factors use in oncology practice: an Italian experience   | 10.1007/s40276-015-0026-1     |                | 1      |
| Tringali Michele  | Implementation of EUnetHTA core Model® in Lombardia: the VTS framework.  | 10.1017/S0266462313000639     | 24451150       | 19     |
| Tringali Michele  | Exploring values of health technology assessment agencies using reflective multicriteria and rare disease case   | 10.1017/S0266462317000915     | 29019295       | 0      |

\* Autocertificated

| Grant                        |      |       |                      |                  |
|------------------------------|------|-------|----------------------|------------------|
| Funded Institution / Country | Year | Title | Position in Projects | Collaborator     |
| None                         | 0    | None  | Collaborator         | Tringali Michele |

Sent date: 20/05/2018 21.34

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Sent date of moratorium changes: 01/06/2018 15.17

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
| <p><b>Project Code:</b> NET-2018-12368077-2</p>   | <p><b>Principal Investigator:</b> Maria Frigerio</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Regione Lombardia - Direzione Generale Sanità</p>   |
| <p><b>Project Type: WP PROJECT - 2</b></p>  |  |

| Total proposed budget ( Euro ) |                   |                   |   |   |   |
|--------------------------------|-------------------|-------------------|---|---|---|
| Costs                          | TOTAL BUDGET      | Co-Funding        | Project costs proposed to funding Organization (no MOH request) | List of costs proposed for funding to the MOH | Percentage of total proposed to the MOH |
| 1a Staff Salary                | 112.142,00        | 112.142,00        | 0,00  | not permitted                                 | 0,00                                    |
| 1b Researchers' Contracts      | 220.000,00        | 0,00              | 150.000,00  | 70.000,00                                     | 50,00                                   |
| 2 Equipment (Leasing - Rent)   | 50.500,00         | 0,00              | 0,00  | 50.500,00                                     | 36,07                                   |
| 3a Supplies                    | 0,00              | 0,00              | 0,00  | 0,00  | 0,00                                    |
| 3b Model Costs                 | 0,00              | 0,00              | 0,00  | 0,00  | 0,00                                    |
| 3c Subcontracts                | 0,00              | 0,00              | 0,00  | 0,00  | 0,00                                    |
| 3d Patient Costs               | 0,00              | 0,00              | 0,00  | 0,00  | 0,00                                    |
| 4 IT Services and Data Bases   | 0,00              | 0,00              | 0,00  | 0,00  | 0,00                                    |
| 5 Publication Costs            | 2.750,00          | 0,00              | 0,00  | 2.750,00                                      | 1,96                                    |
| 6 Convegni                     | 1.350,00          | 0,00              | 0,00  | 1.350,00                                      | 0,96                                    |
| 7 Travels                      | 2.750,00          | 0,00              | 0,00  | 2.750,00                                      | 1,96                                    |
| 8 Overheads                    | 12.650,00         | 0,00              | 0,00  | 12.650,00                                     | 9,04                                    |
| 9 Coordination Costs           | 0,00              | 0,00              | 0,00  | 0,00  | 0,00                                    |
| <b>Total</b>                   | <b>402.142,00</b> | <b>112.142,00</b> | <b>150.000,00</b>   | <b>140.000,00</b>                             | <b>100,00</b>                           |

Report the Co-Funding Contributor:

3 man-month salary of PI, 5 man-month salary of Co-PI, 6 man-month salary of four research collaborators.

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
| <p><b>Project Code:</b> NET-2018-12368077-2</p>   | <p><b>Principal Investigator:</b> Maria Frigerio</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Regione Lombardia - Direzione Generale Sanità</p>   |
| <p><b>Project Type: WP PROJECT - 2</b></p>  |  |

| <b>Budget Justification</b>  |  |
|------------------------------|--|
| 1a Staff Salary              | 4 man-month salary of PI and 10 man-month salary of Co-PI  |
| 1b Researchers' Contracts    | Regione Lombardia: 1 Cardiologist (3 year) + 1 Cardiac Nurse (3 year); MOH: 1 Management Engineer (3 Year)                     |
| 2 Equipment (Leasing - Rent) | Leasing/renting of Tele-cardiology service   |
| 3a Supplies                  | None   |
| 3b Model Costs               | None   |
| 3c Subcontracts              | None   |
| 3d Patient Costs             | None   |
| 4 IT Services and Data Bases | None   |
| 5 Publication Costs          | The results will be published at the end of the projects   |
| 6 Convegni                   | Estimate of expenditure for conferences for the dissemination of research results  |
| 7 Travels                    | Travel and accommodation expenses incurred by researchers for the participation to conferences to disseminate research results |
| 8 Overheads                  | -  |
| 9 Coordination Costs         | None   |

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|  <p><i>Ministero della Salute</i><br/>         Direzione Generale della Ricerca Sanitaria<br/>         e Biomedica e della Vigilanza sugli Enti<br/> <b>BANDO RICERCA FINALIZZATA 2018</b><br/>         esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>         Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
| <p><b>Project Code:</b> NET-2018-12368077-2</p>   | <p><b>Principal Investigator:</b> Maria Frigerio</p>  |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>  | <p><b>Applicant Institution:</b> Regione Lombardia - Direzione Generale Sanità</p>  |
| <p><b>Project Type: WP PROJECT - 2</b></p>  |   |

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
| <p><b>Project Code:</b> NET-2018-12368077-3</p>   | <p><b>Principal Investigator:</b> Banfi Giuseppe</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto Ortopedico Galeazzi</p>  |
| <p><b>Project Type: WP PROJECT - 3</b></p>  |  |

**Major Diagnostic Category\*:** Ortopedia

**Project Classification IRG:** Healthcare Delivery and Methodologies

**Project Classification SS:** Health Services Organization and Delivery - HSOD

**Project Keyword 1:** Healthcare organizations, programs, and delivery of services; including those delivered in non-traditional settings; integrated care delivery systems; disease management and modeling; continuous quality improvement; characteristics of the organization and patient outcomes; organizational performance and efficiency; cost-benefit analysis; economics of health care and pharmacoconomics.

**Project Keyword 2:** Health care governance and sustainability

**Project Keyword 3:** Health technology assessment and clinical practice guidelines

**Project duration (months):** 36

**Project Request:**      **Animals:**                       **Humans:**                       **Clinical trial:**

**The object/s of this application is/are under patent copyright Y/N:**

| Investigators, Institution and Role in the Project |       |               |   |                              |            |
|--|-------|---------------|---|------------------------------|------------|
|  | Co-PI | Key Personnel | Institution/Org./Pos.   | Role in the project          | Birth Date |
| 1  | X     | Sirtori Paolo | IRCCS Istituto Ortopedico Galeazzi-<br>Equipe Universitaria di Ortopedia<br>Rigenerativa e Ricostruttiva (E.U.O.R.R.) | Expert Research Collaborator | 25/01/1963 |

## Overall Summary

Fast Track (FT) is a specific surgical process aimed at completely recovering the patient after elective surgery. Such a process has been recently introduced also in hip and knee arthroplasty, where the classical procedure includes some days in orthopaedic ward followed by a two weeks of rehabilitation, generally performed into the hospital, which could be the same of surgical treatment or different, but specialized in reeducation to walking and using legs.

The project is aiming at evaluating, through the standardized approach of Health Technology Assessment, the real impact on hospital efficiency, efficacy on the patients, and on organization of hospital and of community healthcare. The data supplied by the project could be useful to define guidelines and innovative reimbursement policies by National Healthcare Service.

## Background / State of Art

Fast Track (FT) is a specific surgical process aimed at completely recovering the patient after elective surgery. Such a process has been recently introduced also in hip and knee arthroplasty, where the classical procedure includes some days in orthopaedic ward (average in Italy: 7 days) followed by a two weeks of rehabilitation, generally performed into the hospital, which could be the same of surgical treatment or different, but specialized in reeducation to walking and using legs.

IRCCS Galeazzi is a teaching and research hospital in Milano specialized in orthopaedic surgery. Galeazzi is the first

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| <p><b>Project Code:</b> NET-2018-12368077-3</p>   | <p><b>Principal Investigator:</b> Banfi Giuseppe</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto Ortopedico Galeazzi</p>  |
| <p><b>Project Type: WP PROJECT - 3</b></p>  |  |

hospital in Italy for total arthroplasties (hip, knee, and ankle) performing yearly more than three thousands procedures. The leading experience in arthroplasties is moving the hospital towards new processes for engaging patients, especially through new informatics procedures, for enhancing efficiency, through electronic systems to follow and trace patients into the hospital, and for following patients after discharge, through telemedicine and continuous connection with the treated subjects. In particular, Galeazzi developed specific, local registries for hip and knee arthroplasties, and also for ankle one, while a National registry is lacking. These registries are mainly based on electronic devices to facilitate the compliance of patients and to reduce the surgeon involvement when different forms should be filled. The evaluation of outcomes of arthroplasties by surgeons and by patients are parallel and independent, collecting data on quality of life and of range of movement and of pain through international validated scores. The patients are defining their quality of life, after surgery and rehabilitation, by the Patient Related Outcome Measurements (PROMs), which are the recommended procedure by OECD (Organisation for Economic Co-operation and Development, including 35 member Countries, section Health) to evaluate outcomes; Galeazzi, for instance, is included in a specific Working group of OECD, together with some Countries having National registries, for standardizing the use of PROMs (1).

Galeazzi is characterized by high efficiency and high throughput, but is aiming at evaluating and improving the measurement of outcome and efficacy. The Health Technology Assessment concept is already accepted and used in Galeazzi for evaluating procedures and instrumentations. The present attention paid to healthcare based value needs of correct estimation of costs, which is currently performed in the hospital, but also the measurement of outcomes, i.e. the real efficacy of treatments. Thus, registries are developed for that purpose. There is an economic benefit of decreasing length of stay (LOS) in hospital, but the shorten hospitalization could decrease some possible adverse events on patients, as risk of surgical site infection (2).

### Hyphotesis and Specific AIMS

#### Hyphotesis and Significance:

FT protocols have developed in United States and, later, in different Countries to devise a multimodal treatment plan to increase efficiency and to improve outcomes (3,4). The protocol is multiprofessional while includes skills of anaesthesiologists, orthopaedic surgeons, nurses, and physiotherapists, and knowledge on fluid therapy, pain control, blood balance, preoperative education and assessment, early mobilization. Thus, a specific organization of hospital process and ward is needed (5,6).

The FT process is based on special assistance to the patient including conversations and meetings with anaesthesiologists, surgeons, nurses, physiotherapists; the use of specific booklets or smartphone applications is particularly appreciated to prepare patient to the selection for FT and to follow him after discharge (7);

Very low surgical invasiveness, considering also shorter periods of catheterization, artificial nutrition, and drainage;  
- Special anaesthesiological procedures to reduce surgical stress; previous data, have suggested that spinal anesthesia may be preferable compared to general anesthesia. Nowadays preliminary data suggest that we should reconsider these data and that general anesthesia may be preferable in a fast-track program. Also, the traditional use of a stay in the post-anaesthesia

care unit (PACU) should be reconsidered, since the use of an opioid-sparing fast-track setup may reduce or even eliminate the conventional stay in the PACU unit.

The criticism of general anesthesia has to be improved using today's advanced techniques leading to optimized prevention of nausea and vomiting as well as the reduction of opioid-induced hyperalgesia.

Short presurgical fasting, and early regular nutrition and mobilization.

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
| <p><b>Project Code:</b> NET-2018-12368077-3</p>   | <p><b>Principal Investigator:</b> Banfi Giuseppe</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto Ortopedico Galeazzi</p>  |
| <p><b>Project Type: WP PROJECT - 3</b></p>  |  |

- Reduce bleeding and the following anemia:

These topics are important to be considered in optimizing fast-track and include pre-, intra- and postoperative action

- a) Preoperative anaemia should be recognised, and potentially treated with iron or others
- b) the best effort should be made in order to reduce intraoperative bleeding. The influence of surgical approaches on bleeding have not been extensively proved but minimally invasive surgery has been suggested to reduce blood loss. Several review studies have proved that the use of topical or systemically tranexamic acid makes a substantial difference for blood loss. Transfusion is linked to an increased LOS (Length of stay) and co-morbidity.

**Preliminary Data:**

Galeazzi started to apply FT for hip and knee arthroplasties for some patients in 2018, recruited into the general population selected for the surgery applying strict inclusion criteria, elaborated from experiences published in current scientific literature. The patients are becoming from different surgical teams; the program includes a multidisciplinary collaboration (anaesthesiologists, surgeons, nurses, and physiotherapists), who are involved in a general agreement on defined evidence-based perioperative care principles, monitoring of data, and adjustment of the programme on the basis of scientific evidence. The programme is directly followed by health managers of the hospital, where a specific system to trace all patients procedures is existing, registering, besides the medical reports, the efficiency data.

**Specific Aim 1:**

A focus on the pathogenesis of muscle weakness is also needed, since quadriceps strength is reduced by 30% or 80% soon after total hip or knee arthroplasty, respectively. Data from randomised trials have cast doubt on the conventional use of physiotherapy after these procedures, but most of these studies have initiated physiotherapy weeks after the operation. Future efforts should instead focus on early postoperative muscle strength training. Since early mobilisation is essential to success, early dizziness and postoperative orthostatic intolerance due to reduced peripheral vascular contraction when a patient is in an upright position.

**Minimally invasive surgical technique**

Minimally invasive surgery does not mean short skin incision but represent a surgical act in respect of the soft tissues, above all muscles e tendons. In fact recently minimally invasive term has been changed in "tissue sparing".

Target control anesthesia

Short presurgical fasting period

Low fluid intake

Early nutrition after surgery

Short periods of catheterization and drainage

No bladder catheterization is performed in FT patients; the drainage in the surgical site, when positioned, is always removed the day after surgery

Pain control:

Effective postoperative pain management is necessary for early recovery after total hip or knee arthroplasties and, evidence based techniques include spinal anesthesia, peripheral nerve blocks, and non-steroidal antiinflammatory drugs combined with paracetamol. Simple, intraoperative, high-volume local anesthetic wound infiltration has proven to be effective for early pain relief after total knee arthroplasty, less after total hip arthroplasty. Although single-dose or continuous peripheral nerve blocks can optimise analgesia, the risk of muscle weakness and falls might preclude their continued use.

Early mobilization

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| <p><b>Project Code:</b> NET-2018-12368077-3</p>   | <p><b>Principal Investigator:</b> Banfi Giuseppe</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto Ortopedico Galeazzi</p>  |
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Patients and caregivers preparation for selection

It is clear that FT process needs of cooperation among different professionals, and between professionals and personnel involved in organizational process.

The inclusion criteria for unicompartmental knee arthroplasty (UKA), total knee arthroplasty (TKA) and total hip arthroplasty (THA) are patients living in Regione Lombardia, aging from 18 and 75 years, women having a weight < 70 Kg, ASA I and II classes, social conditions allowing rapid discharge from hospital and assuring rehabilitation at home, lack of surgical complications.

The discharge criteria for UKA, TKA are ability for autonomous wearing, ability to use bed (get off and get in), autonomy for personal hygiene, ability to sit, knee bending at 90°, complete extension of knee, ability to raise leg maintaining the knee extended, level 6 of FIM score (physiotherapeutic score).

The discharge criteria for THA are ability for autonomous wearing, ability to use bed (get off and get in), autonomy for personal hygiene, ability to sit, hip flexibility at 90°, complete extension of hip, ability to raise leg maintaining the knee extended, level 6 of FIM score (physiotherapeutic score), ability to walk with only one crutch

**Specific Aim 2:**

not applicable

**Specific Aim 3:**

not applicable

**Experimental Design Aim 1:**

HTA evaluation of the Specific Aim 1

**Experimental Design Aim 2:**

not applicable

**Experimental Design Aim 3:**

not applicable

**Picture to support preliminary data:**

Galeazzi-Picture.pdf

**Methodologies and statistical analyses:**

The HTA evaluation of FT we propose is integrated into a project intended to supply decision makers about procedures and guidelines. We will supply our data, accurately elaborated and interpreted, to various cooperators of the whole project to define and measure indicators, to define guidelines and to calculate costs and budget impact and, finally, to decide possible modifications of healthcare organization and procedures reimbursement.

The evaluation of FT process should be performed by Health Technology Assessment (HTA) method, namely EuNeHTA procedure, to define efficiency and efficacy of early discharge of patient after knee or hip arthroplasty.

Criticism and difficulties for widespread FT program include the diversity of hospital settings, inadequate staffing of wards, use of opioid-based analgesia regimens, insufficient postoperative mobilisation of patients, absence of well defined

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discharge criteria, and suboptimum pre-operative patient information.

FT programmes include a multidisciplinary collaboration (anaesthesiologists, surgeons, nurses, and physiotherapists), who are involved in a general agreement on defined evidence-based perioperative care principles, monitoring of data, and adjustment of the programme on the basis of scientific evidence.

For instance, FT programs have been developed for different surgical procedures leading to higher patient satisfaction and lower morbidity.

#### Expected outcomes:

Expected outcomes are improvement of preoperative conditions of patients thanks to specific preparation. Indicator: patient satisfaction before discharge (evaluated by a specific scales)

Fast recovery from surgery. Indicators: Significant reducing in LOS, in comparison with not FT patients; Not increasing in short-term complications and in hospital readmission rate after 30-90 days in comparison with not FT patients.

Improvement of blood management. Indicator: Minimal blood loss (evaluated by delta hemoglobin loss); in comparison with not FT patients

Movement indicators improved after surgery in short, medium and long term. Indicator: specific physical reeducation scores, as Functional Independence Measure (FIM); Early capability to start the normal relational life, in comparison with not FT patients by specific scores as autonomy profile of modified Barthel index; PROMs collected into the registry and Minimal Importance Change on PROMs

Efficiency increase, with a positive impact on direct and indirect costs, especially on optimization of human resources.

Indicator: budget impact analysis

Improvement of integration of hospital with community and practitioners. Indicator: PROMs collected into the registry; indirect costs analysis.

#### Risk analysis, possible problems and solutions:

The high number of arthroplasties performed in Galeazzi allows the recruitment of high number of patients for FT. The aim of the Institute is the recruitment in the FT process of almost one half of the patients. Thus, the risk for possible insufficient quantity of data is very low and negligible. In any case, possible cooperation with some different orthopaedic wards could solve the problem

#### Significance and Innovation

HTA of hip and knee arthroplasty FT could supply data for defining common and standardized procedures (8), developing guidelines, and proposing new reimbursement modes, as so-called bundled DRG. This evaluation should provide data to decision makers useful to define new organizational models for pre-hospitalization, follow-up during hospitalization and reeducation of the treated joint after discharge. Possible decrease of direct and indirect costs on FT patients and the impact at different levels could be calculated.

The project is innovative for Italy, while data, especially outcomes, on FT in our Country are lacking. One retrospective study has been published in the field, lacking an economical and organizational impact evaluation (9). The project is innovative also because the data collected in literature are generally becoming from general hospitals, while specific multidisciplinary experience of personnel is particularly important to compare regularly treated and FT patients.

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| <p><b>Project Code:</b> NET-2018-12368077-3</p>   | <p><b>Principal Investigator:</b> Banfi Giuseppe</p>   |
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### Description of the complementary and synergy research team

The team who manages the project is including an expert of scientific programmes and HTA evaluation (BG) and a orthopaedic surgeon, responsible for FT process in Galeazzi (SP). Besides the proposants, the team is including physical therapists devoted to the FT programme, data manager, research nurse, physical therapy physician, anaesthesiologists, biomedical engineers, dietotherapists. The whole team is assuring the complete evaluation of all aspects of the FT programme. The experience of proposants is assuring the correct scientific and practical approach to the process.

### Training and tutorial activities

Tutorial activities will be developed directly by orthopaedic surgeon responsible of the process for young postgraduated MDs. Training of specialized personnel will be defined by single components of the whole team who manages the process. The expert on HTA will train the components of the team who did not have specific knowledge on the field about the different items needed to complete the HTA evaluation.

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8. D'Ambrosi R, Banfi G, Usulli FG. Total ankle arthroplasty and national registers: What is the impact on scientific production? *Foot Ankle Surg* 2018; Epub
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### Timeline / Deliverables / Payable Milestones

- 18 Month: Release of Intermediate Data Analysis
- 36 month: Final evaluation and interpretation of data

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### Milestones 18 month

Release of Intermediate Data Analysis

### Milestones 36 month

Final evaluation and interpretation of data

### Gantt chart

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### Equipment and resources available

The Orthopaedic Hospital Galeazzi (IRCCS Galeazzi) is a teaching and research hospital in Milano, Italy. The research activities concerning the diseases of movement apparatus are accredited by Ministry of Health since 2006, thus Galeazzi is one of IRCCS, that means Institutes for Care and Scientific Research. IRCCS Galeazzi is the first orthopaedic hospital in Italy for some complex surgeries, as arthrodesis, hip, knee and ankle arthroplasties, and covers all orthopaedic diseases. Moreover, movement disorders and metabolic diseases are also treated. Besides orthopaedics, some additional specialties are present into the hospital, as rehabilitation, dermatology, oral surgery, maxillo-facial surgery, plastic surgery, neurosurgery, endocrinology. The IRCCS Galeazzi aim is to define, program and perform a top-level care associated with high quality research in bone and muscle diseases, following a 40-years tradition, innovating assistance through new procedures, new bioengineering techniques and evidence-based and translational medicine. The link between the high quality care and innovative and clinically-based research allow to project, develop and release new organizational models for healthcare, to increase the skills and qualification of healthcare personnel, to improve learning for graduates and postgraduates students, to increase the correct information on services, treatments and outcomes for citizens.

Specific equipment:

Web based registry for arthroplasties with PROMs;

Hospital ward devoted to FT equipped with instruments and devices for monitoring patients;

Hospital exercise space equipped with instruments for reeducating patients after surgery.

### Translational relevance and impact for the National Health System (SSN)

The impact of the project on National Healthcare Service should be high. The project, innovative for our Country, and even original for EU, can supply data to define specific decisions for FT arthroplasty processes. The project has the characteristics of the Value Based Healthcare concept, supplying data and knowledge to define the needed requirements for engaging, preparing, treating and following the patient. The observed and interpreted data can supply useful process indicators, even to define "bundled DRG" for FT to cut general costs, to improve efficiency and efficacy, and to integrate hospital with community healthcare. Moreover, the project will supply data for defining economical models and universal clinical guidelines

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### PRINCIPAL INVESTIGATOR PROFILE

|                                |  |
|--------------------------------|--|
| <p>Name<br/>Banfi Giuseppe</p> | <p>Institution: Istituto Ortopedico Galeazzi<br/>Department/Unit: Scientific Direction<br/>Position Title: Scientific Director</p> |
|--------------------------------|--|

### Personal Statement

Project will define a HTA eval. of FT, supplying data and knowledge to define the needed requirements for engaging, preparing, treating and following the patient. Observed and interpreted data can supply useful process indicators, even to define "bundled DRG" for FT to cut general costs, to improve efficiency and efficacy, and to integrate hospital with community healthcare, data for defining economical models and universal clinical guidelines.

Key person responsibility: management of the proj. , training of different operators involved in the process for HTA model, implementation of different items of HTA model on process, Interrelationship, the definition of indicators, interpretation of the results, and, finally, proposal of conclusive data for healthcare experts and decision makers

| Education/Training - Institution and Location | Degree  | Year(s) | Field of study                  |
|---|---|---------|---------------------------------|
| University of Pavia, Italy                    | Degree in Medicine                              | 6       | Medicine                        |
| University of Milan, Italy                    | Postgraduate in Hygiene and Preventive Medicine | 4       | Hygiene and Preventive Medicine |

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| Positions   |                           |   |  |           |         |
|---|---------------------------|---|--|-----------|---------|
| Institution                                       | Division / Research group | Location                                | Position   | From year | To year |
| GRUPPO OSPEDALIERO SAN DONATO FOUNDATION          | na                        | C.SO PORTA VIGENTINA 18, MILANO         | SCIENTIFIC DIRECTOR  | 2008      | 2018    |
| IRCCS ISTITUTO ORTOPEDICO GALEAZZI                | na                        | VIA R. GALEAZZI 4, MILANO               | SCIENTIFIC DIRECTOR  | 2007      | 2018    |
| FONDAZIONE ISTITUTO INSUBRICO RICERCA PER LA VITA | na                        | VIA LEPETIT 34, GERENZANO (VA)          | MEMBER OF BOARD OF DIRECTORS   | 2012      | 2018    |
| FONDAZIONE CENTRO SAN RAFFAELE                    | na                        | VIA OLGETTINA 60, MILANO                | GENERAL DIRECTOR   | 2012      | 2012    |
| MINISTRY OF HEALTH                                | na                        | Viale Giorgio Ribotta 5, Roma           | Member of "Methods, Training and Communication" Working Group of the Ministry of Health's Governing Body   | 2016      | 2018    |
| REGIONE LOMBARDIA                                 | na                        | Piazza Città della Lombarida 1, Milano  | Vice President of HTA Programmes Emerging Technologies Commission and Member of the Health Technology Assessment (HTA) Commission  | 2009      | 2018    |
| IRCCS Ospedale San Raffaele                       | na                        | VIA OLGETTINA 60, MILANO                | President of the "Health Organization, Innovation and Leadership" Research Center including the definition of Early HTA projects EATRIS, the European infrastructure for translational medicine. | 2013      | 2018    |
| Libera Università Carlo Cattaneo (LIUCC)          | na                        | Corso G. Matteotti 22, Castellanza (VA) | Teacher of the Advance Course on HTA and Master "per Coordinamento Professioni sanitarie"  | 2006      | 2018    |
| UNIVERSITY VITA-SALUTE SAN RAFFAELE               | na                        | VIA OLGETTINA 58, MILANO                | FULL PROFESSOR OF CLINICAL BIOCHEMISTRY AND CLINICAL MOLECULAR BIOLOGY   | 2017      | 2018    |
| UNIVERSITY VITA-SALUTE SAN RAFFAELE               | na                        | VIA OLGETTINA 58, MILANO                | VICE RECTOR FOR RESEARCH   | 2017      | 2018    |

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**Official H index:** 30.0 ( autocertificata )

**Source:** Scopus

**Scopus Author Id:** 7102710315

**ORCID ID:** 0000-0001-9578-5338

**RESEARCH ID:** K-6585-2015

**Awards and Honors:**

He introduced HTA evaluation in Galeazzi, and experimented also early HTA, in cooperation with EATRIS, european infrastructure for advanced therapies.

He has expertise in economical evaluation of medical processes, cooperating with the Liuc economical academy on programs for cost-effectiveness and cost-opportunity calculation.

He introduced fast track procedures in Galeazzi, coordinating various professionals, in a general project for applying the Value Based Healthcare

**Other CV Informations:**

Giuseppe Banfi was Medical Supervisor of IRCCS Galeazzi from 2003 to 2008 and Scientific Director of the same Institute from 2008 until now. The specific experience on management of a specialized hospital, leading in orthopaedic sciences in Italy, is peculiar and crucial especially for proposing, managing, evaluating, assessing, translating, organizing innovation in orthopaedic procedures. Moreover, Giuseppe Banfi developed specific expertise in Health Technology Assessment, actively participating in different commissions of Regione Lombardia from 2009, contributing to assess the Regional system for assessment and appraisal of medical procedures.

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### Selected peer-reviewed publications of the PI

| Valid for PI minimum expertise level   |                                  |          |         |     |
|--|----------------------------------|----------|---------|-----|
| Title  | DOI                              | PMID     | Cit. ** | P.* |
| Banfi G, Lombardi G, Colombini A, Lippi G. Bone metabolism markers in sports medicine.   | 10.2165/11533090-000000000-00000 | 20632739 | 56      | F   |
| Colombini A, Lombardi G, Corsi MM, Banfi G. Pathophysiology of the human intervertebral disc.  | 10.1016/j.biocel.2007.12.011     | 18243770 | 72      | L   |
| Lombardi G, Vitale JA, Logoluso S, Logoluso G, Cocco N, Cocco G, Cocco A, Banfi G. Circannual rhythm of plasmatic vitamin D levels and the association with markers of psychophysical stress in a cohort of Italian professional soccer players. Chronobiology International 2017;34(4):471-479<br>IF: 2,562 | 10.1080/07420528.2017.1297820    | 28306393 | 5       | L   |
| Ferrari D, Lombardi G, Banfi G. Concerning the vitamin D reference range: pre-analytical and analytical variability of vitamin D measurement. Biochemia Medica 2017;27(3):030501<br>IF: 2,934  | 10.11613/BM.2017.030501          | 28900363 | 1       | L   |
| Moroni A, Miscione MT, Orsini R, Micera G, Mosca S, Sinapi F, De Girolamo L, Banfi G. Clinical and radiographic outcomes of the Birmingham Hip Resurfacing arthroplasty at a minimum follow-up of 10 years: results from an independent centre. Hip International 2017;27(2):134-139<br>IF: 1,055            | 10.5301/hipint.5000424           | 28362050 | 1       | L   |
| Lombardi G, Barbaro M, Locatelli M, Banfi G. Novel bone metabolism-associated hormones: the importance of the pre-analytical phase for understanding their physiological roles. Endocrine 2017;56(3):460-484<br>IF: 3,131  | 10.1007/s12020-017-1239-z        | 28181144 | 2       | L   |
| Xu J, Lombardi G, Jiao W, Banfi G. Effects of Exercise on Bone Status in Female Subjects, from Young Girls to Postmenopausal Women: An Overview of Systematic Reviews and Meta-Analyses. Sports Medicine 2016;46(8):1165-82<br>IF: 5,038   | 10.1007/s40279-016-0494-0        | 26856338 | 19      | L   |
| Randelli P, Arrigoni P, Aliprandi A, Sdao S, Ragone V, D'Ambrosi R, Randelli F, Cabitza P, Banfi G. Repair versus shaving of partial-thickness articular-sided tears of the upper subscapularis tendon. A prospective randomized controlled trial. Joints 2016;3(3):109-15                                   | 10.11138/jts/2015.3.3.109        | 26889466 | 3       | L   |

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
| <p><b>Project Code:</b> NET-2018-12368077-3</p>   | <p><b>Principal Investigator:</b> Banfi Giuseppe</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto Ortopedico Galeazzi</p>  |
| <p><b>Project Type: WP PROJECT - 3</b></p>  |  |

| Title  | DOI                          | PMID     | Cit. ** | P.* |
|--|------------------------------|----------|---------|-----|
| Lombardi G, Sanchis-Gomar F, Perego S, Sansoni V, Banfi G.<br>Implications of exercise-induced adipo-myokines in bone metabolism.<br>Endocrine 2016; 54(2):284-305   | 10.1007/s12020-015-0834-0    | 26718191 | 14      | L   |
| Mariotti M, Carnovali M, Banfi G.<br>Danio rerio: the Janus of the bone from embryo to scale.<br>Clinical Cases in Mineral and Bone Metabolism 2015;12(2):188-94   | 10.11138/ccmbm/2015.12.2.188 | 26604948 | 2       | L   |
| Lombardi G, Perego S, Luzi L, Banfi G.<br>A four-season molecule: osteocalcin. Updates in its physiological roles.<br>Endocrine 2015;48(2):394-404   | 10.1007/s12020-014-0401-0    | 25158976 | 24      | L   |
| Randelli P, Randelli F, Ragone V, Menon A, D'Ambrosi R, Cucchi D, Cabitza P, Banfi G.<br>Regenerative Medicine in Rotator Cuff Injuries.<br>BioMed Research International 2014;  | 10.1155/2014/129515          | 25184132 | 21      | L   |
| Randelli P, Randelli F, Arrigoni P, Ragone V, D'Ambrosi R, Masuzzo P, Cabitza P, Banfi G.<br>Optimal glenoid component inclination in reverse shoulder arthroplasty. How to improve implant stability.<br>Musculoskeletal Surgery 2014; 98 Suppl 1:15-8  | 10.1007/s12306-014-0324-1    | 24659201 | 10      | L   |
| Drago L, De Vecchi E, Romano' CL, Vassena C, Banfi G.<br>Behaviour of perioperative values of haemoglobin, haematocrit and red blood cells in elderly patients undergoing lower limb arthroplasty: a retrospective cohort study on non-transfused patients.<br>International Journal of Immunopathology and Pharmacology 2013;26(2):427-33 | 10.1177/039463201302600215   | 23755757 | 1       | L   |
| Lanteri P, Lombardi G, Colombini A, Banfi G.<br>Vitamin D in exercise: Physiologic and analytical concerns.<br>Clinica Chimica Acta 2013;415:45-53<br>IF: 2,850  | 10.1016/j.cca.2012.09.004    | 22975529 | 15      | L   |
| Moja L, Piatti A, Pecoraro V, Ricci C, Virgili G, Salanti G, Germagnoli L, Liberati A, Banfi G.<br>Timing Matters in Hip Fracture Surgery: Patients Operated within 48 Hours Have Better Outcomes.<br>A Meta-Analysis and Meta-Regression of over 190,000 Patients<br>PLoS One 2012;7(10):e46175<br>IF: 4,092                              | 10.1371/journal.pone.0046175 | 23056256 | 123     | L   |
| Lanteri P., Lombardi G., Colombini A., Grasso D., Banfi G.<br>Stability of osteopontin in plasma and serum.<br>Clinical Chemistry and Laboratory Medicine 2012;50(11):1979-84<br>IF: 2,069   | 10.1515/cclm-2012-0177       | 22718644 | 12      | L   |

