XIII Seminar - Phd Day

An empathic approach to science: how to rebuild communities?

Organized by
the Italian National Institute of Health
and Sapienza University of Rome
Istituto Superiore di Sanità
Rome, October 3, 2022

Edited by
M. Micocci, E. Tortellini, G. Volonnino and S. Bocci

ISTITUTO SUPERIORE DI SANITÀ

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ABSTRACT BOOK

Edited by
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The PhD Day represents a traditional, successful event in the activities of the PhD in Advances in infectious diseases, microbiology, legal medicine and public health sciences. As the first meeting to be held in presence after the COVID-19 pandemic, the XIII meeting tries to deepen the aspects related to the state of communities after such a challenging condition. In particular, we will explore how an empathic approach should be beneficial in many areas of our activities, including our ways to participate to, and cooperate with, the scientific community.

Key words: Infectious diseases, microbiology, legal medicine, public health, empathy, community

Il PhD Day rappresenta un evento ormai tradizionale e di successo nelle attività del Dottorato di ricerca in *Advances in infectious diseases, microbiology, legal medicine and public health sciences.* Essendo il primo incontro da svolgersi in presenza dopo la pandemia, il XIII meeting ha l'obiettivo di approfondire gli aspetti correlate allo stato delle comunità dopo tali complesse e difficili condizioni. In particolare, cercheremo di esplorare come un approccio empatico potrebbe avere effetti positive in molte aree delle nostre attività, incluso il nostro modo di partecipare alla e collaborare con la comunità scientifica.

Parole chiave: Malattie infettive, microbiologia, medicina legale, sanità pubblica, empatia, comunità

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INDEX

PROGRAMME

Monday, October 3, 2022

8.45   Access and Registration

Preliminary welcome
Alfonso Mazzaccara, Training Office, Italian National Institute of Health, Rome, Italy
Anna Teresa Palamara, Department of Infectious Diseases, Italian National Institute of Health, Rome, Italy
Stefano D'Amelio, Department of Public Health and Infectious Diseases, Sapienza University of Rome, Rome, Italy
Carlo Della Rocca, Dean of the Faculty of Pharmacy and Medicine, Sapienza University of Rome, Rome, Italy

Session I

Chairpersons: **Corrado De Vito, Felice Marco Damato, Gianpietro Volonnino**

9.30   Lecture
Dalla percezione del dolore all'empatia
Salvatore Maria Aglioti

10.15   Lecture
L'empatia nella qualità della relazione terapeutica e per la prevenzione del *burn-out*
Cristiano Violani

10.35   Lecture
Maxi Emergenze e ricostruzione psicosociale
Giuseppe Tolve

11.00   Coffee Break

11.15-13.15
PHD CANDIDATES' COMMUNICATIONS
Chairpersons: **Paola Frati, Annalisa Rosso, Erika Renzi**

Forensic application of monoclonal anti-human Glycophorin A antibody to establish vitality of the injuries
Benedetta Baldari

Choosing non-institutional sources of information
about childhood vaccinations. A cross-sectional study
Vito Cerabona

Telemedicine in multiple sclerosis and dementia.
Opportunities of digital communication to support neurological chronic patient
Marta Chiappetta

Evaluation of e-learning activities at the Istituto Superiore di Sanità.
Focus on training for preparedness and response in the COVID-19 emergency
Alessandra Di Pucchio

PRe.Val.E clinical outcome indicator "proportion of PCI STEMI
treated within 90 minutes": preliminary results of the self-monitoring
in the Sandro Pertini Hospital, Rome
Arianna Di Rocco

Elevate to alleviate - evidence based vascular nursing study
Nicola Ielapi

Methodological approaches in the use of big data and real-world data
in public health: a systematic review
Giuseppe Migliara

Lifestyle behaviors among canadian nurses working night shifts
in the COVID-19 era: a cross-sectional study
Chidiebere Emmanuel Okechukwu

Dermal Filler complications and medico-legal implications
Maria Giuseppina Onesti

Performance indicators in litigation management: methodological proposal
for internal and external quality control
Matteo Scopetti

Rehabilitation and assistive technology for refugees and asylum seekers
Marco Tofani

Prediction of potential loss for health facilities through analysis
of previous litigations concerning medical liability
Rocco Valerio Viola

13.15 Lunch Break

13.15-14.15

POSTER SESSION

Health determinants in ethnic minorities with Alzheimer's Disease
and identification of early diagnosis strategies in individuals
with mild cognitive impairment
Antonio Ancidoni

Safety and health protection in maxi emergencies
Paolo Anibaldi

The "LAZIO ADVICE" telemedicine platform: first results of general
practitioners usage, facilitators and barriers
in the Local Health Authority Roma 1
Andrea Barbara

Evaluation of epidemiological trend of repeated point-prevalence studies
of healthcare-associated infections in a large teaching hospital
Domenico Barbato

A new trap prototype for sand flies surveillance: preliminary field collections
in dog shelter of Southern Italy
Ilaria Bernardini

The role of microbial translocation and gut microbiome in patients
with Kpc-Producing Klebsiella Pneumoniae (Kpc-Kp) rectal colonization
as a risk factor for subsequent bloodstream infections
Francesca Cancelli

Development of molecular assays on Plasmodium Falciparum
gametocytes for functional analysis and novel diagnostics
on malaria parasite transmission
Mariagrazia Ciardo

Study about the association between vaccination with attenuated live
flu vaccine and COVID-19 in the pediatric population
Rosario Andrea Cocchiara

New immunohistochemical markers for the differential diagnosis
between hanging and simulated hanging
Alessandra De Matteis

Evaluation of the ecotoxicity induced by veterinary pharmaceuticals
and their mixtures on the aquatic vertebrate Danio Rerio *through*
a one health approach
Kevin di Domenico

An organotypic model of retinal Toxoplasma gondii *infection:*
increased production of GSTO1, PNFKB AND IL-6
Veronica Rodriguez Fernandez

Concomitant medication polypharmacy, interactions and over the counter
medicament in a cohort of HIV elderly patients
Paolo Vassalini

Mosquito Alert: a citizen science project for improved mosquito surveillance
Silvia Venturini

Session II

Chairpersons: **Silvio Paone, Marco Pombi, Eeva Tortellini**

14.15   Lecture
        Human-Primates coexistence
        Noemi Spagnoletti

14.35   Lecture
        The example of the Public Cuban Biotech in controlling SARS-CoV-2
        Fabrizio Chiodo

15.00-17.00
        PHD CANDIDATES' COMMUNICATIONS

Inflammatory mechanisms in Caco-2 cells exposed to Anisakis-*derived*
messengers of pathogenicity
Ilaria Bellini

Toward the development of a new molecular method to study malaria
transmission: gene expression analysis of Plasmodium falciparum
ookinete-specific markers in Anopheles coluzzii *mosquitoes*
Giulia Bevivino

Beneficial effects of oral bacteriotherapy in COVID-19 patients
Luigi Celani

Detection of measles specific IGM/IGG by in house ELISA based
on recombinant N protein
Maedeh Kojouri

New entomological sampling method for arbovirus surveillance:
field test in Italy and Djibouty
Sara Manzi

PREFACE

The PhD Day represents a traditional, successful event in the activities of the PhD in Advances in infectious diseases, microbiology, legal medicine and public health sciences. As the first meeting to be held in presence after the COVID-19 pandemic, the XIII meeting tries to deepen the aspects related to the state of communities after such a challenging condition. In particular, we will explore how an empathic approach should be beneficial in many areas of our activities, including our ways to participate to, and cooperate with, the scientific community.

The event aims at encouraging sharing and spreading the PhD students' results and research projects. Their works will be presented as either oral communications or abstracts or posters. This will permit to a wide audience to get in touch with the most updated researches in the field.

As usual, the PhD students of the third year will present orally their results. In this edition, students at the second year will present in a virtual poster session their studies, while the abstracts of first year students studies are included in the "New research topics" section of the abstract book.

The Scientific Staff

Ilaria Bellini, Arianna Di Rocco,
Giovanni Galeoto, Erika Renzi, Marco Tofani,
Silvia Venturini, Livia Besi,
Felice Marco Damato, Nicola Di Fazio,
Alessandra Di Pucchio
Ilaria Bernardini

Session I

PhD candidates' communications

Chairpersons

Corrado De Vito, Felice Marco Damato, Gianpietro Volonnino

FORENSIC APPLICATION OF MONOCLONAL ANTI-HUMAN GLYCOPHORIN A ANTIBODY TO ESTABLISH VITALITY OF THE INJURIES

Benedetta Baldari (1), Luigi Cipolloni (2), Maria Rosaria Aromatario (1), Paola Frati (1), Vittorio Fineschi (1)

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(2) Department of Clinical and Experimental Medicine, University of Foggia, Foggia, Italy

Background: Monoclonal antibodies against Glycophorin A Antibody (GPA) - group of RBC - are employed in immunohistochemical staining during post-mortem examination. Through this method, it is possible to point out the RBC presence in tissues in order to evaluate the vitality both of soft tissue injuries and bone fractures sampled.

Methods: On all sample collected during autopsy, 4 μm-thick paraffin-embedded sections were cut and stained with H&E staining following the standard protocol. In addition, anti-human GPA antibody immunohistochemistry investigation was performed using antibodies anti-glycophorin A. Pre-treatment was necessary to facilitate antigen retrieval and to increase membrane permeability to antibodies anti-glycophorin A boiling 0.25 M EDTA buffer, at 20°C.

Results: 20 cases were selected analyzing the documentation of peculiar autopsies performed by the Institute of Legal Medicine of Rome and Foggia from 2010 to 2022: 5 samples of fractured bones and 15 samples of soft tissues. 5 cases were enrolled as controls. Confirming the anti-human GPA antibody immunohistochemistry investigation was found positive in fractured bones and in the 2 cases of retina; it was possible to demonstrate the vitality at the moment of the lesion. Monoclonal antibodies against GPA resulted contrasting in the hanging cases, indicating in some cases the presence of RBC and in others the absence of RBC. In 1 strangulation case, anti-human GPA antibody immunohistochemistry investigation was found positive. The results in the control cases have been negative.

Discussion: This experimental application demonstrated that the use of monoclonal antibody anti-human GPA on bone and retina - particularly in cases of corpses with advanced putrefaction phenomena - could be important to verify whether the lesion is vital or not. Furthermore, the contrasting results on the neck skin in hanged individual could be related to the RBC absence. According to literature, the presence of hemorrhagic infiltration is not generally observable in hanging cases. Though certainly not conclusive, more investigation are necessary.

INFLAMMATORY MECHANISMS IN CACO-2 CELLS EXPOSED TO *ANISAKIS*-DERIVED MESSENGERS OF PATHOGENICITY

Ilaria Bellini (1)**,** Daniela Scribano (1), Meysam Sarsha (1), Cecilia Ambrosi (1), Antonella Pizzarelli (1), Anna Teresa Palamara (2), Stefano D'Amelio (1), Serena Cavallero (1)

(1) Department of Public Health and Infectious Diseases, Sapienza University of Rome, Rome, Italy

(2) Department of Infectious Diseases, Italian National Institute of Health, Rome, Italy

Background: Anisakiasis is a zoonosis caused by consumption of raw fish parasitized with *Anisakis* spp. third stage larvae (L3). Even if humans are accidental host, a single L3 is sufficient to induce mild to severe symptoms. In fact, larval migration in the gastrointestinal tract, the excreted/secreted products and Extracellular Vesicles (EVs) can progressively determine allergic reactions, erosive ulcerous lesions and granulomas. Despite its relevance for public health, investigations on host's inflammatory and immune response are still very scarce. Furthermore, reports of tumors co-occurrence with *Anisakis* L3 are increasing, suggesting exposure as a risk factor. The aim of this study was to investigate the inflammatory pathway in *in vitro* human epithelial colorectal adenocarcinoma cells (Caco-2) exposed to the live L3, the Crude Extract (CE) and the exosomes enriched fraction (EV), as representative of mechanical action of L3, whole body of senescent larvae and inflammation silencing, respectively.

Methods: L3 were collected from fishes from selected area (FAO37) and species identification were carried according to diagnostic molecular keys. CE were analyzed using Qubit4 and EVs isolated through commercial kit were characterized using western blot and Nanoparticle tracking analyses. The activation of inflammatory response key molecules (ERK1/2, NF-kB), the gene expression and amounts of the pro-inflammatory cytokines (IL-6, IL-8) were analyzed by Western Blot, RT-PCR and ELISA, respectively.

Results: ELISA tests carried out on Caco-2+L3 showed a progressive decrease of IL-6 ($P<0.01$) and IL-8 if compared to controls. Interestingly, no signals were obtained for IL-6 in Caco-2+EVs ($P<0.01$) and IL-8 was downregulated ($P<0.01$). Contrariwise, CE induced a strongly increased secretion of IL-6 ($P<0.01$) and a decreasing trend was observed for IL-8. Real-time PCR results on Caco-2+L3, CE and EVs suggested a detectable early effect on cytokines expression (1h). Western Blot analyses are still ongoing.

Conclusions: The results obtained showed an intricate host-parasite interplay, characterized by an early phase where the active L3 and its released EVs may modulate the immune response to find a long-lasting niche where survive, and a second phase where L3 senescence may induce host immune response activation, leading to the granuloma formation.

TOWARD THE DEVELOPMENT OF A NEW MOLECULAR METHOD TO STUDY MALARIA TRANSMISSION: GENE EXPRESSION ANALYSIS OF *PLASMODIUM FALCIPARUM* OOKINETE-SPECIFIC MARKERS IN *ANOPHELES COLUZZII* MOSQUITOES

Giulia Bevivino, Fabrizio Lombardo, Bruno Arcà, Marco Pombi, David Modiano
Department of Public Health and Infectious Diseases, Sapienza University of Rome, Rome, Italy

Background: So far, *Plasmodium* transmission from the human host to the mosquito vector has been studied through *in vivo* and *ex vivo* experiments. However, these approaches are significantly hampered by logistical, ethical, and technical obstacles both in the field and in the laboratory. The aim of this project is to develop sensitive molecular methods to detect and quantify the ookinete stage of *Plasmodium falciparum* in *Anopheles coluzzii* mosquitoes. Nucleic acid extraction (gDNA and total RNA) from mosquitoes collected during the first 24 hours after an infectious blood meal (during the *Plasmodium* ookinete stage), would allow the simultaneous molecular identification both of the parasite and of the human host, originating from the last blood meal before mosquito capture. Therefore, this tool might allow to study the influence of the human genetic background on the efficiency of *P. falciparum* transmission from human to mosquito bypassing most of the above-mentioned obstacles.

Methods: *An. coluzzii* mosquitoes were experimentally infected with *P. falciparum* and collected at 12-18-24 and 36 hours post-infection, spanning the formation and maturation of the ookinete stage. RNA and gDNA were extracted from single mosquitoes and a SYBR green qPCR assay was developed to analyze across the four time-points the transcriptional profile of 4 selected ookinete-specific genes, encoding for: the Circumspozoite and TRAP-Related Protein (CTRP), Secreted Ookinete Adhesive Protein (SOAP), von Willebrand factor A domain-related Protein (WARP) and Chitinase 1 (CHT1) protein. Furthermore, external calibration standard curves were designed to achieve absolute quantifications of markers inside single infected mosquitoes.

Results: RTqPCR analysis showed a transcriptional modulation of ctrp, soap, warp and cht1 transcripts during ookinete development, with a peak in transcript abundance at 24 hpi during midgut invasion. The absolute quantification analysis showed to be suitable for quantifying ookinete transcripts with a good reproducibility among different markers.

Discussion: This study represents a first transcriptional analysis and molecular quantification of *P. falciparum* ookinete marker genes inside single *An. coluzzii* mosquitoes. Next experimental steps will involve the selection of the most promising marker and the validation of our protocol on field-collected mosquitoes. This pilot study is a first step in the development of more robust and agile conditions to investigate, on a large scale, the role of human, parasite, and mosquito genetic variability in malaria transmission.

BENEFICIAL EFFECTS OF ORAL BACTERIOTHERAPY IN COVID-19 PATIENTS

Luigi Celani, Gabriella d'Ettorre
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Background: SARS-CoV-2 may impact on host microbiota and gut inflammation, infecting intestinal epithelial cells. Furthermore, some patients after the resolution of the disease, experience symptoms associated with a syndrome known as Long-Covid characterized by symptoms such as fatigue, "brain fog", similar diffuse pains. The aim of this study was to compare the rate of mortality, the need of ICU hospitalization and the length of hospitalization in patients with severe COVID-19 pneumonia who received the best available therapy (BAT) *vs* patients treated with BAT and supplemented with oral bacteriotherapy. We also analyzed the effect of probiotic supplementation in preventing chronic fatigue.

Methods: We performed an observational cohort study included 200 adults with COVID-19 pneumonia. All patients received therapeutic regimens including low molecular weight heparin plus one or more between hydroxychloroquine, azithromycin, antivirals, and Tocilizumab. Oral Bacteriotherapy (OB) was used as complementary treatment. Subsequently, to evaluate the effect on chronic fatigue, a subgroup of 58 patients hospitalized for COVID-19 was analyzed. 24 (41.4%) received OB during hospitalization (OB+) while 34 (58.6%) taken only the standard treatment (OB–). Serum metabolomic profiling of patients has been performed at both hospital acceptance (T0) and discharge (T1). Six months after discharge, fatigue perceived by participants was assessed by administrating the Fatigue Assessment Scale.

