

## PhD Course in Public Health XXXVIII cycle, a.y. 2022/2023

### PhD Executive Positions

**N. 1 linked to research project:** *"Health Technology Assessment of Human Papillomavirus (HPV) testing as the primary screening test for the population based cervical cancer screening program of the Metropolitan Area of Milan."*

**Company:** Agenzia per la Tutela della Salute della Città Metropolitana di Milano

**Curriculum:** Health Services Research and Technology Assessment

**Abstract:**

Human Papillomavirus (HPV) test was introduced in 2017 as a primary screening test for cervical cancer among the Italian Essential Levels of Care (LEA). In the Metropolitan Area of Milan, the implementation of a population based screening program, offering a primary HPV test every 5 years to women aged between 30 and 64 years and a Liquid-Based Citology (LBC) every 3 years to unvaccinated women aged among 25 and 29 years, started in 2022. In the Lombardy region, vaccination against HPV started in 2008. The first cohort of fully vaccinated women reaches 25 years of age in 2022. According to the recommendations of the Cervical Cancer Screening Italian Group (GISCI), fully vaccinated women will be eligible for an HPV test every 5 years starting from 30 years of age. In addition, the 2020-2025 National Vaccine Prevention Plan (PNPV) recommends HPV vaccination catch-up during the first LBC screening test, for 25-yo women who hadn't been previously vaccinated. The combination of cervical cancer screening programs, based on primary tests with better sensitivity and specificity and more accurate in identifying treatable precancers, and the HPV vaccination policy, recently extended to male teenagers, will largely impact the epidemiology of both HPV infection and cervical carcinoma, as well as of other HPV-related cancers.

Aim of the present project is the conduction of a comprehensive assessment of cost, outcomes and cost-effectiveness of the current screening strategy, compared to a primary Papanicolaou smear screening strategy every three years, and to the no-screening alternative.

**N. 1 linked to research project:** *"Improving non-invasive ventilation in patients with acute respiratory failure"*

**Company:** ASST Grande Ospedale Metropolitano Niguarda

**Curriculum:** Pathophysiology and disease prevention

**Abstract:**

Non-invasive ventilation (NIV) is widely used in Emergency Departments (ED) to treat acute respiratory failure. It is strongly recommended in patients with cardiogenic acute pulmonary edema and COPD exacerbation, in

which reduces the rate of endotracheal intubation (ETI) and mortality.<sup>1</sup> Even though the evidence is still scanty, NIV is largely used as first treatment also in patients with de novo hypoxemic acute respiratory failure, in particular in pneumonia and ARDS, with high failure rates (22% for mild ARDS, 42% for moderate ARDS, 47% for severe ARDS) and risk of patient self-inflicted lung injury (PSILI).<sup>1-3</sup> Several predictors of failure have been proposed to better identify patients failing an initial trial of NIV: in particular, a severe hypoxia (P/F <150), high tidal volumes ( $V_t > 9.5$  mL / kg), and high inspiratory efforts, whose non-invasive evaluation still represents a challenge and an area of research interest.<sup>2,4,5</sup> Furthermore, the best non-invasive respiratory support modality (CPAP, BiPAP, single-tube circuit with leaks or bi-tube), the best interface (helmet, face mask), the best setting of ventilatory parameters (best PEEP, and pressure support), are not well defined yet. The research project aims to optimize the use of NIV in patients with acute respiratory failure in the EDs and in Sub-Intensive Care Units, and to evaluate the performance and usefulness of non-invasive methods of monitoring respiratory effort and function (e.g. pulmonary, cardiac and diaphragmatic ultrasound, and electrical impedance tomography).

Bibliografia

**N. 1 linked to research project:** *"Patients with a Fontan circulation beyond the fourth decade of life"*

**Company:** IRCCS Policlinico San Donato S.p.A.

**Curriculum:** Biostatistics and Epidemiology

**Abstract:**

Background

Survival after the Fontan operation is improving and many of these patients now live well into adulthood. Data on the late morbidity and mortality of Fontan patients in their 4th decade of life are lacking.

Study aims

To evaluate the late outcome of adult patients with a Fontan circulation who have survived beyond 35 years of age.

Study design

Retrospective data-only study therefore patient-level consent not required.

Study period: 1/1/2005 – present

Inclusion criteria: Consecutive patients with a Fontan circulation including atriopulmonary (AP), modified AP, Kawashima, lateral tunnel (LT) and extracardiac conduit (ECC), who became 35 years old during the study period.

Exclusion criteria: Unpalliated univentricular patients, patients with partial cavopulmonary shunts e.g. Glenn or other palliative shunts (e.g. Blalock-Taussig shunt, central shunt) not followed by a Fontan-type procedure.

Information collected:

- Demographics
- Underlying CHD, associated defects
- Dominant ventricle morphology
- Age at Fontan surgery
- Type and timing of Fontan
- Timing and type of Fontan revision (same type of operation, revised due to complication) or conversion (change in Fontan type e.g. AP to TCPC)

The following data were collected at baseline assessment i.e. at/just after 35th birthday, and at the latest follow-up / last follow-up before death or transplantation:

- NYHA functional class
- Bloods including haemoglobin, creatinine, estimated glomerular filtration rate, urea, (eGFR), iron studies, liver function including albumin, b-type natriuretic peptide
- Ventricular function (qualitative: normal or mild, moderate, or severe impairment)
- Degree of systemic atrioventricular valve regurgitation (nil, mild, moderate, severe)

- History of atrial thrombosis or thromboembolic events
- History of arrhythmia, heart failure admission
- History of protein losing enteropathy (PLE) or Fontan-associated liver disease (FALD)
- Date of follow-up
- Date and cause of death
- Date and type of transplantation
- New complications during follow-up: arrhythmia, heart failure exacerbation, thromboembolic event, PLE, FALD

Statistical analysis planned:

Descriptive statistics of cohort.