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
| <p><b>Project Code:</b> NET-2018-12368077-3</p>   | <p><b>Principal Investigator:</b> Banfi Giuseppe</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto Ortopedico Galeazzi</p>  |
| <p><b>Project Type: WP PROJECT - 3</b></p>  |  |

| Title  | DOI                          | PMID     | Cit. ** | P.* |
|--|------------------------------|----------|---------|-----|
| Colombini A., Corsetti R., Machado M., Graziani R., Lombardi G., Lanteri P., Banfi G.<br>Serum Creatine Kinase Activity and Its Relationship With Renal Function Indices in Professional Cyclists During the Giro d'Italia 3-Week Stage Race.<br>Clinical Journal of Sport Medicine 2012;22(5):408-13<br>IF: 2,110 | 10.1097/JSM.0b013e31825e66cc | 22744001 | 10      | L   |
| Lombardi G., Lanteri P., Colombini A., Banfi G.<br>Blood biochemical markers of bone turnover: pre-analytical and technical aspects of sample collection and handling.<br>Clinical Chemistry and Laboratory Medicine 2012;50:771-789<br>IF: 2,069  | 10.1515/cclm-2011-0614       | 22628324 | 27      | L   |
| Lombardi G, Colombini A, Freschi M, Tavana R, Banfi G.<br>Seasonal variation of bone turnover markers in top-level female skiers.<br>European Journal of Applied Physiology 2011;111:433-40<br>IF: 2,214   | 10.1007/s00421-010-1664-7    | 20878421 | 16      | L   |

\* Position: F=First L=Last C=Correspondent

\*\* Autocertificated

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
| <p><b>Project Code:</b> NET-2018-12368077-3</p>   | <p><b>Principal Investigator:</b> Banfi Giuseppe</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto Ortopedico Galeazzi</p>  |
| <p><b>Project Type: WP PROJECT - 3</b></p>  |  |

| For evaluation CV   |                              |          |        |
|---|------------------------------|----------|--------|
| Title   | DOI                          | PMID     | Cit. * |
| Drago L, De Vecchi E, Romano' CL, Vassena C, Banfi G. Behaviour of perioperative values of haemoglobin, haematocrit and red blood cells in elderly patients undergoing lower limb arthroplasty: a retrospective cohort study on non-transfused patients.  | 10.1177/039463201302600215   | 23755757 | 1      |
| Moroni A, Miscione MT, Orsini R, Micera G, Mosca S, Sinapi F, De Girolamo L, Banfi G. Clinical and radiographic outcomes of the Birmingham Hip Resurfacing arthroplasty at a minimum follow-up of 10 years: results from an independent centre. Hip International 2017;27(2):134-139<br>IF: 1,055 | 10.5301/hipint.5000424       | 28362050 | 1      |
| Lombardi G, Barbaro M, Locatelli M, Banfi G. Novel bone metabolism-associated hormones: the importance of the pre-analytical phase for understanding their physiological roles. Endocrine 2017;56(3):460-484<br>IF: 3,131   | 10.1007/s12020-017-1239-z    | 28181144 | 2      |
| Xu J, Lombardi G, Jiao W, Banfi G. Effects of Exercise on Bone Status in Female Subjects, from Young Girls to Postmenopausal Women: An Overview of Systematic Reviews and Meta-Analyses. Sports Medicine 2016;46(8):1165-82<br>IF: 5,038  | 10.1007/s40279-016-0494-0    | 26856338 | 19     |
| Randelli P, Arrigoni P, Aliprandi A, Sdao S, Ragone V, D'Ambrosi R, Randelli F, Cabitza P, Banfi G. Repair versus shaving of partial-thickness articular-sided tears of the upper subscapularis tendon. A prospective randomized controlled trial. Joints 2016;3(3):109-15                        | 10.11138/jts/2015.3.3.109    | 26889466 | 3      |
| Lombardi G, Sanchis-Gomar F, Perego S, Sansoni V, Banfi G. Implications of exercise-induced adipo-myokines in bone metabolism. Endocrine 2016; 54(2):284-305<br>IF: 3,878   | 10.1007/s12020-015-0834-0    | 26718191 | 14     |
| Mariotti M, Carnovali M, Banfi G. Danio rerio: the Janus of the bone from embryo to scale. Clinical Cases in Mineral and Bone Metabolism 2015;12(2):188-94  | 10.11138/ccmbm/2015.12.2.188 | 26604948 | 2      |
| Lombardi G, Perego S, Luzi L, Banfi G. A four-season molecule: osteocalcin. Updates in its physiological roles. Endocrine 2015;48(2):394-404<br>IF: 3,878   | 10.1007/s12020-014-0401-0    | 25158976 | 24     |
| Randelli P, Randelli F, Ragone V, Menon A, D'Ambrosi R, Cucchi D, Cabitza P, Banfi G. Regenerative Medicine in Rotator Cuff Injuries. BioMed Research International 2014;2014:129515  | 10.1155/2014/129515          | 25184132 | 21     |

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
| <p><b>Project Code:</b> NET-2018-12368077-3</p>   | <p><b>Principal Investigator:</b> Banfi Giuseppe</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto Ortopedico Galeazzi</p>  |
| <p><b>Project Type: WP PROJECT - 3</b></p>  |  |

| Title   | DOI                       | PMID     | Cit. * |
|---|---------------------------|----------|--------|
| Randelli P, Randelli F, Arrigoni P, Ragone V, D'Ambrosi R, Masuzzo P, Cabitza P, Banfi G.<br>Optimal glenoid component inclination in reverse shoulder arthroplasty. How to improve implant stability.<br>Musculoskeletal Surgery 2014; 98 Suppl 1:15-8 | 10.1007/s12306-014-0324-1 | 24659201 | 10     |

\* Autocertificated

| Grant                        |      |   |                      |
|------------------------------|------|---|----------------------|
| Funded Institution / Country | Year | Title   | Position in Projects |
| Ministry of Health/Italy     | 2006 | RF-IOG-2006-335297<br>MARKERS CELLULARI E MOLECOLARI NEL PRP (PLATELET RICH PLASMA) DI PAZIENTI CON PATOLOGIE OSTEOARTICOLARI                                 | Coordinator          |
| Ministry of Health/Italy     | 2010 | RF-2010-2322039<br>Porous titanium combined with an osteoinductive hydrogel and cells: an innovative strategy to improve prosthetic implants osseointegration | Coordinator          |

**Employment contract extension:**

( Data changed during the moratorium period )

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
| <p><b>Project Code:</b> NET-2018-12368077-3</p>   | <p><b>Principal Investigator:</b> Banfi Giuseppe</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto Ortopedico Galeazzi</p>  |
| <p><b>Project Type: WP PROJECT - 3</b></p>  |  |

### Biographical Sketch Contributors 1

|                                       |   |
|---------------------------------------|---|
| <p><b>Name:</b><br/>Sirtori Paolo</p> | <p><b>Institution</b> IRCCS Istituto Ortopedico Galeazzi- Equipe Universitaria di Ortopedia Rigenerativa e Ricostruttiva (E.U.O.R.R.)<br/><b>Department/Unit</b> Equipe Universitaria di Ortopedia Rigenerativa e Ricostruttiva (E.U.O.R.R.)<br/><b>Position Title</b> Medical Doctor</p> |
|---------------------------------------|---|

| Education/Training - Institution and Location | Degree                                       | Year(s) | Field of study  |
|---|--|---------|-----------------|
| University of Milan, Italy                    | Degree in Medicine                           | 1989    | Medicine        |
| University of Milan, Italy                    | Postgraduate in Orthopaedic and Traumatology | 1994    | Hip replacement |

**Personal Statement:**

The project will define a HTA evaluation of FT, supplying data and knowledge to define the needed requirements for engaging, preparing, treating and following the patient. The observed and interpreted data can supply useful process indicators which can be used for defining guidelines for orthopaedic surgeons and for different professionals involved in the FT patient management.

The responsibility of key person (SP) includes the evaluation of inclusion and exclusion criteria, the evaluation of surgical approaches, the coordination of different professionals involved in the process to define the best practices according with current literature, interrelationship with patients and caregivers, interrelationship with community healthcare professionals, especially practitioners.

| Institution                            | Division / Research group | Location                        | Position                           | From year | To year |
|--|---------------------------|---------------------------------|------------------------------------|-----------|---------|
| UNIVERSITY OF SHEFFIELD MEDICAL SCHOOL | nd                        | 25 Beech Hill Road Sheffield UK | FELLOW RESEARCH IN BONE METABOLISM | 1991      | 1992    |
| UNIVERSITY VITA-SALUTE SAN RAFFAELE    | nd                        | VIA OLGETTINA 58, MILANO        | TEMPORARY PROFESSOR in ORTHOPAEDIC | 2007      | 2010    |
| IRCCS Ospedale San Raffaele            | nd                        | VIA OLGETTINA 60, MILANO        | Senior Orthopaedic Surgeon         | 1994      | 2012    |
| IRCCS ISTITUTO ORTOPELICO GALEAZZI     | nd                        | VIA R. GALEAZZI 4, MILANO       | Consultant Orthopaedic Surgeon     | 2012      | 2018    |

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| <p><b>Project Code:</b> NET-2018-12368077-3</p>   | <p><b>Principal Investigator:</b> Banfi Giuseppe</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto Ortopedico Galeazzi</p>  |
| <p><b>Project Type: WP PROJECT - 3</b></p>  |  |

### Awards and Honors

**Official H index:** 4.0 ( autocertificata )

**Source:** Scopus

**Scopus Author Id:** 6602551250

**ORCID ID:** 0000-0001-8740-9957

**RESEARCH ID:** J-4609-2018

**Awards and Honors:**

None.

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
| <p><b>Project Code:</b> NET-2018-12368077-3</p>   | <p><b>Principal Investigator:</b> Banfi Giuseppe</p>   |
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| <p><b>Project Type: WP PROJECT - 3</b></p>  |  |

### Expertise Research Collaborators

| Selected peer-reviewed publications of the Research Group / Collaborators |  |                        |         |        |
|---|--|------------------------|---------|--------|
| Collaborator  | Title  | DOI                    | PMID    | Cit. * |
| Sirtori Paolo   | A comparative study on biochemical markers of bone collagen breakdown in post-menopausal women.                  | 10.1006/phrs.1997.0220 | 9367668 | 3      |
| Sirtori Paolo   | Effect of short course of 1,25-dihydroxyvitamin D3 biochemical markers of bone remodelling in stmenopausal women | 10.1006/phrs.1996.0049 | 8971958 | 3      |

\* Autocertificated

| Grant                        |      |       |                      |               |
|------------------------------|------|-------|----------------------|---------------|
| Funded Institution / Country | Year | Title | Position in Projects | Collaborator  |
| NA                           | 0    | NA    | Collaborator         | Sirtori Paolo |

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| <p><b>Project Code:</b> NET-2018-12368077-3</p>   | <p><b>Principal Investigator:</b> Banfi Giuseppe</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto Ortopedico Galeazzi</p>  |
| <p><b>Project Type: WP PROJECT - 3</b></p>  |  |

| Total proposed budget ( Euro ) |                   |                   |   |   |   |
|--------------------------------|-------------------|-------------------|---|---|---|
| Costs                          | TOTAL BUDGET      | Co-Funding        | Project costs proposed to funding Organization (no MOH request) | List of costs proposed for funding to the MOH | Percentage of total proposed to the MOH |
| 1a Staff Salary                | 112.142,00        | 112.142,00        | 0,00  | not permitted                                 | 0,00                                    |
| 1b Researchers' Contracts      | 220.000,00        | 0,00              | 150.000,00  | 70.000,00                                     | 50,00                                   |
| 2 Equipment (Leasing - Rent)   | 50.500,00         | 0,00              | 0,00  | 50.500,00                                     | 36,07                                   |
| 3a Supplies                    | 0,00              | 0,00              | 0,00  | 0,00  | 0,00                                    |
| 3b Model Costs                 | 0,00              | 0,00              | 0,00  | 0,00  | 0,00                                    |
| 3c Subcontracts                | 0,00              | 0,00              | 0,00  | 0,00  | 0,00                                    |
| 3d Patient Costs               | 0,00              | 0,00              | 0,00  | 0,00  | 0,00                                    |
| 4 IT Services and Data Bases   | 0,00              | 0,00              | 0,00  | 0,00  | 0,00                                    |
| 5 Publication Costs            | 2.750,00          | 0,00              | 0,00  | 2.750,00                                      | 1,96                                    |
| 6 Convegni                     | 1.350,00          | 0,00              | 0,00  | 1.350,00                                      | 0,96                                    |
| 7 Travels                      | 2.750,00          | 0,00              | 0,00  | 2.750,00                                      | 1,96                                    |
| 8 Overheads                    | 12.650,00         | 0,00              | 0,00  | 12.650,00                                     | 9,04                                    |
| 9 Coordination Costs           | 0,00              | 0,00              | 0,00  | 0,00  | 0,00                                    |
| <b>Total</b>                   | <b>402.142,00</b> | <b>112.142,00</b> | <b>150.000,00</b>   | <b>140.000,00</b>                             | <b>100,00</b>                           |

Report the Co-Funding Contributor:

3 man-month salary of PI and 11 man-month salary of Co-PI

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
| <p><b>Project Code:</b> NET-2018-12368077-3</p>   | <p><b>Principal Investigator:</b> Banfi Giuseppe</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto Ortopedico Galeazzi</p>  |
| <p><b>Project Type: WP PROJECT - 3</b></p>  |  |

| <b>Budget Justification</b>  |  |
|------------------------------|--|
| 1a Staff Salary              | 3 man-month salary of PI and 11 man-month salary of Co-PI  |
| 1b Researchers' Contracts    | Regione Lombardia: 1 Orthopedist (3 year) + 1 Physiotherapist (3 year); MOH: 1 Data manager (3 Year)                           |
| 2 Equipment (Leasing - Rent) | Leasing/renting of Tele-rehabilitation service   |
| 3a Supplies                  | -  |
| 3b Model Costs               | -  |
| 3c Subcontracts              | -  |
| 3d Patient Costs             | -  |
| 4 IT Services and Data Bases | -  |
| 5 Publication Costs          | The results will be published at the end of the projects   |
| 6 Convegni                   | Estimate of expenditure for conferences for the dissemination of research results  |
| 7 Travels                    | Travel and accommodation expenses incurred by researchers for the participation to conferences to disseminate research results |
| 8 Overheads                  | -  |
| 9 Coordination Costs         | -  |

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|  <p><i>Ministero della Salute</i><br/>         Direzione Generale della Ricerca Sanitaria<br/>         e Biomedica e della Vigilanza sugli Enti<br/> <b>BANDO RICERCA FINALIZZATA 2018</b><br/>         esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>         Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
| <p><b>Project Code:</b> NET-2018-12368077-3</p>   | <p><b>Principal Investigator:</b> Banfi Giuseppe</p>  |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>  | <p><b>Applicant Institution:</b> Istituto Ortopedico Galeazzi</p>   |
| <p><b>Project Type: WP PROJECT - 3</b></p>  |   |

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| <p><b>Project Code:</b> NET-2018-12368077-4</p>   | <p><b>Principal Investigator:</b> Cherubini Antonio</p>  |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistono significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto Nazionale di Riposo e Cura per Anziani</p>   |
| <p><b>Project Type: WP PROJECT - 4</b></p>  |  |

**Major Diagnostic Category\*:** Ortopedia

**Project Classification IRG:** Healthcare Delivery and Methodologies

**Project Classification SS:** Health Services Organization and Delivery - HSOD

**Project Keyword 1:** Healthcare organizations, programs, and delivery of services; including those delivered in non-traditional settings; integrated care delivery systems; disease management and modeling; continuous quality improvement; characteristics of the organization and patient outcomes; organizational performance and efficiency; cost-benefit analysis; economics of health care and pharmacoeconomics.

**Project Keyword 2:** Health care governance and sustainability

**Project Keyword 3:** Health technology assessment and clinical practice guidelines

**Project duration (months):** 36

**Project Request:**      **Animals:**                       **Humans:**                       **Clinical trial:**

**The object/s of this application is/are under patent copyright Y/N:**

| Investigators, Institution and Role in the Project |       |                        |   |                       |            |
|--|-------|------------------------|---|-----------------------|------------|
|  | Co-PI | Key Personnel          | Institution/Org./Pos.                                 | Role in the project   | Birth Date |
| 1  | X     | Dell'Aquila Giuseppina | IRCCS Istituto Nazionale di Riposo e Cura per Anziani | Research Collaborator | 16/11/1977 |
| 2  |       | Conti Giancarlo        | Regional Health Agency, Marche Region                 | Research Collaborator | 30/08/1964 |
| 3  |       | Bustacchini Silvia     | IRCCS Istituto Nazionale di Riposo e Cura per Anziani | Research Collaborator | 25/03/1961 |

## Overall Summary

Nursing home (NH) residents are characterized by multimorbidity, disability and frailty. In the literature hospitalization rates ranged from 9% to 59%, in an Italian study it was 11.6%. Hospitalization might give rise to worsening health, increasing disability and mortality. Their clinical care should be based on the methodology of comprehensive geriatric assessment (CGA). Preliminary evidence suggests that frail NH residents might benefit from CGA in terms of reduced hospitalization events. A major issue is the lack of specialists to implement CGA in NH. This problem could be overcome by means of technology. The use of technology to support geriatric consultation has been rarely reported. Our hypothesis is that implementing a geriatric telemangement governance model may reduce hospitalization, improve patient outcomes and reduce health care costs in NH residents recently discharged from the hospital.

## Background / State of Art

Nursing home (NH) residents are characterized by advanced age, multimorbidity, frailty and disability (Lattanzio, 2010). Their clinical care should be based on comprehensive geriatric assessment (CGA). CGA is a multidisciplinary process focused on determining the clinical profile across multiple dimensions, residual abilities, prognosis, leading to a

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| <p><b>Project Code:</b> NET-2018-12368077-4</p>  | <p><b>Principal Investigator:</b> Cherubini Antonio</p>  |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistono significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                   | <p><b>Applicant Institution:</b> Istituto Nazionale di Riposo e Cura per Anziani</p>   |
| <p><b>Project Type: WP PROJECT - 4</b></p>   |  |

personalized care plan. While CGA benefits have been consistently demonstrated in the hospital setting, this methodology has been less evaluated in NHs. There is preliminary evidence suggesting that NH residents might benefit from CGA in terms of improved quality of care and reduced hospitalization. Older nursing home residents often experience acute diseases or worsening of chronic diseases that require hospitalization. In an Italian study 11.6% of NH residents were hospitalized once during 1 year (Cherubini, 2012). Hospitalization might have a negative impact on NH residents, with increased risk of complications (e.g. adverse drug reactions, delirium, falls), worsening health and increasing disability. Hospitalization is also associated with increased health care costs. Several studies investigated the factors associated with hospital admission in NH residents: both resident characteristics and NH characteristics have been implicated. Among the former, older age and specific condition (e.g. infections, delirium, congestive heart failure, hip fracture, gastrointestinal bleeding and disability) increased the probability of hospitalization, whereas dementia and terminal conditions decreased it. Facility characteristics have been associated with the risk of hospitalization. Lack of physicians during off hours might be one cause of inappropriate hospitalizations. Inadequately trained nursing staff, lack of possibility of administering intravenous therapy also increase hospitalization. On the other hand, a higher level of qualified staff can decrease this risk. At least part of the hospitalizations from NHs have been considered potentially avoidable. NH residents discharged from the hospital have an even higher risk of readmission. Poor communication between hospital and NH staff; inaccurate discharge summaries; lack of medication reconciliation; pending test results; lack of follow-up, all contribute to poor care transition and increase the risk of re-hospitalization. There is limited evidence that CGA performed on NH residents recently discharged from the hospital can reduce rehospitalization (Cordato, 2018). However, a major issue is the lack of specialist resources to implement CGA in NHs. This problem could be overcome by means of technology. Long-term care is an area in which the adoption of technology might significantly improve health care. Telemedicine is feasible and effective for the delivery of specialist care to residents for selected medical disciplines. However, the application of telemedicine strategies to support geriatric consultation has been rarely reported in the literature (Edirippulige, 2013).

## Hyphotesis and Specific AIMS

### Hyphotesis and Significance:

In recent years, innovative technologies have been introduced in medicine. Their use within a governance model may help improving patient outcomes and reducing healthcare costs. This is needed for NH residents, who have multimorbidity, polypharmacy, frailty and disability: extremely costly conditions to individuals and the health-care system (currently organised to manage single conditions). This approach is inadequate to satisfy the needs of NH residents. Identifying a new governance strategy for this vulnerable population is crucial. Our main hypothesis is that implementing a geriatric telemangement governance model dealing with older multimorbid NH residents may improve patient outcomes and reduce health care costs.

### Preliminary Data:

There is solid evidence that CGA improves outcomes in hospitalized older patients: CGA increases the likelihood to be alive and in their own homes at 3 to 12 months after discharge (Ellis 2017). CGA is currently used in many NHs across the world. After the mandatory implementation of CGA in USA NHs, improvement in clinical outcomes of NH residents, improvement of care processes and greater participation of healthcare professionals in team work were shown. More recent studies confirm that NH residents may benefit from CGA in terms of improved quality of care and reduced hospitalization. In a trial

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| <p><b>Project Type: WP PROJECT - 4</b></p>   |  |

comparing a geriatrician led outreach service to usual care for older residents discharged from the hospital (the intervention group received a post-discharge NH visit within 96 hours), there was a significant reduction in outpatient visits at 6 months in the intervention group but no difference in readmission rates (Harvey, 2014). Another intervention study on recently hospitalized NH residents showed that Regular Early Assessment Post-Discharge (REAP) protocol (first NH visit within 1 week after discharge and then monthly visits for 6 months by a geriatrician and a nurse practitioner) reduced two-thirds hospital readmissions compared to usual care (Cordato, 2018).

A major issue is the lack of specialists to implement CGA in NHs. This problem could be overcome by means of technology, which can allow to deliver specialist consultation to residents. The application of telemedicine strategies to support geriatric consultation has been rarely reported (Edirippulige, 2013).

**Specific Aim 1:**

To develop a geriatric telemangement governance model for older multimorbid patients discharged from hospital to nursing homes. The model will integrate geriatric specialists with NH staff and general practitioners (GPs).

**Specific Aim 2:**

To implement the model in some NHs in Marche Region

**Specific Aim 3:**

To measure the performance of the model in terms of effectiveness and cost-effectiveness.

**Experimental Design Aim 1:**

A multidisciplinary group (geriatricians, NH staff and GPs) will be created to discuss the key elements of the intervention and anticipate possible challenges. The technology used is well standardized, nevertheless it will be tested on few NH residents before the beginning of the study.

**Experimental Design Aim 2:**

The implementation of the governance model will be performed in an intervention study carried out in NH residents recently discharged from hospital. The intervention will consist in geriatric telemangement by means of videoconsultation where the geriatrician will discuss each patient with the GP (who provides primary medical care to NH residents) and NH staff. During the follow up, at least 2 videoconsultations will be scheduled (month 1 and 3).

Moreover, the geriatrician will be available to provide on demand consultation. The telemangement model will be integrated with the regional ICT infrastructure.

**Experimental Design Aim 3:**

A before and after evaluation of the effects of the implementation of the geriatric telemangement governance model on risk of hospitalization, geriatric syndromes (falls, delirium, pressure sores), number of drug and of inappropriate prescriptions. NH staff and GPs adherence to the intervention, satisfaction and perception of usefulness will be evaluated.

**Picture to support preliminary data:**

INRCA MARCHE picture def.pptx

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| <p><b>Project Code:</b> NET-2018-12368077-4</p>  | <p><b>Principal Investigator:</b> Cherubini Antonio</p>  |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistono significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                   | <p><b>Applicant Institution:</b> Istituto Nazionale di Riposo e Cura per Anziani</p>   |
| <p><b>Project Type: WP PROJECT - 4</b></p>   |  |

**Methodologies and statistical analyses:**

Design: a. a retrospective analysis of outcomes and healthcare resource use among older subjects admitted in participating NHs after discharge from hospitals; b. a prospective intervention study to investigate impact of a geriatric telemangement program on cost-effectiveness and clinical outcomes in NH residents after discharge from hospitals.

Inclusion criteria: Retrospective study: all long term residents aged 70 years and more admitted to NHs after hospital discharge during previous 2 years. Prospective study: all long term residents aged 70 years and more discharged from hospital within 1 week from NH admission.

**Exclusion criteria:**

Residents admitted for a short period of time; lack of informed consent; terminal condition.

Primary endpoints: Hospital readmission rate during 6 month follow-up after index NH admission. If a resident will be admitted to hospital more than once, only the first hospitalization will be considered.

**Secondary endpoints:**

Secondary endpoints: a. number of drugs b. use of potentially inappropriate drugs ; c. pressure sores; d. falls; e. delirium; f. intervention adherence g. NH staff satisfaction and perceived usefulness; h. GP perceived usefulness i. number of hospital days l. number of emergency department visits.

**Intervention:**

The telemangement system will include specialist geriatric consultation. The model will be a hub-and-spoke model. The telemangement system will be equipped with a complete enterprise-grade videoconferencing system, and wireless videoconferencing carts will be supplied at each remote site to enable consultation at the bedside. Geriatrician will review diagnoses, treatments, and CGA results. The patient will be interviewed and examined, and then a multidisciplinary case conference with the nurses and GPs will be conducted. The NH staff and GPs will receive a specific training. The technological solution is based on already available telemedicine platform certified according to ISO 13485. The security of data is guaranteed by the certified web platform.

**Sample size:**

300 subjects will be recruited both for retrospective and prospective study. Considering that 8% of Italian NH residents are admitted to hospital once during 6 months of follow-up, and assuming a drop out rate of 20%, 245 subjects are enough to assure the same effect size with a power of 80% and alpha error of 0.05.

**Assessments:**

CGA will be carried out by a multidisciplinary team led by the geriatrician together with the GP and NH staff. Geriatrician will review diagnoses, treatments, and CGA results. The patient will be interviewed and examined, and then a multidisciplinary case conference will be held. Health technology assessment (HTA) will evaluate the effectiveness, safety, economic and social consequences of model implementation, by collecting data on healthcare resources consumption and costs both in retrospective and prospective studies. A Resource Utilization Questionnaire will retrieve data on: 1) healthcare

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services, 2) drug consumption and non drug interventions, 3) other health-related costs: e.g. informal care, out-of-pocket patient/caregiver expenditures, 4) NH staff and patients/caregivers satisfaction. HTA report will be developed with a specific tool.

#### Statistical analyses:

Descriptive analyses: continuous variables (CV) are presented as means ( $\pm$  SD, range); categorical variables as percentages. The Shapiro-Wilk test is used to evaluate normality in distributions of CV. For normally distributed data, standard parametric tests are used, otherwise non-parametric tests are applied. Then study variables will be compared temporally by repeated measures ANOVA with Bonferroni correction for post-hoc comparisons, to bring out statistically significant differences between baseline and follow-up. In a second step, models of multivariate regression and Cox proportional hazard regressions will be performed.

#### Expected outcomes:

The model is expected to improve the clinical management of complex multimorbid older NH residents. Besides providing equity of access to specialist geriatric services, the telemangement service should enable nursing homes to better manage a more-complex caseload, which may result in fewer transfers to acute care hospitals. These effects may improve the clinical and financial viability of NHs and contribute to lower demand for hospitals. Moreover, the telemangement intervention is expected to improve other outcomes relevant to NH residents, as well as NH staff and GP satisfaction. The HTA process will contribute to assess the clinical performance of the telemangement system, to evaluate its effectiveness (main predictors of costs and cost-effectiveness ratio of the intervention) and its contribution to quality of care in the organization and to produce a basis for the evaluation of transferability of the results to other settings and for decision making.

#### Risk analysis, possible problems and solutions:

Careful risk assessment has been carried out and specific assumptions have been drawn considering that external or internal factors may interfere with achieving project objectives:

1. DELAY IN ETHICAL COMMITTEE APPROVAL: IRCCS INRCA has its own institutional ethics committee, making a delay in approval unlikely.
2. ISSUES ON IMPLEMENTATION OF THE TELEMAGEMENT PLATFORM: We preventively addressed technical issues with the implementation of the web-platform leveraging the revision of the existing information systems.
3. DELAY OF SUBJECTS ENROLMENT: Training and ongoing support will be provided to NHs. Back-up NHs will be identified as needed.
4. HIGH NUMBER OF SUBJECTS LOST AT FOLLOW-UP: some NH residents may die during follow-up. Moreover, they and their family might ask to exit from the study. A detailed information will be provided to the participants and their family. GPs will be involved.
5. FAILURE TO KEEP TO TIME SCHEDULE: a Project Manager will be appointed by the Principal Investigator to guide and manage the study.

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### Significance and Innovation

The current health care system is not adequate to satisfy the needs of multimorbid frail older NH residents. This project aims at developing an innovative geriatric telemanagement governance model that might substantially improve ability of NH to provide personalized care to these subjects. This model, by implementing a strong collaboration between the hospital and nursing homes, makes available comprehensive geriatric assessment to the frail institutionalized older population most in need of it, potentially leading to improved clinical outcomes and reduced healthcare costs.

### Description of the complementary and synergy research team

The Project WP team consists of senior researchers with complementary expertise in clinical healthcare and research in geriatrics, including experience in nursing home, and in the field of economic evaluations in healthcare and HTA.

Prof Cherubini (PI): coordination and management of the project; design, development and implementation of the model and of the interventional study; analysis and dissemination of the results.

Dr Dell'Aquila (Co-PI): study design and protocol definition, study implementation and follow-up as a geriatrician with a significant knowledge and experience in the nursing home setting.

Ing Conti (in collaboration with Dr Sisti and Dr Papa - Marche Regional Health Agency): implementation of HTA methodologies within Health Regional System and coordination of technological system requirements and integration, HTA reporting.

Dr Bustacchini (with Dr Bevilacqua and Ing Rossi - INRCA Center of Innovative Models for Aging Care and Technology): input on study design and protocol definition, evaluation and reporting of the effectiveness and safety, economic and social consequences of the implementation of a telemanagement system.

### Training and tutorial activities

It will be necessary to make training courses to increase the geriatric knowledge of healthcare staff and general practitioners in the nursing homes involved in the project. The topics of these courses will be the characteristics of older complex patient, multimorbidity, frailty, disability, geriatric syndromes (dementia, delirium, falls, instability, adverse reactions to drugs, immobilization syndrome), comprehensive geriatric assessment and therefore the definition of a personalized care plan. Furthermore, technical training will be carried out on the use of the technology made available to NHs.

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<http://www.adhophta.eu/toolkit/index.html>

### Timeline / Deliverables / Payable Milestones

Deliverables (DO) and Milestones (MSO) (please refer to the attached GANTT Chart)

D01 - Midterm project report (Month 18)  
D02 - Final project report (Month 36)  
MS01 - First Project Meeting (Month 2)  
MS02 - Implementation of the teleconsultation platform (Month 9)  
MS03 - Training of nursing home staff and primary care physicians (month 12)  
MS04 - Retrospective study (Month 15)  
MS05 - Mid-term Project Meeting (Month 18)  
MS06 - Intervention study (Month 27)  
MS07 - Third Project Meeting (Month 34)  
MS08 - Final conference (Month 36)

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### Milestones 18 month

MS01 - First Project Meeting (Month 2)  
 MS02 - Implementation of the teleconsultationplatform (Month 9)  
 MS03 - training of nursing home staff and primary care physicians (month 12)  
 MS04 - Retrospective study (Month 15)  
 MS05 - Mid-term Project Meeting (Month 18)

### Milestones 36 month

MS06 - Intervention study (Month 27)  
 MS07 - Third Project Meeting (Month 34)  
 MS08 - Final conference (Month 36)

### Gantt chart

INRCA MARCHE GANTT WP def.xlsx

### Equipment and resources available

This complex research project will require a solid infrastructure comprising the availability of specific resources, instruments and tools.

The infrastructure required for the project is already available. INRCA regularly provides health services through ICT (in particular tele-cardiology). The telemedicine platform used is certified according to ISO 13485 and offer the possibility of a wide range of services. The platform has been designed to provide remote care and monitor chronic and vulnerable patients (already tested with older people) and may be used to monitor patients in different care settings, measuring vital parameters simply with a kit of medical devices (blood pressure monitor, scales, oximeter, ECG, etc.). The solution also has real-time audio-video conferencing functions, and audio-video broadcasting.

Marche Region will make available is Health data center infrastructure that allow the connection of the solution the regional EMR.

Data management will be ensured through a central database which will be set up as a secure Internet based system linked to the study web site and the remote data capture application.

The INRCA Clinical Trials Office and Research Quality Management will set requirements for developing and conducting the study according to ethics and good clinical practice conformity, regulatory standards and following the established operating procedures.

Subcontractor will be necessary to implement the data exchange between the tele-monitoring platform and the Regional EMR to guarantee:

- the availability of all the information on the patient history during the videoconsultation carrying out of the CGA;
- the collection of all the information on the access of the patient to the healthcare system and monitor the use of resource to assess the impact of the intervention.