Results: Out of the 200 patients, 112 received BAT without oral bacteriotherapy, and 88 BAT with oral bacteriotherapy. Crude mortality was 22%. In the group of patients treated with BAT plus oral bacteriotherapy 11% died as compared to 30% in the group of patients treated with BAT ($p<0.001$). By multivariate analysis, age >65 years, C-Reactive Protein >41.8 mg/L, Platelets <150.000 mmc, and cardiovascular events were associated with the increased risk of mortality. Oral bacteriotherapy was associated with a reduced risk for death. From the group of 58 patients investigated for chronic fatigue, 70.7% reported fatigue while 29.3% were negative for such condition. The OB+ group showed a lower proportion of subjects reporting fatigue than the OB– one ($p<0.01$). Furthermore, OB+ subjects were characterized by significantly increased concentrations of serum Arginine, Asparagine, Lactate opposite to lower levels of 3-Hydroxyisobutirate.

Discussion: this study suggests a possible role for oral bacteriotherapy in the management of patients hospitalized for COVID-19 pneumonia and point out how the administration of probiotics may prevent the development of chronic fatigue by impacting key metabolites involved in the utilization energy pathways.

CHOOSING NON-INSTITUTIONAL SOURCES OF INFORMATION ABOUT CHILDHOOD VACCINATIONS. A CROSS-SECTIONAL STUDY

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(3) Department of Sciences of Public Health and Pediatrics, University of Turin, Turin, Italy
(4) Local Health Unit, City of Turin, Turin, Italy

Background: The source of information about childhood vaccination accessed by parents plays a fundamental role in the onset of vaccine hesitancy. A cross-sectional study was carried out (i) to investigate the sources of information used by the parents of kids attending schools of all levels in Rome and Turin and (ii) to identify predictors that led to choosing alternative sources of information.

Methods: Two validated tools were anonymously administered online to the parents: the "Parent Attitudes about Childhood Vaccines Survey" (PACVs) and the "Health Literacy Vaccinale degli adulti in Italiano" (HLVa-IT). A logistic regression model was built to identify predictors of alternative sources of information on the topic.

Results: 2301 answers were collected from June to October 2021. Most of the respondents were mothers (81%), married (73%), with a mean age of 47.7 years (±6.4), with a degree or post-degree education (59%) and employment (90%); 11% of the respondents gathered information from tv and newspapers and 10% from the internet. Results of the logistic regression model show that fathers are more prone to use alternative sources of information (OR 1.43, p=0.004) as well as those who have negative attitudes toward childhood vaccinations (OR 2.72, p<0.001). Statistically significant associations were also found with a low perceived quality of the healthcare system, the higher kid's age, being atheist or agnostic, and requiring more information about vaccinations. People who had never paid attention to information material about vaccination or were never invited to get a vaccine were more inclined to use alternative sources of information.

Conclusions: Selecting an alternative source of information, as opposed to a conventional and institutional one, can result in significant skepticism or even refusal of childhood vaccinations. School-based educational interventions can effectively improve vaccine acceptance in both adults and children.

TELEMEDICINE IN MULTIPLE SCLEROSIS AND DEMENTIA. OPPORTUNITIES OF DIGITAL COMMUNICATION TO SUPPORT NEUROLOGICAL CHRONIC PATIENT

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Background: Telemedicine combines medical and informatics techniques that provide care at a distance by eliminating time, place, and cost barriers associated with access to care. Its potential benefits emerged especially during the COVID-19 pandemic. Telemedicine is a diagnostic-therapeutic service that can be used in a variety of clinical settings and by all health care providers; it also supports the patient and creates a link between different places of care (hospitals, specialist outpatient clinics, and those of the General Practitioner). Telemedicine expresses its potential especially in the management and monitoring of chronic diseases. It proves to be very useful in the neurological field in the treatment of neurodegenerative diseases such as Multiple Sclerosis and Dementia, contexts in which remote support ensures continuity of care for the patient and caregivers.

Methods: The evaluation of telemedicine in the two clinical areas examined was supported by a review of the scientific literature, comparison through research based on observation of in-person visits and tele-visits and qualitative research tools (interviews, surveys, case studies) that enabled the identification of limitations and potentialities of the use of digital tools, including from a technical and organizational perspective. The focus of the research was particularly on the clinician's communication approach to the patient and on all those elements that facilitate the integration of Telemedicine and the traditional visit.

Results: In the management of the pathologies examined, telemedicine improves the quality of life of the patient himself and his caregivers because it allows him to be assisted at home with medical services that complement those provided in the hospital. Furthermore, constant remote monitoring represents psychological support that makes the patient feel safe, avoids the risk of complications, and ensures more frequent contact with the clinician because it overcomes the barriers related to movement, especially in patients who have walking difficulty and those with dementia who tend to perceive disorientation outside the home environment.

Discussion: The results obtained demonstrate how the innovative medical assistance modality implemented with Telemedicine contributes to improving the care of the chronic neurological patient, strengthening the care network, and supporting the patient in the path of the disease. To obtain successful integration of this method, it is essential to organize an effective remote setting through training in the proper use of digital tools and support of new communication strategies between health care providers and patients.

EVALUATION OF E-LEARNING ACTIVITIES AT THE ISTITUTO SUPERIORE DI SANITÀ. FOCUS ON TRAINING FOR PREPAREDNESS AND RESPONSE IN THE COVID-19 EMERGENCY

Alessandra Di Pucchio (1), Donatella Barbina (1), Debora Guerrera (1), Andrea Vittozzi (2), Federica Maria Regini (1), Pietro Carbone (1), Alfonso Mazzaccara (1)
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Background: On February 28th 2020, the Istituto Superiore di Sanità (ISS) launched the e-learning course "Health Emergency from the Novel Coronavirus SARS-CoV-2: Preparedness and Response". The course was delivered on the EDUISS platform (https://www.eduiss.it) to train as many health professionals as possible throughout the national territory in the very first phase of the pandemic. This study focuses on the course's evaluation, in terms of the approach and instruments.

Materials and Methods: The Problem Based Learning (PBL), in the e-Learning adapted version developed by ISS, was the educationa l approach underpinning the e-Learning course. The Learning Management System (LMS) used was Totara Learn version 11. The course was asynchronous low interaction, e-mail assistance, free of charge access, delivered in Italian language. Three training units were included, developed with the contribution of seventeen experts from various institutions. PBL was used to create the learning activities associated to the learning outcomes. Formative and Summative assessment methods aligned to the learning outcomes were included. Kirkpatrick's evaluation model was applied to define the level of evaluation: learners reaction assessed by a standard satisfaction questionnaire (Likert type); a pre/post test including a set of 18 Multiple Choice Questions (MCQs) was developed to measure learning level (learning outcomes: knowledge); a standard quality questionnaire including items to measure whether the learned knowledge were transferable to the workplace (self-assessment). A final CME certification test including 63 MCQs for summative assessment (learning outcomes: knowledge). Totara tools were also used to track course completion rates and perform ongoing evaluations.

Results: Of the 205,830 participants, 160,207 (74%) successfully completed the course (completers). Completers: came from all Italian regions and belonged to all thirty different health professions of the Italian National Health Service; 94% of them reported high level of satisfaction; a significant improvement of completer's knowledge was reported after the course attendance ($t = 312.761$, $p = 0.00001$); the average score on the final CME test was 87.9/100 (SD 6.72, Range 76-100). Analysis of the psychometric characteristics of the evaluation tools were also performed.

Discussion and Conclusion: The e-Learning activities performed by ISS during the COVID-19 emergency has been nationally and internationally recognized. Starting from the lessons learned, a prototype course based on competence-oriented active learning - Problem Based Learning is going to be delivered.

P.RE.VAL.E CLINICAL OUTCOME INDICATOR "PROPORTION OF PCI STEMI TREATED WITHIN 90 MINUTES": PRELIMINARY RESULTS OF THE SELF-MONITORING IN THE SANDRO PERTINI HOSPITAL, ROME

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(3) Health Information Systems Unit, Sandro Pertini Hospital, ASL Roma 2, Rome, Italy

Background: The *P.Re.Val.E* (Regional Outcome Evaluation Program) annually publishes data about performance in the Lazio regional Health System. "Proportion of patients with STEMI treated with Percutaneous Coronary Intervention (PCI) within 90 minutes" is a quality indicator for efficacy and timeliness in STEMI (ST-segment Elevation Myocardial Infarction) treatment.

Objectives: Create an internal monitoring system, with detailed procedures, in order to evaluate the performance in the clinical indicator of the STEMI treatment, in advance of the regional outcomes evaluation program, starting from the data provided by the ASL Roma 2 Health Information System.

Methods: Data were obtained by crossing the SIO (Hospital Information System) and SIES (Health Emergency Information System) regional information flows, containing data validated by the Lazio Region. The inclusion and exclusion criteria of the *P.Re.Val.E* protocol were applied to the database obtained.

By internal audit, was performed a critical periodical review of STEMI cases in medical records, ICD-9-CM procedure codes and SDO "Scheda di Dimissione Ospedaliera" - Hospital Discharge Form).

Results: Have been included 113 medical records during the period January 01 - December 31 in 2021. A total of 56 STEMI cases has been treated with PCI within 90 minutes (49,6%). From that analysis, mainly two types of critical issues emerged: firstly, errors were documented in coding ICD-9-CM, over reporting AMI diagnosis, reported wrong date or hours of procedures (19/56 cases, 33,9); secondly emerged a delay in clinical network (22/56 cases, 39,3%) especially in atypical clinical presentation of STEMI, hemodynamic instability at presentation, ST– elevation absent at first admission ECG, etc.

Conclusion: An autonomous and computerized internal monitoring system allows to carry out a self-analysis of the internal health network. Obtaining information on health benefits over short periods, such as quarterly, and in advance of the annual report, would allow the necessary changes to be made to improve the quality of the health service.

ELEVATE TO ALLEVIATE - EVIDENCE BASED VASCULAR NURSING STUDY

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Background: Venous return in the circulatory system of lower limbs results from the interaction of several mechanisms and reflects the balance between blood inflow and outflow. Blood outflow improves during the lying position especially with leg elevation both in patients with Chronic Venous Disease (CVD) and in healthy subjects in sedentary settings with short-term immobilization. This study evaluated the level of comfort of hospital inpatients, without CVD, lying with a moderate leg elevation during hospital stay.

Methods: This was a clinical trial examining 60 consecutive patients referred to vascular surgery, cardiac surgery, and nephrology units. After inclusion, patients were randomly assigned to two groups: A (leg elevation) in which patients were made to lie in the hospital bed with moderate elevation of the legs, and B (no leg elevation) in which patients were made to lie in the hospital bed without leg elevation.

Results: The whole population consisted of 40 patients undergoing leg elevation (group A) and 20 without leg elevation (group B). During each day of hospitalization, measurements such as ankle and calf circumference, heart rate, blood pressure, and body temperature were collected. Subjective data such as perceived heaviness in the lower limbs, comfort perception and hours of sleep were also collected. In this study, patients of group A recorded a decrease in calf and ankle circumference (delta in ankle and calf circumference (difference between end of study visit and baseline visit) were significantly decreased in group A *vs* group B (p<0.001 for both sides), and patients perceived less leg heaviness and even reported more leg comfort compared to patients of group B (p<0.001)). Among patients of group A, the bigger advantage in terms of comfort perception was recorded in patients with 15° leg elevation.

Discussion: Moderate leg elevation during hospital stay seems to effectively improve leg comfort in hospitalized patients.

DETECTION OF MEASLES SPECIFIC IGM/IGG BY IN HOUSE ELISA BASED ON RECOMBINANT N PROTEIN

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Background: The World Health Organization (WHO) has set a goal of eradicating measles globally through mass vaccination. High-quality surveillance is required for efficient monitoring of eradication aims. The identification of measles-specific IgM/IgG antibodies is widely utilized for laboratory confirmation within the WHO worldwide measles and rubella laboratory network. A specific IgM/IgG in-house ELISA was developed using a recombinant measles Nucleocapsid (N) protein expressed in *Escherichia coli*.

Methods: Viral RNA was extracted from Measles virus genotype B3 strain MVs/Padova.ITA/24.17/1[B3] isolated from infected Vero E6 cells (C1008 [Vero 76, clone E6, Vero E6] – ATCC). The N gene was amplified from viral RNA to produce N recombinant protein. Human serum was diluted and commercial secondary monoclonal anti-human IgM-HRP goat anti-human IgG-HPR antibodies was used. Seventy-six human serum specimens, collected during the surveillance activity for measles disease, were first screened using a commercial IgM/IgG ELISA (SERION) kit. These sera were then processed using our new in-house assay for the presence of anti-measles IgG and IgM and the results were compared with those obtained with the commercial assay.

Results: The N protein was easily purified from *E. coli* cell lysates by a one-step protocol at high level of homogeneity. It was stable at -80°C TN buffer, and used as coating antigen in ELISA. For the development of the assay several quantities of coating antigen were tested (0.5, 0.25, 0.125 μg/well). Sensitivity and specificity of our in-house assay were evaluated and resulted comparable to those obtained with the commercial assay.

Discussion: The in-house IgM/IgG ELISA presented here is a specific and sensible tool in diagnosis of measles in seroprevalence and epidemiological investigations on protective immunity in different populations.

NEW ENTOMOLOGICAL SAMPLING METHOD FOR ARBOVIRUS SURVEILLANCE: FIELD TEST IN ITALY AND DJIBOUTY

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Background: Several strategies are available in mosquito-borne disease surveillance, according to target species and surveillance goals. In this study, we propose an innovative method to simplify pathogen detection from mosquitoes. To this aim we modified a BG sentinel trap to include a sugar delivery system equipped with a nucleic acid preserving substrate (FTA-card). During sugar feeding, pathogens in mosquito saliva are released on a honey-soaked FTA-card, remaining detectable for several days at environmental conditions. To define the applicability of the system we tested the modified trap in Italy and Djibouti exploring the performance in relation to i) a standard surveillance method (analysis of mosquitoes trapped with CDC-CO_2) ii) different target species iii) sampling scheme and iv) long term storage.

Methods: All mosquitoes collected in Italy (Jul-Aug 2019 and 2021) and Djibouti (Jan-Feb 2020) were morphologically identified to define the species. Each card was tested through RNA extraction and PCR for arboviruses detection. In samples collected in Italy we also processed mosquitoes in pools of up to 100 specimens as described for FTA-cards. Collected data were analysed through statistical software R with Mann-Whitney U test and GLM models.

Results: Data collected in Italy in 2019 show that the CDC-CO_2 trap catches 1.6 times more mosquitoes than the modified BG-sentinel under the same condition (GLM, $p < 0.001$; 95%CI=1.2-2.2). In relation to mosquito species, the proposed method collects less *Cx. pipiens* (median BG=96, CDC=189; Mann-Whitney U test, $p<0.001$), but shows best performance in trapping *Ae. albopictus* (median BG=7.5, CDC=1; Mann-Whitney U test, $p<0.0001$) and no difference for *Oc. caspius* (median BG=8.5, CDC=10.5; Mann-Whitney U test, $p=0,8$). Both trap types detect West Nile (WNV) and Usutu (USUV) viruses. Positive events from FTA-cards (N=2/72) are later and less than events reported with standard method (positive pool/tested mosquitoes, N=15/16646). In 2021 we modified the sampling scheme increasing traps and working days up to 4-day sampling. In this collection, the proposed system (N=2/50) highlight USUV circulation first of the standard method (N=2/919). FTA-cards collected in Djibouti show the circulation of WNV (N=2/71) and DENV (N=1/71) in different dates and traps, according to the presence of vector species in the corresponding trap.

Discussion: The detection of pathogens from FTA-cards in field show that the proposed system could be used for arbovirus surveillance. Under the same condition, our results suggest a low sensitivity of the modified trap compared to standard method, at least for USUV and WNV surveillance. The performance could be enhanced increasing the number of traps and working days and resulting particularly advantageous in long-term storage of arboviruses and in minimize the samples to detect arboviruses circulation in mosquitoes.

ISOLATION AND CHARACTERIZATION OF BACTERIOPHAGES WITH CLINICAL POTENTIAL APPLICATION AGAINST KLEBSIELLA PNEUMONIAE CARBAPENEMASE (KPC) PRODUCING KLEBSIELLA PNEUMONIAE

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Background: Bacteriophage are bacteria-infecting viruses with an obligate requirement for a host. Their abundance and distribution is depending on that of their host organisms. The interactions between bacteria and phages are complex and the role of phages in driving bacterial diversity in colonised microenvironments, such as the intestinal tract of hospitalised patients, is not yet well understood. Very few studies have focused on the isolation and characterisation of phages against KPC-producing Klebsiella pneumoniae (Kp) isolated from patient with diagnosis of intestinal colonization. The main objective underlying this research is to find new phages with potential clinical application against KPC-producing-Kp through the isolation and characterization of phages and the identification of those useful for a future clinical application (either as a decolonization strategy or as an adjuvant therapy for infections caused by KPC-Kp).