Survival analysis with death as end-point and also combined end-point of death or heart / heart-lung transplantation. Kaplan-Meier curves. Univariable and multivariable Cox proportional hazards analysis to identify predictors of an adverse outcome.

Study timeframe

Data collection:

Royal Brompton Hospital (complete), Southampton (complete), San Donato (2.5 months to end-September)

Data analysis and manuscript preparation: October-November 2021

Manuscript submission: December 2021.

**N. 1 linked to research project:** *"Innovative Healthcare and Welfare Models: Designing, Implementation, Assessment"*

**Company:** CUTE S.r.l.

**Curriculum:** Health Services Research and Technology Assessment

**Abstract:**

In economically advanced countries, the growing average age, the progressive socio-demographic changes and the epidemiological trends of the population have induced in the last decades the genesis of Health and Social-Welfare initiatives and models to contrast, mitigate and prevent structural problems (eg. Long term care, Taking Charge of Chronicity, Integrated Hospital-Territory Management, Support for Fragile People, ...). It is common evidence that many of these initiatives and models - originally considered adequate, robust and well developed - in the Pandemic COVID19 period showed various gaps in the systems and processes of continuity of prevention, treatment and diagnosis (as well as in emergency management).

In an equally evident way, potentially available "supports" - from Telemedicine to Big Data - have in fact proved to be an enormous unexpressed potential, becoming today, more than ever, key factors for future planning of policies and ecosystems of Public Health.

Supported by an epochal International "Recovery Plan", the National, Regional and Local Governance Systems have the opportunity to direct resources towards skills, organizational and instrumental solutions that will determine to a large extent the ability to protect citizens' health and social well-being for the next decades.

The PhD project will develop methodologies and tools for the design, implementation and governance of Innovative Welfare Models in which Health Services and Technologies find effective use to promote, achieve and guarantee sustainable and resilient welfare.

## **N.2 vincolate ai progetti:**

- 1) *"Le cardiomiopatie aritmogene ereditarie"*
- 2) *"Raccolta dati e follow-up di pazienti affetti da insufficienza tricuspidalica secondaria"*.

**Ente/Società:** ISTITUTO AUXOLOGICO ITALIANO

**Curriculum:** Fisiopatologia clinica e prevenzione delle malattie

### **Abstract:**

#### Progetto 1

Valutazione in una popolazione di pazienti affetti da cardiomiopatie aritmogene ereditarie di fattori genetici e clinici che possano essere implicati nella genesi e progressione della malattia e che quindi possano aiutare nella diagnosi, stratificazione del rischio e predizione della risposta terapeutica dei pazienti affetti. Per la parte genetica verranno ricercati nuovi geni associati alle diverse cardiomiopatie oggetto di studio e contestualmente verranno valutati fattori genetici non causali che possano avere un ruolo di modificatori della progressione di malattia. Per la parte clinica verranno valutati markers biochimici e variabili ricavate da indagini di imaging (ecocardiografia, risonanza magnetica nucleare cardiaca e scintigrafia miocardica).

#### Progetto 2

I dati saranno raccolti in modo prospettico, iniziando come studio a singolo centrico con la possibilità di ampliare la casistica aggiungendo altri centri satelliti tramite collaborazioni scientifiche.

Verranno raccolti dati completi derivati da: ecocardiogramma transtoracico bidimensionale e tridimensionale, metodiche di imaging di II livello quando eseguite (risonanza magnetica cardiaca, cardio-TAC, cateterismo cardiaco destro).

Gli obiettivi della analisi dei dati raccolti saranno:

- i) valutazione dei parametri di funzione ventricolare destra per capire quali correlano con la prognosi (eventi : morte e ospedalizzazioni per scompenso, progressione della patologia tricuspidalica con necessità di intervento chirurgico o transcateretere);
- ii) valutazione del ruolo del cateterismo da sforzo ed ecocardiogramma da sforzo in aggiunta all'ecocardiografia a riposo per la stratificazione prognostica di questi pazienti;
- iii) valutazione dei fattori clinici di progressione della insufficienza tricuspidalica in storia naturale.

## **N. 1 linked to research project:** *"Social fragility as a health determinant"*

**Company:** AGENZIA DI TUTELA DELLA SALUTE DI BERGAMO

**Curriculum:** Health Services Research and Technology Assessment

### **Abstract:**

The social determinants of health (SDH) are defined by the WHO as "non-medical factors that influence health outcomes". They include income, education, employment, housing and social inclusion among others and numerous studies suggest that they can account for 30 to 55% of the health outcomes<sup>1</sup>.

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<sup>1</sup> [https://www.who.int/health-topics/social-determinants-of-health#tab=tab\\_1](https://www.who.int/health-topics/social-determinants-of-health#tab=tab_1)

Frailty is a widely used concept that describes a state of increased vulnerability to adverse health outcomes that increases with the accumulation of physical, psychological, and social deficits. Among them social frailty is the most unexplored domain<sup>2</sup>.

The study aims to evaluate the feasibility and to possibly quantify an overall frailty score by complementing administrative databases comprising health records (hospital discharges, outpatient visit, ED access, drug prescriptions, health exemptions etc.), social frailty data (municipality social-services dossiers, deprivation index etc.), geographical data and accessibility (5A's of Access) related to the province of Bergamo.

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<sup>2</sup> Bunt S, Steverink N, Olthof J, van der Schans CP, Hobbelen JSM. Social frailty in older adults: a scoping review. *Eur J Ageing*. 2017;14(3):323-334. Published 2017 Jan 31. doi:10.1007/s10433-017-0414-7