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti</p> <p><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV - Geriatric Telemangement of HEALTH conditions in nursing home residents recently discharged from the hospital GET HEALTH</p> |
| <p><b>Project Code:</b> NET-2018-12368077-4</p>  | <p><b>Principal Investigator:</b> Cherubini Antonio</p>  |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                   | <p><b>Applicant Institution:</b> Istituto Nazionale di Riposo e Cura per Anziani</p>   |
| <p><b>Project Type: WP PROJECT - 4</b></p>   |  |

### Translational relevance and impact for the National Health System (SSN)

The topic of the research project (Telemangement of health conditions in nursing home residents recently discharged from the hospital) is relevant for the NHS in term of epidemiological impact, innovation related to the development and implementation of a new governance model of care for patients at higher risk of adverse outcomes, and possible reduction of costs. The model implementation outcomes will be evaluated in a multidisciplinary framework including health problem and characteristics of the application, safety and clinical effectiveness, patient, caregiver and professional perspectives, economic and organizational aspects, socio-cultural, ethical and legal aspects. The resulting HTA report will inform recommendations and tools for the transferability of the results to other regional health care systems and long term care settings, helping final users to decide whether this model is relevant to their own setting.

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| <p><b>Project Type: WP PROJECT - 4</b></p>  |  |

### PRINCIPAL INVESTIGATOR PROFILE

|  |  |
|--|--|
| <p><b>Name</b><br/>Cherubini Antonio</p> | <p><b>Institution</b> Istituto Nazionale di Riposo e Cura per Anziani<br/><b>Department/Unit</b> Geriatria e Accettazione Geriatrica di Urgenza<br/><b>Position Title</b> Director</p> |
|--|--|

### Personal Statement

Prof Cherubini will be the Principal Investigator and coordinator of the WP. Given his role, he will supervise all the project phases, actively participating to each step of the project.

| Education/Training - Institution and Location | Degree                                       | Year(s) | Field of study             |
|---|--|---------|----------------------------|
| University of Padova                          | PhD in experimental and clinical gerontology | 2000    | Gerontology and Geriatrics |
| University of Perugia                         | Geriatrician                                 | 1996    | Geriatrics                 |
| University of Perugia                         | Medical doctor                               | 1992    | Medicine and Surgery       |

### Positions

| Institution           | Division / Research group   | Location | Position            | From year | To year |
|-----------------------|---|----------|---------------------|-----------|---------|
| IRCCS-INRCA           | Geriatrics, geriatric emergency care and Center for research on aging | Ancona   | Director            | 2012      | 2018    |
| University of Perugia | Geriatrics  | Perugia  | Associate Professor | 2004      | 2012    |
| University of Perugia | Geriatrics  | Perugia  | Researcher          | 1999      | 2004    |

**Official H index:** 56.0 ( autocertificated )

**Source:** Scopus

**Scopus Author Id:** 7005767834

**ORCID ID:** 0000-0003-0261-9897

**RESEARCH ID:** Not available

### Awards and Honors:

None.

### Other CV Informations:

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti</p> <p><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV - Geriatric Telemanagement of HEALTH conditions in nursing home residents recently discharged from the hospital GET HEALTH</p> |
| <p><b>Project Code:</b> NET-2018-12368077-4</p>  | <p><b>Principal Investigator:</b> Cherubini Antonio</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                   | <p><b>Applicant Institution:</b> Istituto Nazionale di Riposo e Cura per Anziani</p>  |
| <p><b>Project Type: WP PROJECT - 4</b></p>   |   |

He has performed research at the Geriatric Research Education Clinical Center, VA hospital, Gainesville, Fl.; at the Dept of Neurology, Massachusetts General Hospital, Harvard Medical School, Boston, Ma; at the Human Nutrition research Center on Aging, Tufts university, Boston, Ma; at the Longitudinal branch Section, National Institute of Aging, Baltimore, Md, USA. He is member of the Academic Board of the EUGMS (2013-) and member of the Geriatric Expert Group at the European Medicine Agency (2011-). He is currently member of the Ethics committee of the IRCCS-INRCA and previously of Ethics committee of the Marche region. Author of more than 250 papers in peer reviewed journ. and of five books. Associate Editor of European Geriatric Medicine and of Jour. of Gerontology and Geriatrics.

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| <p><b>Project Code:</b> NET-2018-12368077-4</p>  | <p><b>Principal Investigator:</b> Cherubini Antonio</p>  |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                   | <p><b>Applicant Institution:</b> Istituto Nazionale di Riposo e Cura per Anziani</p>   |
| <p><b>Project Type: WP PROJECT - 4</b></p>   |  |

### Selected peer-reviewed publications of the PI

| Valid for PI minimum expertise level   |                                  |          |         |     |
|--|----------------------------------|----------|---------|-----|
| Title  | DOI                              | PMID     | Cit. ** | P.* |
| Is polypharmacy an independent risk factor for adverse outcomes after an emergency department visit?   | 10.1007/s11739-016-1451-5        | 27075646 | 2       | L   |
| Systematic review of systematic reviews of non-pharmacological interventions to treat behavioural disturbances in older patients with dementia. The SENATOR-OnTop series           | 10.1136/bmjopen-2016-012759      | 28302633 | 13      | L   |
| Efficacy of Non-Pharmacological Interventions to Prevent and Treat Delirium in Older Patients: A Systematic Overview. The SENATOR project ONTOP Series                             | 10.1371/journal.pone.0123090     | 26062023 | 27      | L   |
| Evidence of and recommendations for non-pharmacological interventions for common geriatric conditions: the SENATOR-ONTOP systematic review protocol                                | 10.1136/bmjopen-2014-007488      | 25628049 | 20      | L   |
| Association of habitual dietary resveratrol exposure with the development of frailty in older age: the Invecchiare in Chianti study.   | 10.3945/ajcn.115.118976          | 26490492 | 10      | L   |
| The Relationship between Urinary Total Polyphenols and the Frailty Phenotype in a Community-Dwelling Older Population: the InCHIANTI Study   | 10.1093/gerona/glv026            | 25838546 | 12      | L   |
| Anticholinergic Drug Use and Negative Outcomes Among the Frail Elderly Population Living in a Nursing Home   | 10.1016/j.jamda.2014.08.002      | 25282629 | 30      | L   |
| Underrecognition and undertreatment of dementia in Italian nursing homes   | 10.1016/j.jamda.2012.05.015      | 22727993 | 24      | F   |
| Predictors of hospitalization in Italian nursing home residents: the U.L.I.S.S.E. Project.   | 10.1016/j.jamda.2011.04.001      | 21621481 | 32      | F   |
| Adverse drug events as a cause of hospitalization in older adults.   | 10.1007/BF03319101               | 23446784 | 47      | L   |
| The persistent exclusion of older subjects from ongoing trials on heart failure  | 10.1001/archinternmed.2011.31    | 21444844 | 139     | F   |
| The prevention of adverse drug reactions in older subjects   | 10.2174/138920011796504482       | 21495975 | 14      | F   |
| Fighting against age discrimination in clinical trials.  | 10.1111/j.1532-5415.2010.03032.x | 20863340 | 87      | F   |
| Potentially inappropriate drug prescriptions and risk of hospitalization among Italian older nursing home residents: the U.L.I.S.S.E. project on behalf of the Ulisse study group. | 10.2165/11538240-000000000-00000 | 20809664 | 73      | L   |
| Low plasma N-3 fatty acids and dementia in older persons: the InCHIANTI study  | 10.1093/gerona/62.10.1120        | 17921425 | 57      | F   |

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV - Geriatric Telemanagement of HEALTH conditions in nursing home residents recently discharged from the hospital GET HEALTH</p> |
| <p><b>Project Code:</b> NET-2018-12368077-4</p>   | <p><b>Principal Investigator:</b> Cherubini Antonio</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto Nazionale di Riposo e Cura per Anziani</p>  |
| <p><b>Project Type: WP PROJECT - 4</b></p>  |   |

| Title   | DOI                                  | PMID     | Cit. ** | P.* |
|---|--------------------------------------|----------|---------|-----|
| Vitamin E levels, cognitive impairment and dementia in older persons: the InCHIANTI study.                                | 10.1016/j.neurobiolaging.2004.09.002 | 15748776 | 65      | F   |
| Elderly patients with cognitive impairment have a high risk for functional decline during hospitalization: the GIFA study | 10.1093/gerona/60.12.1576            | 16424291 | 62      | L   |
| Marked decrease in plasma antioxidants in aged osteoporotic women: results of a cross-sectional study.                    | 10.1210/jc.2002-021496               | 12679433 | 350     | L   |
| Validation of the five-item Geriatric Depression Scale in elderly subjects in three different settings.                   | 10.1034/j.1600-0579.2003.00216.x     | 12752847 | 182     | L   |
| Antioxidant profile and early outcome in stroke patients Stroke   | 10.1161/01.STR.31.10.2295            | 11022053 | 157     | F   |

\* Position: F=First L=Last C=Correspondent

\*\* Autocertificated

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti</p> <p><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV - Geriatric Telemanagement of HEALTH conditions in nursing home residents recently discharged from the hospital GET HEALTH</p> |
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| <p><b>Project Type: WP PROJECT - 4</b></p>   |   |

| For evaluation CV   |                                  |          |        |
|---|----------------------------------|----------|--------|
| Title   | DOI                              | PMID     | Cit. * |
| Predictors of Functional Changes in Italian Nursing Home Residents: The U.L.I.S.S.E. Study.   | 10.1016/j.jamda.2015.11.004      | 26715356 | 2      |
| Polypharmacy in Nursing Home Residents: What Is the Way Forward?  | 10.1016/j.jamda.2015.07.008      | 26293420 | 13     |
| Anticholinergic Drug Use and Negative Outcomes Among the Frail Elderly Population Living in a Nursing Home  | 10.1016/j.jamda.2014.08.002      | 25282629 | 30     |
| Prevalence and potentially reversible factors associated with anorexia among nursing home residents: results from the ULISSE project  | 10.1016/j.jamda.2012.10.022      | 23218843 | 23     |
| Underrecognition and undertreatment of dementia in Italian nursing homes  | 10.1016/j.jamda.2012.05.015      | 22727993 | 24     |
| Predictors of hospitalization in Italian nursing home residents: the U.L.I.S.S.E. Project.  | 10.1016/j.jamda.2011.04.001      | 21621481 | 32     |
| Potentially inappropriate drug prescriptions and risk of hospitalization among Italian older nursing home residents: the U.L.I.S.S.E. project on behalf of the Ulisse study group.                    | 10.2165/11538240-000000000-00000 | 20809664 | 73     |
| Health care for older people in Italy: the U.L.I.S.S.E. Project (Un Link Informatico sui Servizi Sanitari Esistenti per l'anziano - A computerized network on health care services for older people). | 10.1007/s12603-010-0056-3        | 20191260 | 19     |
| Pain in European long-term care facilities: cross-national study in Finland, Italy and the Netherlands  | 10.1016/j.pain.2009.10.008       | 19910119 | 63     |
| Hip fracture in Nursing Homes: an Italian study on prevalence, latency, risk factors, and impact on mobility  | 10.1007/s002230001212            | 11685420 | 18     |

\* Autocertificated

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| <p><b>Project Code:</b> NET-2018-12368077-4</p>  | <p><b>Principal Investigator:</b> Cherubini Antonio</p>  |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                   | <p><b>Applicant Institution:</b> Istituto Nazionale di Riposo e Cura per Anziani</p>   |
| <p><b>Project Type: WP PROJECT - 4</b></p>   |  |

| Grant                          |      |  |                      |
|--------------------------------|------|--|----------------------|
| Funded Institution / Country   | Year | Title  | Position in Projects |
| Innovative medicine initiative | 2014 | Sarcopenia & Physical frailty IN older people: multi-component Treatment strategies  | Collaborator         |
| Ministry of Health             | 2013 | Emergenza e Continuità dell'assistenza: implementazione di un modello organizzativo integrato ospedale-territorio per la presa in carico dei pazienti anziani complessi. | Collaborator         |
| European Commission            | 2013 | PROFOUND- Prevention of Falls Network for Dissemination  | Collaborator         |
| Ministry of Health             | 2012 | Assegnazione dei criteri di priorità per la presa in carico degli anziani affetti da multimorbilità. Implementazione del sistema MAPLe in Italia.                        | Coordinator          |
| European Commission            | 2012 | SENATOR- Development and clinical trials of a new Software ENgine for the Assessment & Optimization of drug and non-drug Therapy in Older persons                        | Collaborator         |
| Ministry of Health             | 2011 | Establishing and linking cognitive and disease and functional outcomes in the InCHIANTI study through physicians interview and consultation of medical record.           | Coordinator          |
| Ministry of Health             | 2010 | La definizione del case-mix nelle cure domiciliari: implementazione del sistema RUG-III HC in Italia   | Collaborator         |
| Umbria Region                  | 2008 | Il punto unico di accesso come nuovo modello organizzativo per la presa in carico delle persone anziane disabili nella rete dei servizi sociosanitari territoriali       | Coordinator          |
| European Commission (FP7)      | 2008 | PREDICT- Increasing the Participation of the Elderly in Clinical Trials  | Collaborator         |
| Ministry of Health             | 2007 | Scompenso cardiaco. Modelli Riabilitativi Multi-disciplinari: i nuovi "farmaci" per il paziente anziano con scompenso cardiaco cronico                                   | Collaborator         |

**Employment contract extension:**

( Data changed during the moratorium period )

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV - Geriatric Telemanagement of HEALTH conditions in nursing home residents recently discharged from the hospital GET HEALTH</p> |
|   | <p><b>Project Code:</b> NET-2018-12368077-4</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistono significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto Nazionale di Riposo e Cura per Anziani</p>  |
| <p><b>Project Type: WP PROJECT - 4</b></p>  |   |

### Biographical Sketch Contributors 1

|  |                        |  |
|--|------------------------|--|
| <p><b>Name:</b><br/>Dell'Aquila Giuseppina</p> | <b>Institution</b>     | IRCCS Istituto Nazionale di Riposo e Cura per Anziani            |
|  | <b>Department/Unit</b> | Geriatrics, geriatric Emergency and center for research on aging |
|  | <b>Position Title</b>  | Physician  |
|  |                        |  |

| Education/Training - Institution and Location | Degree       | Year(s) | Field of study       |
|---|--------------|---------|----------------------|
| University of Perugia                         | Geriatrician | 2007    | Geriatrics           |
| University of Perugia                         | MD           | 2003    | Medicine and Surgery |

**Personal Statement:**

Dr. Dell'Aquila will be the co PI of the WP. She will collaborate with the design of the intervention, the training of primary care physicians and nursing home staff and the performance of the observational study.

| Institution   | Division / Research group   | Location      | Position  | From year | To year |
|---|---|---------------|-----------|-----------|---------|
| IRCCS - Istituto Nazionale di Riposo e Cura per Anziani | Geriatrics, geriatric emergency care and Center for research on aging | Ancona, Italy | Physician | 2012      | 2018    |
| Residenza Protetta 'Veralli Cortesi'- nursing home      | Nursing home care   | Todi, Italy   | Physician | 2008      | 2012    |

**Awards and Honors**

**Official H index:** 12.0 ( autocertificated )

**Source:** Scopus

**Scopus Author Id:** 25031443100

**ORCID ID:** 0000-0002-9297-5088

**RESEARCH ID:** Not available

**Awards and Honors:**

None

|   |  |
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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV - Geriatric Telemangement of HEALTH conditions in nursing home residents recently discharged from the hospital GET HEALTH</p> |
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| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto Nazionale di Riposo e Cura per Anziani</p>   |
| <p><b>Project Type: WP PROJECT - 4</b></p>  |  |

### Biographical Sketch Contributors 2

|   |   |
|---|---|
| <p><b>Name:</b><br/>Conti Giancarlo</p> | <p><b>Institution</b> Regional Health Agency, Marche Region<br/><b>Department/Unit</b> P.F. HEALTH TECHNOLOGY ASSESSMENT AND BIOMEDICAL TECHNOLOGIES<br/><b>Position Title</b> DIRECTOR</p> |
|---|---|

| Education/Training - Institution and Location | Degree   | Year(s) | Field of study                               |
|---|--|---------|--|
| MACERATA E CAMERINO UNIVERSITY                | MASTER   | 2011    | HEALTH LEGISLATION AND LAW                   |
| TRIESTE UNIVERSITY                            | MASTER   | 2002    | CLINICAL ENGINEERING                         |
| BVQI - MILANO                                 | INTERNATIONAL REGISTER OF CERTIFICATED AUDITORS (IRCA) LEAD AUDITOR REGISTRATION | 1998    | QUALITY SYSTEMS LEAD AUDITOR TRAINING COURSE |
| BOLOGNA UNIVERSITY                            | MASTER'S DEGREE  | 1998    | ELECTRONIC ENGINEERING                       |

**Personal Statement:**

Giancarlo Conti will support the implementation of Health Technology Assessment methodologies within Health Regional System. He will carry out a context analysis and define technological requirements for integration of the tele-health system with the regional ICT health infrastructure. Moreover, he will coordinate the analysis of technical regulations and preparation of quality requirements (technological, structural, and organizational) for authorization and institutional accreditation.

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV - Geriatric Telemanagement of HEALTH conditions in nursing home residents recently discharged from the hospital GET HEALTH</p> |
| <p><b>Project Code:</b> NET-2018-12368077-4</p>   | <p><b>Principal Investigator:</b> Cherubini Antonio</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistono significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto Nazionale di Riposo e Cura per Anziani</p>  |
| <p><b>Project Type: WP PROJECT - 4</b></p>  |   |

| Institution                                    | Division / Research group                                | Location      | Position       | From year | To year |
|--|--|---------------|----------------|-----------|---------|
| AUSL MODENA (COUNTY HEALTH AUTHORITY)          | CLINICAL ENGINEERING                                     | MODENA        | SENIOR MANAGER | 2001      | 2005    |
| ASUR MARCHE (MARCHE REGIONAL HEALTH AUTHORITY) | CLINICAL ENGINEERING                                     | ANCONA        | DIRECTOR       | 2005      | 2008    |
| ASUR MARCHE (MARCHE REGIONAL HEALTH AUTHORITY) | TECHNICAL SERVICES, HERITAGE, CLINICAL ENGINEERING       | FANO          | DIRECTOR       | 2008      | 2010    |
| UNITED HOSPITALS OF MARCHE NORTH               | WORKS AND TECHNOLOGIES DEPARTMENT PESARO                 | Marche Region | DIRECTOR       | 2011      | 2012    |
| UNITED HOSPITALS OF MARCHE NORTH               | CLINICAL ENGINEERING AND HEALTH TECHNOLOGY ASSESSMENT    | PESARO        | DIRECTOR       | 2011      | 2015    |
| MARCHE REGION                                  | HEALTH DEPARTMENT  | ANCONA        | SENIOR MANAGER | 2016      | 2017    |
| REGIONAL HEALTH AGENCY OF MARCHE REGION        | HEALTH TECHNOLOGY ASSESSMENT AND BIOMEDICAL TECHNOLOGIES | ANCONA        | DIRECTOR       | 2017      | 2018    |

### Awards and Honors

**Official H index:** 0.0 ( autocerficated )

**Source:** Scopus

**Scopus Author Id:** Not available

**ORCID ID:** Not available

**RESEARCH ID:** Not available

#### Awards and Honors:

None

|   |  |
|---|--|
|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV - Geriatric Telemangement of HEALTH conditions in nursing home residents recently discharged from the hospital GET HEALTH</p> |
| <p><b>Project Code:</b> NET-2018-12368077-4</p>   | <p><b>Principal Investigator:</b> Cherubini Antonio</p>  |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto Nazionale di Riposo e Cura per Anziani</p>   |
| <p><b>Project Type: WP PROJECT - 4</b></p>  |  |

### Biographical Sketch Contributors 3

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|--|--|
| <p><b>Name:</b><br/>Bustacchini Silvia</p> | <p><b>Institution</b> IRCCS Istituto Nazionale di Riposo e Cura per Anziani<br/><b>Department/Unit</b> Scientific Direction - Research, Innovation and Technology Transfer Unit<br/><b>Position Title</b> Head of Unit</p> |
|--|--|

| Education/Training - Institution and Location   | Degree                       | Year(s) | Field of study  |
|---|------------------------------|---------|---|
| Catholic University, Rome, Italy  | MD                           | 1986    | Medicine  |
| Catholic University, Rome, Italy -  | Postgraduate School          | 1990    | Respiratory Medicine  |
| University La Sapienza, Rome, Italy - Postgraduate School in Pharmacology                         | Postgraduate School          | 1994    | Clinical Pharmacology   |
| University of Milan, Milan, Italy - Institute of Pharmacology                                     | MSc                          | 2003    | Health Economics and Pharmacoeconomics  |
| European Academy for Medicine of Ageing - Institute for Biomedicine of Ageing, Nuremberg, Germany | Advanced Postgraduate Course | 2014    | Scientific, clinical, educational and managerial competences in medical gerontology, including principles of geriatric care, Evidence Based Medicine in Geriatrics, cognitive and behavioural issues. |

**Personal Statement:**

Dr. Silvia Bustacchini will support activities for project design and implementation, including the impact evaluation of the geriatric telemangement governance model.

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV - Geriatric Telemanagement of HEALTH conditions in nursing home residents recently discharged from the hospital GET HEALTH</p> |
| <p><b>Project Code:</b> NET-2018-12368077-4</p>   | <p><b>Principal Investigator:</b> Cherubini Antonio</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistono significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto Nazionale di Riposo e Cura per Anziani</p>  |
| <p><b>Project Type: WP PROJECT - 4</b></p>  |   |

| Institution   | Division / Research group  | Location                   | Position  | From year | To year |
|---|--|----------------------------|---|-----------|---------|
| Catholic University - School of Medicine                            | Unit of Respiratory Medicine   | Rome, Italy                | Fellowship  | 1986      | 1989    |
| Pharma Industry: Fisons then Rhone-Poulenc Rorer nt                 | Medical Direction and Clinical Research Department                       | Rome and then Milan, Italy | Clinical Research Manager   | 1989      | 1997    |
| Pharma Industry: Pfizer National and Regional Healthcare Operations | Outcomes Research Unit   | Rome, Italy                | Outcomes Research Manager   | 1997      | 2004    |
| Pharma Industry: IDI Farmaceutici                                   | Medical Direction and Clinical Research Department                       | Rome, Italy                | Responsible for Medical Direction and Regulatory Affairs Qualified Person for Pharmacovigilance | 2005      | 2009    |
| Italian National Research Center on Aging (IRCCS INRCA)             | Scientific Direction / Research, Innovation and Technology Transfer Unit | Ancona, Italy              | Responsible   | 2009      | 2018    |

### Awards and Honors

**Official H index:** 14.0 ( autocertificated )

**Source:** Scopus

**Scopus Author Id:** 35794883400

**ORCID ID:** 0000-0002-8166-3265

**RESEARCH ID:** I-3122-2012

#### Awards and Honors:

None

|   |   |
|---|---|
|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV - Geriatric Telemanagement of HEALTH conditions in nursing home residents recently discharged from the hospital GET HEALTH</p> |
| <p><b>Project Code:</b> NET-2018-12368077-4</p>   | <p><b>Principal Investigator:</b> Cherubini Antonio</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistono significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto Nazionale di Riposo e Cura per Anziani</p>  |
| <p><b>Project Type: WP PROJECT - 4</b></p>  |   |

### Expertise Research Collaborators

| Selected peer-reviewed publications of the Research Group / Collaborators |  |                                    |          |        |
|---|--|------------------------------------|----------|--------|
| Collaborator  | Title  | DOI                                | PMID     | Cit. * |
| Dell'Aquila Giuseppina  | Predictors of Functional Changes in Italian Nursing Home Residents: The U.L.I.S.S.E. Study.  | 10.1016/j.jamda.2015.11.004        | 26715356 | 2      |
| Bustacchini Silvia  | The economic burden of inappropriate drug prescribing, lack of adherence and compliance, adverse drug events in older people a systematic review                                   | 10.1007/BF03319105                 | 23446788 | 37     |
| Dell'Aquila Giuseppina  | Underrecognition and undertreatment of dementia in Italian nursing homes   | 10.1016/j.jamda.2012.05.015        | 22727993 | 24     |
| Dell'Aquila Giuseppina  | Predictors of hospitalization in Italian nursing home residents: the U.L.I.S.S.E. Project.   | 10.1016/j.jamda.2011.04.001        | 21621481 | 32     |
| Bustacchini Silvia  | The economic burden of chronic obstructive pulmonary disease in the elderly: results from a systematic review of the literature.   | 10.1097/01.mcp.0000410746.82840.79 | 22209929 | 22     |
| Dell'Aquila Giuseppina  | Potentially inappropriate drug prescriptions and risk of hospitalization among Italian older nursing home residents: the U.L.I.S.S.E. project on behalf of the Ulisse study group. | 10.2165/11538240-000000000-00000   | 20809664 | 73     |
| Bustacchini Silvia  | Pharmacoeconomics and aging.   | 10.2165/11534680-000000000-00000   | 20136171 | 12     |

\* Autocertificated

| Grant                                 |      |  |                      |                    |
|---------------------------------------|------|--|----------------------|--------------------|
| Funded Institution / Country          | Year | Title  | Position in Projects | Collaborator       |
| Italian Ministry of Health            | 2016 | Report-AGE Project: clinical and biological predictors of physical function decline in older patients with chronic cardiovascular diseases. RF-2013-02358848 | Coordinator          | Bustacchini Silvia |
| European Commission under: FP7-HEALTH | 2012 | Intervention Research On Health Literacy among Ageing population. Project ID: 305831   | Collaborator         | Bustacchini Silvia |

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Sent date of moratorium changes: 01/06/2018 15.17

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV - Geriatric Telemanagement of HEALTH conditions in nursing home residents recently discharged from the hospital GET HEALTH</p> |
| <p><b>Project Code:</b> NET-2018-12368077-4</p>   | <p><b>Principal Investigator:</b> Cherubini Antonio</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto Nazionale di Riposo e Cura per Anziani</p>  |
| <p><b>Project Type: WP PROJECT - 4</b></p>  |   |

| Total proposed budget ( Euro ) |                   |                   |   |   |   |
|--------------------------------|-------------------|-------------------|---|---|---|
| Costs                          | TOTAL BUDGET      | Co-Funding        | Project costs proposed to funding Organization (no MOH request) | List of costs proposed for funding to the MOH | Percentage of total proposed to the MOH |
| 1a Staff Salary                | 150.000,00        | 150.000,00        | 0,00  | not permitted                                 | 0,00                                    |
| 1b Researchers' Contracts      | 290.000,00        | 0,00              | 150.000,00  | 140.000,00                                    | 50,00                                   |
| 2 Equipment (Leasing - Rent)   | 131.000,00        | 0,00              | 66.000,00   | 65.000,00                                     | 23,21                                   |
| 3a Supplies                    | 0,00              | 0,00              | 0,00  | 0,00  | 0,00                                    |
| 3b Model Costs                 | 0,00              | 0,00              | 0,00  | 0,00  | 0,00                                    |
| 3c Subcontracts                | 58.000,00         | 0,00              | 30.000,00   | 28.000,00                                     | 10,00                                   |
| 3d Patient Costs               | 0,00              | 0,00              | 0,00  | 0,00  | 0,00                                    |
| 4 IT Services and Data Bases   | 25.000,00         | 0,00              | 15.000,00   | 10.000,00                                     | 3,57                                    |
| 5 Publication Costs            | 11.600,00         | 0,00              | 6.000,00  | 5.600,00                                      | 2,00                                    |
| 6 Convegni                     | 5.800,00          | 0,00              | 3.000,00  | 2.800,00                                      | 1,00                                    |
| 7 Travels                      | 6.400,00          | 0,00              | 3.000,00  | 3.400,00                                      | 1,21                                    |
| 8 Overheads                    | 52.200,00         | 0,00              | 27.000,00   | 25.200,00                                     | 9,00                                    |
| 9 Coordination Costs           | 0,00              | 0,00              | 0,00  | 0,00  | 0,00                                    |
| <b>Total</b>                   | <b>730.000,00</b> | <b>150.000,00</b> | <b>300.000,00</b>   | <b>280.000,00</b>                             | <b>100,00</b>                           |

Report the Co-Funding Contributor:

for staff salary

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV - Geriatric Telemanagement of HEALTH conditions in nursing home residents recently discharged from the hospital GET HEALTH</p> |
| <p><b>Project Code:</b> NET-2018-12368077-4</p>   | <p><b>Principal Investigator:</b> Cherubini Antonio</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistono significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto Nazionale di Riposo e Cura per Anziani</p>  |
| <p><b>Project Type: WP PROJECT - 4</b></p>  |   |

| <b>Budget Justification</b>  |   |
|------------------------------|---|
| 1a Staff Salary              | Permanent staff contributing to project activities                                  |
| 1b Researchers' Contracts    | Contract personnel to be involved in the project                                    |
| 2 Equipment (Leasing - Rent) | Workstation and medical devices for nursing home                                    |
| 3a Supplies                  | None  |
| 3b Model Costs               | None  |
| 3c Subcontracts              | Integration of the telemanagement platform with regional electronic medical records |
| 3d Patient Costs             | None  |
| 4 IT Services and Data Bases | Cost of IT services for data collection, management and analysis                    |
| 5 Publication Costs          | Cost for publications in open access journals                                       |
| 6 Convegni                   | Dissemination activities  |
| 7 Travels                    | Visit to participating sites for monitoring and review quality of the projects      |
| 8 Overheads                  | 10% overhead  |
| 9 Coordination Costs         | None  |

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|  <p><i>Ministero della Salute</i><br/>         Direzione Generale della Ricerca Sanitaria<br/>         e Biomedica e della Vigilanza sugli Enti<br/> <b>BANDO RICERCA FINALIZZATA 2018</b><br/>         esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>         Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV - Geriatric Telemanagement of HEALTH conditions in nursing home residents recently discharged from the hospital GET HEALTH</p> |
| <p><b>Project Code:</b> NET-2018-12368077-4</p>   | <p><b>Principal Investigator:</b> Cherubini Antonio</p>  |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>  | <p><b>Applicant Institution:</b> Istituto Nazionale di Riposo e Cura per Anziani</p>   |
| <p><b>Project Type: WP PROJECT - 4</b></p>  |  |

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <b>Project Title:</b><br>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV |
| <b>Project Code:</b> NET-2018-12368077-5  | <b>Principal Investigator:</b> Lorusso Vito  |
| <b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4                       | <b>Applicant Institution:</b> Istituto tumori Giovanni Paolo II  |
| <b>Project Type: WP PROJECT - 5</b>   |  |

**Major Diagnostic Category\*:** Ortopedia

**Project Classification IRG:** Healthcare Delivery and Methodologies

**Project Classification SS:** Health Services Organization and Delivery - HSOD

**Project Keyword 1:** Healthcare organizations, programs, and delivery of services; including those delivered in non-traditional settings; integrated care delivery systems; disease management and modeling; continuous quality improvement; characteristics of the organization and patient outcomes; organizational performance and efficiency; cost-benefit analysis; economics of health care and pharmacoeconomics.

**Project Keyword 2:** Health care governance and sustainability

**Project Keyword 3:** Health technology assessment and clinical practice guidelines

**Project duration (months):** 36

**Project Request:**      **Animals:**                       **Humans:**                       **Clinical trial:**

**The object/s of this application is/are under patent copyright Y/N:**

| Investigators, Institution and Role in the Project |       |                        |                                   |                       |            |
|--|-------|------------------------|-----------------------------------|-----------------------|------------|
|  | Co-PI | Key Personnel          | Institution/Org./Pos.             | Role in the project   | Birth Date |
| 1  | X     | Giotta Francesco       | IRCCS-Cancer Institute            | Research Collaborator | 20/03/1962 |
| 2  |       | massafra raffaella     | Istituto Tumori Giovanni Paolo II | Research Collaborator | 21/05/1973 |
| 3  |       | Zito Francesco Alfredo | IRCCS-Cancer Institute            | Research Collaborator | 07/01/1959 |

## Overall Summary

Aim of this study is the experimentation of the integrated use of the HTA methodology with machine learning techniques used for the construction of automated decision support systems to clinicians in the development of personalized treatment paths.

The proposed methodology envisages the HTA approach in defining the Apulian Breast Units care pathway starting from the assessment of the national and international reference guidelines and adopting the AGREE method, reviewing literature (metanalysis and HTA reports), implementing innovative technologies based on their effectiveness, providing in deep analysis of the epidemiological, structural and regional organizational context, and evaluating the impact of the new organizational model (Breast Unit care Pathway as technology itself). Moreover a machine learning approach will be applied to the management of a complex multidisciplinary care path as it appears to be that of a ABUCP, and it will provide elements to support clinicians decision

## Background / State of Art

Compared to the incidence of all other cancers (except those of the skin), breast cancer is the most frequently diagnosed among women (28%). There are several risk factors related to reproductive, hormonal, dietary and metabolic factors, previous radiotherapy and previous dysplasias or hereditary breast cancers.

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Sent date of moratorium changes: 01/06/2018 15.17

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti</p> <p><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
| <p><b>Project Code:</b> NET-2018-12368077-5</p>  | <p><b>Principal Investigator:</b> Lorusso Vito</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                   | <p><b>Applicant Institution:</b> Istituto tumori Giovanni Paolo II</p>   |
| <p><b>Project Type: WP PROJECT - 5</b></p>   |  |

The early diagnosis, more and more frequent because of the growing adherence to the screening campaigns on the one hand and the improvement of treatments on the other, have led to the increase of survival for breast cancer (in Italy, the 5-year survival is equal to 87%, while 10 years from diagnosis it drops to 80%).