Methods: We collected different environmental samples of sewage water that is proven a rich source of bacteria. The isolation of KPC-Kp strains took place between 2019-2021 from clinical samples obtained during routine testing from patients with colonization or infection hospitalized at the Teaching Hospital Policlinico Umberto I of Rome, Italy. As controls strains, we collected susceptible Kp strains in 2022 in Charitè University of Berlin. Isolation of cocktails of phages and purification of single phages against the bacteria collection were then performed in triplicate. After isolation, we performed the DNA extraction and sequencing to better characterise the phages.

Results: We collected 18 samples from the enrichment treatment of sewage water and tested all samples against 17 strains of Klebsiella pneumoniae, in total 306 samples were analyzed with spot test method. We found the presence of single plaques until dilution -7 of the purified sewage water. We collected 63 "cocktails" where we observed a big spot lysis and in parallel we obtained a collection of 25 single phages from a single plaques; we performed 3-5 round of purification and the almost of the phage titration was around 10^8 PFU/mL and 10^{10} PFU/mL and the average of the titration was 2x 10^8 PFU/mL.

Discussion: Phages can be seen as new antimicrobial strategies against multi-drug resistant bacteria including KPC-Kp. This study could open up new and effective therapeutic strategies based on the use of phages to combat or prevent colonization and subsequent infection with KPC-Kp.

METHODOLOGICAL APPROACHES IN THE USE OF BIG DATA AND REAL-WORLD DATA IN PUBLIC HEALTH: A SYSTEMATIC REVIEW

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Background: Since the past few years, there has been a growing interest for the use of massive amounts of data - i.e. the Big Data - in medical research, for their potential role in changing the approach to personal care, medical care and public health. In this perspective, Big Data can provide great support in epidemiological research, in the analysis of the health needs, in prevention, treatment and management of medical conditions and in the development of healthcare policies. However, the analysis of such a huge amount of data poses significant challenges in obtaining evidence-based information. The aim of this systematic review is to address the methodologies used to deal with Big Data in medical research, focusing on the ways in which Big Data can be effectively used in a public health perspective.

Methods: A systematic review of the literature was performed, searching in PubMed, Scopus and Web of Science databases. Papers reporting the use of Big Data methodologies in public health will be included. The methodologies of collection, analysis and use of Big Data, as well as the challenges encountered and the strategies implemented to overcome them, will be reported. A particular interest will be placed on whether the study was guided by a hypothesis to be proved or whether a data-driven approach was used.

Results: The search retrieved 2880 records on PubMed, 8237 on Web of Science, and 15243 on Scopus. After removing duplicates, the 16348 records remained, that were at first screened for title and abstract selecting 361 records to be assessed by full text screening, selecting the papers falling into one of these six topic: i) Identification of risk factors for diseases in general population; ii) Identification of risk predictors or risk stratifiers for diseases in general population; iii) Use of technologies for disease surveillance; iv) Analysis of electronic medical records; v) Design of public health interventions, or conception and simulation of public health interventions; vi) Allocation of resources in health services. The full text screening is currently in progress and 92 records have been included for the systematic review.

Discussion: Although the study is still in progress, the great interest around big data in public health is evident from the number of records included in the systematic review, and the identification and understanding of the most suitable methodologies to provide good quality evidence in public health studies is therefore crucial.

LIFESTYLE BEHAVIORS AMONG CANADIAN NURSES WORKING NIGHT SHIFTS IN THE COVID-19 ERA: A CROSS-SECTIONAL STUDY

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Background: Anxiety, fear, and quarantine predisposes nurses to substance use in the era of Coronavirus disease 2019 (COVID-19) pandemic. Numerous nurses working night shifts tend to counter fatigue and sleepiness at work by taking caffeine excessively. The use of sleep-promoting medications and alcohol to initiate sleep during the day have been observed among nurses working night shift and the dependence on sleep-promoting medications have adverse health effects. The objective of this study is to determine the prevalence of substance use (nicotine, caffeine, cannabis, sleep-promoting medication, and alcohol use) in a sample of nurses working night shifts in the province of Saskatchewan, Canada, in the COVID-19 era. In addition, the association between job stress, sleep quality, anxiety, and depression.

Methods: Registered nurses working permanent or rotating night shifts between 25 to 65 years old, in the province of Saskatchewan, will be invited to participate in this online survey. Sociodemographic characteristics such as age, gender, race/ethnicity, level of education, years of working experience as a nurse, marital/relationship status, and hours of work per shift will be assessed. Various questionnaires will be used to assess job stress, substance use, sleep quality and mood among the participants.

Expected Results: At the end of this study, we expect an increase in substance use among Canadian nurses working night shifts in the era of COVID-19 pandemic and a significant association between sleep problem and depression.

Discussion: This study will reveal the possible association between working night shift and substance use among nurses during COVID pandemic. This study will also determine any possible association between job stress, sleep problem, anxiety, and depression.

DERMAL FILLER COMPLICATIONS AND MEDICO-LEGAL IMPLICATIONS

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Background: In the last decade, the number of dermal filler injections is significantly increased: they are considered minimally invasive procedure. Despite this, they are not free of complications. Filler can be classified in biodegradable and permanent: silicone, a permanent filler forbidden by FDA in 1992 and in Italy in 1993, is still used in some areas of the world causing major complications. Recently, in Italy, an unauthorized person performed a silicone injection in the mammary area to a patient at home, causing her decease. Filler complications can be triggered by vaccination, as the world observed during the pandemic due to SARS-CoV-2.

Methods: From 2000 and 2022, 215 patients had been evaluated at the Filler Complication Ambulatory of Plastic Surgery Department in Teaching Hospital Policlinico Umberto I of Rome. Anamnestic data and possible previous treatments' information were collected. We clinically evaluated signs and symptoms. Ultrasound was performed as first line imaging technique to identify type and amount of filler. Magnetic Resonance Imaging was performed for the most complicated cases. Every patient was treated with personalized therapy. Informed consent was obtained from every patient before the treatment.

Results: We observed major complications were associated to permanent ones (70%). Time range between the first injection and the sign/symptom varied between weeks and years. SARS-CoV-2 vaccine could have been caused dermal reactions if injected right after or before it. We also noticed that the number of medico-legal issues were mainly linked to permanent filler and only in few cases for the reabsorbable ones. Sometimes, they showed after absorbable filler injection in patients who were already treated with permanent ones.

Discussion: Dermal filler procedures should not be underestimated by the patients nor by the physicians who performs the procedure. Complications can always occur, and prompt diagnosis and treatment should be performed by certified experts to avoid the worst results. They should be performed in authorized structures by trained and expert specialist. Informed consent must always be collected. Patients must be aware of the kind of filler injected, the steps of procedures and all the related complications. The card of the injected filler should always be given to the patient. The plastic surgeon has an obligation of mean and he/she must not give unrealistic expectations: these, as the complications, can lead to claim for compensations from unsatisfied or misinformed patients. Moreover, filler injections should be performed 14 days before or after the vaccination for SARS-CoV-2.

MODULATION OF HOST IMMUNITY TO MALARIA BY *SCHISTOSOMA HAEMATOBIUM*

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Background: Several studies suggest that helminths infection might affect immunity to malaria in populations living in areas of co-endemicity. However, limited evidence is available on the impact of *Schistosoma haematobium* infection on immunity to *Plasmodium falciparum* and on the immunological mechanisms involved. The general aim of the research project was to investigate the modulation of host immunity to malaria by *S. haematobium*. The specific objectives were: 1) to assess the association between markers of *S. haematobium* infection on the prospective risk of *P. falciparum* malaria; 2) to investigate the impact of exposure to *S. haematobium* antigens on the course of *P. berghei* infection in mice; 3) to characterize the immunomodulatory properties of *S. haematobium* antigens in Dendritic Cells.

Methods: 1) IgM and IgG against *S. haematobium* Soluble Worm Antigen Protein (SWAP) and Soluble Egg Antigen (SEA) were measured by an in-house ELISA protocol in plasma samples collected from N=452 subjects. 2) Two experiments were conducted each involving two groups of 5 female CD1 mice that were inoculated, intra-peritoneally with either HIPSE or PBS and 1 day later infected with a clone of *P. berghei* expressing GFP. 3) Maturation of human DCs was induced in RPMI 1640 with 10% heat-inactivated FBS, 100U/ml penicillin and 0.1 ng/ml streptomycin by addition of 10μg/ml of 3 different tetraspanins or LPS, maturation markers and production of cytokines were measured by Cytofluorimetry and Luminex assay respectively.

Results: 1) Association analysis showed a significant increase in the incidence of *P. falciparum* infection among anti-*S. haematobium* seropositive subjects (IRR=1.30, 95%CI= 1.09-1.57, p-value=0.004). 2) A slower growth of parasite density in HIPSE treated mice versus controls was observed in both experiments, however differences were not significant. 3) The three tetraspanins induced the expression of maturation markers and a secretion of TNFα, IL6 and IL10.

Discussion: Results suggest an association between *S. haematobium* and increased prevalence of *P. falciparum* malaria *in natura* and provide initial evidence of immunomodulatory properties of *S. haematobium* antigens *in vivo* and *in vitro*.

CLINICAL AND PROGNOSTIC SIGNIFICANCE OF MERKEL CELL POLYOMAVIRUS (MCPYV) IN NON-SMALL CELL LUNG CANCER (NSCLC)

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Background: Merkel Cell Polyomavirus (MCPyV) is a double-stranded DNA virus associated with Merkel Cell Carcinoma (MCC). Considering the widespread prevalence of the virus across the body, the involvement of MCPyV in tumours other than MCC, such as Non-Small-Cell Lung Carcinoma (NSCLC), cannot be excluded. A potential association between MCPyV infection and EGFR expression it has also been suggested since BRAF gene, a downstream target of EGFR pathway, was found to be higher expressed in MCPyV+ samples than negative ones. Moreover, this correlation, it would seem associated with worse prognosis. Therefore, in this study the prevalence of MCPyV in NSCLC, and the prognosis through the screening of EGFR were investigated.

Methods: Formalin-Fixed Paraffin-Embedded tissue (FFPE) and corresponding nonmalignant lung tissue were obtained from 90 NSCLC patients. After DNA and RNA extraction, to detect MCPyV DNA, a quantitative real-time PCR (qPCR) was performed. To study the expression of viral RNA transcripts and virally encoded protein, a qualitative PCR, employing three set of primers (LT1, LT3 and VP1), was used. EGFR mutation analysis was carried out. PCR products were sequenced in service.

Results: MCPyV DNA was detected in 14/90 FFPE and in 1/90 nonmalignant lung tissue. qPCR showed viral DNA loads ranging from 1×10^2 to 5.5×10^2 copies/ug. By qualitative PCR, MCPyV DNA were detected in 3 samples with LT1 primer, in 7 with LT3 primer, and in 4 with VP1 primer. Four out of ten samples also expressed the LT gene transcript, whereas no VP1 gene transcript was found. Sequence analysis of the LT gene of these 4 samples showed, in 3 samples, amino-acid substitutions at the C terminus of LT. None of these mutations caused stop codons. In contrast, the LT gene of 1 tumor, presented a frameshift mutation which generated stop codons. These mutations occurred downstream from the Rb-binding domain causing a truncated exon 2 encoding LT helicase. Analysis of EGFR showed that the infection rate of MCPyV, was higher in NSCLCs with EGFR mutations than without EGFR mutations; however, this difference was not statistically significant (>0.05).

Discussion: Although the viral prevalence in NSCLCs was low, the tumor-specific molecular signatures support the possibility that MCPyV could be associated with the pathogenesis of NSCLCs. Moreover, since MCPyV infection is observed in occurrence of EGFR mutation, our results could indicate that MCPyV could be considered an EGFR mutagen and might spark interests to deepen the prognostic value of EGFR in NSCLCs.

CORRELATIONS BETWEEN CHRONIC INTESTINAL PSEUDO-OBSTRUCTION (CIPO), GUT MICROBIOTA AND INTESTINAL SEROTONIN-RELATED GENES EXPRESSION

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Background: The Chronic Intestinal Pseudo-Obstruction (CIPO) is a rare disease characterized by symptoms and radiological signs suggestive of intestinal obstruction, in the absence of lumen-occluding lesions, resulting from an extremely severe impairment of propulsive motility. Serotonin (5-HT) release, a local mediator and neurotransmitter, is linked to intestinal peristaltic and secretory reflexes. The intestinal microbiota and the Enteric Nervous System (ENS) interact through the synthesis, the release and the subsequent receptors' activation of serotonin. The interplay among ENS/5-HT and dysbiosis in CIPO remains largely unclear. The project aim was to assess correlations between gut microbiota, intestinal serotonin-related genes expression and the disease in CIPO pediatric patients. To this purpose Mucosa-Associated Microbiota (MAM) has been characterized, and changes in Gastrointestinal (GI) serotonin pathway have been evaluated.

Methods: We collected biopsies of colon, ileum and duodenum from 7 pediatric CIPO patients and 7 age-/sex-matched healthy controls at Cesare Arrigo Hospital (Alessandria). After DNA extraction, the MAM was assessed by next generation sequencing (NGS) of the V3-V4 region of the bacterial RNA 16s, in an Illumina Miseq platform. The expression of genes implicated in serotoninergic pathway (*TPH1, SLC6A4, 5-HTR3* and *5-HTR4*) was established by qPCR, after total RNA extraction from the same tissue samples. Correlation analyses were performed to highlight relationships between MAM and the expression of genes linked to the production (*TPH1*), transport (*SLC6A4*) and reception (5-*HTR3*, 5-*HTR4*) of 5-HT, and clinical parameters of CIPO patients.

Results: Our results showed, a MAM different in its composition and biodiversity respect to controls. Network analysis evidenced in CIPO patients a microbial ecosystem with fewer species, less connected, and with a greater number of non-synergistic relationships respect to controls. Preliminary results on qPCR analysis revealed an alteration in the expression of *TPH1* and *SLC6A4* genes resulted to be significantly less expressed in the colon district of CIPO patients respect to controls.

Discussion: Results showed, for the first time in CIPO patients, a specific MAM associated to CIPO patients and an alteration in the synthesis and transport of intestinal serotonin. A possible malfunctioning in the serotonin pathway, maybe linked or triggered by an altered microbiota, could be a mechanism underlying the intestinal mobility disorder in CIPO patients. Our results could also represent the first step to design a new therapy targeting microbiota, improving treatment outcomes and quality of life of CIPO patients.

MOLECULAR CHARACTERIZATION AND PREVALENCE OF PROTOZOAN AND METAZOAN PARASITES INFECTING NON-HUMAN PRIMATES IN NATURAL AND CAPTIVE CONDITIONS

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Background: Non-Human Primates (NHP) have been found infected with a diversity of intestinal zoonotic protozoan and metazoan parasites of public health concern. Ecosystem transformation increases the contact between humans and NHP, incrementing the chances of zoonotic parasite transmission. Likewise, contact with captive NHP can represent an occupational risk for humans, leading to parasitic infections. This study aims to evaluate the prevalence of intestinal parasites infecting NHP living in fragmented forests in Colombia and in a wildlife recovery centre in Italy, and to molecularly characterize selected parasite species of zoonotic interest, in order to identify potentially zoonotic pathogens and to explore their transmission pathways.

Methods: Faecal samples were collected from free-ranging NHP *Alouatta seniculus, Ateles hybridus, Aotus griseimembra, Aotus brumbacki, Cebus versicolor, Saimiri cassiquiarensis*, and *Sapajus apella* living in forest fragments in Central Colombia, as well as from captive NHP *Macaca tonkeana, Macaca fascicularis,* and *Sapajus apella* living at *Parco Faunistico Piano dell'Abatino, in Rieti* (Lazio Region). Two hundred fifteen and 33 faecal samples were collected from free-ranging and captive NHP, respectively. Flotation and faecal smears were performed in order to identify parasites based on morphology.

Results: About 91% of the samples were positive for intestinal parasites. Protozoans (*Blastocystis* sp., Balantiididae, *Dientamoeba* sp., *Entamoeba* sp., *Giardia* sp.), cestodes (*Hymenolepis* sp.), trematodes (*Controrchis* sp.), nematodes (*Ascaris* sp., *Strongyloides* sp., *Trypanoxyuris* sp., Ancylostomatidae), and acanthocephalans were found infecting free-ranging NHP. *Ascaris lumbricoides, Giardia intestinalis* and *Blastocystis hominis* were identified through molecular techniques, from samples of free-ranging NHP. Captive primates were found infected with protozoans (*Entamoeba coli, Dientamoeba* sp., *Iodamoeba* sp., *Balantidium*-like cysts) and nematodes (*Oesophagostomum* sp., *Strongyloides* sp., *Trichuris* sp.).

Discussion: This study contributes new information of intestinal parasites infecting wild NHP exposed to anthropogenic disturbance. The finding of parasites with zoonotic potential suggests epidemiological implications in NHP conservation and human health, at the human-NHP interface, in transformed ecosystems. Additionally, the results of this study could be useful in the design of public health policies, and within NHP conservation programs.

PERFORMANCE INDICATORS IN LITIGATION MANAGEMENT: METHODOLOGICAL PROPOSAL FOR INTERNAL AND EXTERNAL QUALITY CONTROL

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Background: The development of tools and the implementation of methodologies capable of making healthcare services measurable and documentable in order to quantify the results in terms of quality of care, is not a topic of recent acquisition. Litigation management can have a significant impact in the context of clinical governance and improvement of care performance only if it can provide for the quantitative and qualitative review of cases, communication with the professionals involved and sharing of data with the different structures involved. The main objective of the study is to describe in detail the entire development process of a group of Key Performance Indicators for monitoring and implementing performance in the management of medical liability litigation. The approach outlined will also help to define reference standards to be used for comparative purposes for the assessment of claims management performance.