It has become a priority for all health organizations to identify and develop welfare models capable of responding to the complexity of the phenomena associated with this pathology and appropriately addressing its ever-expanding and mutating welfare burden.

Since 2003, the European Parliament had already identified in the Breast Unit as the optimal response to this welfare question, referring to the requirements of EUSOMA (European Society of Breast Cancer Specialists), asked the Member States that all women with breast cancer were treated by a multidisciplinary team and a network of certified senological centers was organized. In 2006 a new resolution established that these centers had to be implemented by 2016 in order to increase the survival and quality of life of women with breast cancer. Also in 2006, the European Commission published the fourth edition of the European Guidelines for Quality Assurance in Breast Cancer Screening and Diagnosis where, in chapter 9, the EUSOMA article on the requirements of a Breast Unit was reported. In June 2014, the Working Group for the definition of specific organizational and assistance modalities of the network of senology structures (DD 04-09-2012) elaborated the manual "Guidelines on the organizational and assistance modalities of the Senology Centers network". It is an integral part of the agreement ratified on December 18, 2014 between the Government, the Regions and the Autonomous Provinces of Trento and Bolzano, in which the Regions and the PA undertake to incorporate the technical contents and the path of assistance to the patient affected by breast cancer within 6 months from the stipulation. The document referred to in the agreement between Government and Regions defines the Center of Senology as "a model of assistance specialized in the diagnosis, treatment and psychophysical rehabilitation of women with breast cancer where the management of the patient's path is entrusted to a multidisciplinary group of dedicated professionals with specific experience in the field of senology". The Center of Senology must possess the requisites foreseen at European level and in particular it must treat every year more than 150 new cases of breast cancer, adopt guidelines for the diagnosis, treatment of the tumor at all the stages and for the psychophysical rehabilitation of the patient. It must also use a database for data collection. Data collection, training and research are among the qualifying tools of the center.

Apulia Region would adopt a specific care pathways as an important tool to support clinical governance and to guarantee equity in Health Care services asses.

HTA is a multidisciplinary process that summarizes information about the medical, social, economic and ethical issues related to use of a health technology (any health intervention: screening, vaccines, diagnostics, medicines, devices, education, rehabilitation, public health interventions, organization of health services) in a systematic, transparent, unbiased, robust manner. It aims to inform policy at national, regional or hospital level.

In Apulia Region the HTA approach is identified as a useful methodology to develop and assess Clinical/care pathways. The strategic Regional Agency for Health care and welfare (AReSS) is in charge for developing clinical networks and care pathways.

## Hyphotesis and Specific AIMS

### Hyphotesis and Significance:

Evidence from epidemiological data shows how female breast cancer involves a constant expansion of the care load for the Italian Health System and Regional Health Systems both in terms of primary and secondary prevention (lifestyles and

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
| <p><b>Project Code:</b> NET-2018-12368077-5</p>   | <p><b>Principal Investigator:</b> Lorusso Vito</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto tumori Giovanni Paolo II</p>   |
| <p><b>Project Type: WP PROJECT - 5</b></p>  |  |

screening campaigns) and in terms of treatment path (diagnostic analysis, therapeutic approach, rehabilitation and end of life pathways). In this context, the Breast Units are an effective tool to face this big killer.

Several studies show that those treated in specialized senological centers with multidisciplinary approaches, have more chances to heal [1-4]: women treated in these centers have a survival rate that is 18% higher than those who it is aimed at non-specialized facilities, and they also have a better quality of life [5].

Our main Hypothesis is that the integrated use of real world data through a decision support system and the HTA approach could improve clinical appropriateness, breast units performances, clinical governance and health outcomes.

#### Preliminary Data:

The data of each patient who has undertaken the path of the Breast Unit, have been builded a database with the following data: woman's personal data, lesion identification by pathological anatomy report, data on chemo-, hormone-, and radio-therapy, data on diagnostic tests and lesion surgery (fig.1-3).

The group has experience in the development of expert systems and machine learning algorithms for the characterization and classification of breast lesions, also developed in collaboration with researchers of the National Institute of Nuclear Physics (INFN). In particular, Dr. Massafra is co-author of several scientific papers [8-11].

#### Specific Aim 1:

One of the requisites required by Eusoma is the drafting, written and shared among all the BU members, of a Diagnostic Therapeutic Assistance Path (PDTA) to be implemented in the Health Units of belonging. The national and regional legislation has set as a priority for every Health Authority the implementation of PDTAs for some diseases with greater social and health impact.

OR1 - CONSTRUCTION OF A PDTA REGIONAL FOR BREAST UNIT

OR1.1 - CRITICAL ANALYSIS OF THE MOST RECENT NATIONAL AND INTERNATIONAL GUIDELINES FOR THE BREAST NETWORKS

OR1.2 - ANALYSIS OF THE REGIONAL SCENARIO

OR1.3 - REGIONAL PDTA DEFINITION

#### Specific Aim 2:

For the management of a multidisciplinary center of senology it is necessary to have databases for the management of all the clinical conditions in which women can be found starting from the negativity to the screening until the psycho-functional rehabilitation. To this end, the architecture of a database will be defined for the management of clinical care data referring to patients with a neoplastic or hypothesized lesion.

In particular, the ORs are:

OR2 - DATABASE FOR THE DATA MANAGEMENT OF INDIVIDUAL PATIENTS

OR2.1 DEFINITION AND STUDY OF THE USEFUL INFORMATION FLOW

OR2.2 BUILDING OF A DATABASE IN ELECTRONIC FORMAT

OR3 - PERFORMANCES OF PERSONALIZED THERAPEUTIC PATHWAY

Qualitative and quantitative evaluation of the processes and results of the Breast Unit pathways using indicators known to the state of the art and definition of new ones.

OR3.1 - STATE OF ART REVIEW

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| <p><b>Project Code:</b> NET-2018-12368077-5</p>   | <p><b>Principal Investigator:</b> Lorusso Vito</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto tumori Giovanni Paolo II</p>   |
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OR3.2 - STATISTICAL ANALYSIS OF GENERATED DATA FLOW

OR4 - DEVELOPMENT OF AN AUTOMATED METHOD TO SUPPORT THERAPEUTIC DECISIONS

OR4.1 - DEVELOPMENT OF AN AUTOMATED MODEL FOR THE DEFINITION OF PERSONALIZED THERAPEUTIC ROUTES

OR4.2 - VALIDATION OF THE AUTOMATED SYSTEM

OR4.3 EVALUATION OF EFFECTS OF THERAPEUTIC OPTIONS ON THE FOLLOW-UP

**Specific Aim 3:**

OR5 INTEGRATION OF BU CARE PATHWAY ASSESSMENT WITH THE DECISION SUPPORT SYSTEM (DSS)

OR5.1 DEVELOPING THE BREAST UNIT CARE PATHWAY WITH HTA APPROACH

OR5.2 IMPROVING THE BREAST UNIT CARE PATHWAY WITH REAL DATA

**Experimental Design Aim 1:**

The Clinical Practice Guidelines (CPGs) have been redefined as "tools to support the decision of the clinician and the patient, through clear description and critical evaluation of the available scientific evidence (including the risk/benefit ratio) that underpins the clinical recommendations, making them understandable and adapting them to the expectations of the individual patient" Institute of Medicine Washington DC: Standards for developing trustworthy Clinical Practise Guidelines 2011 (SIGN Handbook for developers 50)

The drafting of the PDTA will follow some basic steps as indicated by the Italian Group Method for Evidence-Based Medicine:

1. definition of priority (of the compilation of a PDTA) linked both to the clinical and social impact of the pathology, its frequency and variability;
2. establishment of the working group;
3. Finding (search for Guidelines-LG), Appraisal (qualitative critical evaluation of LG), Integrating (bibliographic integration), Adapting (Adapting LG to local context), Updating (Update).

**Experimental Design Aim 2:**

The Breast Units must achieve the necessary measures to achieve a minimum standard with respect to quality indicators indicated by Eusoma. For the purposes of qualitative and quantitative assessment of the processes and results of the Breast Unit, the already known indicators will be analyzed. Other indicators of interest, characterizing our center will be built from the data collected in the management database during the project, relating for example to the diagnostic performance of technologically advanced imaging instruments such as CEM and fusion imaging.

On the basis of the retrospective data on the paths concluded by the patients entered in the Breat Unit, for which the follow-up of the therapeutic/diagnostic path is therefore known, models of artificial intelligence and machine learning techniques will be implemented in order to define predictive models support to the multidisciplinary team in therapeutic decisions.

**Experimental Design Aim 3:**

HTA is a form of policy research that systematically examines the short- and long-term consequences, in terms of health and resource use, of the application of a health technology, a set of related technologies or a technology-related issue. In the HTA context, technology has a wide-ranging definition that includes products (medicines, devices etc.), procedures (surgical interventions, multimodal treatment concepts etc.) and systems (prevention and managed care programmes etc.);

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| <p><b>Project Code:</b> NET-2018-12368077-5</p>   | <p><b>Principal Investigator:</b> Lorusso Vito</p>   |
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hence a breast unit care pathway is a 'health technology'. HTA is a multidisciplinary process summarising information about medical, social, economic and ethical issues related to the use of a health technology in a systematic, transparent, unbiased, robust manner. Following this approach, we will produce a HTA report by comparing and synthesizing information and evidence on BU organization and management, investigating all the relevant domains, as identified by EUnetHTA, the European network for Health Technology Assessment.

**Picture to support preliminary data:**

PUGLIA\_NET\_v5-Picture.docx

**Methodologies and statistical analyses:**

The definition of the most appropriate therapeutic pathway requires an extensive knowledge domain that includes medical imaging data of different modalities, biological and genetic, diagnostic tests and biomarkers, risk factors and clinical trials. The goal is to integrate information from multiple sources and exploit them prospectively for decision support.

On the basis of the acquired knowledge domain, multivariate statistical models, artificial intelligence systems and machine learning algorithms will be implemented.

In the field of pattern recognition and computational learning theory, machine learning algorithms, on the other hand, are methods of data analysis aimed at automating the creation of analytical statistical models and allowing intelligent machines to improve over time, exactly as happens with the human brain [6]. Special algorithms are iteratively trained on a database and knowledge provided by Breast Unit, and 'learn' to make decisions and make predictions without further human intervention. These models will be trained on the various types of information extracted from the clinical history and personal data of the patients who have concluded a path within the Breast Unit and for which therefore the therapeutic, diagnostic and operative follow-up is known.

The PI and the researchers will analyze the information flow in input (paths and follow-up) and the reliability of the predictive models generated, in order to identify any critical issues and suggest any corrective measures.

Machine learning algorithms can also be trained to automate the process of detection and diagnosis of breast lesions in support of imaging analysis instruments: starting from particular statistical, morphological and morphometric features extracted from images containing lesions of various natural, automated systems learn to recognize and classify normal, abnormal (benign and malignant) findings.

**Expected outcomes:**

In the first instance, a PDTA will be defined, optimized and contextualised to the regional reality capable of satisfying the needs of patients and improving their quality life. To this end, based on HTA evaluations, new highly innovative imaging diagnostic instruments will be introduced efficiently in the therapeutic and screening pathway.

Furthermore, appropriate quality indicators will be used to evaluate different aspects of the Breast Unit program, such as the diagnostic and surgical outcome, the process, post-therapeutic interventions or surgery complications.

Finally, the availability of such database offers a considerable array of knowledge useful for the implementation of a computerized system to support the decisions of clinicians for the identification of new patterns of personalized medicine. Multivariate statistical models based on machine learning algorithms will be developed to predict diagnostic follow-up of personalized therapeutic pathways based on retrospective analysis of completed therapeutic pathways, clinical data and patient demographics. They will provide the medical staff with timely advice in the decision-making process, to support their own expert, generating, in real time, a personalized forecast of optional therapeutic pathways foreseen by the PDTA. These

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models, fueled over time by new cases, will automatically self-train to update predictive models and improve forecasts. The results of the WP5 will also concern participation at the Network ensuring all the required support to the WP2 Niguarda, WP7 SSSA and WP8 Azienda Zero (WP5 will collect data on performance and all the other requested information, participating at the tutorial activities carried out by WP SSSA, Niguarda and Azienda Zero). The scientific results will be disseminated within the national and international scientific community through participation in national and / or international conferences related to the subject matter of the project.

#### **Risk analysis, possible problems and solutions:**

During the start-up phase of the project there could be difficulties related to the timing of the recruitment of contract staff with a delay in achieving the project objectives. To tackle this potential risk, the research group will make use of the expertise of researchers in force at the Institute, also of collaboration with entities that have expressed interest in the research objectives and who will collaborate in the realization of the same, such as Regional Agency for Health and Social Services (AReSS in charge with the development of different regional clinical networks and care pathways, and where the Regional Health Technology Assessment Centre RHTAC - is located) and National Institute for Nuclear Physics (INFN). The A.Re.S.S. it aims to organize and improve, through the monitoring and continuous verification of the outcomes, the responsiveness of the regional health system to the needs and expectations of the health demand of the citizens of Puglia. The experiences of the A.Re.S.S. concern the use of HTA methodologies for the evaluation of therapeutic/care pathways and innovative technologies.

#### **Significance and Innovation**

The objective of this project is to optimize the coordination and multidisciplinary management of cancer cases, and to exploit the different information in a perspective way for decision support. In this context, the project aims to develop an innovative software system that provides intuitive graphical interfaces and automated diagnostic and therapeutic tools for the personalized analysis of individual cases and the identification of any critical pathways based on follow-up analysis clinicians.

The implementation of the therapeutic decision support system, would allow a more efficient, integrated and shared management of all the health information and clinical history of the patients, favoring the study of the most critical pathologies and the realization of a more effective preventive intervention. This inevitably translates into a control of health expenditure.

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| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto tumori Giovanni Paolo II</p>   |
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### Description of the complementary and synergy research team

The research group is multidisciplinary and all of the research group members collaborate in the Breast Unit of the Institute. Research group will make use of the collaboration of other doctors belonging to Institute who actively participate in the Breast Unit program:

CM Ressa, Breast Unit Coordinator  
V Didonna, Medical Physics Director  
P Tesauro, Direction Physician  
A Lapietra, Quality Manager  
M Lioce, Radiotherapy Director  
S Diotaiuti, Senological Surgery Director  
R Dentamaro, Radiol. Director  
P Tamborra, Medical Physic  
D La Forgia, Radiol. Physician  
A Latorre, Oncology Physician  
A Nardone, Radiotherapy Physician  
I Pastena, Pathological Anatomy Physician  
V Desantis, Plastic Surgery Physician

This group collaborates with other research units with many experience in the sector that have expressed their interest in the project proposal, such as the INFN of Bari and A.Re.S.S. (Dr. E. A. Graps, RHTAC Director) (see section E). The expertise of the INFN team is related to this project are the analysis and processing of images, pattern recognition and machine learning, with related applications in medical big data analytics. The expertise of A.Re.S.S. team is related to this project regard to the use of methods for multidimensional and multidisciplinary analysis of the clinical, social, organizational, economic, ethical and legal implications of a technology, through the evaluation of multiple dimensions such as effectiveness, safety, costs, impact social and organizational.

### Training and tutorial activities

At least once a week, meetings will be organized dedicated to the discussion and collegial assessment of individual clinical cases, to the planning of diagnostic-therapeutic strategies, treatment and rehabilitation. These appointments, coordinated by the research group Dr. Francesco Giotta, Medical Director of Medical Oncology, will participate all the members of the team of professionals of the Breast Unit, representing the various complex operating units of the center of senology. Due to their multidisciplinary nature and the moments dedicated to scientific updating, these meetings will represent a highly formative moment for the participants.

For this reason, we intend to request credits for Continuing Medical Education (ECM) for the professional figures of: Oncologist, Radiotherapist, Surgeon, Anatomic Pathologist, Radiodiagnost, Medical Physicist, Cardiologist, Anesthetist, Nurse.

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## Timeline / Deliverables / Payable Milestones

At 18th month a report on first results of analysis will be delivered.

At 36th month the full report on performed activities and achieved aims will be delivered.

### Milestones 18 month

Definition of Key Performance Indicators (KPI) for measuring the performance and quality of therapeutic treatments, with reference to diagnostics in general, surgery, radiotherapy, medical therapy, expected time and follow-up. These indicators must have certain characteristics, such as: reliability (measurements must be reproducible at different times and possibly in different observatories), validity, usability, feasibility.

### Milestones 36 month

HTA evaluation of national and international reference guidelines, from the analysis of the epidemiological, structural and regional organizational context.

Definition of a Diagnostic-Therapeutic and Assistance (PDTA) path integrated into the reality of the regional context in order to offer highly professional care and a high level of specialization starting from the screening phase up to the psycho-

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functional rehabilitation.

## Gantt chart

Gantt Puglia.pdf

## Equipment and resources available

k1: The Institute has highly innovative diagnostic imaging instruments, such as CESM, fusion imaging, tomosynthesis, MRI driven biopsies, for which it is intended to start performance and cost / benefit analysis for the integration of the same in the PDTA as alternative methods to the traditional ones.

From October 2014 the Breast Unit was established at the IRCCS 'Giovanni Paolo II'; weekly meetings were held, discussing on about 280 cases per year.

In order to define a regional PDTA, it is primarily necessary to carry out an HTA analysis of the national and international guidelines (AGREE method) and of the regional context in which this instrument is inserted. Specific knowledge of HTA approach is necessary. Multidisciplinary skills are essential to conduct analysis in different domains to investigate the health regional contest, the safety and the management costs of different technologies encompassed in the BUCP, the organisational model costs, etc.

For this purpose, HTA experts (Epidemiologist, Clinical engineer, health Economist) are necessary during the entire duration of the project, both through 'in kind' contribution of ARESS professionals and using the project funds.

k2: In this project the goal of Istituto Nazionale di Fisica Nucleare (INFN) is to optimize the developed machine learning methods.

Using the database available at the research center and that will be collected during the study (with the possibility of collecting data in a multicentric way between one or more regions of the NET program), in this project the INFN group (coordinated by Dr. S. Tangaro, Ph.D.) aims to develop a system that compares two types of methods of analysis and prediction: 'supervised', where the system is trained on the data label proposed by the Breast Unit, and "non-supervised", where the system of performs a function to describe hidden structure from "unlabeled" data based on appropriate optimization.

The use of Cloud services provide a scalable set of services that can be fitted on the computational complexity of the user data.

In this context, the experiences of the INFN Bari group include: (i) Development of Computer Aided Detection Systems (CAD) for the analysis of biomedical images, in particular mammographic images; (ii) Analysis of magnetic resonance images (MRI) to study the morphological alterations caused by diseases; (iii) Development of complex statistical tools for the analysis of medical data.

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### Translational relevance and impact for the National Health System (SSN)

The Cancer Institute Giovanni Paolo II - IRCCS di Bari - is the central hub of the cancer network in Puglia and is a recognized Breast Unit center of excellence in the treatment of breast cancer.

From a perspective viewpoint, the PDTA definition model, the automated database for the shared management of the findings and the diagnostic predictive models of artificial intelligence that are intended to be developed for the Breast Unit center, once validated and consolidated, can be generalized and extended to the whole cancer network of the region, with consequent positive effects in terms of rationalization of the costs of the National Health Service and reduction of social costs.

The implementation of the therapeutic decision support system, will allow a more efficient, integrated and shared management of the health information and clinical history of the patients, favoring the study of the most critical pathologies and the realization of a more effective preventive intervention.

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| <p><b>Project Type: WP PROJECT - 5</b></p>  |  |

### PRINCIPAL INVESTIGATOR PROFILE

|                              |  |
|------------------------------|--|
| <p>Name<br/>Lorusso Vito</p> | <p>Institution<br/>Istituto tumori Giovanni Paolo II</p> <p>Department/Unit<br/>Medical Oncology Department</p> <p>Position Title<br/>Chief of Medical Oncology Operative Unit</p> |
|------------------------------|--|

### Personal Statement

The complex structure of Medical Oncology is at the heart of the coordination functions of clinical research activities, as can be inferred from the analysis of the state of the art. Regardless of the development phase of the neoplastic pathology, in order to better orient the medical treatment, it is necessary to study the biological characteristics of the neoplasm in collaboration with pathological anatomy and the molecular biology laboratory. The expert systems will allow to identify the main factors of outcome indicators, in particular on time-related parameters.

| Education/Training - Institution and Location | Degree              | Year(s) | Field of study       |
|---|---------------------|---------|----------------------|
| Università Cattolica del Sacro Cuore di Roma  | Speciality          | 1995    | Haematology          |
| Università degli Studi di Bari                | Speciality          | 1982    | Oncology             |
| Università degli Studi di Bari                | Board Certification | 1978    | Medicine and Surgery |

### Positions

| Institution                      | Division / Research group    | Location             | Position            | From year | To year |
|----------------------------------|------------------------------|----------------------|---------------------|-----------|---------|
| IRCCS Istituto Tumori            | Oncologia Medica             | Bari, Italy          | Head of Unit        | 2012      | 2018    |
| Azienda Ospedaliera 'Vito Fazzi' | Oncologia Medica             | Lecce, Italy         | Head of Unit        | 2006      | 2012    |
| IRCCS Istituto Tumori            | Oncologia Medica             | Bari, Italy          | Head of Unit        | 2001      | 2006    |
| IRCCS Istituto Tumori            | Oncologia                    | Bari, Italy          | Associate Assistant | 1990      | 2018    |
| Arcispedale S.Maria Nuova        | Servizio di Oncologia Medica | Reggio Emilia, Italy | Full-time Assistant | 1981      | 2018    |

**Official H index:** 35.0 ( autocertificated )

**Source:** Scopus

**Scopus Author Id:** 35356695200

**ORCID ID:** Not available

**RESEARCH ID:** Not available

### Awards and Honors:

Since 1980 he is a member of the Italian Association of Medical Oncology (AIOM) of which he was also a member of the board of directors in the years 1991-1995. Since 1988 he is a member of the American Society of Clinical Oncology (ASCO). Since 1990 he is a member of the European Society of Medical Oncology (ESMO). In 1993 was member of the Commission for Phase I Clinical Trials in the IRCCS Istituto Tumori 'Giovanni Paolo II'.

### Other CV Informations:

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
| <p><b>Project Code:</b> NET-2018-12368077-5</p>   | <p><b>Principal Investigator:</b> Lorusso Vito</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto tumori Giovanni Paolo II</p>   |
| <p><b>Project Type: WP PROJECT - 5</b></p>  |  |

In 1998 he carried out a Training Course in Health Management divided into 5 modules: Planning and Control, Health Services Economics, Human Resources Management, Quality System in Health Services, Evaluation of Healthcare Activities.

He was a lecturer at the University of Bari of Medical Oncology Lessons for the students of the Degree Course in Prevention Techniques in the Environment and in the Workplace (2005) and at the University of Modena and Reggio Emilia at the School of Specialization in Oncology (2007).

In 2008 he was Co-director of the first level University Master "Data Manager in Oncology. Expert in the design and management of a clinical study " University of Salento.

From the year 2009 to the year 2012 he was Professor of Oncology at the Degree Course in Nursing in Lecce.

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
| <p><b>Project Code:</b> NET-2018-12368077-5</p>   | <p><b>Principal Investigator:</b> Lorusso Vito</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>            | <p><b>Applicant Institution:</b> Istituto tumori Giovanni Paolo II</p>   |
| <p><b>Project Type: WP PROJECT - 5</b></p>  |  |

### Selected peer-reviewed publications of the PI

| Valid for PI minimum expertise level  |                               |               |         |     |
|---|-------------------------------|---------------|---------|-----|
| Title   | DOI                           | PMID          | Cit. ** | P.* |
| Amifostine as chemoprotectant in metastatic breast cancer patients treated with doxorubicin.  | 10.3892/or.10.1.163           | 12469164      | 9       | L   |
| Phase I/II study of gemcitabine plus mitoxantrone as salvage chemotherapy in metastatic breast cancer.  | 10.1038/sj.bjc.6600780        | 12592360      | 7       | F   |
| A phase I study of capecitabine in combination with vinorelbine in advanced breast cancer.  | 10.3816/CBC.2003.n.019        | 12864942      | 19      | F   |
| Rationale for the use of gemcitabine in breast cancer (Review).   | 10.3892/ijo.24.2.389          | 14719116      | 17      | L   |
| Biomarkers predictive for clinical efficacy of taxol-based chemotherapy in advanced breast cancer.  | 10.1093/annonc/md902          | 15923415      | 104     | L   |
| Oral vinorelbine plus capecitabine (oralvinctin) combination in patients with advanced breast cancer (ABC). A phase II study of the GOIM (Gruppo Oncologico dell'Italia Meridionale).     | 10.1093/annonc/dl942          | 16760280      | 24      | F   |
| Clinical and therapeutic perspectives of gene expression profiling for breast cancer.   | 10.1093/annonc/dm226          | 17591834      | 4       | L   |
| Role of liposomal anthracyclines in breast cancer.  | 10.1093/annonc/dm229          | Not available | 31      | F   |
| Role of gemcitabine in metastatic breast cancer patients: a short review.   | 10.1016/j.breast.2007.10.009  | 18037292      | 37      | L   |
| How should we prescribe lapatinib to our patients: once daily or twice daily, and at what dose?   | 10.1200/JCO.2008.20.0345      | 9064955       | 5       | L   |
| Bevacizumab in the treatment of HER2-negative breast cancer.  | Not available                 | 19707460      | 6       | F   |
| Intravenous versus oral vinorelbine plus capecitabine as second-line treatment in advanced breast cancer patients. A retrospective comparison of two consecutive phase II studies.        | 10.1016/j.breast.2010.01.015  | 20167491      | 6       | F   |
| Lapatinib in breast cancer: clinical experiences and future perspectives.   | 10.1016/S0305-7372(10)70024-4 | 21129615      | 16      | L   |
| Which role for EGFR therapy in breast cancer?   | 10.2741/249                   | 22202041      | 1       | F   |
| Non-pegylated liposome-encapsulated doxorubicin plus cyclophosphamide or vinorelbine in metastatic breast cancer not previously treated with chemotherapy: a multicenter phase III study. | 10.3892/ijo.2014.2604         | 25176223      | 5       | F   |

\* Position: F=First L=Last C=Correspondent

\*\* Autocertificated

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
| <p><b>Project Code:</b> NET-2018-12368077-5</p>   | <p><b>Principal Investigator:</b> Lorusso Vito</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto tumori Giovanni Paolo II</p>   |
| <p><b>Project Type: WP PROJECT - 5</b></p>  |  |

| For evaluation CV  |                                |               |        |
|--|--------------------------------|---------------|--------|
| Title  | DOI                            | PMID          | Cit. * |
| Liposomal-encapsulated doxorubicin plus cyclophosphamide as first-line therapy in metastatic breast cancer: A phase II multicentric study.   | 10.1093/annonc/mdm228          |               | 15     |
| A randomised factorial trial of sequential doxorubicin and CMF vs CMF and chemotherapy alone vs chemotherapy followed by goserelin plus tamoxifen as adjuvant treatment of node-positive breast cancer.        | 10.1038/sj.bjc.6602355         | Not available | 22     |
| Randomized clinical trial of adjuvant fluorouracil, epirubicin, and cyclophosphamide chemotherapy for patients with fast-proliferating, node-negative breast cancer.   | 10.1200/JCO.2001.19.19.3929    | 11579113      | 25     |
| Tumor-proliferative Activity, Progesterone Receptor Status, Estrogen Receptor Level, and Clinical Outcome of Estrogen Receptor-positive Advanced Breast Cancer.  | Not available                  | 2334898       | 34     |
| Time to progression in metastatic breast cancer patients treated with epirubicin is not improved by the addition of either cisplatin or lisdamine: Final results of a phase III study with a factorial design. | 10.1200/JCO.2002.08.012        | 12377958      | 40     |
| Phase II study of vinorelbine with protracted fluorouracil infusion as a second- or third-line approach for advanced breast cancer patients previously treated with anthracyclines.                            | 10.1200/JCO.2000.18.19.3370    | 11013277      | 46     |
| Efficacy and safety of zoledronic acid in patients with breast cancer metastatic to bone: A multicenter clinical trial.  | 10.1634/theoncologist.11.7-841 | Not available | 49     |
| Treatment of triple negative breast cancer (TNBC): Current options and future perspectives.  | 10.1016/S0305-7372(10)70025-6  | Not available | 67     |
| Lack of benefit of maintenance paclitaxel in first-line chemotherapy in metastatic breast cancer   | 10.1200/JCO.2006.06.1812       | Not available | 68     |
| Cytoskeleton and paclitaxel sensitivity in breast cancer: The role of $\beta$ -tubulins.   | 10.1002/ijc.22557              | Not available | 107    |

\* Autocertificated

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
| <p><b>Project Code:</b> NET-2018-12368077-5</p>   | <p><b>Principal Investigator:</b> Lorusso Vito</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto tumori Giovanni Paolo II</p>   |
| <p><b>Project Type: WP PROJECT - 5</b></p>  |  |

| Grant   |      |  |                      |
|---|------|--|----------------------|
| Funded Institution / Country                    | Year | Title  | Position in Projects |
| Ministero della Sanità                          | 2002 | Progetto Globale Prostata  | Coordinator          |
| Ministero della Sanità                          | 2002 | Incidenza della malattia di Alzheimer nei pazienti affetti da neoplasie e lungo sopravvivenuti. Rilevo epidemiologico in rapporto all'utilizzo di farmaci antitumorali con possibile danno endoteliale | Coordinator          |
| Ministero della Sanità                          | 2002 | Studio multicentrico randomizzato di fase II nel carcinoma transizionale dell'urotelio in stadio avanzato o metastatico tra gemcitabina + cisplatino e gemcitabina + cisplatino + taxolo               | Coordinator          |
| Ministero della Sanità                          | 2002 | Carcinoma ovarico. Studio randomizzato di fase II tra le associazioni di cisplatino, taxolo e lonidamina versus cisplatino, ifosfamide e lonidamina. Studio di fase II randomizzato                    | Coordinator          |
| Ministero della Sanità                          | 2002 | Taxolo e Lonidamina nel carcinoma epatico non operabile. Studio di fase I/II   | Coordinator          |
| Ministero della Sanità                          | 1993 | Reversione con Lonidamina della resistenza al cisplatino nella terapia del carcinoma ovarico in stadio avanzato  | Coordinator          |
| Associazione Italiana per la Ricerca sul Cancro | 1996 | Valutazione della sequenza chemioterapia DHAP-trapianto di midollo autologo di progenitori emopoietici circolanti (PEC) nei linfomi non Hodgkin a basso grado  | Coordinator          |

**Employment contract extension:**

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
| <p><b>Project Code:</b> NET-2018-12368077-5</p>   | <p><b>Principal Investigator:</b> Lorusso Vito</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto tumori Giovanni Paolo II</p>   |
| <p><b>Project Type: WP PROJECT - 5</b></p>  |  |

### Biographical Sketch Contributors 1

|  |   |
|--|---|
| <p><b>Name:</b><br/>Giotta Francesco</p> | <p>Institution: IRCCS-Cancer Institute<br/>Department/Unit: Medical Oncology<br/>Position Title: Medical Director - I Level</p> |
|--|---|

| Education/Training - Institution and Location | Degree                                | Year(s) | Field of study |
|---|---------------------------------------|---------|----------------|
| University of Bari                            | Specialization In Oncology            | 1991    | Medicine       |
| University of Bari                            | Master Degree in medicine and surgery | 1988    | Medicine       |

#### Personal Statement:

The coordination activity of the breast unit is part of the "clinical governance" tools which allow the carrying out of clinical activities, aimed at accountability and participation, in the strategic and management choices, of all the subjects involved in the provision of health services. Multidisciplinary and multi-professional integration, by defining organizational models and operational tools, must make it possible to develop an excellence diagnostic therapeutic assistance pathway.

| Institution              | Division / Research group | Location | Position         | From year | To year |
|--------------------------|---------------------------|----------|------------------|-----------|---------|
| IRCCS - Cancer Institute | Oncology                  | Bari     | MEDICAL DIRECTOR | 1990      | 2018    |

#### Awards and Honors

**Official H index:** 15.0 ( autocertificated )

**Source:** Scopus

**Scopus Author Id:** 6603316944

**ORCID ID:** Not available

**RESEARCH ID:** Not available

#### Awards and Honors:

From the 2014 the dr. Giotta Francesco is coordinator of the breast team of the Cancer Institute Giovanni Paolo II

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
| <p><b>Project Code:</b> NET-2018-12368077-5</p>   | <p><b>Principal Investigator:</b> Lorusso Vito</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto tumori Giovanni Paolo II</p>   |
| <p><b>Project Type: WP PROJECT - 5</b></p>  |  |

### Biographical Sketch Contributors 2

| <p><b>Name:</b><br/>massafra raffaella</p>     | <p>Institution: Istituto Tumori Giovanni Paolo II<br/>Department/Unit: Medical Physics Department<br/>Position Title: Medical Physics Expert</p> |         |                          |
|--|--|---------|--------------------------|
| Education/Training - Institution and Location  | Degree   | Year(s) | Field of study           |
| University of Napoli Federico II               | master in technologies for space remote - first level  | 2003    | Physics IMAGING ANALISIS |
| Bari 1999                                      | Responsible Expert in MRI  | 2005    | Medical Physics          |
| Ministero del Lavoro e delle Politiche Sociali | certification of radiation protection expert first degree  | 2005    | Radiation Protection     |
| University of Napoli Federico II               | Diploma of Specialization in Health Physics  | 2005    | Health Physics           |
| University of Bari Aldo Moro                   | Master Degree in Physics   | 2001    | Physics                  |

**Personal Statement:**

Matured experience in research imaging analysis with applications of supervised algorithms for the analysis of electrophysiological signals in collaboration with the TIRES Center of Excellence. He has collaborated in the development of CAD systems for the recognition of mammary lesions in mammograms (MAGIC-5 experiment - Medical Applications on a Grid Infrastructure Connection), financed by INFN, with which he currently collaborates. She is in charge of High Specialization in Special Techniques of intraoperative breast radiotherapy.

| Institution   | Division / Research group               | Location          | Position   | From year | To year |
|---|---|-------------------|--|-----------|---------|
| Istituto Tumori Giovanni Paolo II   | U.O. S. D. Fisica Sanitaria             | Bari              | Physics Director highly specialized position                   | 2009      | 2018    |
| Azienda Ospedaliero Universitaria O.O.R.R. di Foggia + A.S.L. BAT             | U.O. C. Radiotherapy                    | Foggia - Barletta | Physics Director   | 2007      | 2009    |
| Istituto Tumori Giovanni Paolo II   | U.O. C. Fisica Sanitaria                | Bari              | Medical Physics Expert (Position of professional collaborator) | 2006      | 2007    |
| Istituto Nazionale di Fisica Nucleare (INFN)                                  | Physics Department                      | Bari              | Research Collaborator (term-contract worker)                   | 2006      | 2006    |
| Tecnologie Innovative per la Rivelazione e L'Elaborazione del Segnale (TIRES) | Physics Department - University of Bari | Bari              | Research Collaborator (term-contract worker)                   | 2002      | 2002    |

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
| <p><b>Project Code:</b> NET-2018-12368077-5</p>   | <p><b>Principal Investigator:</b> Lorusso Vito</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto tumori Giovanni Paolo II</p>   |
| <p><b>Project Type: WP PROJECT - 5</b></p>  |  |

### Awards and Honors

**Official H index:** 6.0 ( autocertificated )

**Source:** Scopus

**Scopus Author Id:** 10044673400

**ORCID ID:** Not available

**RESEARCH ID:** Not available

### Awards and Honors:

Since 2007 she is a member of AIFM (Italian Medical Physics Association).