Methods: The study was conducted through the analysis of data relating to the claims management activity carried out at the Teaching Hospital Policlinico Umberto I of Rome between 2012 and 2018. The data collected from the Legal Affairs Office of the health facility were used to set up the database. To develop a significant index for measuring the quality of the services provided, the Process Analysis Method was followed for the selection of the indicators.

Results: The present study included a sample of 936 claims reported between 2012 and 2018. As regards the volumes of services, the Teaching Hospital Policlinico Umberto I of Rome represents a highly specialized healthcare facility, with 1,235 beds, 41,000 annual hospitalizations, 24,000 days hospital admissions, 140,000 accesses to the emergency department and 1,000,000 annual procedures between instrumental diagnostics and specialist examination. In general, a positive impact of the performance indicators on the internal quality control system of litigation management was noted. The results obtained also provided extremely useful information on the role of collecting, analyzing and communicating performance data in the quality management system.

Discussion: The usefulness of implementing a set of indicators for performance evaluation was demonstrated. The performance was identified as an important factor influencing the healthcare safety, also in the field of medico-legal services. The methodology and the scientific perspective of the medico-legal activity allow - unlike the investigations carried out by non-governmental organizations and insurance companies - to obtain relevant results for the purposes of clinical governance in relation to the knowledge and consideration of the different phases and protagonists of care paths.

RATES AND DETERMINANTS OF HOSPITAL-ACQUIRED INFECTIONS AMONG ICU PATIENTS UNDERGOING CARDIAC SURGERY IN DEVELOPING COUNTRIES: RESULTS FROM THE EMERGENCY'NGO HOSPITAL IN SUDAN

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Introduction: Knowledge of local and regional Antimicrobial Resistance (AMR) is crucial for clinical decision making especially in critically ill patients. The aim of this study was to investigate rate and pattern of infections in valvular heart disease patients admitted to the Intensive Care Unit (ICU) at the Salam Centre for Cardio Surgery of Khartoum, Sudan (EMERGENCY'NGO).

Methods: This is a retrospective, observational, single large international reference center (Regional Program) study enrolling patients admitted to our ICU from January 1st to December 31th 2019 (Khartoum, Sudan). Data collected for each patient included demographic, operating theater/ICU data and microbiological cultures.

Results: Over the study period, 611 patients were enrolled (Elective surgery *n*=491, Urgent surgery *n*=34 and Urgent medical *n*=86). Infection rate was 14.2% and resulted higher on medicals than in surgical patients (25.6% *vs* 12.4%; p=0.002; OR=2.43) and in those undergoing urgent surgery *vs* elective patients (29.4% *vs* 11.2%; p=0.004; OR=3.3). Infection was related to (a) SOFA score (p<0.001), (b) time in ICU (p<0.001), (c) days from ICU admission to OT (p=0.003). A significant relation between type of admission (elective, urgent surgery or medical) and presence of infections was found (p<0.001). Mortality rate was higher in infected patients (infected *vs* infection-free: 10.3% *vs* 2.1%; p<0.001; OR=5.38 95% CI 2.16-13.4 p<0.001).

Conclusions: Hospital-acquired infections remain a relevant preventable cause of mortality in our particular population.

REHABILITATION AND ASSISTIVE TECHNOLOGY FOR REFUGEES AND ASYLUM SEEKERS

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Background: Good health and wellbeing for all, including those with disabilities, is one of the main sustainable development goals. Migrants with disability represent an underserved group of individuals who are forced to leave their countries. Data on refugees and asylum seekers with disabilities are lacking. Refugees have poor access to rehabilitation and Assistive Technologies (AT), although laws and policies in Italy guarantee this type of healthcare. However, there are several limitations to the successful implementation of these services.

Methods: We analysed Italian policies on migration and health, and data from *Sistema Accoglienza e Integrazione* (SAI - Reception and Integration System). Qualitative interview were also performed thanks to the collaboration of different reception centres in Italy.

Results: National health system is regionally based and therefore healthcare facilities and services vary in terms of quality in different regions of Italy. The latest available data from SAI revealed large disparities in services for refugees with disability between Italian regions. Only 10 regions have specific services for people with disabilities. The center area has the best distribution of services, with all four regions providing services dedicated to people with disabilities. The region with the most capacity to assist refugees with disabilities is the Apulia region: 5.48% of total availability is dedicated to people with disabilities. Overall, the SAI can accommodate a total of 32,456 people, but only 2.81% of available posts are reserved for people with disabilities.

Discussion: There are no consistent and systematic national initiatives in Italy to organize or improve rehabilitation and AT services for refugees and asylum seekers. Italy, together with Greece and Spain, is the first gateway to Europe and therefore a specific vulnerability assessment should be considered in reception centres and during the identification process. Although there are national policies guaranteeing access to rehabilitation and AT, people are not aware of these possibilities and regional differences in services for refugees and asylum seekers with disabilities are evident. Training healthcare professionals and social and community workers on migration and disability is recommended. Community-Based Inclusive Development approach should be considered an effective strategy. Therefore, national stakeholders, together with regional governments, should collaborate to remove barriers to the access of rehabilitation and AT, as well as to guarantee equity in healthcare and a good quality of life for all.

PREDICTION OF POTENTIAL LOSS FOR HEALTH FACILITIES THROUGH ANALYSIS OF PREVIOUS LITIGATIONS CONCERNING MEDICAL LIABILITY

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Background: In healthcare institutions, clinical risk management includes a set of methods, tools and actions that allow risk assessment and treatment in order to improve patient safety. Medical liability litigation is part of the clinical risk. To the best of our knowledge there are no standardized tools or objective references to quantify the probability of loss for Institutions deriving from a civil trial concerning medical liability.

Methods: We performed a retrospective analysis of civil litigation involving health facilities in Sapienza University to set up a single data warehouse. We collected and organized according to known variables available. We defined our categories of interest as for the incident type, patient outcome, payments occurred for compensation. We used a further classification about areas of inappropriateness found. Results were extracted and coupled by pivot charts.

Results: All claims of the last decade were included. We indexed 567 cases, among 47 different units; 42% concerned 5 high-incidence wards. 91 cases were liquidated before judicial course; 131 hesitated in compensation for a total amount of 16 million 625 thousand euros. Cumulative amount of clinical performance was 10 million 320 thousand euros, while 1 million 788 thousand depended on organization defects.

Discussion: Data collected reflects a ratio between claims and hospitalizations of 26.8. We observed a gradual decrease in the last three years of the study period. Based on ICPS classification, we found high incidence of fatal cases (20% of total). Although 75% of compensated claims preceded judicial sentences, their cumulative amount counted for less than a half. The general judicial conversion rate of unpaid claims, on the other hand, is affected by the short time interval since the opening of the claims in the last two years of the examined period. Neurosurgical complaints are fewer than orthopedic ones, but they bring higher compensation, since the damages are more serious. Similarly, radiology and civil liability complaints lead to low compensation, despite the large number. The number of disputes, especially the catastrophic ones, is hardly predictable. The management of healthcare-associated infections is a fundamental problem, which increases litigation. This study confirms the relevance of the healthcare-associated infections in clinical risk management. The analysis of malpractice claims data allows the detection of the patterns and the consequences of iatrogenic errors; the risk manager can improve safety in a more targeted manner.

Poster Session

HEALTH DETERMINANTS IN ETHNIC MINORITIES WITH ALZHEIMER'S DISEASE AND IDENTIFICATION OF EARLY DIAGNOSIS STRATEGIES IN INDIVIDUALS WITH MILD COGNITIVE IMPAIRMENT

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Background: Alzheimer's Disease (AD) is a condition that affects all ethnocultural realities, and AD prevalence is rising more rapidly in low and middle-income countries where life expectancy is increasing. Migration flows are progressively increasing worldwide, and inevitably, healthcare systems are demanded to develop adequate support for the diagnosis, management and treatment of patients that belong to different ethnocultural backgrounds. Mild Cognitive Impairment (MCI) is a clinical condition that occurs before dementia onset and is characterized by cognitive disturbances. These two clinical entities need to be better described in people with a migrant background.

Methods: National surveys, population-based studies and studies on healthcare administrative databases will be essential to comprehend the dementia phenomenon in Italian-born patients as well as in patients with different cultural backgrounds.

Results: Preliminarily, a national survey was conducted in 343 Italian Centres for Cognitive Disorders and Dementia (CCDDs) to obtain information on the number of migrants referred to CCDDs in 2019, the challenges encountered in the diagnostic approach, and potential facilitators in the provision of care. A significant number of migrants are being referred to CCDDs in 2019. However, CCDDs are still not equipped to deliver diversity-sensitive care and support for people with dementia. A population-based, cohort study was also conducted in the Lazio Region to identify migrants living with dementia based on data from health administrative databases and to investigate possible differences in the prevalence, clinical correlates, and treatment of dementia between migrant and Italian-born patients. The main results from this study identified that migrants have a lower age-standardized prevalence of dementia and reduced access to dedicated treatments and services than Italians-born patients. Concurrently, to understand the prevalence of use and consumption of Anti-Dementia Drugs (ADDs) (years 2018-2020) among people residing in Italy aged >65 (Italians and migrants), a descriptive study using administrative healthcare databases was conducted. Results from this study identified that 38% of ADDs is not reimbursed by the NHS. This data, together with other results, extends knowledge on the use of ADDs, providing useful comparisons with the prescription pattern of ADDs from other countries.

Discussion: Based on data from health administrative databases, a population-based, cohort study will be conducted in the Umbria region to identify people with MCI and dementia and their ADDs prescription pattern. This study will aim to have a closer look at living people with MCI or dementia with a migration background.

SAFETY AND HEALTH PROTECTION IN MAXI EMERGENCIES

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Background: The COVID-19 pandemic has severely tested traditional models for healthcare facilities. The initial difficulties faced by the National Health System negatively affected clinical and economic outcomes. Generally speaking, any catastrophic event with unknown characteristics, and which overwhelms the "normal" operational abilities, requires the development of new organizational models. These new models should enable all stakeholders to coordinate their actions and effectively meet health care demands. The primary goal is to increase public health and safety via the development of organizational models which are flexible and can be easily amended based on the organization's specific needs. The secondary goal is to identify/develop real-time clinical pathways able to resolve the emergency, as well as providing a protocol to manage its aftermath.

Methods: The present study was founded on the identification of a methodology for safeguarding the safety of care in the context of maxi-emergencies. Specifically, a five-step process has been implemented for realizing the quality objectives:

1) Operational strategy and strategic time management;
2) Timely processing of available data;
3) Creation of protected paths involving victims and operators;
4) Training for operators involved in the emergency (not only for health professionals);
5) Regular re-training.

In this context, we can look at Disaster management as a multidisciplinary team of experts who rapidly enact solutions for the emergency using the most accurate scientific evidence to best allocate available resources.

Results: The theorized methodology made it possible to develop care models and plan actions for the improvement of clinical and economic outcomes. It was also possible to create a multidisciplinary and transversal organizational system to cope with maxi-emergencies, characterized by a strong preventive perspective for the management of disasters.

Discussion: In the case of maxi emergencies, it is necessary to take actions to reduce public health damage, knowing however that it will be impossible to reduce the risk to zero. Those who deal in public health face a challenge that can be better tackled with a "programming" mindset. The word programming may seem far-removed from the idea of an emergency, yet in our research we aim to demonstrate that it is precisely through a forward-thinking, programming mindset that we can be prepared to face a healthcare maxi emergency and give concrete answers, which will allow to protect public health.

THE "LAZIO ADVICE" TELEMEDICINE PLATFORM: FIRST RESULTS OF GENERAL PRACTITIONERS USAGE, FACILITATORS AND BARRIERS IN THE LOCAL HEALTH AUTHORITY ROMA 1

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Background: Telemedicine provides the use of information and communication technologies to deliver healthcare services at a distance. It represents a valuable tool for COVID-19 patients, allowing clinical assessment, monitoring of vital parameters, remote visits and prescription of treatment or hospitalization in case of clinical worsening.

The study aims to evaluate the use, barriers and facilitators of the "Lazio ADVICE" telemedicine platform according to General Practitioners (GPs) and Family Paediatricians (FPs) of the LHA Roma 1 to contrast the COVID-19 pandemic and its implementation.

Methods: An interview-based survey was performed in December 2020, composed of questions investigating the demographic information of GPs/FPs, the knowledge of the platform, frequency of utilization, usefulness, strengths and weaknesses and hypothesis of future implementation proposed. Sample size and randomization to obtain a casual ordered list of GPs/FPs and statistical analyses were performed. The participation of GPs/FPs was voluntary, unpaid and informed consent was requested.

Results: We interviewed 214 physicians (21,75% of the total population): 89 (41,59%) were users and 125 (58,41%) non-user.Among the users, 19 (21,35%) used the platform every day or even several times a day, 40 (44,34%) several times a week but less than one access per day, 30 (33,71%) several times a month up to one entry per week. Most of them (92,26%) consider the platform useful. Suggested improvements: integration between applications (ADVICE and the software used by GP/FPs; 86,26%), presence of data regarding COVID-19 diagnosis and contact tracing (69,6%), facilitating access and usability (52,81%). Difficulties: poor integration among software and work routine (76,4%), deficiencies regarding contact tracing aspects e.g. viewing pdf of swab results (67,41%), access and usability issues (53,93%). Among the non-users, 14 (11,2%) didn't know the platform existence, 60 (48%) never tried and 51 (40,8%) tried to use it. Reported reasons for the interruption of use were not very user-friendly (45,1%), perceived useless (37,26%), non-optimal functioning (23,53%) and lack of time (19,61%).

Discussion: Lazio Region has adopted innovative strategies to develop an adequate response to the coronavirus pandemic, such as "Lazio ADVICE". Despite contrasting results and opinions, the COVID-19 pandemic has accelerated the implementation of telemedicine services around the Region, starting a positive and continuous exchange of experiences,

activities and best practices among physicians and all LHAs. Telemedicine for monitoring patients has potential but certainly has to compete with a niche already occupied i.e. by telephone consultations; consequently, to be competitive, it must offer something different or additional.

EVALUATION OF EPIDEMIOLOGICAL TREND OF REPEATED POINT-PREVALENCE STUDIES OF HEALTHCARE-ASSOCIATED INFECTIONS IN A LARGE TEACHING HOSPITAL

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Background: Healthcare-Associated Infections (HAIs) are the most frequent adverse events in healthcare settings. They are associated with increased mortality and Antimicrobial Resistance (AMR), leading to prolonged hospital stays and consistent financial loss for healthcare systems. Similarly, Antimicrobial Use (AMU) and AMR represent a growing threat to global public health and the sustainability of healthcare services.

Objectives: The objective of this study is to estimate the burden of HAIs and antimicrobial use in the Teaching Hospital Policlinico Umberto I (THPUI) of Rome describing the trend of prevalence of HAIs across the years, comparing data about: a) patients; b) invasive procedures; c) infections; d) prescribed antimicrobials; e) clinical setting; f) risk factors for HAIs. Data were collected according to ECDC point prevalence survey protocol in the same months of three different years (2018, 2019 and 2021). Descriptive statistics for all variables were calculated. Univariate analysis was used to assess possible associations between variables and HAIs. Variables with a significance level of $p<0.25$ were included in a multiple logistic regression model.

Results: A total of 2,362 patients were included in three repeated Point Prevalence studies from 2018 and 2021; of these patients, 13.9% presented with at least one HAI. The prevalence of patients with HAI was 13.3% (106/799) in 2018, 11.1% (91/818) in 2019 and 17.6% (131/745) in 2021. Bloodstream infections were the most common, accounting for 31.8% of total infections, followed by urinary tract infections (24.0%) and pneumonia (22.7%). Overall, 397 microorganisms were isolated, with Enterobacteriaceae being the most frequent [39.5% (157/397)]. At the time of the survey, 49.8% (1,177/2,362) patients were receiving antimicrobial therapy. The multivariate analysis showed a significant association between HAI and patients' age (OR=1.01; 95% CI:1.01-1.02), use of medical devices (OR=4.81; 95% CI:3.12-7.41), length of stay (OR=1.02; 95% CI:1.01-1.02) and exposure to prophylactic antimicrobial therapy (OR=0.54; 95% CI:0.36-0.80).

Discussion: The ECDC methodology proved to be applicable to THPUI, where HAI prevalence was higher than the European standard. This highlights the need to implement targeted measures to prevent and control HAIs, including continuous monitoring to evaluate the effectiveness of such interventions and economic impact. This methodology and related tools used in this study could be exported into other local and regional healthcare settings in order to create a standardised approach for the management of HAIs and to compare similar contexts.

A NEW TRAP PROTOTYPE FOR SAND FLIES SURVEILLANCE: PRELIMINARY FIELD COLLECTIONS IN DOG SHELTER OF SOUTHERN ITALY

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Background: Phlebotomines are vectors of several human and zoonotic diseases such as *Leishmania* spp., *Bartonella bacilliformis* and Phleboviruses. Among the major sand fly vectors in Italy, *Phlebotomus perniciosus* and *Ph. perfiliewi* are the most widespread. A prerequisite to prevent and control sand flies and the diseases they transmit is knowing their presence in the environment through entomological surveillance. Standard sampling techniques for adult sand flies are sticky papers and suction trap (e.g. CDC), but they maintain specimens alive only few hours. The aim of this study is to evaluate several traps that can be potentially modified to collect sand flies and preserve them alive for at least 24 hours for subsequent breeding, competence studies or molecular analysis.

Methods: Preliminary field experiments were performed in a dog shelter in Valenzano (Bari, Italy) from September to October 2021, where three traps were compared through a Latin squared design: CDC light trap, BG-pro trap, and a prototype trap (both never tested for sand fly sampling) placed in three different sites ± 30m far from each other and rotated in position every night. The new prototype consists in a sideway suction trap that catch specimens in a collection chamber (7,5 l) at its bottom where air circulation is allowed by a central hole. High humidity is maintained inside the trap through 7% HEC idrogel solution. The collected specimens can feed on sucrose solution (1:10) placed inside the chamber.

Results: A total of 50 Ph. perniciosus (mean proportion per night = 5.5; SD = 6.5; min= 1; max = 16) were collected by BG-pro trap, following by CDC light trap (N = 36; mean proportion per night = 4.0; SD= 4.2; min = 1; max = 12) and new prototype (N = 23; mean proportion per night = 2.5; SD = 4.36; min = 1; max = 13). In all cases sex ratio was unbalanced in favour of males (BG-pro = 60%; CDC light trap = 74%; New Prototype = 78%) and no alive specimens were registered in the traps.

Discussion: The results, although preliminary, indicated BG-pro trap as a promising tool for sand fly sampling, while the new trap showed the lowest performance among the three traps. It should be taken into account that this sampling was conducted at the end of the sand fly activity period, where densities are particularly low. Therefore, other samplings to be conducted during the peak of sand fly seasonal activity are needed, where optimal conditions to evaluate the trap performances will be available. Once identified the best trap, its design will be modified to host collected specimens in optimal conditions according to project aims.

THE ROLE OF MICROBIAL TRANSLOCATION AND GUT MICROBIOME IN PATIENTS WITH KPC-PRODUCING KLEBSIELLA PNEUMONIAE (KPC-KP) RECTAL COLONIZATION AS A RISK FACTOR FOR SUBSEQUENT BLOODSTREAM INFECTIONS

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Background: The spread of antibiotic resistant bacteria in clinical settings has reached a very worrisome level worldwide, especially carbapenem-resistant *Klebsiella pneumoniae* (Kp). In the majority of cases, KPC-producing *Klebsiella pneumoniae* (KPC-Kp) rectal colonization is expression of an altered microbiota as a consequence of previous antimicrobial therapies, which have a detrimental effect towards the gut flora homeostasis. Colonization by KPC-Kp is considered to be a prerequisite for subsequent infection, especially Bloodstream Infections (BSI).

Methods: Patients with KPC-Kp rectal colonization hospitalized in Intensive Care Unit (ICU) and non-ICU wards of the Teaching Hospital Policlinico Umberto I of Rome, Sapienza University of Rome will be enrolled in the study. To detect KPC-Kp rectal colonization, periodicals (i.e., every week) rectal swabs will be performed. Subjects will be further divided into those developing nosocomial KPC-Kp BSI (BSI+) and those not developing nosocomial KPC-Kp BSI (BSI-) during the 30-day follow-up period. Markers of Microbial Translocation [LPB (Lipopolysacharide Binding Protein); EndoCab IgM] and Intestinal Damage [I-FABP (Intestinal Fatty Acid Binding Protein)] will be evaluated using enzyme-linked immunosorbent assays in plasma.

Results: Not all the KPC-Kp colonized patients develop subsequent BSI; however, since BSIs caused by KPC-Kp are associated with high morbidity and mortality, it is important to identify the risk factors for developing BSI in patients with KPC-Kp colonization in order to promptly start adequate antibiotic therapy in patients with suspicion of infection. We conducted a pilot study to assess BSI in COVID era. Among 1,099 patients admitted in Infectious Diseases Department (non ICU) between March to December 2020, 84 (7.6%) BSI we observed. 7/84 (8.3%) BSI were due to Multi-Drug Resistant (MDR) pathogens (*A. baumannii XDR* e *K. pneumoniae KPC*), each patient was previously colonized by pathogens which caused bacteremia. However only 30/1099 (2.7%) patients were colonised by MDR pathogens. It appears that colonized patients by MDR pathogens have high risks to have bacteremia but not all patient developed that. Therefore, the aim of our study is to research risk factors for bacteremia in subjects with MDR rectal colonization.

Discussion: The innovative hypothesis of this project is that during KPC-Kp rectal colonization a certain degree of gut permeability and microbial translocation as well as an alteration of gut microbiome occur, possibly influencing the risk of subsequent BSI. The importance of the results of this project resides on the clinical consequences, either in terms of improving the clinical management of KPC-Kp infections by reducing the time to start the appropriate therapy or in terms of antimicrobial stewardship principles by using "the right therapy for the right patient".

DEVELOPMENT OF MOLECULAR ASSAYS ON *PLASMODIUM FALCIPARUM* GAMETOCYTES FOR FUNCTIONAL ANALYSIS AND NOVEL DIAGNOSTICS ON MALARIA PARASITE TRANSMISSION

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Background: The transmission of *Plasmodium falciparum* malaria parasite from human host to mosquito vector depends on the presence of gametocytes, the sexually dimorphic stages of the parasite circulating in human peripheral blood. For transmission to succeed, both mature male and female gametocytes must be taken up by a female Anopheles mosquito during the blood meal as the first step is the fusion of one male and one female gamete. To define a parameter to measure the gametocyte sex ratio is relevant to predict parasite infectiousness to mosquito, to deploy transmission-blocking interventions targeting the parasite sexual stages and to test gametocytocidal compounds to investigate possible sex specific effect of these compounds.

Methods: Real time PCR assay (DCt) based on two sex-specific transcripts, pfCCp4 for female and pfMGET for male gametocytes was used to measure the sex ratio of a population of gametocytes. Gametocyte sex-ratio values independently obtained with the above Real time assay and with Immunofluorescence Assays (IFA) were compared in three *P. falciparum* laboratory lines, two wild type (NF54 and HB3) and one transgenic (Dyn- GFP). As it is impossible to physically separate wild type male and female gametocytes, preparations in which the number of male and female gametocytes was derived by the sex ratio determined by the above IFA, were used to calculate the copy number of the pfCCp4 and pfMGET transcripts in female and male gametocytes.

Results: Preliminary experiments showed that the gametocyte sex ratio obtained using the DCt value correlated with the sex ratio independently determined by IFA analysis only in the wild type lines NF54 and HB3 but not in the case of the transgenic line. Preliminary results indicated that in gametocytes of all three P. falciparum lines the copy number of pfMGET is higher than the that of pfCCp4. The Real time PCR assay was used on gametocytes treated for 48h with 1 microM of compounds MMV048 and MMV07116. Results indicated that neither compound differently affected the viability of male and female gametocytes.

Discussion: DCt can be used to measure sex ratio of wild type gametocytes. It also can be used to test additional compounds to test possible sex-specific activity against gametocytes. Molecular sex specific assays can allow to understand the influence of the sex ratio and its perturbations by drug treatment on parasite transmissibility in mosquitoes.

STUDY ABOUT THE ASSOCIATION BETWEEN VACCINATION WITH ATTENUATED LIVE FLU VACCINE AND COVID-19 IN THE PEDIATRIC POPULATION

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Background: Vaccination generates a specific immunological memory capable of responding in a fast and targeted manner in case of exposure to the target pathogen. It has recently emerged that vaccines can induce heterologous or Non-Specific Effects (NSE). In particular, epidemiological studies have shown that vaccination with Live Attenuated Vaccines (LAV) is associated with an increase in overall infant survival and a lower incidence of respiratory infections caused by unrelated pathogens. The immunological mechanisms responsible for NSEs are based on the induction of innate immune memory also called trained immunity. Considering the broad immune protection mediated by trained immunity and the epidemiological evidence of non-specific protection, including viral respiratory tract infections conferred by LAV, it was observed that LAV may also have protective effects against 2019 Coronavirus disease (COVID -19). In the pediatric population, the clinical manifestation of SARS-CoV-2 infection is generally benign, although in some cases the infection may be complicated by the onset of Multisystemic Inflammatory Syndrome (MIS-C), which is fraught with high morbidity and mortality. Among the factors identified as possible responsible for a lower susceptibility to infection, innate immunity and trained immunity were identified.

Methods: The pediatric population, in the period between October 2021 and January 2022 received the administration of the LAV against influenza nasally. A retrospective cohort study including children aged 0 to 14 resident in ASL Roma1 and 2 will evaluate the effectiveness of the influenza vaccine in reducing the risk of SARS-CoV-2 infection. For each member of the study cohort, the vaccination status for Fluenz tetra, AstraZeneca will be obtained from the ASL register while any SARS-CoV-2 infection and/or relative hospitalization will be extrapolated by accessing the database of the Regional Service of Surveillance of Infectious Diseases (SERESMI) of Lazzaro Spallanzani Institute.

Results: As LAVs have been shown to have heterologous protective effects and as the pivotal role of mucosal immunity in preventing viral respiratory tract infections is increasingly evident, significant efficacy of intranasal LAV against influenza (Fluenz tetra, AstraZeneca) is expected to prevent from SARS-CoV-2 infection in the pediatric population. This study will simultaneously evaluate the effects on SARS-CoV-2 infection, of other pediatric vaccines and in relation to their timing of administration.

Discussion: The vaccination with LAV might demonstrate an association with an increased pediatric survival and a lower incidence of complications after SARS-CoV-2 infection. The trained immunity might play a significant role in impacting on respiratory infections in children.

NEW IMMUNOHISTOCHEMICAL MARKERS FOR THE DIFFERENTIAL DIAGNOSIS BETWEEN HANGING AND SIMULATED HANGING

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Background: The diagnosis of the vitality of an injury, i.e. whether it occurred before or after death, is important in forensic pathology, as the differential diagnosis between death by hanging and simulated hanging (suspension of the victim after murder). The finding of a vital reaction at the cervical skin wound may aid in the diagnosis of hanging, but the finding of ambiguous vital reactions isn't uncommon. There is a real difficulty in interpreting the histology of the skin wound, due to the timing of lesion formation, which may be short and insufficient for the development of a vital reaction. An important aid comes from immunohistochemical methods and the study of miRNAs. The objective of this study is to search for reliable immunohistochemical markers in the differential diagnosis between hanging deaths and simulated hanging.

Methods: 25 skin samples from subjects who died from hanging will be selected and a control group of 10 cases will be recruited (5 negative controls from subjects who died from another non-traumatic cause; 5 positive controls from Glioblastoma and/or Ovarian Carcinoma). The tissue samples will then be treated with anti-CHAF1A Ab (Chromatin Assembly Factor1 SubunitA) and anti-FOXO3 Ab (Forkhead boxO3). The role of CHAF1A is unclear however, molecular studies have confirmed that it binds Histone H3/H4, packing chromatin and making DNA duplication and transcription impossible. CHAF1A is a regulator of apoptosis and its expression would appear related to the Bim protein of the Bcl family, and regulated by FOXO3. FOXO3's role is to mediate the apoptotic cascade, as an intermediary in the Akt/FOXO3/Bim axis. We chose these markers in consideration of the results of our previous study in which we showed that c-FLIP, an early marker of ischaemia/apoptosis, is under-expressed in the wound skin, as the ischaemic insult would result in underexpression of c-FLIP with activation of necroptosis and the proteolytic cascade leading to cell death.

Results: The interest of this study is to verify if the CHAF1A and FOXO3 can be used as diagnostic tools on the skin wound in hanging deaths, and thus to assess the vitality of the wound to allow a differential diagnosis between hanging and simulated hanging. This work also aims to perform a histological study to histologically detect the presence of macroscopically non-visible blood infiltrates and their skin distribution in relation to the action of the ligature mark.

Discussion: There is currently no scientific work in forensic pathology evaluating the expression of CHAF1A and FOXO3, however, their important role in the apoptotic cascade could make them ideal markers for assessing the vitality of a lesion.

EVALUATION OF THE ECOTOXICITY INDUCED BY VETERINARY PHARMACEUTICALS AND THEIR MIXTURES ON THE AQUATIC VERTEBRATE *DANIO RERIO* THROUGH A ONE HEALTH APPROACH

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Background: The release of veterinary pharmaceuticals in the environment as a result of farming practices is one of the major challenges of the last years. Thousands of different compounds end up daily in the aquatic environment where they pose a threat to human and environmental health. Moreover, although the single substances are in many cases present at low concentrations, they can blend in mixtures that might show an overall effect that is often underestimated. For this reason, a deeper knowledge of the consequences that these products and their mixtures can have on the environmental and human health is necessary.

Methods: The aim of this study is to highlight and investigate lethal and sub-lethal effects derived from the exposure of fish embryos to veterinary antibiotics and their mixtures. For this purpose, the vertebrate *Danio rerio,* one of the most promising and widespread animal model, has been chosen. The starting point for this study is the OECD 236 acute toxicity assay, however sub-lethal endpoints such as shape of the eyes, skeletal deformities, organism length, spontaneous activity of the tail and heartbeat have also been taken into account. The data acquisition has been performed with the use of the *Danioscope* software, that allows to acquire images at high resolution.

Results: The preliminary results obtained with single antibiotics show low mortality at every tested concentration. However, the presence of sub-lethal effects even at low concentrations has been recorded. In particular, malformations and premature hatching seem to be the most frequently occurring sub-lethal endpoints.

Discussion: The use of *in vitro* assays based on zebrafish early stages allows to effectively detect chemicals-induced acute toxicity, with effects ranging from lethal to sub-lethal endpoints. In this context, the detection of sub-lethal effects is an important monitoring tool, since it allows to highlight the modes of action of both isolated compounds and mixtures that can have a relevant influence on the environment and also on human health.

PROFILES OF MEDICAL PROFESSIONAL LIABILITY IN THE COVID-19 EMERGENCY. PROSPECTIVE ANALYSIS OF REGULATORY DEVELOPMENTS AND JURISPRUDENTIAL GUIDELINES

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Background: The COVID-19 pandemic of the year 2020, constituting a medical emergency of an exceptional and extraordinary nature, has had important health, social and economic repercussions within national and supranational systems, as in the field of professional medical liability.

Methods: The methods of the project are therefore to assess whether, in the context of the emergency pandemic of COVID-19, it is necessary to update the legislation on medical professional liability. In this regard it will be necessary to analyse the professional responsibility profiles of both the health professional and the structure.

Results: It is expected to obtain clarification on the position of the case law in matters of special difficulty (art. 2236 cc), of the state of necessity, of the shortage of places in intensive care, of the responsibility for nosocomial infection, of the responsibility of healthcare worker, of the responsibility of the facility.

Discussion: The dramatic situation created by the COVID-19 pandemic has led to direct proposals for changes to the rules governing medical liability, also at the direct solicitation of the health professionals engaged in the first line in the emergency. In Italy, some amendments to the Decree-Law March 17, 2020, n. 18 c.d. "Cura Italia" moved in this direction. The multiplicity of the amendments proposed by the politicians indicates the interest in solving a contemporary legal problem that needs answers from the institutions.

PHENOTYPIC AND GENOTYPIC ANALYSIS OF BETA-LACTAM AND CARBAPENEM - RESISTANCE *KLEBSIELLA PNEUMONIAE*

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Background: The increasing phenomenon of antibiotic resistance represented by ESBL and AmpC-producing Gram-negative bacteria poses a threat to public health due to their involvement in serious infections. The production of β-lactamase enzymes such as AmpC β-lactamases (AmpC) and Extended-Spectrum β-Lactamases (ESBL) and the production of carbapenemases are among the main mechanisms of resistance to extended-spectrum cephalosporins and carbapenemases by gram-negative bacteria. With this study we determine resistance in strains of clinical isolates of *Klebsiella pneumoniae* by identifying the production of extended-spectrum β-lactamases and carbapenemases and the frequency of resistance genes NDM, CTX-M, SHV-1, TEM.

Methods: 15 isolates of *Klebsiella pneumoniae* were subjected to phenotypic testing for ESBL detection by microdilution in Muller-Hinton broth with the following antibiotics: cefotaxime, ceftazidime, cefepime, meropenem and ertapenem. A confirmatory test for resistance was carried out by the Kirby-Bauer disk diffusion method. For each strain, genomic DNA was extracted and multiplex PCR was performed for the following genes: blaNDM, blaCTX-M, blaSHV-1, blaTEM.

Results: 79% of the isolated strains show phenotypic resistance to at least one antibiotic belonging to the third-generation cephalosporins, and of these 50% also show resistance to the fourth-generation cephalosporins. The strains resistant to third-generation cephalosporins had MIC>4 mg/mL for cefotaxime, MIC>8 mg/mL for ceftazidime, and MIC>4 mg/mL for cefepime. The same strains were resistant to meropenem with MIC equal to 16 mg/mL and ertapenem with MIC equal to 2 mg/mL. Diffusion tests confirmed antibiotic resistance. Genotypic analysis showed that all strains tested were positive for genes coding for β-lactam resistance such as blaNDM, blaCTX-M, blaSHV-1 and 62% carried the blaTEM gene for carbapenem.