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
| <p><b>Project Code:</b> NET-2018-12368077-5</p>   | <p><b>Principal Investigator:</b> Lorusso Vito</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto tumori Giovanni Paolo II</p>   |
| <p><b>Project Type: WP PROJECT - 5</b></p>  |  |

### Biographical Sketch Contributors 3

|  |  |
|--|--|
| <p><b>Name:</b><br/>Zito Francesco Alfredo</p> | <p>Institution IRCCS-Cancer Institute<br/>Department/Unit Pathological anatomy<br/>Position Title Director of Complex Unit</p> |
|--|--|

| Education/Training - Institution and Location | Degree                                 | Year(s) | Field of study |
|---|--|---------|----------------|
| Bologna Prof. Pileri                          | Stage in oncomatologia                 | 2010    | Medicine       |
| Milano Certiquality                           | Audit ISO 9000                         | 1999    | Medicine       |
| University of Bari                            | Specialization In Oncology             | 1995    | Medicine       |
| University of Bari                            | Specialization In Pathological anatomy | 1989    | Medicine       |
| University of Bari                            | Master Degree in medicine and surgery  | 1985    | Medicine       |

#### Personal Statement:

Pathological Anatomy provides essential information for patients' prognosis and therapy. It is advisable to carry out joint surgical reports for all the Pathological Anatomies of the Region to standardize the clinical-pathological information. It will be useful to minimize the subjectivity of the interpretation of biological characterizations using expert automated systems through the digitalization of the preparations. Dr. Zito in collaboration with Nottingham University published on *Journal of Histopathology* a diagnostic reproducibility study on digitalized breast biopsies.

| Institution              | Division / Research group         | Location | Position             | From year | To year |
|--------------------------|-----------------------------------|----------|----------------------|-----------|---------|
| IRCCS                    | Department of Services            | Bari     | Medical Chief        | 2017      | 2018    |
| Azienda Sanitaria Locale | Department of Laboratory Medicine | Bari     | Medical Chief        | 2013      | 2017    |
| Azienda Sanitaria Locale | Pathological anatomy              | Bari     | Medical Chief        | 2010      | 2013    |
| IRCCS                    | Pathological anatomy              | Bari     | Medical Director     | 1990      | 2002    |
| IRCCS                    | Histopathology Health Unit        | Bari     | Responsible Director | 2002      | 2010    |

#### Awards and Honors

**Official H index:** 19.0 ( autocertificated )

**Source:** Scopus

**Scopus Author Id:** 55735407400

**ORCID ID:** Not available

**RESEARCH ID:** Not available

**Awards and Honors:**

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|  <p><i>Ministero della Salute</i><br/>         Direzione Generale della Ricerca Sanitaria<br/>         e Biomedica e della Vigilanza sugli Enti<br/> <b>BANDO RICERCA FINALIZZATA 2018</b><br/>         esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>         Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
| <p><b>Project Code:</b> NET-2018-12368077-5</p>   | <p><b>Principal Investigator:</b> Lorusso Vito</p>  |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>  | <p><b>Applicant Institution:</b> Istituto tumori Giovanni Paolo II</p>  |
| <p><b>Project Type: WP PROJECT - 5</b></p>  |   |

Dr. Zito is President of the Management College of the Bari Cancer Institute. He is, in second mandate, Regional Secretary of the Italian Society of Pathological Anatomy (SIAPEC). In 2015 he was awarded the AITIC AWARD on Breast Cancer Youth.

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
| <p><b>Project Code:</b> NET-2018-12368077-5</p>   | <p><b>Principal Investigator:</b> Lorusso Vito</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Istituto tumori Giovanni Paolo II</p>   |
| <p><b>Project Type: WP PROJECT - 5</b></p>  |  |

### Expertise Research Collaborators

| Selected peer-reviewed publications of the Research Group / Collaborators |   |   |               |        |
|---|---|---|---------------|--------|
| Collaborator  | Title   | DOI   | PMID          | Cit. * |
| massafra<br>raffaella   | Distributed medical images analysis on a Grid infrastructure.   | <a href="https://doi.org/10.1016/j.future.2006.07.006">https://doi.org/10.1016/j.future.2006.07.006</a>     | Not available | 23     |
| massafra<br>raffaella   | A completely automated CAD system for mass detection in a large mammographic database   | <a href="https://doi.org/10.1118/1.2214177">https://doi.org/10.1118/1.2214177</a>                           | Not available | 78     |
| Zito Francesco<br>Alfredo   | Trypase-positive mast cells correlate with angiogenesis in early breast cancer patients. International Journal of Oncology  | DOI: 10.3892/ijo_000  | Not available | 59     |
| Zito Francesco<br>Alfredo   | Changes in CpG islands promoter methylation patterns during ductal breast carcinoma progression.  | DOI: 10.1158/1055-  | Not available | 68     |
| Zito Francesco<br>Alfredo   | Biomarkers predictive for clinical efficacy of taxol-based chemotherapy in advanced breast cancer   | doi:10.1093/annonc/mdi902   | Not available | 104    |
| Zito Francesco<br>Alfredo   | Cytoskeleton and paclitaxel sensitivity in breast cancer: The role of $\beta_2$ tubulins. International journal of cancer   | <a href="https://doi.org/10.1002/ijc.22557">https://doi.org/10.1002/ijc.22557</a>                           | Not available | 107    |
| Zito Francesco<br>Alfredo   | Multicenter validation of a gene expression-based prognostic signature in lymph node-negative primary breast cancer   | DOI: 10.1200/JCO.2005.03.9115   | Not available | 278    |
| Giotta<br>Francesco   | Novel association with gemcitabine and docetaxel as salvage chemotherapy in metastatic breast cancer previously treated with anthracyclines: Results of a multicenter phase II study <sup>1</sup> | <a href="https://doi.org/10.1053/j.seminonc.2004.03.022">https://doi.org/10.1053/j.seminonc.2004.03.022</a> | Not available | 26     |
| Giotta<br>Francesco   | First-line treatment with epirubicin and vinorelbine in metastatic breast cancer. Journal of clinical oncology  | DOI: 10.1200/JCO.2002.06.039  | not available | 29     |
| Giotta<br>Francesco   | A prothrombotic state in breast cancer patients treated with adjuvant chemotherapy. Breast cancer research and treatment  | not available   | 8879681       | 46     |

\* Autocertificated

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| <p><b>Project Type: WP PROJECT - 5</b></p>  |  |

| <b>Grant</b>  |      |  |                      |                           |
|---|------|--|----------------------|---------------------------|
| Funded Institution / Country                                    | Year | Title  | Position in Projects | Collaborator              |
| Ministero della Salute - Programma Integrato Oncologia (P.I.O.) | 2016 | Progetto di ricerca corrente 2016 "Studio e sviluppo di un sistema di supporto alla diagnosi delle neoplasie mammarie basato su imaging multimodale"   | Collaborator         | massafra<br>raffaella     |
| Ministero della Salute - Programma Integrato Oncologia (P.I.O.) | 2012 | Validazione clinica e analitica di markers biomolecolari di diagnosi oncologica su materiale biologico ottenuto con tecniche non invasive  | Coordinator          | Zito Francesco<br>Alfredo |
| Ministero della Salute - Programma Integrato Oncologia (P.I.O.) | 2008 | Il rispetto della Qualità della Vita nel paziente oncologico fragile. Il ruolo della riabilitazione oncologica: dall'approccio multidisciplinare alle Linee Guida - Rispetto della qualità di vita nel paziente oncologico fragile | Collaborator         | Giotta<br>Francesco       |

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| <p><b>Project Type: WP PROJECT - 5</b></p>  |  |

| Total proposed budget ( Euro ) |                   |                   |   |   |   |
|--------------------------------|-------------------|-------------------|---|---|---|
| Costs                          | TOTAL BUDGET      | Co-Funding        | Project costs proposed to funding Organization (no MOH request) | List of costs proposed for funding to the MOH | Percentage of total proposed to the MOH |
| 1a Staff Salary                | 230.000,00        | 230.000,00        | 0,00  | not permitted                                 | 0,00                                    |
| 1b Researchers' Contracts      | 341.996,00        | 0,00              | 220.998,00  | 120.998,00                                    | 43,23                                   |
| 2 Equipment (Leasing - Rent)   | 31.300,00         | 0,00              | 11.300,00   | 20.000,00                                     | 7,15                                    |
| 3a Supplies                    | 105.000,00        | 0,00              | 0,00  | 105.000,00                                    | 37,51                                   |
| 3b Model Costs                 | 0,00              | 0,00              | 0,00  | 0,00  | 0,00                                    |
| 3c Subcontracts                | 30.000,00         | 0,00              | 30.000,00   | 0,00  | 0,00                                    |
| 3d Patient Costs               | 0,00              | 0,00              | 0,00  | 0,00  | 0,00                                    |
| 4 IT Services and Data Bases   | 0,00              | 0,00              | 0,00  | 0,00  | 0,00                                    |
| 5 Publication Costs            | 10.500,00         | 0,00              | 5.100,00  | 5.400,00                                      | 1,93                                    |
| 6 Convegni                     | 5.000,00          | 0,00              | 2.600,00  | 2.400,00                                      | 0,86                                    |
| 7 Travels                      | 10.100,00         | 0,00              | 5.000,00  | 5.100,00                                      | 1,82                                    |
| 8 Overheads                    | 46.000,00         | 0,00              | 25.000,00   | 21.000,00                                     | 7,50                                    |
| 9 Coordination Costs           | 0,00              | 0,00              | 0,00  | 0,00  | 0,00                                    |
| <b>Total</b>                   | <b>809.896,00</b> | <b>230.000,00</b> | <b>299.998,00</b>   | <b>279.898,00</b>                             | <b>100,00</b>                           |

Report the Co-Funding Contributor:

The personnel involved will dedicate from 5% to 20% of the work activity every year for this project. the staff salary budget has been defined on the basis of the salaries of the personnel involved.

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| <p><b>Project Type: WP PROJECT - 5</b></p>  |  |

| <b>Budget Justification</b>  |  |
|------------------------------|--|
| 1a Staff Salary              | -  |
| 1b Researchers' Contracts    | Contracts n.2 expert in biomedical data processing/support system of decision, n.1 expert in health economy, n. 1 data entry |
| 2 Equipment (Leasing - Rent) | software licences (dataBREAST/ matlab)   |
| 3a Supplies                  | Material for diagnosys RM (Resonance Magnetic) guided  |
| 3b Model Costs               | none   |
| 3c Subcontracts              | Istituto Nazionale di Fisica Nucleare for model optimization   |
| 3d Patient Costs             | none   |
| 4 IT Services and Data Bases | none   |
| 5 Publication Costs          | Open access fee  |
| 6 Convegni                   | International congress participation   |
| 7 Travels                    | Meetings for project activity realization and integration  |
| 8 Overheads                  | -  |
| 9 Coordination Costs         | none   |

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| <p><b>Project Code:</b> NET-2018-12368077-6</p>   | <p><b>Principal Investigator:</b> Rostagno Carlo</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Toscana</p>   |
| <p><b>Project Type: WP PROJECT - 6</b></p>  |  |

**Major Diagnostic Category\*:** Ortopedia

**Project Classification IRG:** Healthcare Delivery and Methodologies

**Project Classification SS:** Health Services Organization and Delivery - HSOD

**Project Keyword 1:** Healthcare organizations, programs, and delivery of services; including those delivered in non-traditional settings; integrated care delivery systems; disease management and modeling; continuous quality improvement; characteristics of the organization and patient outcomes; organizational performance and efficiency; cost-benefit analysis; economics of health care and pharmacoconomics.

**Project Keyword 2:** Health care governance and sustainability

**Project Keyword 3:** Health technology assessment and clinical practice guidelines

**Project duration (months):** 36

**Project Request:**      **Animals:**                       **Humans:**                       **Clinical trial:**

**The object/s of this application is/are under patent copyright Y/N:**

| Investigators, Institution and Role in the Project |       |                    |                       |                             |            |
|--|-------|--------------------|-----------------------|-----------------------------|------------|
|  | Co-PI | Key Personnel      | Institution/Org./Pos. | Role in the project         | Birth Date |
| 1  | X     | Boccaccini Alberto | Regione Toscana       | Research collaborator-Chief | 26/10/1956 |
| 2  |       | De Biase Pietro    | Regione Toscana       | Research Collaborator       | 31/07/1966 |

## Overall Summary

Traumatic injuries account for more than 5 million deaths annually . 40 % are related to uncontrolled hemorrhage , the most common preventable cause of death after severe trauma. As Acute Traumatic Coagulopathy evolves over time, the prothrombotic effects of endothelial cell activation eventually predominate with an increased VTE risk . A less severe pro hemorrhagic condition but a more frequent activation of hemostasis with an high incidence of DVT and PE occurs in major lower limb fractures , in particular in elderly patients with hip fracture. Prothrombin Time (PT) and PTT have major limitations in the diagnosis of trauma induced coagulopathy . The introduction in the emergence of viscoelastic tests (rotational thromboelastometry [ROTEM] ) as a point-of-care procedure for detecting acute coagulopathy after trauma . Aim of present study is to assess the role of trauma coagulopathy in politrauma and major orthopedic trauma and the need for personalized anticoagulant prophylaxis

## Background / State of Art

Current available evidence suggests that Acute Traumatic Coagulopathy is due to massive stimulation of thrombin generation, fibrinogen and platelet consumption, and fibrinolysis by damaged tissues. Tissue damage exposes tissue factor (TF), which is present on all cells within the body that are not normally in contact with the blood, and also the sub-endothelial matrix. Tissue factor drives localized thrombin and fibrin generation. Collagen within the sub-endothelial matrix binds to platelet glycoprotein VI and vWF to glycoprotein Ib, causing platelet activation. Activated platelets adhere to damaged tissues and serve as catalysts for amplification of thrombin generation. These processes are reflected in the

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| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                   | <p><b>Applicant Institution:</b> Toscana</p>   |
| <p><b>Project Type: WP PROJECT - 6</b></p>   |  |

findings of observational clinical studies that show reduced clotting factor and physiological anticoagulant levels , high thrombin generating capacity and reduced platelet counts.As ATC evolves over time, the prothrombotic effects of endothelial cell activation eventually predominate, particularly if hypoxia and acidosis are not alleviated. Many factors but released is from the endothelium exacerbates the prothrombotic environment. Full blood viscoelastic hemostatic assays, such as rotational thromboelastometry (ROTEM) may provide a more complete assessment of hemostasis and as point-of-care devices should be able to provide results in a more clinically useful time frame for targeted therapy in both phases of trauma coagulopathy .

### Hyphotesis and Specific AIMS

#### Hyphotesis and Significance:

More than 5 million deaths annually are related to traumatic injuries. Trauma is the first cause of death in people aged < 45 years. Hemorrhage is the most common preventable cause of death after severe trauma and might be controlled by early aggressive therapy. The bleeding trauma patient represents a significant financial burden for societies, therefore improvements in the management of then massively bleeding trauma patient via educational measures and state-of-the-art clinical practice guidelines should improve outcomes by assisting in the timely identification of bleeding sources, followed by prompt measures to minimise blood loss, restore tissue perfusion and achieve hemodynamic stability. Aggressive plasma administration with high plasma/red blood cells ratio is a frequently employed therapeutic intervention. However allogenic blood products transfusion is associated with increased risks of multiple organ dysfunction syndrome (MODS), adult respiratory distress syndrome (ARDS) and infection, which may prolong hospital state and the need for mechanical ventilation. Major orthopedic surgery has been shown to induce a hypercoagulable state in the postoperative period, and this hypercoagulability has been implicated in the pathogenesis of postoperative thrombotic complications, including deep vein thrombosis, pulmonary embolism, myocardial infarction and ischemic stroke The early acute coagulopathy associated with traumatic injury has recently been recognized as a multifactorial primary condition that results from a combination of bleeding-induced shock, tissue injury-related thrombin-thrombomodulin-complex generation and the activation of anticoagulant and fibrinolytic pathways. Prothrombin Time (PT) and PTT , fibrinogen concentration and platelet count are widely used to guide resuscitation in trauma patients however have major limitations in the diagnosis of trauma induced coagulopathy as they are time-consuming, S, moreover they focus on selected aspects of coagulation, which may not be appropriate for ATC g and lack the desirable sensitivity at the critical time of admission. The introduction in the emergence of viscoelastic tests (rotational thromboelastometry [ROTEM] ) as a point-of-care diagnostic procedure has provided promising results in diagnosis and treatment guide of early trauma induced coagulopathy . As ATC evolves over time, the prothrombotic effects of endothelial cell activation eventually predominate, particularly if hypoxia and acidosis are not alleviated. Therefore as the clinical condition evolves VTE risk increases. The primary outcome of the present study is to assess the effects of ROTEM-guided therapy in patients undergoing orthopedic elective surgery and trauma surgery on the use of allogeneic blood products and postoperative complications. The secondary outcome is to determine the impact on mortality and quality of life at 3 months and one-year after the surgery

#### Preliminary Data:

In previous finalized project RF-2010-2316600 - Evaluation of a multidisciplinary team case management on clinical outcome in a tertiary traumatology center- we evaluated the implementation of a Multidisciplinary Working Group that will include several specialists such as Anesthesiologists Geriatricians, Orthopaedics, Radiologist, nursing Service Managers, Nurses, Physiotherapists , Social Service Staff , Health Care and Social Agency staff in the management of fragility fractures. . Among results from that experience , despite a significant improvement in hospital survival, and decrease in

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| <p><b>Project Type: WP PROJECT - 6</b></p>  |  |

number of complications and length of hospitalization , we noticed the persistence of high rate of post-operative deep venous thrombosis despite standard thrombo prophylaxis. On the other hand patients with major trauma are exposed to an high hemorrhagic risk due to trauma coagulopathy . We expect that preliminary data may support the hypothesis that rotational thromboelastometry [ROTEM] may guide a personalized approach to prophylaxis.

**Specific Aim 1:**

Evaluate the relation in polytrauma patients (ISS > 15) between acute trauma coagulopathy and hospital overall mortality , hemorrhagic related deaths and occurrence of MOF. We will evaluate type and number of allogenic blood products used, incidence of perioperative complications (deep venous thrombosis, pulmonary embolism, ARDS, MODS); hospital, 28 days and 3 months mortality; quality of life using EuroQol questionnaire at 3 and 12 months after the surgery.

**Specific Aim 2:**

Evaluation of the incidence of symptomatic VTE and asymptomatic DVT in polytrauma patients and of their relation with hemostatic abnormalities detected by ROTEM. We will evaluate type and number of allogenic blood products used, incidence of perioperative complications (deep venous thrombosis, pulmonary embolism, ARDS, MODS); hospital, 28 days and 3 months mortality; quality of life using EuroQol questionnaire at 3 and 12 months after the surgery.

**Specific Aim 3:**

In patients with lower limb fracture, and in particular in elderly patients with hip fracture, incidence of DVT is high despite routine anticoagulant prophylaxis. In these patients aim of the study will be to evaluate of a relationship exist between hypercoagulability assessed by ROTEM evaluation and the development of DVT. In a following phase , if the hypothesis will be confirmed , we would like to assess the effects of a personalized anticoagulant dosage targeted on ROTEM results

**Experimental Design Aim 1:**

All patients admitted to SOD Cure Intensive del Trauma e Supporti Extracorporei due to major trauma with and injury severity score > 15 will be included in the study . Blood samples for ROTEM and standard laboratory examination will be collected within 30 minutes from admission. The use of blood products during further resuscitation will be guided by targeted directed strategy . ROTEM will be repeated on day 2 after hospitalization . End points of the study will be in hospital overall mortality , hemorrhagic related deaths and occurrence of MOF. Exclusion criteria: patients with congenital or acquired coagulation disorders, stroke or myocardial infarction within 2 months before surgery, use of clopidogrel, or vitamin K antagonist within 2 to 5 days before surgery.

**Experimental Design Aim 2:**

In patients with polytrauma ( experimental aim 1 ) after the initial hemorrhagic phase (Acute Traumatic Coagulopathy) a prothrombotic condition related to endothelial cell activation develops over time with an increased VTE risk . In trauma patients referred to ICU the incidence of symptomatic VTE is close to 5%. DVT monitoring will begin on day 1 after admission and will be repeated on day 5 and thereafter after scheduled orthopedic or/and general surgery when needed . Incidence of symptomatic VTE and asymptomatic DVT diagnosed by doppler ultrasound will be assessed. Factors related to VTE will be searched for in particular will be evaluated the relation with ROTEM hemostatic changes and blood products administration. Exclusion criteria: patients with congenital or acquired coagulation disorders, stroke or myocardial infarction within 2 months before surgery, use of clopidogrel, or vitamin K antagonist within 2 to 5 days before surgery.

**Experimental Design Aim 3:**

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Every patient referred for long bone lower limb or hip fracture will be evaluated in the Emergency Department of Centro TraumatologicoOrtopedico AOU Careggi, Firenze. Orthopedic evaluation and radiological diagnostic investigation will eventually confirm clinical diagnosis. The patient will undergo venous line positioning, examination by the internal medicine specialist, ECG and laboratory examination. Blood sample for ROTEM examination will be collected within 30 minutes. Deep venous thrombosis prophylaxis with low molecular heparin is started as soon as possible. Surgery will be performed within 48 hours. Duplex ultrasound will be scheduled on day 5-7 from surgery for diagnosis of DVT. Exclusion criteria: patients with congenital or acquired coagulation disorders, stroke or myocardial infarction within 2 months before surgery, use of clopidogrel, or vitamin K antagonist within 2 to 5 days before surgery.

**Picture to support preliminary data:**

**Methodologies and statistical analyses:**

Patient data on demographics, time of injury, pre-hospital fluid administration and vital signs will be collected prospectively. Mechanism of injury will be recorded. The severity of clinical conditions at hospital admission will be evaluated by Injury Severity Score. The total amount of packed red blood cell (PRBC) and plasma units required within the first 24 hours will be recorded. Massive transfusion (MT) is defined as the administration of 10 or more units of PRBC within 24 hours. Values are given as mean (standard deviation) unless stated otherwise. Differences among groups with ATC and need for MT were compared to normal groups by Student's t test or Mann-Whitney U test as appropriate. Receiver operating characteristic (ROC) curves and area under the curve (AUC) were used to compare test accuracy. One-way analysis of variance (ANOVA) was used for detection of differences in transfusion requirements between groups. Statistical calculations were made using SPSS 22.0 (IBM Corp Armonk, NY, USA). A P value <0.05 is considered statistically significant.

**Expected outcomes:**

Information about the pathophysiology of hemostatic abnormalities related to trauma and their relation with hemorrhagic or thrombotic events will allow the choice of treatment.

**Risk analysis, possible problems and solutions:**

The main risk associated concerns data availability, adequate classification of trauma severity, correct timing of blood sampling and examination. Standardized techniques of Doppler ultrasound examination among operators will decrease the risk of misinterpretation.

**Significance and Innovation**

The innovative perspective of the WP lies in the fact that we hope to identify patients at high risk of hemorrhagic or thrombotic complications after trauma in order to prevent adverse clinical outcomes through personalization of pharmacological (and non pharmacological) treatment.

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|  <p><i>Ministero della Salute</i><br/>         Direzione Generale della Ricerca Sanitaria<br/>         e Biomedica e della Vigilanza sugli Enti<br/> <b>BANDO RICERCA FINALIZZATA 2018</b><br/>         esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>         Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
| <p><b>Project Code:</b> NET-2018-12368077-6</p>   | <p><b>Principal Investigator:</b> Rostagno Carlo</p>  |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>  | <p><b>Applicant Institution:</b> Toscana</p>  |
| <p><b>Project Type: WP PROJECT - 6</b></p>  |   |

### Description of the complementary and synergy research team

To achieve WP objectives, the research team involves a multi-disciplinary team of experts in different disciplines such as Internal medicine specialists, cardiologists ,anesthesiologists, orthopedics, experts in blood clotting . The research team as whole has expertise in managing patients with severe high impact trauma or elderly patients with fragility fractures . The presence of both experts in the clinical area and methods (hemostasis laboratory ) will assure a more balanced and compete vision . Moreover, WP Careggi will participate at the Network ensuring all the required support to the WP carrying out trasversal activities. In particular, WP Careggi will provide support to WP SSSA and Milan as a direct application on the field.

### Training and tutorial activities

Not applicable

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
| <p><b>Project Code:</b> NET-2018-12368077-6</p>   | <p><b>Principal Investigator:</b> Rostagno Carlo</p>   |
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| <p><b>Project Type: WP PROJECT - 6</b></p>  |  |

### Bibliography

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- Cardenas JC,et al. Measuring thrombin generation as a tool for predicting hemostatic potential and transfusion requirements following trauma. J Trauma Acute Care Surg
- Levrat A,et al. Evaluation of rotation thrombelastography for the diagnosis of hyperfibrinolysis in trauma patients. Br J Anaesth

### Timeline / Deliverables / Payable Milestones

- At month 18 is a report of preliminary results and analysis.
- At month 36 will be produced a full report with analysis of each aim under investigation.

### Milestones 18 month

Milestone expected at month 18 is a report of preliminary results and analysis.

### Milestones 36 month

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
| <p><b>Project Code:</b> NET-2018-12368077-6</p>   | <p><b>Principal Investigator:</b> Rostagno Carlo</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Toscana</p>   |
| <p><b>Project Type: WP PROJECT - 6</b></p>  |  |

At month 36 will be produced a full report with analysis of each aim under investigation.

### Gantt chart

GANTT-CHART-Careggi.xls

### Equipment and resources available

WP activities will be conducted using facilities available at AOU Careggi Firenze , including the available technical equipment

### Translational relevance and impact for the National Health System (SSN)

WP6 will contribute to the development of advanced management methods tools to support clinical management and policy makers in coping with new technologies and innovations once there are introduced.

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| <p><b>Project Type: WP PROJECT - 6</b></p>  |  |

### PRINCIPAL INVESTIGATOR PROFILE

|                                       |  |
|---------------------------------------|--|
| <p><b>Name</b><br/>Rostagno Carlo</p> | <p><b>Institution</b> Toscana<br/><b>Department/Unit</b> Dipartimento Medicina Sperimentale e Clinica / SOD Medicina Interna e post-chirurgica<br/><b>Position Title</b> Associate Professor of Internal Medicine/<br/>CHIEF</p> |
|---------------------------------------|--|

### Personal Statement

He will coordinate the research group involved in the scientific activities of the WP, giving his contribute to a)setting the WP main goals, in accordance with CoPi and other WP Leaders, and with his collaborators on the basis of the background literature analysis, and of the overall Project significance, b)establishing and maintaining relationships with Institutions participating to the project, Regional/Intraregional Institutions to extract data, c)coordinating analysis and interpretation of findings

| Education/Training - Institution and Location | Degree                    | Year(s) | Field of study                            |
|---|---------------------------|---------|---|
| University of Firenze                         | Degree in Medicine (M.D.) | 6       | Medicine and surgery                      |
| University of Firenze                         | Specialty                 | 4       | Cardiology                                |
| University of Firenze and Roma                | Philosophy Doctor         | 4       | Pathophysiology of pulmonary hypertension |

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
| <p><b>Project Code:</b> NET-2018-12368077-6</p>   | <p><b>Principal Investigator:</b> Rostagno Carlo</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Toscana</p>   |
| <p><b>Project Type: WP PROJECT - 6</b></p>  |  |

| Positions                                 |  |          |   |           |         |
|---|--|----------|---|-----------|---------|
| Institution                               | Division / Research group                    | Location | Position  | From year | To year |
| Azienda Ospedaliera Universitaria Careggi | Medicina Interna e Post-chirurgica           | Firenze  | Chief   | 2013      | 2018    |
| University of Florence                    | Dipartimento Medicina Sperimentale e Clinica | Firenze  | Associate Professor of Internal Medicine                        | 2005      | 2018    |
| Azienda Ospedaliera Careggi               | Heart Surgery Division                       | Firenze  | ChiefPost intensive care  | 2005      | 2011    |
| Azienda Ospedaliera Careggi               | Cardiology Division                          | Firenze  | Associate Chief   | 1993      | 2001    |
| Azienda Ospedaliera Careggi               | Cardiology Division                          | Firenze  | Assistant internal medicine                                     | 1991      | 1993    |
| University of Florence                    | Cardiology Division                          | Pisa     | Clinical Researcher   | 1990      | 1991    |
| University of Florence and Roma           | Sector of Medicine                           | Firenze  | Philosophy Doctorate  | 1986      | 1989    |
| University of Florence                    | Cardiology Division                          | Firenze  | Winner of ministerial grant for the frequency to Specialization | 1982      | 1986    |

**Official H index:** 22.0 ( autocertificated )

**Source:** Scopus

**Scopus Author Id:** 57190077736

**ORCID ID:** 0000-0002-7764-8919

**RESEARCH ID:** k-3558-2018

**Awards and Honors:**

Post-graduate scholarship at Liceo Guido Castelnuovo Firenze (1972-1976)

**Other CV Informations:**

Born in Parma November 29th 1957 Director of Medicina Interna e post-chirurgica AOU Careggi. Specialist in Cardiology. PhD in Fisiopatologia Clinica. He is teacher of cardiology and internal medicine at University of Florence. He is member of the ESC W.G. . Fellow of the ANMCO. Particular field of interest have been several aspects heart surgery , treatment of atrial fibrillation, heart failure and physiopathology of pulmonary circulation . In the last four years he worked in the development of a multidisciplinary hip fracture unit with particular interest in comprehensive preoperative evaluation ,

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
| <p><b>Project Code:</b> NET-2018-12368077-6</p>   | <p><b>Principal Investigator:</b> Rostagno Carlo</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Toscana</p>   |
| <p><b>Project Type: WP PROJECT - 6</b></p>  |  |

recognition and treatment of cardiovascular, in particular thromboembolic, and respiratory complications, evaluation of factors associated with early and late mortality after hip surgery

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
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| <p><b>Project Type: WP PROJECT - 6</b></p>  |  |

### Selected peer-reviewed publications of the PI

| Valid for PI minimum expertise level  |                                     |          |         |     |
|---|-------------------------------------|----------|---------|-----|
| Title   | DOI                                 | PMID     | Cit. ** | P.* |
| Hip fracture unit: beyond orthogeriatrics.  | 10.1007/s11739-018-1818-x           | 29508226 | 0       | F   |
| Role of mitral valve repair in active infective endocarditis: long term results.  | 10.1186/s13019-017-0604-6.          | 28521809 | 1       | F   |
| Factors related to sinus rhythm at discharge after radiofrequency ablation of permanent atrial fibrillation in patients undergoing mitral valve surgery.            | 10.1007/s00380-015-0647-3           | 25680414 | 1       | F   |
| Surgical RF ablation of atrial fibrillation in patients undergoing mitral valve repair for Barlow disease.  | 10.1159/000348565                   | 23736042 | 4       | F   |
| Early Lactococcus lactis endocarditis after mitral valve repair: a case report and literature review.   | 10.1007/s15010-012-0377-8.          | 2325172  | 4       | F   |
| Active infective endocarditis: Clinical characteristics and factors related to hospital mortality.  |                                     | 21154258 | 16      | F   |
| Beta-blocker and angiotensin-converting enzyme inhibitor may limit certain cardiac adverse effects of clozapine.  | 10.1016/j.genhosp psych.2007.09.003 | 18433662 | 17      | F   |
| Five-year echocardiographic results of combined undersized mitral ring annuloplasty and coronary artery bypass grafting for chronic ischaemic mitral regurgitation. |                                     | 17989079 | 78      | C   |
| Usefulness of NT-Pro-BNP and Echocardiography in the Diagnosis of Subclinical Clozapine-Related Cardiotoxicity.   | 10.1097/JCP.0b013e318234ee66.       | 22020348 | 8       | F   |
| Atrial fibrillation after cardiac surgery: incidence, risk factors, and economic burden.  | jjvca. 2010.03.009.                 | 20570180 | 38      | F   |
| Prognostic value of 6-minute walk corridor test inpatients with mild to moderate heart failure . Comparison with other methods of functional evaluation.            |                                     | 12798821 | 158     | F   |
| Silent ischemia in unstable angina is related to an altered cardiac norepinephrine handling.  |                                     | 8504506  | 38      | C   |
| Transient intermittent lymphocyte activation is responsible for the instability of angina.  |                                     | 1516190  | 202     | C   |
| Randomised comparison of subcutaneous heparin, intravenous heparin and aspirin in unstable angina.  |                                     | 7739307  | 45      | C   |

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
| <p><b>Project Code:</b> NET-2018-12368077-6</p>   | <p><b>Principal Investigator:</b> Rostagno Carlo</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Toscana</p>   |
| <p><b>Project Type: WP PROJECT - 6</b></p>  |  |

| Title  | DOI | PMID    | Cit. ** | P.* |
|--|-----|---------|---------|-----|
| Effect of heparin, aspirin or alteplase in reduction of myocardial ischemia in refractory unstable angina. |     | 1969013 | 139     | C   |

\* Position: F=First L=Last C=Correspondent

\*\* Autocertificated

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
| <p><b>Project Code:</b> NET-2018-12368077-6</p>   | <p><b>Principal Investigator:</b> Rostagno Carlo</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Toscana</p>   |
| <p><b>Project Type: WP PROJECT - 6</b></p>  |  |

| For evaluation CV   |                              |          |        |
|---|------------------------------|----------|--------|
| Title   | DOI                          | PMID     | Cit. * |
| In Hospital and 3-Month Mortality and Functional Recovery Rate in Patients Treated for Hip Fracture by a Multidisciplinary Team.                                      | 10.1371/journal.pone.0158607 | 27389193 | 3      |
| Acute coronary syndromes with significant troponin increase in patients with hip fracture prior to surgical repair: differential diagnosis and clinical implications. | 10.1007/s11739-015-1348-8    | 26563767 | 3      |
| New Oral Anticoagulants in Prophylaxis of Venous Thromboembolic Disease in Major Orthopedic Surgery.  |                              | 26721520 | 2      |
| Prophylaxis of venous thromboembolism in major orthopedic surgery: a practical approach.  |                              | 2482323  | 4      |
| Small-dose recombinant activated factor VII (NovoSeven) in cardiac surgery.   |                              | 16632803 | 73     |
| .Influence of endothelial nitric oxide synthase gene polymorphisms (G894T, 4a4b, T-786C) and hyperhomocysteinemia on the predisposition to acute coronary syndromes.  |                              | 14999203 | 67     |
| Treatment options for acute venous thromboembolism in the older patient.  |                              | 9442762  | 4      |
| Acute T-cell activation is detectable in unstable angina.   |                              | 9107167  | 167    |
| Aspirin effect on early and late changes in acute lung injury in sheep.   |                              | 8440792  | 16     |
| Age-related changes in the hemostatic system.   |                              | 8477086  | 56     |

\* Autocertificated

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| <p><b>Project Type: WP PROJECT - 6</b></p>  |  |

| Grant                             |           |  |                      |
|-----------------------------------|-----------|--|----------------------|
| Funded Institution / Country      | Year      | Title  | Position in Projects |
| Progetto Ricerca Finalizzata 2010 | 2012-2016 | Evaluation of a multidisciplinary team case management on clinical outcome in a tertiary traumatology centre | Coordinator          |

**Employment contract extension:**

( Data changed during the moratorium period )

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| <br>Ministero della Salute<br>Direzione Generale della Ricerca Sanitaria<br>e Biomedica e della Vigilanza sugli Enti<br><b>BANDO RICERCA FINALIZZATA 2018</b><br>esercizio finanziario anni 2016-2017 | <b>Project Title:</b><br>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV |
| <b>Project Code:</b> NET-2018-12368077-6   | <b>Principal Investigator:</b> Rostagno Carlo  |
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| <b>Project Type: WP PROJECT - 6</b>  |  |

### Biographical Sketch Contributors 1

|  |                                |   |                         |
|--|--------------------------------|---|-------------------------|
| <b>Name:</b><br>Boccaccini Alberto                   | Institution<br>Regione Toscana | Department/Unit<br>Dipartimento AOU Careggi Firenze | Position Title<br>Chief |
| <b>Education/Training - Institution and Location</b> | <b>Degree</b>                  | <b>Year(s)</b>                                      | <b>Field of study</b>   |
| University of Florence                               | Specialty                      | 3   | Anaesthesiology         |
| University of Florence                               | Degree in Medicine (M.D.)      | 6   | Medicine                |

#### Personal Statement:

As a scientist with a longstanding expertise in healthcare management and performance evaluation for health systems at both regional, national and international level coupled with strong experiences of collaborations with policy makers and healthcare professionals he will contribute together with the PI to the design and scientific supervision of the WP activities.

| Institution                               | Division / Research group                | Location | Position                  | From year | To year |
|---|--|----------|---------------------------|-----------|---------|
| Azienda Ospedaliera Universitaria Careggi | UO Anestesia e Rianimazione in Ortopedia | Firenze  | Director                  | 2016      | 2018    |
| Azienda Ospedaliera Careggi               | UO Anestesia e Rianimazione              | Firenze  | Senior Anaesthesiologist  | 1991      | 2016    |
| Ex USL 10G                                | UO Anestesia e Rianimazione              | Firenze  | Assistant Anaesthesiology | 1990      | 1991    |

#### Awards and Honors

**Official H index:** 4.0 ( autocertificated )

**Source:** Scopus

**Scopus Author Id:** 57198043012

**ORCID ID:** Not Available

**RESEARCH ID:** Not Available

#### Awards and Honors:

At present Chief of Department of Orthopedic Anesthesiology Azienda Ospedaliera Univeristaria Careggi- Firenze, teacher of Anesthesiology at University of Florence . Author of several papers published in International and national Journals

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| <p><b>Project Code:</b> NET-2018-12368077-6</p>   | <p><b>Principal Investigator:</b> Rostagno Carlo</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Toscana</p>   |
| <p><b>Project Type: WP PROJECT - 6</b></p>  |  |

### Biographical Sketch Contributors 2

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| <p><b>Name:</b><br/>De Biase Pietro</p> | <p>Institution: Regione Toscana<br/>Department/Unit: Department of Traumatology and Orthopedics<br/>Position Title: Director</p> |
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| Education/Training - Institution and Location | Degree                    | Year(s) | Field of study               |
|---|---------------------------|---------|------------------------------|
| University of Florence                        | Specialty                 | 3       | Physiatry medicine           |
| University of Florence                        | Specialty                 | 3       | Traumatology and Orthopedics |
| University of Florence                        | Degree in Medicine (M.D.) | 6       | Medicine                     |

**Personal Statement:**

As a scientist with a longstanding expertise in healthcare management and performance evaluation for health systems at both regional, national and international level coupled with strong experiences of collaborations with policy makers and healthcare professionals he will contribute together with the PI to the design and scientific supervision of the WP activities

| Institution         | Division / Research group                            | Location | Position   | From year | To year |
|---------------------|--|----------|------------|-----------|---------|
| AOU Careggi Firenze | Department of Traumatology and General Orthopedics   | Firenze  | Director   | 2016      | 2018    |
| ASL Arezzo          | Orthogeriatrics Unit of the Orthopedic Department    | Arezzo   | Head       | 2011      | 2016    |
| AOU Careggi Firenze | Oncology Orthopedics and Reconstructive Surgery Unit | Firenze  | Consultant | 1999      | 2011    |

**Awards and Honors**

**Official H index:** 11.0 ( autocertificated )

**Source:** Scopus

**Scopus Author Id:** 6602521309

**ORCID ID:** not available

**RESEARCH ID:** not available

**Awards and Honors:**

At present Director of Department of Department of Traumatology and General Orthopedics Azienda Ospedaliera Universitaria Careggi- Firenze, teacher of Orthopedics at University of Florence . Author of several papers published in International and national Journals. NATO mission in the former Yugoslavia during the period from 26/07/1996 to 24/09/1996 and was awarded the NATO medal for services rendered during this period.

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| <p><b>Project Code:</b> NET-2018-12368077-6</p>   | <p><b>Principal Investigator:</b> Rostagno Carlo</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Toscana</p>   |
| <p><b>Project Type: WP PROJECT - 6</b></p>  |  |

### Expertise Research Collaborators

| Selected peer-reviewed publications of the Research Group / Collaborators |   |                                |          |        |
|---|---|--------------------------------|----------|--------|
| Collaborator  | Title   | DOI                            | PMID     | Cit. * |
| De Biase Pietro   | Application of bone morphogenetic proteins to femoral non-unions: a 4-year multicentre experience   |                                | 20082793 | 52     |
| De Biase Pietro   | Extraarticular knee resection with prosthesis-proximal tibia-extensor apparatus allograft for tumors invading the knee  | 10.1007/s11999-011-1882-2      | 21484473 | 22     |
| De Biase Pietro   | The use of an injectable calcium sulphate/calcium phosphate bioceramic in the treatment of osteonecrosis of the femoral head  | 10.1155/2016/2606521           | 2242693  | 30     |
| De Biase Pietro   | Modular endoprostheses for nonneoplastic conditions: Midterm complications and survival   | 10.1155/2016/2606521           | 28050552 | 1      |
| Boccaccini Alberto  | The optimal dose of local anaesthetic in the orthogonal two-needle technique. Extent of sensory block after the injection of 20, 30 and 40 mL of anaesthetic solution |                                | 9202914  | 10     |
| Boccaccini Alberto  | Ultrasound identification of nerve cords in the infraclavicular fossa: A clinical study   |                                | 22240617 | 7      |
| Boccaccini Alberto  | Respiratory effect of interscalene brachial plexus block vs combined infraclavicular plexus block with suprascapular nerve block for arthroscopic shoulder surgery    | 10.1016/j.jclinane.2017.11.029 | 29195098 | 0      |

\* Autocertificated

| Grant                        |      |       |                      |                    |
|------------------------------|------|-------|----------------------|--------------------|
| Funded Institution / Country | Year | Title | Position in Projects | Collaborator       |
| NA                           | 0    | NA    | Coordinator          | Boccaccini Alberto |

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| Total proposed budget ( Euro ) |                   |                  |   |   |   |
|--------------------------------|-------------------|------------------|---|---|---|
| Costs                          | TOTAL BUDGET      | Co-Funding       | Project costs proposed to funding Organization (no MOH request) | List of costs proposed for funding to the MOH | Percentage of total proposed to the MOH |
| 1a Staff Salary                | 45.000,00         | 45.000,00        | 0,00  | not permitted                                 | 0,00                                    |
| 1b Researchers' Contracts      | 140.000,00        | 0,00             | 0,00  | 140.000,00                                    | 50,00                                   |
| 2 Equipment (Leasing - Rent)   | 105.500,00        | 0,00             | 25.500,00   | 80.000,00                                     | 28,57                                   |
| 3a Supplies                    | 0,00              | 0,00             | 0,00  | 0,00  | 0,00                                    |
| 3b Model Costs                 | 0,00              | 0,00             | 0,00  | 0,00  | 0,00                                    |
| 3c Subcontracts                | 0,00              | 0,00             | 0,00  | 0,00  | 0,00                                    |
| 3d Patient Costs               | 0,00              | 0,00             | 0,00  | 0,00  | 0,00                                    |
| 4 IT Services and Data Bases   | 28.000,00         | 0,00             | 10.000,00   | 18.000,00                                     | 6,43                                    |
| 5 Publication Costs            | 10.600,00         | 0,00             | 5.000,00  | 5.600,00                                      | 2,00                                    |
| 6 Convegni                     | 2.800,00          | 0,00             | 0,00  | 2.800,00                                      | 1,00                                    |
| 7 Travels                      | 5.600,00          | 0,00             | 0,00  | 5.600,00                                      | 2,00                                    |
| 8 Overheads                    | 32.500,00         | 0,00             | 4.500,00  | 28.000,00                                     | 10,00                                   |
| 9 Coordination Costs           | 0,00              | 0,00             | 0,00  | 0,00  | 0,00                                    |
| <b>Total</b>                   | <b>370.000,00</b> | <b>45.000,00</b> | <b>45.000,00</b>  | <b>280.000,00</b>                             | <b>100,00</b>                           |

Report the Co-Funding Contributor:

Staff-salary dedicated to the project

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| <p><b>Project Type: WP PROJECT - 6</b></p>  |  |

| <b>Budget Justification</b>  |  |
|------------------------------|--|
| 1a Staff Salary              | PI and CoPI have a permanent position in SSN   |
| 1b Researchers' Contracts    | 1 research contract for 3 years - 1 contract for post-doc grant for 3 years  |
| 2 Equipment (Leasing - Rent) | 1 rotational Thromboelastogrph - 1 echograph   |
| 3a Supplies                  | -  |
| 3b Model Costs               | -  |
| 3c Subcontracts              | -  |
| 3d Patient Costs             | -  |
| 4 IT Services and Data Bases | Software/database/It services will be purchased  |
| 5 Publication Costs          | The results will be published at the end of the projects   |
| 6 Convegni                   | Estimate of expenditure for conferences for the dissemination of research results  |
| 7 Travels                    | Travel and accommodation expenses incurred by researchers for the participation to conferences to disseminate research results |
| 8 Overheads                  | -  |
| 9 Coordination Costs         | -  |

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| <p><b>Project Code:</b> NET-2018-12368077-7</p>   | <p><b>Principal Investigator:</b> Passino Claudio</p>  |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Toscana</p>   |
| <p><b>Project Type: WP PROJECT - 7</b></p>  |  |

**Major Diagnostic Category\*:** Ortopedia

**Project Classification IRG:** Healthcare Delivery and Methodologies

**Project Classification SS:** Health Services Organization and Delivery - HSOD

**Project Keyword 1:** Healthcare organizations, programs, and delivery of services; including those delivered in non-traditional settings; integrated care delivery systems; disease management and modeling; continuous quality improvement; characteristics of the organization and patient outcomes; organizational performance and efficiency; cost-benefit analysis; economics of health care and pharmacoconomics.

**Project Keyword 2:** Health care governance and sustainability

**Project Keyword 3:** Health technology assessment and clinical practice guidelines

**Project duration (months):** 36

**Project Request:**      **Animals:**                       **Humans:**                       **Clinical trial:**

**The object/s of this application is/are under patent copyright Y/N:**

| Investigators, Institution and Role in the Project |       |               |                            |                           |            |
|--|-------|---------------|----------------------------|---------------------------|------------|
|  | Co-PI | Key Personnel | Institution/Org./Pos.      | Role in the project       | Birth Date |
| 1  | X     | Nuti Sabina   | Scuola Superiore Sant'Anna | Co-Principal Investigator | 06/06/1959 |

## Overall Summary

Once protocols, guidelines are set and innovations introduced a crucial factor is to measure performance in order to put into action feedback and feedforward actions. Scholars asked for implementing measuring systems to assess the performance obtain in real setting.

aims at developing the general aim 3 of the overall proposal: to develop a method to measure the performance of the model created and tested by the Regions based on the recent innovation introduced. The system will be designed considering multiple dimensions and different data sources available. In particular, the WP7 will implement the performance measurement for the orthopedic and cardiovascular disease areas across the regions involved. Primary data will be collected across the institutions involved.

## Background / State of Art

Governance of healthcare systems requires multiple strategies, actions, as well as tools to manage performance in order to achieve value for money (Nuti et al. 2015). Advancements in knowledge and innovation aspire to enhance health benefits. Agencies are now focusing on regulating the introduction of effective innovation based on multicriteria assessment models (Banta, 2003). Yet evidence is scarce on what happens after the introduction phase, i.e. what is the gap between the evidence based on RCT studies and the results obtained in the implementation phase in real world (Berger et al 2017, Gill et al. 2016).

For instance, ARNO database highlighted that CHF patients in Italian healthcare organizations have different characteristics

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than those enrolled into RCT studies (e.g. more elder and more female patients) (Maggioni et al. 2016). More research should be carried out measuring the impact on real world conditions.

Systematic performance measurement, related to the results obtained thanks to the innovation introduced, may help policy makers, professionals and managers to understand whether guidelines and protocols should be changed in using such technologies or to monitor if such guidelines and protocols have been properly applied.

SSSA WP aims at developing performance measurement systems to assess the results obtained along clinical care pathways after the introduction of innovative drugs (e.g. direct oral anticoagulants, sacubitril/valsartan), devices (e.g. transcatheter aortic valve implantation) and technology (e.g. telemonitoring), also by using patient reported outcome and experience. Particularly, SSSA will assess the performance of cardiovascular (particularly focusing on heart failure, HF) and orthopedic care, comparing results both within the region and across the regions participating to the Network.

## Hyphotesis and Specific AIMS

### Hyphotesis and Significance:

The introduction of a new or innovative technology in the health care pathway or into the organization in general has to be assessed not only in the adoption phase (ex-ante) but also in the current application (ex-post). In particular, the systematic monitoring of performance results of the overall pathway, including specific indicators for the innovative technology, may help not only to better assess the overall impact of this innovation along the patient's path but also to reshape organizational aspects to improve the effective integration of innovation into the path. In this perspective, information gathered from patients both on outcome and experience are valuable

### Preliminary Data:

The research group of SSSA has gained extensive experience in collection, harmonization, and use of big data to promote performance measurement and information sharing directed to policy-makers and managers. Researchers have been involved in the development of the multi-dimensional Inter-Regional Performance Evaluation System (IRPES) that uses standardized and interoperable administrative data flows to assess healthcare performance between and within regions, health authorities and public health districts. The IRPES system discloses healthcare performance in multiple domains. The IRPES system is made up of more than 300 indicators which measure the multidimensional performance of each healthcare organization (Nutti et al. 2015). The following are monitored: population's health status; capacity to pursue regional strategies; clinical performance; efficiency and financial performance; patient satisfaction; and staff satisfaction. The indicators are calculated yearly, by using administrative databases. The aim of the IRPES is to assess and monitor health system performance at a regional and local level: indicators are computed with regional and local granularity (both local health authorities and teaching hospitals). In addition, the SSSA may rely on the expertise acquired in building up PROs and PREs in several care pathways (Nutti et al 2017). In addition a number of clinical indicators have been so far identified for assessing prognosis in HF (Emdin et al 2009), whose applicability in evaluating the impact of a specific intervention could be tested.

### Specific Aim 1:

The first aim of the WP7 is the identification of indicators to be monitored in order to analyze performance gap between real world evidence and literature and/or guidelines and protocols. Selection of indicators will be agreed with clinical professionals involved in the Network project, related to the clinical guidelines applied on the topic investigated by the Network.

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**Specific Aim 2:**

To identify and development specific questionnaires to be administered to patients in order to understand the real impact of the innovation introduced

**Specific Aim 3:**

Overall multicriteria performance assessment of selected innovation in CHF and orthopedic paths both in terms of appropriate application of guidelines, clinical indicators and patients reported outcome and experience

**Experimental Design Aim 1:**

Identification of the innovation/technologies to be analyzed in Tuscany related to the CHF and orthopedic paths (and others selected by the other Network partners). Selection & development of indicators will be based on literature review and expert discussions. Research protocols shared across the Network members will drive the linkage and extraction of patient information from the administrative databases (e.g. inhabitants and mortality registry, GPs records, specialist care, drug dispensing, hospital discharge, long-term care, palliative care).

**Experimental Design Aim 2:**

Primary data will be collected using validated international PRO survey. Such instruments are based on underlying conceptual framework developed from extensive qualitative research with patients, examination of the research literature, and engagement of healthcare professionals

**Experimental Design Aim 3:**

Identification of eligible patients will be based on the definition of a common shared protocol from enrolled providers. Eligible patients will be asked for a consent to be enrolled in the study. Information on HQoL, preferences, overall satisfactions and use of services (in terms of process, quality of care) will be collected as part of the customer satisfaction assessment (therefore, no ethical committee approval is required). Systematic collection will be developed using webbased survey. In addition, qualitative methods will be used to assess caregivers experience in coping with the disease, such as focus group activities. Patients information together with administrative data collected across the Regions will be used to compare the expected outcome (from literature, guidelines or local registries (Arzilli C et al 2018) and the real word evidence

**Picture to support preliminary data:**

**Methodologies and statistical analyses:**

Retrospective observational studies will be developed using regional/hospital administrative healthcare and clinical data at individual level following validated protocols. Indicators measuring quality, process, use of resources across the care path and outcomes will be measured for the integrated care path. Mixed models will be used to evaluate how patterns of care may vary according to macro-level determinants and individual socioeconomic characteristics. Measures of use of resources (costs) and outcomes will be jointly analysed to determine value for money. The set of measured indicators will be compared across Network care providers in a benchmarking framework. For the cohort of CHF patients, administrative data will also be linked at network level.

Periodical surveys will be conducted on CHF and orthopedic patients in Tuscany (and eventually also in other organizations of the Network) to collect patient reported outcome and experience measures to be included into the overall performance

Sent date: 20/05/2018 21.34

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Sent date of moratorium changes: 01/06/2018 15.17

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assessment system at healthcare pathway level.

All the results will be disseminated and discussed with multiple stakeholders of the Network

#### Expected outcomes:

- Literature review on expected outcome for HF patients and orthopedic paths for the selected innovations
- Selection of measurements based on literature review, clinical expert meetings, international guidelines and data availability for the innovations introduced in the Network
- scientific review of the use and impact of PROMs for specific interventions
- Reports on the gap between the real world evidence and the expected standard results.

#### Risk analysis, possible problems and solutions:

The main risk associated concerns data availability. We have reduced this risk by designing two strategies to get appropriate data: a) to use regional administrative databases and b) to pool data from hospital level administrative database in a sample of hospitals/local health authorities. To assure complete access to data the PI and CoPI will monitor/support the procedure of data collection. For data analysis, the major risk is associated with the homogeneity of coding and labelling of records across multiple databases. We mitigate this risk by involving healthcare professionals to discuss and share common protocols for data collection.

#### Significance and Innovation

The innovative perspective of the WP lies in the fact that we will set up a systematic monitoring systems for real world evidence aimed at giving an objective measure of the impact of a specific innovation using a multidimensional approach. This approach could provide the stakeholders of the participating Regions the key elements for understanding the best way to implement new technologies in the different care paths.

#### Description of the complementary and synergy research team

To achieve WP objectives, the research team involves a multi-disciplinary team of experts in different disciplines such as healthcare management, health economics and statistics. The research team as whole has also expertise in use of extensive and well characterized individual health data, including administrative data, clinical registries and data from surveys to patients and clinical professionals. The research team has experience in engaging patients (patient associations) and caregivers for focus group activities especially in the area of chronic care. Prior experience also in running expert meetings with clinicians, nurses and scientific groups to gather inputs and assess respective needs and expectations is ground in the research team.

The presence of both experts in the clinical area and methods will assure a more balanced and complete vision supporting the WP and Network project activities.

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti</p> <p><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
| <p><b>Project Code:</b> NET-2018-12368077-7</p>  | <p><b>Principal Investigator:</b> Passino Claudio</p>  |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                   | <p><b>Applicant Institution:</b> Toscana</p>   |
| <p><b>Project Type: WP PROJECT - 7</b></p>   |  |

### Training and tutorial activities

WP7 mission is among others to support and give guidance to the Network members on the identification of performance measures. To this end, residential training meetings will be scheduled with the Network members to provide fundamentals and advanced knowledge on the effective use of performance evaluation tools for healthcare improvements. To facilitate knowledge transfer, case studies could be developed. The WP will also devote time and resource to the training of healthcare professionals involved in the collection of patient data (e.g. PROMs).

### Bibliography

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9. S.Nuti, F. Vola, A. Bonini, M. Vainieri (2015) Making governance work in the health care sector: evidence from a 'natural experiment' in Italy. *Health Economics Policy and Law*
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### Timeline / Deliverables / Payable Milestones

- D01 Selection of innovation to be tested (Report)- Month 6
- D02 Selection of performance measurement indicators to be collected harmonizing and standardizing information from administrative health databases (Report)-Month 8
- D03 Systematic literature review of the use and impact of PROMs for specific innovation (Report)-Month 15
- D04 Presentation of the platform to collect patient survey data (demonstration) Month 20
- D05 Report on preliminary data from the analysis of indicators based on administrative healthcare data (Report)-Month 30
- D06 Report summarising the results of the analysis of both indicators from administrative and survey data (Report)-Month 34

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
| <p><b>Project Code:</b> NET-2018-12368077-7</p>   | <p><b>Principal Investigator:</b> Passino Claudio</p>  |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Toscana</p>   |
| <p><b>Project Type: WP PROJECT - 7</b></p>  |  |

### Milestones 18 month

Milestone expected at month 18 is a report on the identification of innovation to be tested, their expected outcome from literature, and preliminary data analyses.

### Milestones 36 month

At month 36 a full report with the gap analysis between the literature and the real world data collected using administrative data, patients reported experience and outcome and registries.

### Gantt chart

WP7-Gantt-SantAnna.docx

### Equipment and resources available

WP7 activities will be conducted using facilities available at the Scuola Superiore Sant'Anna of Pisa, including the available technical equipment of the Management and Health Laboratory. Since 2006, the Laboratory has been administering questionnaires to patients/health service users. To manage the data-collecting phase, the Laboratory is equipped with a scanner for the optical reading of paper questionnaires and with Computer Assisted Telephone Interviewing and Computer Assisted Web Interviewing platforms. This technical equipment makes possible to define the administration strategy accordingly to the objective and the characteristics of the population target of the study. Additionally, statistical software packages are available to the research team to conduct analysis, such as SAS and STATA software, that allow performing analysis on big data.

### Translational relevance and impact for the National Health System (SSN)

WP7 will contribute to the development of advanced management methods tools to support clinical management and policy makers in coping with new technologies and innovations once they are introduced.

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
| <p><b>Project Code:</b> NET-2018-12368077-7</p>   | <p><b>Principal Investigator:</b> Passino Claudio</p>  |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Toscana</p>   |
| <p><b>Project Type: WP PROJECT - 7</b></p>  |  |

### PRINCIPAL INVESTIGATOR PROFILE

|                                 |  |
|---------------------------------|--|
| <p>Name<br/>Passino Claudio</p> | <p>Institution<br/>Toscana<br/>Department/Unit<br/>Institute of life sciences<br/>Position Title<br/>Associate Professor</p> |
|---------------------------------|--|

### Personal Statement

Together with CoPi, he will coordinate the research group involved in the scientific activities of the WP7, giving his contribute in a) setting the WP main goals, in accordance with CoPi, with other WP Leaders, and with his collaborators on the basis of the background literature analysis, and of the overall Project significance, b) defining analysis tools, caring for standardization of approaches with regard to comparative analysis among Regional Networks, c) establishing and maintaining relationships with Institutions participating to the project, Stakeholders representatives, Regional/Intraregional Institutions to extract data, d) coordinating analysis and interpretation of findings.

| Education/Training - Institution and Location | Degree                    | Year(s) | Field of study       |
|---|---------------------------|---------|----------------------|
| University of Pavia                           | Degree in Medicine (M.D.) | 6       | Medicine and surgery |
| University of Pavia                           | Specialty                 | 4       | Cardiology           |
| University of Pisa                            | Specialty                 | 4       | Sports medicine      |

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
| <p><b>Project Code:</b> NET-2018-12368077-7</p>   | <p><b>Principal Investigator:</b> Passino Claudio</p>  |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Toscana</p>   |
| <p><b>Project Type: WP PROJECT - 7</b></p>  |  |

| Positions   |   |          |  |           |         |
|---|---|----------|--|-----------|---------|
| Institution   | Division / Research group                       | Location | Position                                       | From year | To year |
| Scuola Superiore Sant'Anna  | Institute of Life Sciences                      | Pisa     | Associate Professor of Cardiovascular Medicine | 2015      | 2018    |
| Fondazione Toscana Gabriele Monasterio per la Ricerca Medica e di Sanità Pubblica | Cardiology and Cardiovascular Medicine Division | Pisa     | Associate Chief                                | 2014      | 2018    |
| Fondazione Toscana Gabriele Monasterio per la Ricerca Medica e di Sanità Pubblica | Cardiovascular Medicine Division                | Pisa     | Chief  | 2012      | 2014    |
| Scuola Superiore Sant'Anna  | Sector of Medicine                              | Pisa     | Assistant professor                            | 2006      | 2012    |
| CNR-Institute of Clinical Physiology  | Cardiology Division                             | Pisa     | Clinical Researcher                            | 2000      | 2006    |

**Official H index:** 39.0 ( autocertificated )

**Source:** Scopus

**Scopus Author Id:** ID: 56868372700

**ORCID ID:** <http://orcid.org/0000-0002-0723-4753>

**RESEARCH ID:** K-3809-2018

**Awards and Honors:**

Graduate scholarship at the Collegio Ghislieri in Pavia (1988-1994)

Post-graduate scholarship at the Collegio Ghislieri in Pavia (1994-1996)

**Other CV Informations:**

20-year clinical experience in cardiovascular disease. Vice-Director of the Division of Cardiology and Cardiovascular Medicine at the Fondazione Toscana Gabriele Monasterio. Author of 228 papers in peer-reviewed journals, editor of 2 books, member of the Editorial Board of PlosOne and reviewer for several international Journals. Internationally recognized high quality research output, via collaborations with renowned international research groups, namely in the field of cardiovascular diseases, heart failure and regulatory control of cardiovascular system. Member of Tuscany Regional Ethical Committee, Nord-West section, since 2010; Advisor for clinical trialing for the Fondazione G. Monasterio of Pisa.