Discussion: This study shows the prevalence of genes that confer resistance to carbapenems and beta-lactams and that they are not expressed in all strains in which they are present. Therefore, it is important to assess antibiotic susceptibility, phenotypic screening, and genotypic screening for the implementation of strict antibiotic control policies in health care settings.

COST ANALYSIS OF HEALTH CARE-ACQUIRED INFECTIONS IN A TEACHING HOSPITAL: A COMPARISON OF METHODS

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Background: Healthcare-Associated Infections (HAIs) lead to prolonged hospitalization and increased costs for medical care. Investigators generally estimate only direct additional costs, particularly, additional Length Of Stay (LOS) which represents the most expensive element. Aim of this study is to compare internationally used methods, to estimate extra LOS attributable to HAIs and economic burden, by applying them to the same population.

Methods: The study was carried out through the analysis of hospital admissions at Sant'Andrea Teaching Hospital in Rome (400 beds). All patients developing HAIs, according to CDC criteria, were considered cases. In matched control method, for each infected patient we selected 2 uninfected hospitalized patients according to the following criteria and scoring system: primary diagnosis (ICD-9-CM) (5 points), same admission ward (5 points), LOS in controls equal at least to the interval from admission to infection in cases (5 points), DRG (4 points), age ± 3 years (4 points), same gender (2 points). Once the pairs were matched, we estimated the number of extra days by subtracting the average LOS of the non-infected patients from that of the infected ones. The Appropriateness Evaluation Protocol (AEP) method is based on a list of objective criteria. The original AEP protocol was modified adapting some others criteria, finally thirty objective items were incorporated (Full AEP form), ten of which can be met because of HAIs presence (Partial AEP form). All hospitalization days deemed appropriate according to the "full AEP form" but inappropriate according to the "partial AEP form" were defined as extra LOS attributable to the infection.

Results: To date, we enrolled 63 cases. The mean hospital stay in cases was 39.4±27 days (median 29, range 5-115), whereas in control group 21±16.3 (median 16; range 1-99). The attributable extra LOS estimated by matched comparison was 18.4 per patient. We stratified results for each hospital ward and we found an extra LOS of 17 days for medical and surgical wards and 24 for intensive care units. Overall, the AEP method showed a lower number of extra LOS with 10 days per patient: specifically, 9 days for medical wards, 10 for surgical wards and 8.5 for intensive care units. For statistical regression method analyses the variables to be collected were identified. We considered the type of infection, the responsible microorganism, comorbidities, previous hospitalizations, clinical severity (using the Charlson Comorbidity Score), information on main clinical problem and procedures.

Discussion: The present study may estimate with different methods that HAIs are associated with longer hospital stays and increased costs. Economic evaluation provides valuable information for implementing health policies and preventing HAIs.

PAIN THERAPY IN ALBANIA, A DESCRIPTIVE RESEARCH AIMED TO HIGHLIGHTING THE RIGHT MEANS TOWARDS A PAIN-FREE PATIENT

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Background: While observing Health Care System in Albania, one of the weak points is the ongoing Pain Management culture. Situation is confusing because there are several issues that need solutions, starting from lack of Pain Evaluation and Management Guidelines, lack of financial support for pain-free hospitals further more lack of proper education of medical staff regarding Pain Management and lack of patient's psychological support. So I found it more accurate to start with a descriptive research that puts into focus some of the most basic issues in clinic's daily Pain Management.

Methods: This is a descriptive observational study. The used method is data collection. Data were collected in the regional hospital of Gjirokaster, (in Albania) from Surgical, Emergency and Obstetrics-Gynecology Unit's archive through analyzing medical records of patients being hospitalized from June 2016 until December 2019. Data were taken manually since the hospital doesn't have a digital database. A total amount of 7,605 patient's medical data were collected, respectively 2,383 from Surgical Unit, 2,844 from Emergency Unit and 2,378 from Obstetrics-Gynecology Unit. A questionnaire about Pain Management were distributed to medical staff in three of the biggest cities of Albania: Tirane, Fier and Vlore as well as in Gjirokaster.

Results: From the database we see that: first, pain is being treated without a Pain Evaluation Scale. Second, there is no documented continuous observation of pain and analgesic drug's effectiveness. Third, patient of same sex and diagnose haven't been treated the same way. Furthermore, opioids are the less prescribed drugs and from all the variety of opioids we see that only Codeine and Morphine have been used, and this happens rarely. Finally, neither peripheral nerve block nor other alternative methods were used at all.

Discussion: As previously observed, later confirmed by the results of this study, we conclude that in order to improve Pain Therapy in Albania we have to build up a multi-focused strategic plan starting from Nursing and Medical Study Program having to include in their curricula Pain Therapy, continuous updated Pain Therapy education of medical staff, financial support from Ministry of Health and Social Protection aiming pain- free hospitals as well as set-up a working group that will infer a national guideline for Pain Evaluation and Management.

PREVALENCE AND EFFECT OF CONCURRENT AND SECONDARY INFECTIONS ON MORTALITY IN PATIENTS WITH COVID-19 HOSPITALIZED AT A RESPIRATORY SUB-INTENSIVE CARE UNIT DURING THE SECOND PANDEMIC WAVE IN ITALY

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Background: Little is known about co-infections and secondary infections in sub-intensive care units. This study targets patients hospitalized in a respiratory sub-intensive care unit with the aims to i) assess the prevalence of concurrent and secondary infections in COVID-19 patients, ii) evaluate the risk factors for secondary infections development and iii) assess the impact of secondary infections on in-hospital mortality.

Methods: Single-center, retrospective analysis of prospectively collected data on patients with COVID-19 pneumonia from November 2020 until April 2021. Inclusion criteria were: i) diagnosis of COVID-19 respiratory failure and/or ARDS; ii) hospitalization in a sub-intensive respiratory care unit and iii) age >18 years. Exclusion criteria were: i) patients admitted for less than 48 hours and ii) patients with missing data.

Results: A total of 201 patients were included in the study. 106 (52%) presented with severe COVID-19 infection. Co-infections were 4 (1.9%), all due to *Mycoplasma pneumoniae* whereas 46 patients (22%) developed a secondary infection, mostly primary bloodstream infections (23 episodes, 35.9%), pneumonia (19, 29.6%), and urinary infections (18, 28.5%). First infective episode was diagnosed after a median of 14.5 days from admission. In 40.6% of cases, MDR pathogens were detected, with *Acinetobacter baumannii* isolated in 47% of them. Overall mortality rate was 30%. Mortality rate (p=0.0001), in-hospital stay (p=0.001) and colonization with MDR pathogens (p=0.0001) were higher in patients with secondary infections. Patients with secondary infections and patients who died presented on admission a higher rate of severe COVID-19 and a higher Charlson Comorbidity Index (p=0.0001). Prior (ie 30-d) infection (OR 5.3, p=0.03) and exposure to antibiotic therapy in last 30-d (OR 5, p=0.037) were independent risk factors for new onset secondary infection development. Independent risk factors for in-hospital mortality were age >65 years (OR 6.8, p=0.002), Charlson CI > 5 (OR 5, p=0.001), severe COVID-19 (OR 2.7, p=0.019), count of lymphocytes < 750/mmc (OR 2.4, p=0.031) and the development of secondary infections (OR 2.7, p=0.024). XDR *Acinetobacter baumannii* resulted independently associated with 14-d mortality (OR 5, p=0.018).

Discussion: Likewise in ICU, in sub-intensive care unit COVID-19 severity and risk factors for infections act synergistically on the development of secondary infections and mortality. Conversely, co-infection presents a lower rate of prevalence.

IMMUNOLOGICAL EFFECTS OF OLT1177 ON PBMC PRODUCTION OF PRO-INFLAMMATORY CYTOKINES AMONG PEOPLE LIVING WITH HIV

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Background: Despite virological control with Antiretroviral Therapy (ART), People Living With HIV-1 infection (PLWH) show chronic immune activation/hyper-inflammation with higher concentrations of IL-1β and IL-18 compared to healthy controls, inducing HIV-related non-AIDS-defining comorbidities, such as cardiovascular and/or neurocognitive disease. OLT1177 is small synthetic molecule, which targets specifically the NLRP3 inflammasome and prevents the release of IL-1β and IL-18 from NLRP3 inflammasome expressing cells, such as Peripheral Blood Mononuclear Cells (PBMC). OLT1177 has been shown to be well tolerated in humans and available as oral capsule formulation. We aim to assess whether that *ex vivo* OLT1177 reduces IL-1β and IL-18 production by PBMC of PLWH under virologic control and optimal compliance to ART but affected by cardiovascular and/or neurocognitive disease. Secondary objectives of the study are to measure blood levels of pro- and anti-inflammatory cytokines as well as of intestinal translocation markers, to check their association with biological response to OLT1177 *ex vivo*, and ultimately to define a clinical inflammatory/translocation cut-off to detect PLWH who could benefit from treatment with OLT1177.

Methods: PBMC will be isolated from each PLWH and divided in two groups, one receiving and other not receiving pre-treatment with OLT1177; subsequently, PBMC will be cultured with antigenic stimuli of different nature (bacterial, viral, fungal) for 24 hours and lastly pro- and anti-inflammatory cytokines (including IL-1β and IL-18) will be measured in the supernatant.

Results: To date, we have almost completed the study population screening. 20 PLWH without comorbidities, 20 PLWH with cardiovascular disease and 20 PLWH with neurocognitive disease have been enrolled. We are currently completing the recruitment of people without HIV infection, before starting laboratory analyses. We expect to show a significant reduction of IL-1β and IL-18 concentration in the supernatant of PBMC treated with OLT1177 compared to the supernatant of PBMC treated with placebo, after antigenic stimulation *ex vivo*, independently from HIV-1 infection status.

Future perspectives: If the expected results will be satisfied, a clinical trial to assess the efficacy of OLT1177 in decreasing *in vivo* the chronically high levels of IL-1β and IL-18 detected among PLWH would be the natural perspective of the current study, with focus on cardiovascular and neurocognitive disorders.

GENTAMICIN LOADED NIOSOMES: ANTIMICROBIAL ACTIVITY AGAINST UROPATHOGENIC *ESCHERICHIA COLI* STRAINS

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Background: Urinary Tract Infections (UTIs) are the most frequent community and hospital-acquired infections. Uropathogenic *Escherichia Coli* (UPEC) is the major causative agent of UTIs. UPEC initially colonize the human host adhering to the bladder epithelium and invade urothelial epithelial cells, where they can replicate forming Intracellular Bacterial Communities (IBCs) and persist establishing Quiescent Intracellular bacterial Reservoirs (QIRs). It has been shown as intravesical instillations of Gentamicin (GM), a broad-spectrum antibiotic that exhibits a concentration-dependent activity and a post-antibiotic effect, reduce the frequency of UTIs. Despite this, the oral GM administration is not effective due to low bioavailability and poor penetration into cells. To overcome the issue, the use of nanocarriers, as drug-delivery systems, received particular attention. Among these, niosomes, vesicular systems whose components are non-ionic surfactants and cholesterol, have been well studied. This work aimed to evaluate the effect of niosomes against invasive intracellular UPEC strains.

Methods: in this work a deep physical-chemical characterization in term of stability over time/biological media and drug entrapment efficiency was carried out. Thanks to the niosomes intimate structure, both lipophilic and hydrophilic moiety-drugs, have been loaded inside the nanocarriers (co-loading of GM and Nile Red), to better evaluate the intracellular uptake. Minimum Inhibitory Concentration and Minimum Bactericidal Concentration of these sample was estimated by the broth micro-dilution method against UPEC strains. The cytotoxicity was determined on human T-24 bladder cells by MTT assay. The antiinvasive ability of niosomes against UPEC strains in T-24 cell monolayers were assessed by the gentamicin protection assay.

Results: all the samples were found to be suitable for the hypothesized application, presenting nanometric dimensions and showing a good stability profile. The internalization of these samples occurred in T-24 cells already after 7 hs of contact. These preparations showed bactericidal activity in a dose dependent manner against UPEC strains. Conversely, they had no cytotoxic effect on the T-24 cells. From the reduction of viable counts on plate it was possible to note that GM delivered in niosomes inhibited the invasion of UPEC strains into cells. This leads us to hypothesize a release of the antibiotic inside the cell.

Discussion: from these preliminary results we can speculate that the delivery of antibiotic by niosomes may be very promising, but some aspects need to be elucidated for a potential application in the therapeutic field.

IDENTIFYING DRIVERS OF EMERGING INFECTIOUS DISEASES AND ARBOVIRAL DISEASES IN JORDAN THROUGH THE ONE HEALTH APPROACH

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Background: Zoonosis occur when the necessary conditions arise for a pathogen to emerge in susceptible populations. These conditions can drive the emergency through a wide variety of mechanisms, called drivers, such as climate change, land use for agricultural and pastures purpose, and social inequality. Studying the zoonosis drivers helps predict the next outbreak and what the hotspots will be. The goal of this thesis is to identify the drivers in the different sectors (human, animal, environment, socio-economic) most associated with arboviruses and Emerging Infectious Diseases (EIDs) and, subsequently, the indicators that help identify hotspots based on the presence of drivers.

Methods: A scoping review is carried out to understand which are the main drivers responsible for arboviral diseases and EIDs and what national and international plans propose to do to address them. After identifying the main drivers and the approaches used to address them, a study will begin in Jordan with the MediLabSecure network. EIDs and arboviral diseases considered priority and the drivers most correlated to their outbreaks will be identified. Based on the results obtained, some indicators will finally be identified to understand which may be the hotspots of the selected diseases in the country.

Results: The literature shows that the main drivers of EIDs and arboviral diseases are climate change, land use and human movements. National and international plans address these drivers with trainings and community-inclusive processes; the development of longitudinal data sets for understanding the biological drivers of viral evolution, spillover, amplification; the identification of areas that can directly contribute to zoonotic spillover risk; and the strengthening of surveillance and laboratories capacities.

Discussion: This study makes it possible to recognize the hotspots of diseases considered a priority in Jordan. In this way, it will be possible to concentrate the search for any outbreaks in specific areas and have a more targeted and less expensive search.

HSV-1 BRAIN INFECTION AND COMPLEMENT ACTIVATION: POSSIBLE ROLE IN NEURODEGENERATION

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Background: Among the multiple factors that may contribute to the pathogenesis of Alzheimer's Disease (AD), numerous experimental and epidemiological evidence suggests that recurrent Herpes Simplex Virus-1 (HSV-1) infection reaching the brain is one of the risk factors for the disease onset and/or progression. However, the molecular mechanisms linking HSV-1 infection to neuronal dysfunctions have yet to be fully elucidated. Genetic, proteomic, and immunologic evidence suggests that dysregulation of the complement cascade, a key component of the innate immune system that is rapidly recruited to allow the clearance of pathogens and promote tissue repair, is involved in the pathogenesis of AD. It is also known that proteins of the classical complement pathway play a role in the process of synaptic elimination or neuronal pruning in the brain, an important event in neurodegeneration.

Methods: Primary neuronal cultures were isolated from the brain of rat embryos (E18). Neurons were mock- and HSV-1-infected at different multiplicity of infection and the efficacy of HSV-1 infection was evaluated by Standard Plaque Assays (SPA). Cells were analysed for the expression of complement components and PSD95 (postsynaptic marker) at protein and mRNA levels with Western Blotting (WB) and RT-PCR, respectively. Immunofluorescence analyses (IF) were also carried to detect specifically C3 expression. Neutralization assay was performed with the aid of a specific antibody directed against the complement component C3.

Results: We found that HSV-1 infection in cultured rat brain cells induces an increase of C1q and C3 mRNA expression, detected by RT-PCR, and also a dose-dependent increase of C1q, C3, and C4 detected by WB. The C3 increase after HSV-1 infection was also confirmed by IF. Results from a neutralization assay showed that in HSV-1 infected neurons the inhibition of the C3 component rescued the HSV-1 induced decrease of PSD-95.

Discussion: The dose-dependent increase of complement proteins after HSV-1 infection in cultured rat brain cells indicates that complement may play a role in the immune response to HSV-1 infection in rat brain. The decrease of the synaptic marker PSD-95 expression after HSV-1 infection in cultured rat brain cells indicates a possible HSV-1 induced synaptic reduction. Finally, the preliminary results of C3 neutralization assay suggest that the complement protein C3 may be involved in the process of synaptic reduction that follows HSV-1 infection. Overall, these results suggest a possible complement-dependent synaptic damage triggered by HSV-1 brain infection, thus strengthening the causal link between HSV-1 and neurodegeneration.

ORAL FLUID AS A NEW INVESTIGATIVE MATRIX TO DETERMINATE OGSR EXPOSURE

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Background: The increased use of ammunition without lead and heavy metals is observed; this lead to a growing interest in the detection of Organic Gunshot Residues (OGSR) as evidence of firearms related crimes. The purpose of this work is the development of a reliable analytical method by means of UHPLC-HRMS for the determination in Oral Fluids (OF) of the most common explosives and the most used stabilizers.