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
| <p><b>Project Code:</b> NET-2018-12368077-7</p>   | <p><b>Principal Investigator:</b> Passino Claudio</p>  |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Toscana</p>   |
| <p><b>Project Type: WP PROJECT - 7</b></p>  |  |

### Selected peer-reviewed publications of the PI

| Valid for PI minimum expertise level  |                                      |          |         |     |
|---|--------------------------------------|----------|---------|-----|
| Title   | DOI                                  | PMID     | Cit. ** | P.* |
| Ventricular repolarization is prolonged in nondipper hypertensive patients: Role of left ventricular hypertrophy and autonomic dysfunction    | 10.1097/00004872-200302000-00038     |          | 42      | F   |
| Neuro-hormonal activation predicts ventilatory response to exercise and functional capacity in patients with heart failure.                   | 10.1016/j.ejheart.2005.05.007        | 16112902 | 40      | F   |
| Aerobic training decreases B-type natriuretic peptide expression and adrenergic activation in patients with heart failure                     | 10.1016/j.jacc.2005.12.050           | 16682309 | 97      | F   |
| Prognostic value of combined measurement of brain natriuretic peptide and triiodothyronine in heart failure                                   | 10.1016/j.cardfail.2008.08.008       | 19181292 | 25      | F   |
| Combined increased chemosensitivity to hypoxia and hypercapnia as a prognosticator in heart failure   | 10.1016/j.jacc.2009.02.030           | 19460611 | 54      | L   |
| Thirty years of the heart as an endocrine organ: physiological role and clinical utility of cardiac natriuretic hormones.                     | 10.1152/ajpheart.00226.2011          | 21551272 | 112     | L   |
| Prognostic value of plasma renin activity in heart failure.   | 10.1016/j.amjcard.2011.03.034        | 21545993 | 36      | L   |
| Metabolic exercise test data combined with cardiac and kidney indexes, the MECKI score: A multiparametric approach to heart failure prognosis | 10.1016/j.ijcard.2012.06.113         | 22795401 | 57      | L   |
| Markers of fibrosis, inflammation, and remodeling pathways in heart failure.  | 10.1016/j.cca.2014.09.006            | 25218738 | 25      | F   |
| Cheyne-Stokes Respiration, Chemoreflex, and Ticagrelor-Related Dyspnea  | 1004-12-2016<br>10.1056/NEJMc1601662 | 27602681 | 2       | L   |
| Influence of central apneas and chemoreflex activation on pulmonary artery pressure in chronic heart failure                                  | 10.1016/j.ijcard.2015.09.007         | 26397412 | 4       | L   |
| Hypovitaminosis D in patients with heart failure: effects on functional capacity and patients' survival.                                      | 10.1007/s12020-017-1282-9            | 28337657 | 2       | L   |
| Prognostic Significance of Central Apneas Throughout a 24-Hour Period in Patients With Heart Failure  | 10.1016/j.jacc.2017.07.740           | 28882233 | 2       | L   |
| Predicting readmissions after hospitalization for heart failure: Medical reasoning vs calculators.  | 10.1016/j.ijcard.2017.03.045         | 28407979 | 0       | L   |

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
| <p><b>Project Code:</b> NET-2018-12368077-7</p>   | <p><b>Principal Investigator:</b> Passino Claudio</p>  |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Toscana</p>   |
| <p><b>Project Type: WP PROJECT - 7</b></p>  |  |

| Title  | DOI                      | PMID     | Cit. ** | P.* |
|--|--------------------------|----------|---------|-----|
| N-terminal fraction of pro-B-type natriuretic peptide versus clinical risk scores for prognostic stratification in chronic systolic heart failure. | 10.1177/2047487318766580 | 29569494 | 0       | L   |

\* Position: F=First L=Last C=Correspondent

\*\* Autocertificated

| For evaluation CV  |                                    |          |        |  |
|--|------------------------------------|----------|--------|--|
| Title  | DOI                                | PMID     | Cit. * |  |
| Demonstrable cardiac reinnervation after human heart transplantation by carotid baroreflex modulation of RR interval.  |                                    | 7586257  | 127    |  |
| Human atherosclerotic plaques contain gamma-glutamyl transpeptidase enzyme activity.   | 10.1161/01.CIR.0000120558.41356.E6 | 15037540 | 236    |  |
| Neuro-hormonal activation predicts ventilatory response to exercise and functional capacity in patients with heart failure                                     | 10.1016/j.heart.2005.05.007        | 16112902 | 35     |  |
| Aerobic training decreases B-type natriuretic peptide expression and adrenergic activation in patients with heart failure                                      | 10.1016/j.jacc.2005.12.050         | 16682309 | 97     |  |
| Combined increased chemosensitivity to hypoxia and hypercapnia as a prognosticator in heart failure  | 10.1016/j.jacc.2009.02.030         | 19460611 | 54     |  |
| Metabolic exercise test data combined with cardiac and kidney indexes, the MECKI score: A multiparametric approach to heart failure prognosis                  | 10.1016/j.ijcard.2012.06.113       | 22795401 | 57     |  |
| Myocardial Fibrosis as a Key Determinant of Left Ventricular Remodeling in Idiopathic Dilated Cardiomyopathy A Contrast-Enhanced Cardiovascular Magnetic Study | 10.1161/CIRCIMAGING.113.000438     | 23934992 | 52     |  |
| Neutrophil Gelatinase-Associated Lipocalin for Acute Kidney Injury During Acute Heart Failure Hospitalizations: The AKINESIS Study.                            | 10.1016/j.jacc.2016.06.055         | 27659464 | 9      |  |
| Cheyne-Stokes Respiration, Chemoreflex, and Ticagrelor-Related Dyspnea   | 10.1056/NEJMc1601662               | 27602681 | 2      |  |
| Prognostic Value of Soluble Suppression of Tumorigenicity-2 in Chronic Heart Failure A Meta-Analysis JACC-heart failure  | 10.1016/j.jchf.2016.09.010         | 27816512 | 10     |  |

\* Autocertificated

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| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Toscana</p>   |
| <p><b>Project Type: WP PROJECT - 7</b></p>  |  |

| Grant  |           |   |                      |
|--|-----------|---|----------------------|
| Funded Institution / Country   | Year      | Title   | Position in Projects |
| Scuola Superiore Sant'Anna, Fondazione Monasterio, CNR Institute of Clinical Physiology Funder: Tuscany Region Call 2014 Nutraceutica  | 2015-2017 | CardioMir.San.To: "Studio delle proprietà cardiorigenerative di microRNA contenuti nelle bacche d'uva sangiovese toscano nella prevenzione dello scompenso cardiaco"                              | Collaborator         |
| Scuola Superiore Sant'Anna, Fondazione Monasterio, University of Siena Italy Funder: Tuscany Region Call 2014 Nutraceutica   | 2015-2017 | FATE PRE.SCO "Valorizzazione delle proprietà epigenetiche dei genotipi antichi toscani di frumento tenero biofortificati con ferro e zinco nella prevenzione dell'insufficienza cardiaca cronica" | Collaborator         |
| Fondazione Monasterio, ASL5 and CNR, Italy Funder: Italian Ministry of Health RF-2011-02348236.  | 2014-2017 | CARPEDIEM - Comorbidity And Risk Profiles Evaluation in Diabetes and hEart Morbidities  | Coordinator          |
| Regione Toscana, Italy, Yorkshire, UK, Lodz, Poland Funder: 7th Framework Programme, Regions of Knowledge Health, Grant agreement n.ro 266262  | 2010-2013 | RICHARD: Regional ICT based Clusters for Healthcare Applications and R&D Integration  | Collaborator         |
| CONSORZIO PISA RICERCHE, Fondazione Monasterio, CAEN and Caribel, Italy CITIC and Hospitales Universitarios "Virgen del Rocío", Spain Mediasoft and Zdravstveni Dom Koper, Slovenia Funder: 1st-call of the European AAL Joint Programme | 2009-2011 | Health at Home project (H@H)  | Collaborator         |

**Employment contract extension:**

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| <p><b>Project Code:</b> NET-2018-12368077-7</p>   | <p><b>Principal Investigator:</b> Passino Claudio</p>  |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Toscana</p>   |
| <p><b>Project Type: WP PROJECT - 7</b></p>  |  |

### Biographical Sketch Contributors 1

| <p><b>Name:</b><br/>Nutti Sabina</p>          | <p>Institution Scuola Superiore Sant'Anna<br/>Department/Unit Scuola superiore Sant'Anna<br/>Position Title Full Professor in management</p> |         |                         |
|---|--|---------|-------------------------|
| Education/Training - Institution and Location | Degree   | Year(s) | Field of study          |
| University of Pisa                            | MSc in Political Science   | 5       | POLITICAL SCIENCE       |
| Bocconi University, Milan                     | Master   | 1       | BUSINESS ADMINISTRATION |

**Personal Statement:**

As a scientist with a longstanding expertise in healthcare management and performance evaluation for health systems at both regional, national and international level coupled with strong experiences of collaborations with policy makers and healthcare professionals she will contribute together with the PI to the design and scientific supervision of the WP activities.

| Institution | Division / Research group | Location | Position   | From year | To year |
|-------------|---------------------------|----------|--|-----------|---------|
| SSSA        | Institute of Management   | Pisa     | Deputy Director Advanced Training (Alta Formazione) in healthcare management                                     | 2000      | 2004    |
| SSSA        | Institute of Management   | Pisa     | Associate Professor of Economics and Business Management and responsible of the Management and Health Laboratory | 2005      | 2014    |
| SSSA        | Institute of Management   | Pisa     | Full Professor of Economics and Business Management and responsible of the Management and Health Laboratory      | 2014      | 2018    |

**Awards and Honors**

**Official H index:** 9.0 ( autocertificated )

**Source:** Scopus

**Scopus Author Id:** 26028416800

**ORCID ID:** <https://orcid.org/0000-0002-2093-1828>

**RESEARCH ID:** K-3796-2018

**Awards and Honors:**

Expert Panel members (2016-2019) - European Commission

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV</p> |
| <p><b>Project Code:</b> NET-2018-12368077-7</p>   | <p><b>Principal Investigator:</b> Passino Claudio</p>  |
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| <p><b>Project Type: WP PROJECT - 7</b></p>  |  |

### Expertise Research Collaborators

| Selected peer-reviewed publications of the Research Group / Collaborators |  |                                 |      |        |
|---|--|---------------------------------|------|--------|
| Collaborator  | Title  | DOI                             | PMID | Cit. * |
| Nuti Sabina   | Does feedback influence patient - professional communication? Empirical evidence from Italy  | 10.1016/j.healthpol.2014.02.001 |      | 8      |
| Nuti Sabina   | Applying discrete choice modelling in a priority setting: An investigation of public preferences for primary care models                         | 10.1007/s10198-013-0542-8       |      | 5      |
| Nuti Sabina   | How do hospitalization experience and institutional characteristics influence inpatient satisfaction? A multilevel approach                      | 10.1002/hpm.2201                |      | 9      |
| Nuti Sabina   | The equity lens in the health care performance evaluation system   | 10.1002/hpm.2195                |      | 7      |
| Nuti Sabina   | Is variation management included in regional healthcare governance systems Some proposals from Italy   | 10.1016/j.healthpol.2013.08.003 |      | 12     |
| Nuti Sabina   | Making governance work in the health care sector: Evidence from a 'natural experiment' in Italy  | 10.1017/S1744133115000067       |      | 11     |
| Nuti Sabina   | Bridging the gap between theory and practice in integrated care: The case of the diabetic foot pathway in Tuscany                                | 10.5334/ijic.1991               |      | 2      |
| Nuti Sabina   | Catching and monitoring clinical innovation through performance indicators. the case of the breast conserving surgery indicator                  | 10.1186/s13104-017-2597-6       |      | 0      |
| Nuti Sabina   | Building medical knowledge from real world registries: The case of heart failure   | 10.1016/j.ijcha.2018.03.008     |      | 0      |
| Nuti Sabina   | Patient satisfaction, patients leaving hospital against medical advice and mortality in Italian university hospitals: A cross-sectional analysis | 10.1186/s12913-018-2846-y       |      | 0      |

\* Autocertificated

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| <p><b>Project Code:</b> NET-2018-12368077-7</p>   | <p><b>Principal Investigator:</b> Passino Claudio</p>  |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Toscana</p>   |
| <p><b>Project Type: WP PROJECT - 7</b></p>  |  |

| Grant   |           |   |                      |              |
|---|-----------|---|----------------------|--------------|
| Funded Institution / Country                            | Year      | Title   | Position in Projects | Collaborator |
| European Commission - Structural Reform Support Service | 2017-2018 | Developing Health System Performance Assessment for Slovenia and Latvia   | Coordinator          | Nutti Sabina |
| Agenas - CCM  | 2012-2014 | Valutazione degli esiti per la riduzione delle disuguaglianze di accesso ai servizi di provata efficacia in popolazioni deboli  | Coordinator          | Nutti Sabina |
| Commissione d'Inchiesta del Senato                      | 2009-2011 | Commissione d'Inchiesta del Senato: Attività di ricerca sui livelli di efficienza/efficacia del SSN   | Coordinator          | Nutti Sabina |
| Italian Ministry of Health                              | 2012      | Strumenti e metodi per l'analisi integrata dei risultati a supporto dei processi di valutazione nella sanità pubblica   | Coordinator          | Nutti Sabina |
| Italian Ministry of Health                              | 2008-2007 | Strumenti e metodi per l'analisi integrata dei risultati a supporto dei processi di valutazione nella sanità pubblica   | Coordinator          | Nutti Sabina |
| Funder: Tuscany Region Call 2014 Nutraceutica           | 2015-2017 | FATE PRE.SCO "Valorizzazione delle proprietà epigenetiche dei genotipi antichi toscani di frumento tenero biofortificati con ferro e zinco nella prevenzione dell'insufficienza cardiaca cronica" | Coordinator          | Nutti Sabina |
| EU Commission   | 2018-2021 | HealthPros  | Coordinator          | Nutti Sabina |

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| <p><b>Project Type: WP PROJECT - 7</b></p>  |  |

| Total proposed budget ( Euro ) |                   |                   |   |   |   |
|--------------------------------|-------------------|-------------------|---|---|---|
| Costs                          | TOTAL BUDGET      | Co-Funding        | Project costs proposed to funding Organization (no MOH request) | List of costs proposed for funding to the MOH | Percentage of total proposed to the MOH |
| 1a Staff Salary                | 100.000,00        | 100.000,00        | 0,00  | not permitted                                 |   |
| 1b Researchers' Contracts      | 185.000,00        | 0,00              | 185.000,00  | 0,00  |   |
| 2 Equipment (Leasing - Rent)   | 0,00              | 0,00              | 0,00  | 0,00  |   |
| 3a Supplies                    | 15.000,00         | 0,00              | 15.000,00   | 0,00  |   |
| 3b Model Costs                 | 0,00              | 0,00              | 0,00  | 0,00  |   |
| 3c Subcontracts                | 0,00              | 0,00              | 0,00  | 0,00  |   |
| 3d Patient Costs               | 0,00              | 0,00              | 0,00  | 0,00  |   |
| 4 IT Services and Data Bases   | 15.000,00         | 0,00              | 15.000,00   | 0,00  |   |
| 5 Publication Costs            | 6.000,00          | 0,00              | 6.000,00  | 0,00  |   |
| 6 Convegni                     | 6.000,00          | 0,00              | 6.000,00  | 0,00  |   |
| 7 Travels                      | 2.500,00          | 0,00              | 2.500,00  | 0,00  |   |
| 8 Overheads                    | 25.000,00         | 0,00              | 25.000,00   | 0,00  |   |
| 9 Coordination Costs           | 0,00              | 0,00              | 0,00  | 0,00  |   |
| <b>Total</b>                   | <b>354.500,00</b> | <b>100.000,00</b> | <b>254.500,00</b>   | <b>0,00</b>                                   |   |

Report the Co-Funding Contributor:

Staff Salary

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| <p><b>Project Code:</b> NET-2018-12368077-7</p>   | <p><b>Principal Investigator:</b> Passino Claudio</p>  |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Toscana</p>   |
| <p><b>Project Type: WP PROJECT - 7</b></p>  |  |

| <b>Budget Justification</b>  |   |
|------------------------------|---|
| 1a Staff Salary              | Staff Salary -PI and CoPI have a permanent position in SSSA   |
| 1b Researchers' Contracts    | Researchers Contracts - 1 Research contract for 3 years + 1 post-doc grant for 3 years  |
| 2 Equipment (Leasing - Rent) | none  |
| 3a Supplies                  | Acquire Supplies  |
| 3b Model Costs               | none  |
| 3c Subcontracts              | none  |
| 3d Patient Costs             | none  |
| 4 IT Services and Data Bases | Software/database/IT service will be purchased  |
| 5 Publication Costs          | The results will be published at the end of the projects  |
| 6 Convegni                   | Estimate of expenditure for conferences for the dissemination of research results   |
| 7 Travels                    | Travel and accommodation expenses incurred by researchers for the participation to conferences to disseminate research results. |
| 8 Overheads                  | -   |
| 9 Coordination Costs         | none  |

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| <p><b>Project Code:</b> NET-2018-12368077-8</p>  | <p><b>Principal Investigator:</b> corti maria chiara</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistono significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                   | <p><b>Applicant Institution:</b> Veneto</p>  |
| <p><b>Project Type: WP PROJECT - 8</b></p>   |  |

**Major Diagnostic Category\*:** Ortopedia

**Project Classification IRG:** Healthcare Delivery and Methodologies

**Project Classification SS:** Health Services Organization and Delivery - HSOD

**Project Keyword 1:** Healthcare organizations, programs, and delivery of services; including those delivered in non-traditional settings; integrated care delivery systems; disease management and modeling; continuous quality improvement; characteristics of the organization and patient outcomes; organizational performance and efficiency; cost-benefit analysis; economics of health care and pharmacoeconomics.

**Project Keyword 2:** Health care governance and sustainability

**Project Keyword 3:** Health technology assessment and clinical practice guidelines

**Project duration (months):** 36

**Project Request:**      **Animals:**                       **Humans:**                       **Clinical trial:**

**The object/s of this application is/are under patent copyright Y/N:**

| Investigators, Institution and Role in the Project |       |                     |                       |                       |            |
|--|-------|---------------------|-----------------------|-----------------------|------------|
|  | Co-PI | Key Personnel       | Institution/Org./Pos. | Role in the project   | Birth Date |
| 1  | X     | Andretta Margherita | Azienda Zero          | Research Collaborator | 03/10/1972 |
| 2  |       | Cavazzana Anna      | Azienda Zero          | Research Collaborator | 04/08/1976 |
| 3  |       | Garzotto Francesco  | Azienda Zero          | Research Collaborator | 25/02/1973 |

## Overall Summary

HTA assessments are not always aligned with or integrated into the purchasing process and the definition or update of PDTAs. This project has the aim of implementing an organizational model for the evaluation of purchase requests integrated with HTA and PDTA processes. This model will be defined on the basis of the existing experiences in this field with the contribution of the other regions participating in the network project. The results of this WP applied in Veneto Region will be shared with the other WPs and could be adapted and implemented in the other regions.

## Background / State of Art

In Italy, a validated system in the governance of new acquisitions of medical devices in local health units/ hospitals does not exist. There is furthermore a lack of a national or regional governance system on the introduction of new technologies based on a systematic analysis of all the procurement requests of new technologies.

On the other hand, in Italy has been recently established the 'HTA National Program of Medical Devices' (PNHTADM), a national network of collaboration between the regions for the definition and use of tools for the governance of medical devices and for HTA. The PNHTADM foresees the analysis and assessment of innovative technologies through the production of national HTA reports in order to introduce cost-effective technologies.

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| <p><b>Project Code:</b> NET-2018-12368077-8</p>  | <p><b>Principal Investigator:</b> corti maria chiara</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistono significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                   | <p><b>Applicant Institution:</b> Veneto</p>  |
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HTA is a source of information useful to support the definition of both the needs and the technical characteristics and is therefore relevant for the selection of products for which procurement procedures will be set up. Between HTA and procurement, however, there is a two-way relationship: on one hand, HTA can influence the acquisition process (for the definition of lots / requirements); on the other hand, the purchasing needs may generate the need for an assessment of a new technology / update of a PDTA.

However, the research conducted did not highlight consolidated experiences of structured examples of a "from procurement-to HTA" relationship, i.e. HTA programs that involve the systematic activation of assessments to address/answer the procurement needs (Sorenson, 2008; Sorenson, 2011; Rodriguez, 2017).

Compared to the other direction of the relationship (from HTA to procurement), research has shown a weak link, both nationally and internationally (Miniati 2014, Poder 2017, Messori, 2018, Trippoli 2018). There seems to be a lack of link between HTA regional programs and MD procurement procedures (Callea et al, 2017).

Thus, in the absence of a structured process of integration between HTA and procurement and HTA and PDTA update, the ideal situation would be firstly to develop a local / regional pathway of structured and systematic acquisition requests related to medical devices and then make it possible for the two channels to communicate (so that PNHTADM informs purchases and that the analysis of purchase requests informs HTA/PDTA updating).

The "Cabina di Regia (CdR)", established by a decree of the Minister of Health of 12 March 2015 with the aim of promoting and coordinating the multi-dimensional assessment activities carried out within the PNHTADM, has set up some sub-groups (SG) within the working group (WG) 2 "Methods, training and communication".

The SG 4 is elaborating a document in order to propose a theoretical model of integration between HTA and procurement decision and between HTA and PDTA definition, consistent with the PNHTADM.

## Hyphotesis and Specific AIMS

### Hyphotesis and Significance:

The hypothesis is that the experimental implementation of an organizational model of centralized and systematic collection and analysis of the acquisition requests integrated with the information deriving from HTA (national HTA/regional HTA/guidelines) allows a governance in the introduction/acquisition of new technologies in the NHS, allowing to:

- take informed decisions, which take into account the assessments of PNHTADM (if the technology is prioritized);
- to govern all the requested MDs even if they do not meet the priority criteria foreseen for a national assessment;
- to identify those MDs that need a national assessment, an update of PDTA or the definition of a PDTA/guidance.

Thus, our objective is to implement the objectives of Sub-group 4 of the WG2, making the model operational in Veneto Region, therefore:

1. using existing HTA to support procurement procedures (from HTA to procurement);
2. on the basis of the analysis of purchase requests, deciding what should be evaluated at national level with the methods defined by the PNHTADM, if possible/if prioritized (from procurement to HTA);
3. identifying the technologies that require an update of PDTA / definition of PDTA and / or identification of technologies for

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which a guidance has to be defined.

#### Preliminary Data:

The model provides a structured pathway for the introduction/procurement of technologies, integrated and consistent with the PNHTADM, with which it shares information sources and methods.

In details, the evaluation pathway model refers to the purchase requests for individual products or categories of products with European conformity marking (CE marking) not available in existing contracts / agreements and never previously purchased, whose purchase request is originated from the annual planning of purchases or from extemporaneous purchase requests that are not covered by planning.

The proposed pathway is based on the compilation of two modules. Firstly, a purchase request form must be filled in by the requesting health personnel and transmitted to the center for the evaluation of purchase requests (CVRA) - which can be local or regional depending on the local organization - which verifies the technology (i.e. whether there are recommendations on the appropriate use of this technology at national or regional level or whether there are existing agreements / contracts to which the purchase request can be traced back). In the absence of any recommendations or conventions / contracts, the CVRA shall fill in a second form, which is a supplementary form. In this case, the Region takes a decision on the purchase request.

This pathway requires the activation of a CVRA at a local or regional setting, which has to verify the state of the technologies for which the purchase is requested and to complete the second form. The CVRA must therefore include appropriate professional skills for the performance of these activities.

#### Specific Aim 1:

- to collect organizational models of integration between HTA/procurement/PDTA processes from available documents (SG4 ongoing model) enriched by the other regions/entities participating in the network project, in order to take advantage of their experiences;
- to define in details roles, competences and functions of the subjects involved (at regional and local level), the necessary information flows, the tools needed (e.g. IT infrastructures, forms, etc.) in order to implement the organizational model of governance of the introduction of new MDs;
- to train all the subjects involved (local and regional personnel in Veneto);
- to define how PDTA will be updated according to the new model of procurement.

#### Specific Aim 2:

- To make the model pathway operational (test phase) in Veneto Region.

#### Specific Aim 3:

- To evaluate performance improvement at a regional level
- To evaluate the outcomes of the process in terms of:
  - total number of evaluated requests;
  - number of evaluated requests which have been informed by PNHTADM / reports from other agencies or other regions;
  - number of evaluated requests which led the technology to be reported to the PNHTADM;
  - number of evaluated requests which led to the collection of further details/information;

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| <p><b>Project Type: WP PROJECT - 8</b></p>  |  |

- number of evaluated requests on the basis of the existing information;
- number of evaluated requests, which detected the need of updating a PDTA/guidance.
- To evaluate the information to be sent/collected to/from the other regions and the national/international institutions.

#### Experimental Design Aim 1:

All operating procedures and necessary acts will be drawn up.  
A specific database will be developed.

#### Experimental Design Aim 2:

All the purchase requests of medical devices coming from all the hospital/local health units in Veneto Region will be collected in the specific database, as indicated in the methodology section, and evaluated for a period of one year.

#### Experimental Design Aim 3:

The database will collect all the purchase requests, but also the outcomes of the evaluation processes; thus it will be possible to analyze and consequently improve the outcomes of the process.  
These data will allow understanding the feasibility of the application of the model at a regional level.  
The minimum set of data to be successfully shared with other institutions will be optimized in order to disseminate the ongoing assessments of innovative devices.

#### Picture to support preliminary data:

#### Methodologies and statistical analyses:

This project contemplates the implementation of an organizational model for the evaluation of purchase requests integrated with HTA and PDTA processes.  
A model is being defined by the SG4 of sub-group 2 of 'Cabina di Regia (CdR)', which has also proposed specific forms for information collection. Those forms will be the basis for the database construction. In fact, in order to make the system working, it will be necessary to have a supporting IT structure that follows the purchase requests from the local level up to the regional level. The requests should be on an electronic basis.

Training activities will be scheduled at the 2 university hospitals and the 9 local health units/community hospitals in Veneto Region.

Healthcare Failure Mode and Effects Analysis (HFMEA) is a process used to identify potential failures and their causes before future services are provided. It is a prospective assessment that identifies and improves steps in a process and reasonably ensures a safe and desirable outcome. It can also provide opportunities to improve current services. Often utilized in his original form (FMEA) in the risk analysis for medical devices following the ISO 14971 directive it has recently been adapted to the Patient Safety discipline for the mitigation of risks which could potentially result in patient tragedy. We will utilize HFMEA in order to measure the improvements obtained by the realization of the new governance. The typical

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Severity scale (Catastrophic, Major, Moderate, Minor) will be revisited and described as Heavy, Major, Moderate and Minor and referred to different outcomes: Organizational, Financial (Costs), Safety (patients and operators). Example of potential cause of a Failure could be: Wrong documentation provided, Incorrect methods or material applied, Instructions not clear, Error by lapse, Missed step in a procedure, Mistakes due to excessive pressure or lack of time or incompetence.

The process FMEA was structured according to the following methodology:

- Subject area of analysis (FMEA topic)
- Election of a team experienced in all clinical, technical and financial fields with decision-making capacity
- Creation of a process flow diagram
- Determination of all potential failure modes for each of the subprocess steps in a FMEA worksheet
- Failure mode analysis that considers the probability of the event occurring (P), its severity (S), and the detectability of the event (D)
- Procurement of the risk priority number (RPN) through the multiplication of the three values ( $P \times S \times D$ )
- Prioritization of the failure modes based on their RPN
- Outcome measures to remove or mitigate those potential modes with higher RPNs
- Development of control indicators and evaluation of the proposed actions
- Evaluation of the effects of the proposed actions

#### Expected outcomes:

We expect that the project will allow firstly to make the pathway operational, at least in a limited setting.

The experimental implementation of the organizational model should allow an increased clinical appropriateness, rationalization of expenditure, rational allocation of resources, optimization of the use of assessment and an overall increased governance and control of the introduced technologies.

Furthermore, there should be an integration of regional with inter-regional and national assessments and an optimization of failures evaluated by an original FMEA analysis.

The results of this WP applied in Veneto Region will be shared with the other WPs and could be adapted and implemented in the other regions.

#### Risk analysis, possible problems and solutions:

-Insufficient knowledge of the experimental model could be a risk of the project. Consequently, it is important to spread the model pathway and the use of the database throughout the Veneto Region. This activity has to be done within the planned training.

-Insufficient link between procurement requests and national HTA could be another risk; that is why it is important to strictly monitoring HTA activities/assessment at the national level.

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| <p><b>Project Code:</b> NET-2018-12368077-8</p>  | <p><b>Principal Investigator:</b> corti maria chiara</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistono significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                   | <p><b>Applicant Institution:</b> Veneto</p>  |
| <p><b>Project Type: WP PROJECT - 8</b></p>   |  |

### Significance and Innovation

Research carried out did not highlight consolidated experiences of structured examples of a relationship from procurement to HTA, that is, HTA programs that foresees the systematic activation of assessments to respond to the purchase or purchase planning needs. In this sense, the model of integration between the evaluation of purchase requests and the PNHTADM proposed represents an innovative element on the international scene. Additionally, the pathway may allow the identification of the technologies that require an update of PDTA / definition of PDTA.

### Description of the complementary and synergy research team

A clinician, an engineer and two pharmacists compose the team.  
The clinician has experience in the activity of coordination and management of projects.  
The engineer has experience in process analysis and research projects in the medical devices field.  
The pharmacists have expertise in coordination of regional working groups, production of HTA documents and evidence based recommendations on medical devices, set up of clinical registries and management, primary data analysis and analysis of regional data for medical devices and procedures.  
Thus, the background of the team research is multi-professional and complementary and will assure the needed expertise required for the proposed project.

### Training and tutorial activities

Training related to the project should be performed principally at two levels: at the research team level and the local hospital units' level. The former should be trained for the correct use and management of the database both for supporting the local hospital level for the database implementation and for its correct management and data analysis during the project period, while the latter should be trained on how to access the database and implement data.

Supporting personnel will be made available.

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| <p><b>Project Type: WP PROJECT - 8</b></p>   |  |

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- Rodriguez G. et al, Politiche di acquisto dei dispositivi medici in Piemonte. Maggior diffusione dei principi di HTA e del ruolo delle Società scientifiche, Quotidiano Sanità, 26 luglio 2017.
- Sorenson C, Kanavos P. Medical technology procurement in Europe: a cross-2645 country comparison of current practice and policy. Health Policy. 2011; 100(1):43-50.
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- Poder TG1. Using the Health Technology Assessment toolbox to facilitate procurement: the case of smart pumps in a Canadian hospital. Int J Technol Assess Health Care. 2017 Jan;33(1):54-62. doi: 10.1017/S0266462317000125. Epub 2017 Jun 5
- Messori A, Trippoli S. Value-based procurement of prostheses for total knee replacement. Orthop Rev (Pavia). 2018 Feb 16;9(4):7488. doi: 10.4081/or.2017.7488. eCollection 2017 Dec 14..
- Trippoli S, Caccese E, Marinai C, Messori A. Value-based procurement of medical devices: Application to devices for mechanical thrombectomy in ischemic stroke. Clin Neurol Neurosurg. 2018 Mar;166:61-65. doi:10.1016/j.clineuro.2018.01.028.
- Intesa tra stato e regioni sul documento strategico per l'HTA dei dispositivi medici

### Timeline / Deliverables / Payable Milestones

MM 0-12: Information exchange with the other regions, procedure and roles definition, training of research team and local hospitals/units, database development.

MM 12-24: Operational phase of the project with implementation of the model, technical support to the local units.

MM 24-36: Process analysis and analysis of the outcomes of the process.

### Milestones 18 month

- Roles, competences and functions of the subjects involved defined;
- regional and local centers for the evaluation of purchase requests (CVRA) established;
- all the subjects involved (local and regional personnel in Veneto) trained.

### Milestones 36 month

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| <p><b>Project Code:</b> NET-2018-12368077-8</p>   | <p><b>Principal Investigator:</b> corti maria chiara</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistono significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Veneto</p>  |
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- A comparison between the actual and the new organizational model will result from the FMEA analysis;
- A summary of the number of the successfully evaluated requests will be available and the number of PDTA updated or which has to be updated;
- A short report on the most useful data to be shared for a dissemination of the ongoing activities will be produced. This should allow regional-national interaction regarding the medical devices assessment.

### Gantt chart

Veneto-GANTT CHART.xls

### Equipment and resources available

k1: Medical devices assessment in Veneto Region is performed by an integrated HTA network based on local and regional committees.

A regional network of clinical engineers has also been recently established.

In Veneto Region Azienda Zero has been founded/established, which includes both an HTA unit and a unit dedicated to centralized procurement processes. Moreover, there is a regional commission with the task of evaluating all requests for tenders for the purchase of medical devices / equipment above a defined threshold. The requests forms of devices tenders have been recently harmonized in the Veneto Region as a first step of a centralized evaluation process.

This organization/facilities will participate to the implementation of the model and the new model should be integrated on this facilities of Regione Veneto.

k2- subcontract: A specific software/database is needed to collect all the acquisition requests and the outcomes of the evaluation. Azienda Zero in Veneto Region is lacking in dedicated resources for the development of the IT infrastructure.

### Translational relevance and impact for the National Health System (SSN)

With the aim to implement a governance model for an appropriate, effective and efficient use of resources maintaining the quality of healthcare, we focus on a regional model able to actively interact at inter-regional and national levels. This in agreement with the Italian Healthcare System based on Regional Autonomy under the National Directives.

In this way, both regions and SSN may take advantage on the governance model defined by the present proposal. Firstly an harmonization between guideline, HTA and clinical pathway (PDTA) with the procurement, may allow an improvement of the processes involved in the medical devices assessment. Secondly, the attempt to integrate the processes with other regions go in the direction of an optimized organizational model useful at a National Level.