Methods: For this purpose, SPE was used for the OF clean-up before UHPLC-HRMS analysis. All target analytes were chromatographically separated by means of a Polar-C18 column. A chlorinated compound was added to the mobile phases in order to promote the formation of chloride adduct ions in the electrospray ion source to allow the best conditions for each analyte. The detection was conducted by means of a high-resolution mass spectrometer equipped with Orbitrap technology; Full scan-data dependent was the selected acquisition mode, in order to detect both the precursor ions and/or the most intense fragments for stabilizers.

Results: The method was tested on real samples: a shooting session was performed in an open shooting range; the shooters fired from 2 to 20 rounds with a 9x21 caliber, after which they were sampled. Samples were analyzed confirming that explosives may be detected in OF, the use of this matrix may be of great interest for investigative purposes as it is not affected by secondary transfer. The sampling is fast, not invasive and can be performed by non-medical staff. The study of possible metabolites allows us to assess the presence of the risk factors of the exposed subjects.

Discussion: The high sensitivity of the presented method allows the determination of very low traces of analytes, providing evidence of a direct contact with OGSR and the high specificity provides a high confidence for the analyte identification, minimizing the possibility of false positive results. This represents an interesting starting point for the assessment of the potential exposure to OGSR or the use of firearms at a crime scene. In this work also the persistence of OGSRs in OF was investigated. The preliminary results obtained during this trial are very promising, as a close correlation between the concentration of OGSR in saliva and the time elapsed between sampling and exposure was observed.

HOW TO MEASURE VACCINE HESITANCY IN NURSES? A SYSTEMATIC REVIEW OF THE MEASUREMENT PROPERTIES OF VALIDATED INSTRUMENTS

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Background: The use of a validated and reliable tool to assess vaccine hesitancy in nurses is critical to developing tailored public health strategies to implement adherence to recommended vaccines for healthcare workers and reduce the chance of contracting or spreading vaccine-preventable diseases. The aim of this review is to identify and evaluate the properties of measurement instruments to estimate nurses' knowledge and attitudes about vaccination, vaccination intentions, and vaccine hesitancy.

Methods: A systematic review was conducted through PubMed, Cumulative Index to Nursing and Allied Health (CINAHL), Scopus, Cochrane, Web of Science, Joanna Briggs Database and ERIC - Education Resources Information Center (PROSPERO ID: CRD42020212252). The methodological quality of the instruments properties was assessed using the COnsensus-based Standards for the selection of health status Measurement Instruments (COSMIN) checklist. The quality of the measurement properties of each individual instrument has been investigated by the evaluation criteria theorized by Terwee et al. 2007.

Results: Starting from 4531 articles, twenty instruments were identified in the 21 included studies: 13 instruments assessed influenza vaccination, two instruments examined HPV vaccination, one instrument examined HBV vaccination, one instrument studied pertussis vaccines, and two instruments included recommended vaccination for healthcare workers. A total of 8,297 healthcare workers were involved in the surveys; of these, 5,083 were nurses (61.3%). The King's Nurses Influenza Vaccination Questionnaire is the most widely used instrument in the international community to assess vaccination intentions toward influenza in nurses, its measurement properties have been found to be reliable, and the instrument has been validated in Chinese and English, with an overall positive methodological quality score. Only one instrument was found to assess vaccine hesitancy of recommended vaccines for health care workers, a tool by Rose Wilson in 2019 with good reliability which includes a validated scale for scoring vaccine hesitancy for influenza, HBV, pertussis, MMR, dTPolio, BCG and varicella (Cronbach's alpha = 0.72).

Discussion: Although several instruments to assess vaccine hesitancy in nurses are available throughout literature, it is currently not possible to identify a single validated and internationally accepted instrument. Implementation of a single, universally viable and valid instrument, as previously proposed by the WHO with regard to the general population, seems therefore necessary in order to systematically measure vaccine hesitancy and develop tailored educational strategies.

AN ORGANOTYPIC MODEL OF RETINAL TOXOPLASMA GONDII INFECTION: INCREASED PRODUCTION OF GSTO1, PNFKB AND IL-6

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Background: Ocular Toxoplasmosis (OT) is caused by the parasite *Toxoplasma gondii* and it represents the most common cause of eye inflammation in the world. Histopathology information of active OT lesions in humans is difficult to gather, and the majority of data about the inflammatory response and the morphological changes is based on a murine model of congenital OT. With this study we present an *ex vivo* model that facilitates the observation and manipulation of the infected retina. After stabilization of the cultured retina, we have started to analyze the inflammatory response caused by the parasite in this tissue. The first markers we have searched for are Glutathione S-Transferase Omega-1 (GSTO1) and Nuclear Factor kappa light chain enhancer of activated B cells (NFkB).

Methods: Retinas dissected from 3- to 5-week-old C57BL/6J mice were cut into 4 fragments and transferred onto Millicell-CM culture inserts with ganglion cells up. Eight fragments were transferred on each insert. The inserts were placed in 6-well tissue culture plates with 1 mL of culture medium (50% MEM, 25% Hank's buffer salt solution, 25% Dulbecco's Phosphate Buffered Saline, 25 U/mL penicillin, 25 mg/mL streptomycin, 1 μg/mL amphotericin B, and 200 μM L-glutamine), which was changed every other day, and incubated for 24 hours, 3 days (D), 7D, or 10D. *T.gondii* (RH strain) were maintained in Vero cells. They were used at a concentration of 2,000/well to infect the retinal explants. Control explants were cultured in an unmodified culture medium. For immunostaining, retinal fragments were fixed with 4% paraformaldehyde, embedded in cryo-gel, and cut into 10-μm-thick sections with a cryostat. The primary antibody was a polyclonal goat anti-*T. gondii* and the secondary antibody was conjugated with Alexa-Fluor-488. The sections were counterstained with DAPI. For Western Blot (WB), fragments were homogenized and processed following standard protocols. Primary antibodies were directed to GSTO-1, to NFkB, or to pNFkB. Densitometric analysis of the immunoreactive bands was performed using the software ImageLab and statistical evaluation with ANOVA.

Results: Immunofluorescent, putative *T.gondii* cysts were observed at 3D and 7D in the Inner Nuclear Layer (INL), Outer Plexiform Layer (OPL), and in the Photoreceptor Outer Segment (POS). Results from WB showed an increase in GSTO1 levels at 24h, decreasing at 3D and 7D. In addition, the ratio pNFkB/NFkB increased significantly at 3D, while at 7D it was similar to control values.

Discussion: These results suggest a survival response in host cells by stimulating an antiapoptotic phenotype as previously shown in infected fibroblasts by Molestina in 2003. Further analyses with shorter incubation times will be performed to verify this process in early phases of infection.

CONCOMITANT MEDICATION POLYPHARMACY, INTERACTIONS AND OVER THE COUNTER MEDICAMENT IN A COHORT OF HIV ELDERLY PATIENTS

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Background: advances in Antiretroviral Treatment (ART) over the past 30 years have significantly prolonged the life expectancy of People Living With HIV (PLWH), whose median age has progressively increased. The aging HIV population presents a new clinical concern for HIV providers: adverse effects from polypharmacy. An aging population means more comorbidities and potentially more drug-drug interactions for providers to manage. The increasing complexity of therapeutic regimens may have a negative impact on the quality of life, adherence to treatment and inevitably increases the chance of drug–drug interactions that may lead to unintended adverse events. Furthermore, the use of over the counter medication is rising among the general population and mainly in PLWH, with a further burden of exposition to drug-drug interaction that may be underrate.

Methods: this is a multicentre, cross-sectional study to investigate potential interactions between ART and non-ARV medication in an Italian cohort of older PLWH. Further objectives are to investigate potential interaction among non-ARV medication, and the prevalence of over the counter and non conventional medication and their possible interactions with ARV drugs. Univariate and multivariate logistic regression models were used to examine the factors associated with the presence of drug-drug interactions.

Results: our first data shows that, concerning ART and non-ART medication, the use of nucleoside reverse transcriptase inhibitor+ integrase strand transfer inhibitor rather than nucleoside reverse transcriptase inhibitor + nonnucleoside reverse transcriptase inhibitor and protease inhibitor–based regimens was associated with a reduced risk of potential drug-drug interactions. The use of non-conventional medication, that has been found in a half of the patients, shows a high proportion (35-40%) of potential interaction with ART. It has been found, surprisingly, a high proportion of interaction between over the counter medication commonly used (as minerals) and integrase strand transfer inhibitors.

Discussion: complete the cohort will give a national view of actual harm caused by polypharmacy in PLWH, and develop optimal strategies to facilitate and promote the effective and safe use of medication.

MOSQUITO ALERT: A CITIZEN SCIENCE PROJECT FOR IMPROVED MOSQUITO SURVEILLANCE

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Background: Mosquito Alert Italia is a taskforce of scientific/educational Institutions led by the Medical Entomology group of the Department of Public Health and Infectious Diseases. The taskforce focuses on the implementation of Citizen Science based approaches to complement research on mosquitoes (with particular reference to invasive species), raise awareness on prevention of mosquito infestations and on mosquito-related health risks, and eventually optimize mosquito control interventions. The main asset of the taskforce is Mosquito Alert app, an application for smart phones that allows citizens to send photographic records of mosquitoes and larval sites and to report biting activity to experts.

Methods: Mosquito Alert app was launched all over Europe in October 2020 and a communication strategy integrating press releases, infographic materials, social media campaign, activities for schools and University students and dedicated meeting is ongoing in Italy since then.

Results: From October 2020 to end of 2021, more than 9,000 Italian Citizen have registered to the app with peaks of registrations after press releases and after high media coverage of the first report of invasive *Aedes koreicus* in Lombardia. A total of 7,878 report were received by the experts (i.e. 4,431 mosquito photos, 208 breeding site photos, and 3,239 bite reports), corresponding to 17% of the total reports sent from all over Europe. Most of the reports were sent from regions were participants of Mosquito taskforce are based. Citizen sampling effort across Italy was estimated by number of users in 2km x 2km cells (based on background tracking of device positions) and the probability of each user within a cell to send at least one report. Data from the first half of 2022 are under analyses.

Discussion: Data from 2020-21 and 2022 communication campaigns will be further analysed in order to understand the main triggers and weaknesses in citizen's use of Mosquito Alert app and to develop more efficient dissemination strategies for future years, including operating in linkage with public health administrations involved in mosquito controls, as preliminary attempted in 2022 summer season. The final goal is to develop a self-sustaining approach to complement entomological monitoring data from citizens, in order to increase awareness, promote good preventive practices to contain mosquito nuisance and risk of mosquito-borne disease and to contribute to effectively shift from the "Public understanding of science model" to "Public engagement model".

Session II

PhD candidates' communications

Chairpersons
Silvio Paone, Marco Pombi, Eeva Tortellini

MOLECULAR BASIS OF ANTIMICROBIAL PROPERTIES OF GREEN NANOCOATING EFFECTIVE AGAINST VIRUS AND BACTERIA

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Background: Microbial colonization of surfaces forms a dangerous reservoir for pathogens contributing to spread of infections with impact on human health and a heavy economic burden. Most of pathogenic microorganisms can survive for months on dry surfaces. Several antimicrobial coatings exist in the market based on the leaching of non-environmentally friendly chemicals or based on formulations hazards to human health and environment. The optimization of disinfection approaches based on Metallic nanoparticles, that can remain longer on surfaces, resist to washing and friction and with good safety environment requisites is a challenge.

Objectives: The present project aims to analyze antimicrobial properties of an innovative self-disinfectant nanocoating based on the antimicrobial action by copper nanoparticles drugged with natural peptides effective against a wide range of virus and bacteria.

In particular will be investigated: 1) the activity and efficiency of antibacterial and antiviral surfaces on Staphylococcus aureus, Neisseria meningitidis, SARS-CoV-2 and H1N1 at different concentrations and at different exposure times; 2) the bacterial dynamic transcriptomic events in response of antimicrobial surface from early stage of exposure; 3) changes in SARS-CoV-2 virus and H1N1 virus genome over the time of monolayer exposure.

Expected results: A wide variety of studies have examined the anti-septic properties of copper nanoparticles on bacteria and viruses, but mechanisms behind these approaches need of further investigations. Reactive Oxygen Species (ROS) generated by copper cause damage to cellular biomolecules, including lipids, proteins and DNA. In bacteria ROS induce a large number of genes related to cell damage, cell membrane repair system, and DNA repair system and genome damages in viruses. The present study is aimed to characterize the molecular mechanisms that underlie this innovative intervention strategy.

Future perspectives: Surface disinfection plays a central role on infection inhibition and control strategies adopted in response to transmissible disease outbreaks. The antimicrobial coatings frequently used show serious concerns linked to low product performance, pollution, toxicity and antibiotic resistance. The knowledge of molecular mechanisms that underlie this innovative intervention strategy, could highlight whether one or a combination of several mechanisms at structural, genomic, transcriptomic and proteomic level could trigger possible resistance mechanisms against antimicrobial nanoparticles.

AN INTEGRATED APPROACH TO PREVENT AND CONTROL HEALTHCARE-ASSOCIATED INFECTIONS IN THE MAIN INTENSIVE CARE UNIT OF TEACHING HOSPITAL POLICLINICO UMBERTO I OF ROME

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Background: Healthcare-Associated Infections (HAIs) are the most frequent and serious adverse event in healthcare as they increase mortality and morbidity rates in hospitalized patients. The risk of developing HAIs depends on the infection control practices implemented, the patient's immune status, and the persistence of pathogens inside the ward. Within this context, identifying patients with risk factors for HAI and multidrug-resistant infections is critical to limit the HAI burden.

Objectives: This project aims to: i) evaluate the factors associated with the development of HAIs in the largest Intensive Care Unit (ICU) of the Teaching Hospital Policlinico Umberto I of Rome; ii) implement the genotypic and epidemiological characterization of microorganisms responsible for HAI in the ICU through the application of the PFGE method; iii) assess attitudes and barriers related to hand hygiene procedures among the ICU Healthcare Workers (HCW).

Preliminary results: Using the active HAI surveillance system, data were collected on HAIs involving COVID-19 and non-COVID-19 patients admitted to the ICU from March 1, 2020 to June 6, 2021. 352 COVID-19 and 130 non-COVID-19 patients were included, and 361 HAIs were recorded. We found little difference between the two cohorts in the cumulative incidence of patients with at least one HAI; small differences were observed between patients in the type of HAIs involving different microorganisms: among COVID-19 patients, HAIs were mainly caused by *A. baumannii*, while among non-COVID-19 patients *K. pneumoniae* and *P. aeruginosa* were the most frequently isolated pathogens. In this regard, we characterized the clonal spread of *A. baumannii* among COVID-19 patients admitted during the first year of the pandemic. A total of 193 patients were included and 102 strains were analyzed. All isolates had high antibiotic resistance profiles and were derived from two genotypes. Multivariable analysis showed that previous use of carbapenems was the only risk factor associated with *A. baumannii* acquisition (aOR: 3.34, 95% CI: 1.66-6.72). Finally, as part of the Corporate Hand Hygiene Project 2021, we sought to quantify compliance with hygiene regulations by HCW, within the ICU. Observations were made only by nursing staff (with 85/200 expected observations), which documented 89.9% compliance of hospital staff.

Future perspectives: We plan a periodic in-depth analysis of attitudes and barriers to hand hygiene along with active patient surveillance and epidemiological characterization of the microorganisms responsible for HAIs in the ICU, in order to be able to build an evidence-based strategy for the containment and prevention of HAIs.

PRION DISEASES SURVEILLANCE: FOCUS ON THE UNSOLVED ASPECTS OF THE EPIDEMIOLOGY OF SPORADIC CREUTZFELDT – JAKOB DISEASE (CJD)

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Background: Creutzfeldt-Jakob Disease (CJD) and related syndromes are rare human diseases belonging to the wide group of Transmissible Spongiform Encephalopathies (TSEs) or prion diseases. Humans TSEs include sporadic, genetic, iatrogenic and infectious forms (such as the zoonotic form called variant CJD correlated to the consumption of foods accidentally infected with the Bovine spongiform encephalopathy agent). TSEs are caused by transmissible agents called prions which replicates in the CNS leading to a characteristic neurodegenerative picture including spongiosis, glyosis, neuron loss and the deposition of the pathological Prion Protein (PrP^{TSE}). Surveillance of human TSEs has been established in 1993 in Italy and contributed to the identification and recording of variant CJD in Europe and in Italy. One of the focuses of our current activity is centered on the recognizion of "classic" or novel atypical forms with infectious or zoonotic origin by observing variations in the spatiotemporal distribution of the disease.

Objectives:
- definition of an innovative diagnostic score capable of maximizing the diagnostic accuracy of sCJD;
- estimation of the incidence/mortality rates of sporadic CJD (sCJD) in Italy;
- analysis of spatial patterns.

Expected results: Reliability of current diagnostic criteria (including validated lab tests) and the added value of new criteria/tests will be continuously estimated in terms of sensitivity, specificity, positive and negative predictive values. The mortality and the incidence rate of sporadic CJD will be calculated. The rates will be calculated raw and specific for gender and/or age, both at the national and regional level, according to the periods set out. Demographic, clinical and diagnostic characteristics of CJD patients will be compared in order to identify any variation in clinical patterns or to characterize and classify atypical cases, as unprecedented forms or pertaining to an already recognized subgroup of prion diseases.

Future perspectives: Defining of an innovative diagnostic score capable of maximizing the diagnostic accuracy of sporadic Creutzfeldt-Jakob Disease (sCJD) through the definition threshold value capable of discriminating between CJD and non-CJD subjects reported as suspected cases.