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| <p><b>Project Code:</b> NET-2018-12368077-8</p>   | <p><b>Principal Investigator:</b> corti maria chiara</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Veneto</p>  |
| <p><b>Project Type: WP PROJECT - 8</b></p>  |  |

### PRINCIPAL INVESTIGATOR PROFILE

|   |   |
|---|---|
| <p><b>Name</b><br/>corti maria chiara</p> | <p><b>Institution</b> Veneto<br/><b>Department/Unit</b> Azienda Zero (Epidemiology Unit)<br/><b>Position Title</b> Director</p> |
|---|---|

### Personal Statement

Principal investigator with the role of overall coordination of activities.

| Education/Training - Institution and Location     | Degree                         | Year(s) | Field of study               |
|---|--------------------------------|---------|------------------------------|
| University of Padova                              | Medical Degree                 | 1985    | Medicine                     |
| University of Padova                              | Board certification, Residency | 1989    | Rheumatology                 |
| University of Padova                              | Ph D.                          | 1993    | Gerontology                  |
| Johns Hopkins School of Hygiene and Public Health | Master in Health Science       | 1994    | Chronic Disease epidemiology |

### Positions

| Institution  | Division / Research group                           | Location           | Position                      | From year | To year |
|--|---|--------------------|-------------------------------|-----------|---------|
| National Institute on Aging, National Institute of Health, USA | Laboratory of Epidemiology, Demography and Biometry | Bethesda, Maryland | Visiting Fellow and Scientist | 1993      | 1997    |
| Azienda Ulss 15  | Hospital Geriatric Ward                             | Cittadella         | Staff Physician               | 1997      | 2004    |
| Azienda Ulss 6 Euganea   | Epidemiology service                                | Padova             | Head                          | 2004      | 2008    |
| Azienda Ulss 6 Euganea   | Health District                                     | Padova             | Director                      | 2008      | 2011    |
| Regione Veneto   | Intermediate and integrated care division           | Venice             | Director                      | 2012      | 2017    |
| Azienda Zero   | Epidemiology and Registries                         | Padova             | Director                      | 2017      | 2018    |

**Official H index:** 32.0 ( autocerficated )

**Source:** Scopus

**Scopus Author Id:** 7101780467

**ORCID ID:** 0000-0002-0727-6929

**RESEARCH ID:** K-8547-2018

### Awards and Honors:

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti</p> <p><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV - Integration of the HTA methodology with the procurement activities and the definition/revision of diagnostic therapeutic assistance paths (PDTAs)</p> |
| <p><b>Project Code:</b> NET-2018-12368077-8</p>  | <p><b>Principal Investigator:</b> corti maria chiara</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistono significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                   | <p><b>Applicant Institution:</b> Veneto</p>  |
| <p><b>Project Type: WP PROJECT - 8</b></p>   |  |

1994 US Dept of Health and Human Serv Award for the scientific contrib. to the planning and implementation of the Women Health and Aging Study.USA

1996 Special Award for important contrib to the research on aging, Nat. Inst. on Aging, Nat. Inst of Health USA

2017 Award by WHO Europ. Cent. for Primary Health Care Div. of Health Systems and Public Health In appreciation for the continuous support of the Net. of Integrated Health Serv. Delivery Focal Points in the WHO EU Region Almaty Kazakhstan

**Other CV Informations:**

Graduated as MD at the Padua University 1985, specialized in Rheumatology, Master in Health Science (Chronic Disease Epidemiology) Johns Hopkins University in Baltimore, (US) PhD in Gerontology University of Padua

1993 to 1997 Visiting fellow and scientist at NIA, NIH in the Epidemiology of Aging and Biometry Program - National Institute on Aging

1998 - 2004 Care of geriatric patients in Hosp, Padova

2004 - 2011 Primary Health Care Management in the Local Trusts of the city area, Padova

2012 - 2016 Director of Integrated Health Care in the Veneto Health Service (Management of Regional Programs of Intermediate Care, Long Term Care in integration with Hospital and Primary Care; Innovative Projects of Population Health Management -Implementation in Veneto of the Johns Hopkins ACG system)

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti</p> <p><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV - Integration of the HTA methodology with the procurement activities and the definition/revision of diagnostic therapeutic assistance paths (PDTAs)</p> |
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| <p><b>Project Type: WP PROJECT - 8</b></p>   |  |

### Selected peer-reviewed publications of the PI

| Valid for PI minimum expertise level   |  |          |         |     |
|--|--|----------|---------|-----|
| Title  | DOI                                      | PMID     | Cit. ** | P.* |
| Coronary heart disease risk factors in older persons   | 10.1007/BF03339560                       | 8737605  | 21      | F   |
| Mortality from infectious diseases in diabetes   | 10.1016/j.numecd.2017.12.007             | 29519560 | 0       | L   |
| Lipoprotein alterations and atherosclerosis in the elderly   | 10.1097/00041433-199708000-00008         | 9253541  | 23      | F   |
| White matter lesions and the risk of incident hip fracture in older persons: Results from the Progetto Veneto Anziani study  | 10.1001/archinte.167.16.1745             | 17846393 | 24      | F   |
| Evidence for a Black-White crossover in all-cause and coronary heart disease mortality in an older population: The North Carolina EPESE  | 10.2105/AJPH.89.3.308                    | 10076478 | 53      | F   |
| Iron status and risk of cardiovascular disease   | 10.1016/S1047-2797(96)00112-3            | 9034408  | 79      | F   |
| Diverging patterns of cardiovascular diseases across immigrant groups in Northern Italy  | 10.1016/j.ijcard.2017.12.014             | 29246427 | 0       | L   |
| Excess mortality in 2015: a time series and cause-of-death analysis in Northern Italy  | 10.1007/s40520-017-0773-0                | 28523608 | 1       | L   |
| Serum iron level, coronary artery disease, and all-cause mortality in older men and women  | 10.1016/S0002-9149(96)00697-2            | 9193009  | 55      | F   |
| The effect of cardiovascular and osteoarticular diseases on disability in older Italian men and women: Rationale, design, and sample characteristics of the Progetto Veneto Anziani (PRO.V.A.) Study | 10.1046/j.1532-5415.2002.50409.x         | 12383151 | 64      | F   |
| Serum albumin and physical function as predictors of coronary heart disease mortality and incidence in older persons   | 10.1016/0895-4356(95)00562-5             | 8636725  | 74      | F   |
| Epidemiology of osteoarthritis: Prevalence, risk factors and functional impact   | 10.1007/BF03327356                       | 14703001 | 107     | F   |
| Clarifying the direct relation between total cholesterol levels and death from coronary heart disease in older persons   | 10.7326/0003-4819-126-10-199705150-00001 | 9148647  | 189     | F   |
| HDL Cholesterol Predicts Coronary Heart Disease Mortality in Older Persons   | 10.1001/jama.1995.03530070037026         | 7629981  | 230     | F   |
| Serum Albumin Level and Physical Disability as Predictors of Mortality in Older Persons  | 10.1001/jama.1994.03520130074036         | 8089886  | 445     | F   |

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| <p><b>Project Code:</b> NET-2018-12368077-8</p>   | <p><b>Principal Investigator:</b> corti maria chiara</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Veneto</p>  |
| <p><b>Project Type: WP PROJECT - 8</b></p>  |  |

\* Position: F=First L=Last C=Correspondent

\*\* Autocertificated

| For evaluation CV  |  |          |        |
|--|--|----------|--------|
| Title  | DOI                                      | PMID     | Cit. * |
| The HELP LDL apheresis multicentre study, an angiographically assessed trial on the role of LDL apheresis in the secondary prevention of coronary heart disease. II. Final evaluation of the effect of regular treatment on LDL cholesterol plasma concentrations and the course of coronary heart disease | 10.1111/j.1365-2362.1994.tb01068.x       | 7890009  | 140    |
| Serum Albumin Level and Physical Disability as Predictors of Mortality in Older Persons  | 10.1001/jama.1994.03520130074036         | 8089886  | 445    |
| HDL Cholesterol Predicts Coronary Heart Disease Mortality in Older Persons   | 10.1001/jama.1995.03530070037026         | 7629981  | 230    |
| Long Term Survival and Use of Antihypertensive Medications in Older Persons  | 10.1111/j.1532-5415.1995.tb07393.x       | 7594151  | 276    |
| Calcium-channel blockade and incidence of cancer in aged populations   | 10.1016/S0140-6736(96)04277-8            | 8757150  | 285    |
| Clarifying the direct relation between total cholesterol levels and death from coronary heart disease in older persons   | 10.7326/0003-4819-126-10-199705150-00001 | 9148647  | 189    |
| Hospital diagnoses, Medicare charges, and nursing home admissions in the year when older persons become severely disabled  | 10.1001/jama.1997.03540330050034         | 9042845  | 195    |
| Cardiovascular events and mortality in newly and chronically depressed persons > 70 years of age   | 10.1016/S0002-9149(98)00077-0            | 9576158  | 174    |
| Serum IL-6 level and the development of disability in older persons  | 10.1111/j.1532-5415.1999.tb01583.x       | 10366160 | 536    |
| Associations of elevated interleukin-6 and C-reactive protein levels with mortality in the elderly   | 10.1016/S0002-9343(99)00066-2            | 10335721 | 1063   |

\* Autocertificated

| Grant  |      |   |                      |
|--|------|---|----------------------|
| Funded Institution / Country                             | Year | Title   | Position in Projects |
| European Commission 134023-LLP-1-2007-1-IT-GRUNDTVIG-GMP | 2007 | EMPOWERING HEALTH LEARNING FOR ELDERLY - EHLE | Coordinator          |

**Employment contract extension:**

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| <p><b>Project Code:</b> NET-2018-12368077-8</p>   | <p><b>Principal Investigator:</b> corti maria chiara</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Veneto</p>  |
| <p><b>Project Type: WP PROJECT - 8</b></p>  |  |

( Data changed during the moratorium period )

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| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistono significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Veneto</p>  |
| <p><b>Project Type: WP PROJECT - 8</b></p>  |  |

### Biographical Sketch Contributors 1

|   |  |
|---|--|
| <p><b>Name:</b><br/>Andretta Margherita</p> | <p><b>Institution:</b> Azienda Zero<br/><b>Department/Unit:</b> HTA department<br/><b>Position Title:</b> Director</p> |
|---|--|

| Education/Training - Institution and Location       | Degree                              | Year(s) | Field of study   |
|---|-------------------------------------|---------|--|
| Università degli Studi di Padova - Padova           | Master's degree                     | 1998    | Pharmaceutical Chemistry and Technology  |
| Università degli Studi di Padova - Padova           | Post-graduate specialization degree | 2002    | Hospital Pharmacy  |
| European Observatory on Health Systems and Policies | summer school                       | 2014    | Observatory Venice Summer School "Rethinking Pharmaceutical policy: Optimising decisions in an era of uncertainty" |

**Personal Statement:**

Co-PI, with the role of support in making the model operational and in data analysis and interpretation, support the PI in the coordination and supervision of activities, support in the database

| Institution             | Division / Research group                                   | Location      | Position  | From year | To year |
|-------------------------|---|---------------|---|-----------|---------|
| Regione Veneto          | Azienda Zero  | Padova, Italy | Director HTA department   | 2018      | 2018    |
| Regione Veneto          | Coordinamento Regionale Unico sul Farmaco (CRUF)            | Verona, Italy | Coordinator of Pharmacoepidemiology and Health Technology Assessment            | 2016      | 2017    |
| Azienda ULSS 20, Verona | Pharmacoepidemiology and drug prescriptions governance Unit | Verona, Italy | Responsible for the pharmacoepidemiology and drug prescriptions governance unit | 2015      | 2016    |
| Azienda ULSS 20, Verona | Territorial Pharmaceutical Service Unit                     | Verona, Italy | Pharmacist Executive  | 2005      | 2016    |

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV - Integration of the HTA methodology with the procurement activities and the definition/revision of diagnostic therapeutic assistance paths (PDTAs)</p> |
| <p><b>Project Code:</b> NET-2018-12368077-8</p>   | <p><b>Principal Investigator:</b> corti maria chiara</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Veneto</p>  |
| <p><b>Project Type: WP PROJECT - 8</b></p>  |  |

### Awards and Honors

**Official H index:** 10.0 ( autocertificated )

**Source:** Scopus

**Scopus Author Id:** 7004201314

**ORCID ID:** 0000-0002-4072-2783

**RESEARCH ID:** K-3619-2018

**Awards and Honors:**

None.

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV - Integration of the HTA methodology with the procurement activities and the definition/revision of diagnostic therapeutic assistance paths (PDTAs)</p> |
| <p><b>Project Code:</b> NET-2018-12368077-8</p>   | <p><b>Principal Investigator:</b> corti maria chiara</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistano significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Veneto</p>  |
| <p><b>Project Type: WP PROJECT - 8</b></p>  |  |

### Biographical Sketch Contributors 2

| <p><b>Name:</b><br/>Cavazzana Anna</p>   | <p><b>Institution</b> Azienda Zero<br/><b>Department/Unit</b> Pharmacy<br/><b>Position Title</b> Executive Pharmacist</p> |         |  |
|--|---|---------|--|
| Education/Training - Institution and Location  | Degree  | Year(s) | Field of study   |
| Università degli Studi di Padova - Padova  | Master's degree   | 2002    | Pharmacy   |
| Università degli Studi di Padova (Italy) and University of Geneva Laboratory "Unité d'Emostase" dell'Hopital Cantonal (Switzerland) in joint supervision | Joint PhD   | 2007    | Experimental and Clinical Rheumatology and Geriatrics in joint supervision with Switzerland                |
| Università degli Studi di Padova - Padova  | Post-graduate specialization degree   | 2010    | Hospital Pharmacy  |
| Università degli Studi di Milano - Istituto Mario Negri - Milano   | Post-graduate academic advanced course  | 2011    | Systematic reviews and meta-analyses for the production of evidencebased guidelines (Cochrane methodology) |
| Università degli Studi di Padova - Padova  | Post-graduate academic master course  | 2012    | Health Technology Assessment   |

**Personal Statement:**

Support in making the model operational and in data analysis and interpretation, support in the database definition and in the training, coordination of the operational phase

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV - Integration of the HTA methodology with the procurement activities and the definition/revision of diagnostic therapeutic assistance paths (PDTAs)</p> |
| <p><b>Project Code:</b> NET-2018-12368077-8</p>   | <p><b>Principal Investigator:</b> corti maria chiara</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistono significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Veneto</p>  |
| <p><b>Project Type: WP PROJECT - 8</b></p>  |  |

| Institution            | Division / Research group                        | Location       | Position                | From year | To year |
|------------------------|--|----------------|-------------------------|-----------|---------|
| Regione Veneto         | Azienda Zero - HTA                               | Padova, Italy  | Executive Pharmacist    | 2018      | 2018    |
| ULSS 8 Berica- Vicenza | Coordinamento Regionale Unico sul Farmaco (CRUF) | Vicenza, Italy | Executive Pharmacist    | 2017      | 2017    |
| Regione Veneto         | Coordinamento Regionale Unico sul Farmaco (CRUF) | Verona, Italy  | Executive Pharmacist    | 2015      | 2017    |
| Regione Veneto         | Coordinamento Regionale Unico sul Farmaco (CRUF) | Verona, Italy  | Collaborator Pharmacist | 2013      | 2015    |
| ULSS 16 - Padova       | Farmacia Ospedaliera Ospedale di Piove di Sacco  | Padova, Italy  | Executive Pharmacist    | 2012      | 2012    |

### Awards and Honors

**Official H index:** 5.0 ( autocertificata )

**Source:** Scopus

**Scopus Author Id:** 12767164000

**ORCID ID:** 0000-0003-3411-2003

**RESEARCH ID:** K-3750-2018

#### Awards and Honors:

no

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV - Integration of the HTA methodology with the procurement activities and the definition/revision of diagnostic therapeutic assistance paths (PDTAs)</p> |
| <p><b>Project Code:</b> NET-2018-12368077-8</p>   | <p><b>Principal Investigator:</b> corti maria chiara</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistono significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Veneto</p>  |
| <p><b>Project Type: WP PROJECT - 8</b></p>  |  |

### Biographical Sketch Contributors 3

|  |   |
|--|---|
| <p><b>Name:</b><br/>Garzotto Francesco</p> | <p><b>Institution:</b> Azienda Zero<br/><b>Department/Unit:</b> Azienda Zero- HTA<br/><b>Position Title:</b> Technical Engineer</p> |
|--|---|

| Education/Training - Institution and Location      | Degree  | Year(s) | Field of study   |
|--|---|---------|--|
| University of Padova                               | Master Degree in Electronics/Biomedical Engineering | 2004    | Electronics/Biomedical Engineering                       |
| University of Padova                               | University of Padova                                | 2004    | Biomedical Engineer                                      |
| National Council of Research (CNR), Padova (Italy) | Post-graduate academic master                       | 2005    | Quality management and Risk analysis for Medical Devices |
| University of Padova                               | Post-graduate academic master                       | 2017    | Statistical Analysis for Clinical Research               |

**Personal Statement:**

Process analysis and evaluation of performance improvement

| Institution          | Division / Research group  | Location    | Position              | From year | To year |
|----------------------|--|-------------|-----------------------|-----------|---------|
| Regione Veneto       | Azienda Zero - HTA   | Padova, IT  | Technical Engineer    | 2018      | 2018    |
| University of Padova | Unit of Biostatistics, Epidemiology and Public Health. Department of Cardiac, Thoracic and Vascular Sciences | Padova, IT  | Associated Researcher | 2017      | 2018    |
| St. Bortolo Hospital | Renal Research Institute, Engineering Clinical Research Dept.  | Vicenza, IT | Head                  | 2006      | 2017    |
| St. Bortolo Hospital | Nephrology Dialysis and Transplant   | Vicenza, IT | Executive Engineer    | 2014      | 2017    |
| Gambro/Baxter        | Marketing and R&D  | Bologna, IT | Project               | 2005      | 2006    |

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti</p> <p><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV - Integration of the HTA methodology with the procurement activities and the definition/revision of diagnostic therapeutic assistance paths (PDTAs)</p> |
| <p><b>Project Code:</b> NET-2018-12368077-8</p>  | <p><b>Principal Investigator:</b> corti maria chiara</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistono significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                   | <p><b>Applicant Institution:</b> Veneto</p>  |
| <p><b>Project Type: WP PROJECT - 8</b></p>   |  |

### Awards and Honors

**Official H index:** 14.0 ( autocertificated )

**Source:** Scopus

**Scopus Author Id:** 36027379000

**ORCID ID:** 0000-0002-0233-3752

**RESEARCH ID:** K-3552-2018

#### Awards and Honors:

2018 American Dialysis Conf: Best Pediatric Ab "Continuous Renal Replacement Therapy in Neonates and Small Infants:Data from Carpediem Retrospective Registry";

2014-2017 Research Project 'Sviluppo di un sistema mecatronico miniaturizzato e portatile per l'ultrafiltrazione extracorporea' Collaborator. Fond Cariverona;

2012 Europ Dialysis Cong. ERA-EDTA: Travel Grant and complimentary reg. for Best Pediatric Ab "Carpediem:Cardio-Renal Pediatric Dialysis Emerg. Machine. A New Hope For Infants"

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV - Integration of the HTA methodology with the procurement activities and the definition/revision of diagnostic therapeutic assistance paths (PDTAs)</p> |
| <p><b>Project Code:</b> NET-2018-12368077-8</p>   | <p><b>Principal Investigator:</b> corti maria chiara</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistono significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Veneto</p>  |
| <p><b>Project Type: WP PROJECT - 8</b></p>  |  |

### Expertise Research Collaborators

| Selected peer-reviewed publications of the Research Group / Collaborators |   |                               |          |        |
|---|---|-------------------------------|----------|--------|
| Collaborator  | Title   | DOI                           | PMID     | Cit. * |
| Andretta Margherita   | Different safety profiles of oral anticoagulants in very elderly non-valvular atrial fibrillation patients. A retrospective propensity score matched cohort study             | 10.1016/j.ijcard.2018.04.117  | 29728333 | 0      |
| Garzotto Francesco  | Continuous renal replacement therapy in neonates and small infants: Development and first-in-human use of a miniaturised machine (CARPEDIEM)                                  | 10.1016/S0140-6736(14)60799-6 | 24856026 | 61     |
| Garzotto Francesco  | RIFLE-Based data collection/management system applied to a prospective cohort multicenter italian study on the epidemiology of acute kidney injury in the intensive care unit | 10.1159/000322161             | 21228585 | 35     |
| Garzotto Francesco  | Multidisciplinary evaluation for severity of hazards applied to hemodialysis devices: An original risk analysis method  | 10.2215/CJN.01740210          | 20813858 | 10     |
| Andretta Margherita   | Monitoring the occurrence of diabetes mellitus and its major complications: The combined use of different administrative databases  | 10.1186/1475-2840-6-5         | 17302977 | 19     |
| Andretta Margherita   | Prevalence, incidence and persistence of antipsychotic drug prescribing in the Italian general population: Retrospective database analysis, 1999-2002                         | 10.1002/pds.1162              | 16287199 | 31     |
| Andretta Margherita   | Antidepressant drug consumption and public health indicators in Italy, 1955 to 2000   | 10.4088/JCP.v66n0612          | 15960569 | 68     |

\* Autocertificated

| Grant   |           |  |                      |                    |
|---|-----------|--|----------------------|--------------------|
| Funded Institution / Country                          | Year      | Title  | Position in Projects | Collaborator       |
| Fondazione Studi Universitari di Vicenza - CARIVERONA | 2014-2017 | Sviluppo di un sistema mecatronico miniaturizzato e portatile per l'ultrafiltrazione extracorporea | Collaborator         | Garzotto Francesco |

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti</p> <p><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV - Integration of the HTA methodology with the procurement activities and the definition/revision of diagnostic therapeutic assistance paths (PDTAs)</p> |
| <p><b>Project Code:</b> NET-2018-12368077-8</p>  | <p><b>Principal Investigator:</b> corti maria chiara</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistono significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                   | <p><b>Applicant Institution:</b> Veneto</p>  |
| <p><b>Project Type: WP PROJECT - 8</b></p>   |  |

| Total proposed budget ( Euro ) |                   |                   |   |   |   |
|--------------------------------|-------------------|-------------------|---|---|---|
| Costs                          | TOTAL BUDGET      | Co-Funding        | Project costs proposed to funding Organization (no MOH request) | List of costs proposed for funding to the MOH | Percentage of total proposed to the MOH |
| 1a Staff Salary                | 134.400,00        | 134.400,00        | 0,00  | not permitted                                 | 0,00                                    |
| 1b Researchers' Contracts      | 360.000,00        | 0,00              | 230.000,00  | 130.000,00                                    | 47,39                                   |
| 2 Equipment (Leasing - Rent)   | 9.000,00          | 0,00              | 0,00  | 9.000,00                                      | 3,28                                    |
| 3a Supplies                    | 5.000,00          | 0,00              | 5.000,00  | 0,00  | 0,00                                    |
| 3b Model Costs                 | 0,00              | 0,00              | 0,00  | 0,00  | 0,00                                    |
| 3c Subcontracts                | 26.000,00         | 0,00              | 13.000,00   | 13.000,00                                     | 4,74                                    |
| 3d Patient Costs               | 0,00              | 0,00              | 0,00  | 0,00  | 0,00                                    |
| 4 IT Services and Data Bases   | 90.000,00         | 0,00              | 0,00  | 90.000,00                                     | 32,81                                   |
| 5 Publication Costs            | 5.000,00          | 0,00              | 0,00  | 5.000,00                                      | 1,82                                    |
| 6 Convegni                     | 3.700,00          | 0,00              | 2.500,00  | 1.200,00                                      | 0,44                                    |
| 7 Travels                      | 3.700,00          | 0,00              | 2.500,00  | 1.200,00                                      | 0,44                                    |
| 8 Overheads                    | 50.240,00         | 0,00              | 25.300,00   | 24.940,00                                     | 9,09                                    |
| 9 Coordination Costs           | 0,00              | 0,00              | 0,00  | 0,00  | 0,00                                    |
| <b>Total</b>                   | <b>687.040,00</b> | <b>134.400,00</b> | <b>278.300,00</b>   | <b>274.340,00</b>                             | <b>100,00</b>                           |

Report the Co-Funding Contributor:

for staff salary

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV - Integration of the HTA methodology with the procurement activities and the definition/revision of diagnostic therapeutic assistance paths (PDTAs)</p> |
| <p><b>Project Code:</b> NET-2018-12368077-8</p>   | <p><b>Principal Investigator:</b> corti maria chiara</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistono significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Veneto</p>  |
| <p><b>Project Type: WP PROJECT - 8</b></p>  |  |

| Budget Justification         |   |
|------------------------------|---|
| 1a Staff Salary              | The involved investigators will dedicate at least a mean of 2 months of work each year for this project. On the basis of the involved investigators' salaries the budget for staff salary has been defined                                    |
| 1b Researchers' Contracts    | We have estimated the need of 4 research contracts who will entirely be dedicated to support the projects activities  |
| 2 Equipment (Leasing - Rent) | Estimate of expenses for personal computers leasing   |
| 3a Supplies                  | Estimate of expenses for stationery supplies  |
| 3b Model Costs               | /   |
| 3c Subcontracts              | A portion of the funding will be dedicated to the software/database management during the three year period of the project  |
| 3d Patient Costs             | /   |
| 4 IT Services and Data Bases | A software/database will be purchased   |
| 5 Publication Costs          | The results will be published at the end of the projects  |
| 6 Convegni                   | Estimate of expenditure for conferences for the dissemination of research results   |
| 7 Travels                    | Travel and accommodation expenses incurred by researchers for the participation to conferences to disseminate research results (MOH funding) . Expenses of the dedicated staff for missions within the Veneto Region (Veneto Region funding)" |
| 8 Overheads                  | /   |
| 9 Coordination Costs         | /   |

( Data changed during the moratorium period )

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti</p> <p><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV - Integration of the HTA methodology with the procurement activities and the definition/revision of diagnostic therapeutic assistance paths (PDTAs)</p> |
| <p><b>Project Code:</b> NET-2018-12368077-8</p>  | <p><b>Principal Investigator:</b> corti maria chiara</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistono significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                   | <p><b>Applicant Institution:</b> Veneto</p>  |
| <p><b>Project Type: WP PROJECT - 8</b></p>   |  |

### Principal Investigator Data - Working package 1 Code: NET-2018-12368077-1

Cognome: ricciardi  
 Nome: gualtiero  
 Codice fiscale:  
 Documento:  
 Data di nascita:  
 Luogo di nascita:  
 Provincia di nascita:  
 Indirizzo lavorativo: viale regina elena 299  
 Città: roma  
 CAP: 00161  
 Provincia: RM  
 Email:  
 Altra email:  
 Telefono:  
 Qualifica: presidente  
 Struttura: presidenza  
 Istituzione: istituto superiore di sanità

### Principal Investigator Data - Working package 2 Code: NET-2018-12368077-2

Cognome: Maria  
 Nome: Frigerio  
 Codice fiscale:  
 Documento:  
 Data di nascita:  
 Luogo di nascita:  
 Provincia di nascita:  
 Indirizzo lavorativo: Piazza Ospedale Maggiore 3  
 Città: Milano  
 CAP: 20162  
 Provincia: MI  
 Email:  
 Telefono:  
 Altro telefono:  
 Fax:  
 Qualifica: Direttore Struttura Complessa  
 Struttura: Cardiologia 2 - insufficienza cardiaca e trapianto

Sent date: 20/05/2018 21.34

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Sent date of moratorium changes: 01/06/2018 15.17

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|---|--|
|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti<br/><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV - Integration of the HTA methodology with the procurement activities and the definition/revision of diagnostic therapeutic assistance paths (PDTAs)</p> |
| <p><b>Project Code:</b> NET-2018-12368077-8</p>   | <p><b>Principal Investigator:</b> corti maria chiara</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistono significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                | <p><b>Applicant Institution:</b> Veneto</p>  |
| <p><b>Project Type: WP PROJECT - 8</b></p>  |  |

Istituzione: ASST Grande Metropolitano Niguarda

### Principal Investigator Data - Working package 3 Code: NET-2018-12368077-3

Cognome: Banfi  
 Nome: Giuseppe  
 Codice fiscale:  
 Documento:  
 Data di nascita:  
 Luogo di nascita:  
 Provincia di nascita:  
 Indirizzo lavorativo: Via Riccardo Galeazzi 4  
 Città: Milano  
 CAP: 20161  
 Provincia: MI  
 Email:  
 Altra email:  
 Telefono:  
 Altro telefono:  
 Qualifica: Direttore Scientifico  
 Struttura: Laboratorio Biochimica Sperimentale e Biologia Molecolare  
 Istituzione: IRCCS Istituto Ortopedico Galeazzi

### Principal Investigator Data - Working package 4 Code: NET-2018-12368077-4

Cognome: Cherubini  
 Nome: Antonio  
 Codice fiscale:  
 Documento:  
 Data di nascita:  
 Luogo di nascita:  
 Provincia di nascita:  
 Indirizzo lavorativo: Via Montagnola 81  
 Città: Ancona  
 CAP: 60121  
 Provincia: AN  
 Email:  
 Altra email:

Sent date: 20/05/2018 21.34

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Sent date of moratorium changes: 01/06/2018 15.17

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti</p> <p><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV - Integration of the HTA methodology with the procurement activities and the definition/revision of diagnostic therapeutic assistance paths (PDTAs)</p> |
| <p><b>Project Code:</b> NET-2018-12368077-8</p>  | <p><b>Principal Investigator:</b> corti maria chiara</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistono significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                   | <p><b>Applicant Institution:</b> Veneto</p>  |
| <p><b>Project Type: WP PROJECT - 8</b></p>   |  |

Telefono:

Qualifica: Direttore

Struttura: UOC Geriatria e Accettazione Geriatrica d'Urgenza

Istituzione: Istituto Nazionale di Riposo e Cura per Anziani V.E. II

### Principal Investigator Data - Working package 5 Code: NET-2018-12368077-5

Cognome: Lorusso

Nome: Vito

Codice fiscale:

Documento:

Data di nascita:

Luogo di nascita:

Provincia di nascita:

Indirizzo lavorativo: Istituto Oncologico Viale Orazio Flacco 65

Città: Bari

CAP: 70124

Provincia: BA

Email:

Altra email:

Telefono:

Altro telefono:

Fax:

Qualifica: Direttore Struttura Completa di Oncologia Medica

Struttura: Istituto Oncologico Giovanni Paolo II

Istituzione: IRCCS

### Principal Investigator Data - Working package 6 Code: NET-2018-12368077-6

Cognome: Rostagno

Nome: Carlo

Codice fiscale:

Documento:

Data di nascita:

Luogo di nascita:

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Indirizzo lavorativo: AOU Careggi Largo Brambilla 3

Città: Firenze

Sent date: 20/05/2018 21.34

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Sent date of moratorium changes: 01/06/2018 15.17

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti</p> <p><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV - Integration of the HTA methodology with the procurement activities and the definition/revision of diagnostic therapeutic assistance paths (PDTAs)</p> |
| <p><b>Project Code:</b> NET-2018-12368077-8</p>  | <p><b>Principal Investigator:</b> corti maria chiara</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistono significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                   | <p><b>Applicant Institution:</b> Veneto</p>  |
| <p><b>Project Type: WP PROJECT - 8</b></p>   |  |

CAP: 50135  
 Provincia: FI  
 Email:  
 Altra email:  
 Telefono:  
 Qualifica: Direttore SOD  
 Struttura: SOD Medicina Interna Post-Chirurgica  
 Istituzione: Azienda Ospedaliero-Universitaria Careggi

#### Principal Investigator Data - Working package 7 Code: NET-2018-12368077-7

Cognome: Passino  
 Nome: Claudio  
 Codice fiscale:  
 Documento:  
 Data di nascita:  
 Luogo di nascita:  
 Provincia di nascita:  
 Indirizzo lavorativo: via Moruzzi 1  
 Città: Pisa  
 CAP: 56124  
 Provincia: PI  
 Email:  
 Altra email:  
 Telefono:  
 Altro telefono:  
 Qualifica: Professore Associato  
 Struttura: Istituto di Scienze della Vita  
 Istituzione: Scuola Superiore Sant'Anna

#### Principal Investigator Data - Working package 8 Code: NET-2018-12368077-8

Cognome: corti  
 Nome: maria chiara  
 Codice fiscale:  
 Documento:  
 Data di nascita:  
 Luogo di nascita:

Sent date: 20/05/2018 21.34

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Sent date of moratorium changes: 01/06/2018 15.17

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|  <p><i>Ministero della Salute</i><br/>Direzione Generale della Ricerca Sanitaria<br/>e Biomedica e della Vigilanza sugli Enti</p> <p><b>BANDO RICERCA FINALIZZATA 2018</b><br/>esercizio finanziario anni 2016-2017</p> | <p><b>Project Title:</b><br/>Definition and testing of a new model of clinical governance based on the integration of tools such as Health Technology Assessment, Clinical Practice Guidelines, Clinical Pathways, and healthcare performance measurement for planning, implementation and management of healthcare interventions in different settings - INTEGRATE-HEALTH-GOV - Integration of the HTA methodology with the procurement activities and the definition/revision of diagnostic therapeutic assistance paths (PDTAs)</p> |
| <p><b>Project Code:</b> NET-2018-12368077-8</p>  | <p><b>Principal Investigator:</b> corti maria chiara</p>   |
| <p><b>Research Type:</b> b) Change-promoting: valutare la sicurezza, efficacia, costo-efficacia, di trattamenti/tecnologie/interventi sanitari per cui sussistono significativi margini di incertezza relativamente agli aspetti menzionati, anche con studi clinici di fase 3 e 4</p>                   | <p><b>Applicant Institution:</b> Veneto</p>  |
| <p><b>Project Type: WP PROJECT - 8</b></p>   |  |

Provincia di nascita:

Indirizzo lavorativo: Passaggio Gaudenzio 1

Città: Padova

CAP: 35131

Provincia: PD

Email:

Altra email:

Telefono:

Altro telefono:

Qualifica: medico dirigente

Struttura: Azienda Zero

Istituzione: Regione Veneto



CAMPOBASSO  
GIOVANNI  
19.04.2021  
09:03:53 UTC



REGIONE PUGLIA  
SEZIONE BILANCIO RAGIONERIA PARERE DI REGOLARITA' CONTABILE  
(D. Lgs. n. 118/11 e s.m.i.)

| UFFICIO | TIPO | ANNO | NUMERO | DATA       |
|---------|------|------|--------|------------|
| SGO     | DEL  | 2021 | 25     | 19.04.2021 |

MIN. SALUTE NET-2018-12368077 Progr. di Rete "DEFINITION AND TESTING OF A NEW MODEL OF CLINICAL GOVERNANCE BASED ON THE INTEGRATION OF TOOLS SUCH AS HTA CLINICAL PRACTICE GUIDELINES, CLINICAL PATHWAYS, AND HEALTHCARE PERFORMANCE MEASUREMENT FOR PLANNING, IMPLEMENTATION AND MANAGEMENT OF HEALTHCARE INTERVENTIONS IN DIFFERENT SETTINGS - INTEGRATE-HEALTH-GOV"- PRESA D'ATTO.

VISTO SI PRENDE ATTO

ANNOTAZIONE:

Responsabile del Procedimento  
PO - CARMEN PARTIPILO

Dirigente  
D.SSA REGINA STOLFA