BIO-SUCCESS: BIOMARKERS SUSTAINABLE COLLECTION AND COMPLETE EXTRACTION IN SALIVAOMICS AND FORENSIC SCIENCES

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Background: Oral fluid has gained acceptance over the past decades as an alternative biological matrix over blood and urine for Driving Under the Influence of Drugs investigations (DUID) and being the field of salivary diagnostics very promising, it has expanded into detection of cancer, heart and infectious diseases, based on the detection of specific biomarkers. Even if extremely simple, sample collection is a waste generator stage because of the means of disposable devices made in plastics which generally involve collection on absorbent material (e.g., foam pad). Commercial devices offer the advantage of improved stability however issues that may arise include the incomplete desorption of lipophilic drugs or the disparate volume collected from different subjects.

Objectives: In this project new biodegradable sampling devices will be developed and tested. To date, different materials such as Polylactic Acid (PLA) or chitosan, which can be safely introduced in the mouth and then easily dissolved in a suitable solvent and/or by means of increased temperatures, have been investigated. 3D printing has been tested as a suitable technology to made cheap and biodegradable swabs with different materials. Another objective has been the development of appropriate sample preparation protocols, based on miniaturized extraction techniques and both targeted and untargeted approaches have been considered. High Performance Liquid Chromatography coupled with tandem Mass Spectrometry (HPLC-MS/MS) allowed the simultaneous identification and quantification of different analytes considered.

Expected (or preliminary) results: PLA has shown some interesting features but his solubilization is not rapid and several mL of acetonitrile are required to dissolve the tampon's head. The dLLME extraction method has proven suitable for the purpose of the work, it is a green extraction method which uses small volumes of organic solvents. The recoveries obtained are on average high for most of the tested analytes, which belong to very different chemical classes, demonstrating the versatility of this technique.

Future perspectives: Considering the limitation of the PLA we will proceed with the reduction of the volume of the tampon's head and the introduction of other materials such as chitosan that can be dissolve in water. This allows to apply another technique of micro-extraction in the liquid phase already tested in our laboratory, the Parallel Artificial Liquid Membrane Extraction (PALME) which requires smaller amount of organic solvent.

HUMAN BIOMONITORING OF MYCOTOXINS IN URINE, SERUM AND BREAST MILK SAMPLES OF THE ITALIAN POPULATION

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Background: The first source of exposure to mycotoxins for humans is represented by the diet. Due to the high diffusion and toxicity of these substances and the growing number of foodstuffs recognized as susceptible to contamination, the competent authorities of many countries consider the problem of mycotoxins among the priorities in terms of food safety.

Objectives: The aim of the PhD project is the mycotoxins risk assessment of the Italian population through Human Biomonitoring Analysis (HBM), analysis will be performed on serum and urine samples of representative adult Italian population. Moreover, breast milk and urine samples will be collected to investigate the exposure of mothers and breast fed infant.

Expected (or preliminary) results: The full achievement of the project objectives will make available to the scientific community a significant amount of data on the incidence of mycotoxins and its biomarkers in biological fluids from the Italian population. Exposure will be assessed with the obtained HBM data and used for risk assessment purpose. Moreover, a LC-HRMS validated method will be available for the determination of mycotoxins and their metabolites in biological fluids.

Future perspectives: Exposure and risk assessed by HBM data will be compared with those obtained by traditional approaches based on occurrence and consumption data, reported in the literature. Data will be also made available to EFSA to conduct future exposure estimates based on the use of biomarkers.

GENOMIC EPIDEMIOLOGY OF AFROTROPICAL MALARIA VECTORS: ANALYSES AND IMPLICATIONS OF CRYPTIC SPECIATION IN THE *ANOPHELES GAMBIAE* COMPLEX

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Background: *Anopheles coluzzii* and *An. gambiae* - the main Afrotropical malaria vectors - have recently diverged and are strongly reproductively isolated. However, stable frequencies of putative hybrids >20% are observed at the Far-West of the species range. Whole genome sequencing data available thanks to the *Anopheles gambiae* 1000 genomes (Ag1000G) project led to attribute to Far-West populations an "uncertain species status", due to admixture of *An. coluzzii/An. gambiae* species-specific Ancestry Informative Markers (AIMs; N = 506).

Objective: Characterize the taxonomic status of Far-West populations and their relationships with *An. coluzzii/An. gambiae* populations from West Africa. This is achieved by analysing high-throughput WGS genomic data by Ag1000G of 1,190 adult females from 3 Far-West populations (FW-pops; 2 from The Gambia - GM - and 1 from Guinea Bissau - GW) and from 5 *An. coluzzii* and 5 *An. gambiae* populations in west Africa.

Preliminary results: Results from PCA analysis of >34M neutral SNPs in the euchromatic region of chromosome-3 and of >8M SNPs in chromosome–X centromeric region clearly separate FW-populations from *An. coluzzii* and *An. gambiae,* as well as identify three FW-clusters: GM1, GM2 and GW1. Comprehensive genomic analyses (i.e. ADMIXTURE, FST, TreeMix, Patterson's D statistics and f3-statistics) suggest that: ii) GM1 – characterized by *An. coluzzii*-like AIMs – is a local *An. coluzzii* population differentiated from other West African populations; i) GM2 is a putative new cryptic taxon characterized by a unique gene-pool and by *An. gambiae*-like AIMs; ii) GW1 is the result of hybridization between *An. coluzzii* and GM2.

Future perspectives: These preliminary results may have a potentially high impact on malaria epidemiology in Far-West Africa. Future perspectives are: i) clarifying the nature of the putative novel FW-taxon and its phylogenetic relationships with the other members of the gambiae complex by phylogenetic and demographic analyses; ii) identifying private alleles or informative markers specific to FW-taxon needed to easily detect FW-taxon individuals in the field and to characterize epidemiological relevant phenotypes that could influence vector capacity and the response to malaria control strategies.

IMPLEMENTATION OF A HEALTH PROMOTION PROGRAM FOR THE REDUCTION OF STRESS, BURNOUT AND ANXIETY IN HEALTHCARE WORKERS INVOLVED IN THE COVID-19 PANDEMIC

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Background: The Coronavirus (COVID-19), identified in early 2020, has unfortunately spread rapidly around the world. Because of the many changes made in hospitals to better cope with this infection, COVID-19 has severely affected the mental and physical health of all workers involved. Several studies carried out in the past year have investigated the experience of workers involved in COVID-19 wards during the first wave. Depression, anxiety and post-traumatic stress disorders were the issues most commonly faced by healthcare professionals.

Objectives: The present research project was therefore created with the aim of reducing stress, burnout, and anxiety in Healthcare Workers (HCWs) directly involved in the COVID 19 pandemic. There are already several studies in the literature demonstrating the effectiveness of yoga and mindfulness in improving the mental health of HCWs. The main purpose of this study, YOMIN (Yoga and Mindfulness), was to conduct a single-arm Clinical Trial (CT) to assess the effectiveness of an intervention based on three types of techniques (MBSR, yoga and YOMIN) in improving mental well-being in HCWs.

Expected (or preliminary) results: The hospital environment can be a big source of stress for HCWs. The aim of this study was to suggest a method to handle the difficult environment in which HCWs work. The training modules were created with the aim of implementing the psychological skills of the nursing staff involved. At the end of the study, thanks to the training course the experimental group is able to work on the different psychological factors and will be less likely to develop work burnout compared to the control group. Establishing an easy-to-access and remote training program, conducted by experts in the field, will allow to increase the psychological well-being of the staff involved, with the aim of decreasing medical errors and increasing standards of care for patients.

Future perspectives: A tracing network and active and continuous surveillance of all the operators involved could allow companies to prevent their healthcare personnel from being so emotionally exhausted that they leave their profession. An adequate orientation and professional selection of personnel, based on self-concept, personality, interests and skills, will allow to maximize the positive effects of work and reduce risks such as work-related stress, burnout and job dissatisfaction.

BEHAVIOR, CARE AND PUBLIC HEALTH: AN INNOVATIVE METHODOLOGY OF ANALYSIS

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Background: The interaction between demographic, environmental and public health dynamics has resulted in an increase in health expenditure that exceeds overall economic growth. The literature indicates that health care spending indexes are often unrelated to a higher level of prevention and health care, but rather to the type of health care provided by Fisher in 2009. The increase in health and technology knowledge has resulted in an increase in life expectancy while life expectancy without disabilities has grown less. The gap between the growth of this variables combined with the birth rate decrease has led to an aging population and, consequently, this has great social and scientific relevance.

Objectives: Considering these phenomena, it is of fundamental importance to develop an efficient information system on health determinants, risk factors and prevention factors linked to the quality of life of the population. The purpose of this project is to analyze how each of the aforementioned variables acts in order to measure their impact on the system itself, studying the interaction between the healthcare environment, economy and health to identify the aspects that have the greatest impact on life expectancy and above all, which ones can extend life expectancy without disabilities. The statistical methodologies related to panel and georeferenced data will be used to create, validate, and estimate a multidimensional and territorial-dynamic model capable of predicting future trends in public health. Particular attention will be given to the effects of the pandemic on social behavior and demographic trends.

Expected results: The model will be using analysis techniques typical of the competition series and cooperation models and used to analyze the dynamics between interacting populations. In addition to the usual driver variables (birth rate, death rate, migration flows, age structure, etc.), the driver variables will be composed of environmental and green economy variables, considered crucial for the sustainability of the system, from which the most appreciable results are expect.

Future perspective: An iterative algorithm can be implemented as a Decision Support System (DSS) in the field of public health, guaranteeing, in quantitative terms, the sustainability of the system and evaluating the policies adopted through the creation of a Key Performance Indicator (KPI).

HUMORAL AND T CELL RESPONSE IN MULTIPLE SCLEROSIS PATIENTS UNDER DIFFERENT DISEASE-MODIFYING THERAPIES IN RESPONSE TO THE THIRD DOSE OF MRNA COVID-19 VACCINE

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Background: Vaccination campaign to contrast the spread of SARS-CoV-2 has raised the issue of vaccine immunogenicity in frail populations, especially Multiple Sclerosis (MS) patients on Disease Modifying Therapies (DMTs) in which a reduced immune response to past vaccinations has been seen.

Objectives: Herein, we describe a biological investigation of humoral and Spike-specific T cell response by production of IFNγ, IL2, and TNFα in MS patients under different DMTs after S peptide libraries stimulation comparing the obtained findings with Healthy Donors (HDs). Two different time-points were evaluated: before (T0) and after 2 months from booster dose of mRNABNT162b2 vaccine (T1). We investigated T cell response evaluating all possible combinations of intracellular expression of IFNγ, IL2, and TNFα in cytokine-producing T cells Moreover, we classified as "activated" those T cells producing one of the three cytokines of interest, and as polyfunctional those T cells producing simultaneously all the three cytokines.

Preliminary results: At T1, both MS patients and HDs showed an increase in anti-S antibody titers (p=0.0017; p=0.0039). Reduced percentage of "activated" and polyfunctional T cells, as well as a different polarization toward one cytokine production by T cells was seen in MS patients (p=0.0111; p=0.0135). Furthermore, stratifying MS patients according to different DMT treatment, dissimilarities in humoral and T cells response in immunomodulating- and immunosuppressive-treated patients were observed, with a drastic reduction of "activated" and polyfunctional T cells in the latter one ("activated" T cells: p=0.0020, p=0.0190; polyfunctional T cells: p=0.0606, p=0.0232). Interestingly, only immunosuppressive-treated patients showed a polarization toward TNFα production by T cells at both time point. Otherwise in immunomodulating-treated patients a more heterogeneous cytokine production was observed.

Future perspectives: Our preliminary results suggest that the immune response to mRNABNT162b2 vaccine is significantly influenced by DMT mechanism of action. Further investigation to better understand how immune response to vaccination in MS patients changes according to different disease treatment are needed.

VALIDATION OF THE "WORK-RELATED QUALITY OF LIFE SCALE" IN A SAMPLE OF REHABILITATION HEALTH WORKERS: CROSS SECTIONAL STUDY

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Background: Work Related Quality of Life (WRQoL) is a multidimensional concept referred to a satisfying work, in fact for many people work is not only a way to get a living, but also an essential activity to maintain a social identity; for this reason, quality of working life is related to general quality of life. Healthcare professionals in contact with patients and their relatives and caregivers, often have to face challenging emotional situations and high levels of stress. Therefore, assessment and monitoring of WRQoL are particularly important in healthcare settings because employee's satisfaction directly affects quality of performances and services offered to patients. Few studies recently have focused on quality of life of rehabilitation health workers; the assessment of perceived WRQoL of these professionals requires valid and reliable tools to realize an effective intervention in order to enable them to cope with work pressures.

Objectives: The primary objective of this study is to validate the Italian version of the WRQoL Scale in an Italian population of rehabilitation health professionals and to investigate its psychometric properties. The secondary objective is to explore correlations between some characteristics of professionals' work situation (date of birth, gender, profession, years of work, type of structure in which they work, Italian region, type of treated patients, type of employment contract and any exemptions for disability) and scores obtained in WRQoL Scale.

Expected results: The Work-Related Quality of Life Scale has been validated in 2020 in an Italian population of nurses and physicians, so we expect that the Italian version of the scale is a valid and reliable tool to also evaluate quality of working life of rehabilitation professionals. Furthermore, we expect different scores about WRQoL between different groups of the studied population.

Future perspectives: WRQoL scale can be useful for coordinators and managers in different work settings to periodically assess satisfaction of employees with their work activity, and also for human resources managers, to test the presence of professionals' well-being in the workplace, identify their needs and intervene if necessary.

ESTIMATING THE MID-LONG TERMS BURDEN OF COVID-19 PANDEMIC ON ITALIAN POPULATION HEALTH STATUS THROUGH THE SURVEILLANCE SYSTEMS *PASSI* AND *PASSI D'ARGENTO*

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Background: The COVID-19 syndemic has been affecting the whole community as per multiple spheres of life. The World Health Organization has invited all countries to develop strategies to strengthen the design and implementation of health policies to create resilient health systems. Since August 2020, *PASSI* and *PASSI d'Argento* (PdA) - two Italian ongoing population-based surveillance systems coordinated by the Italian National Institute of Health (ISS) on adults and elderly, respectively - have been administering a specific COVID module, in addition to the standard questionnaires.

Objectives: The objective is to show the potential of the ongoing surveillance systems in providing evidence for regional health governance to support local health and social services, through the collection of information on the burden of the health emergency on the population nationwide, also in the medium and long term.

Expected (or preliminary) results: The expected results are estimates of the impact of the pandemic phenomenon on working and economic conditions, mental and physical health, in particular on those who report chronic diseases or increased risk conditions; as well as estimates of the use of individual prevention measures and trust in institutions.

Future perspectives: The project is supposed to have a say in making real the scientific commitment to understanding the impact of the COVID-19 pandemic on major health behavioral determinants among the general population. The research flow will build on solid methodologies and practices to promote targeted actions that are needs based and outcome focused.

MECHANISMS OF SARS-COV-2 INFECTION AND PATHOGENESIS

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Background: The COVID-19 pandemic caused by Severe Acute Respiratory Coronavirus 2 (SARS-CoV-2) remains a global emergency due to the rapid spread of its variants. Despite all efforts and the mass vaccination programs, achieving global vaccine coverage remains a major hurdle. SARS-CoV-2 continued to evolve under immune selective pressure, and while transmission levels remain high, there is an increased likelihood of vaccine escape variants evolving. Currently we can rely on the knowledge of different biological features of this virus, but it is also crucial to link those findings to the disease induced by SARS-CoV-2 and its variants infection.

Objectives: The aim of the study is to identify the mechanisms involved in the SARS-CoV-2 infection in different *in vitro* cell models and to evaluate the replicative fitness of its different variants. The study wants to describe an approach to better understand the mechanism used by SARS-CoV-2 for replication and morphogenesis in different cellular lines and culture systems**.** We will investigate the different steps of virus infection in Vero E6, Calu-3 and Caco-2 cell lines.

Expected (or preliminary) results: SARS-CoV-2 infection on Vero E6 cells observed by Transmission Electron Microscopy analysis (TEM) showed very interesting ultrastructural modifications of the infected cells. Subsequently, infected Vero E6 cells were tested in Immunofluorescence Assays (IFAs) to track the progression of viral proteins during virus cycle by labelling them with specific antibodies. The preliminary results show that the Endoplasmic Reticulum and Golgi Apparatus are the cytoplasmic compartments involved in the accumulation of viral structural proteins S, M and N.

Future perspectives: It will be performed co-localization IFAs of the viral genome with the viral proteins produced during the virus life cycle and with the cellular host compartment. This could allow us in determining the strategic and biological importance of these proteins to better understand the different stages of life cycle of SARS-CoV-2 wild-type strain, firstly, and then of its variants.

EVALUATION OF IL-6, TNF-α, VEGF-A, MCP-1 AS POSSIBLE BIOMARKERS TO PREDICT DISEASE SEVERITY IN COVID-19 PATIENTS

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Background: Since December 2019 the Severe Acute Respiratory Syndrome CoronaVirus-2 (SARS-CoV-2) has spread globally, causing a devastating pandemic that has posed enormous healthcare challenges around the world. Patients with the most severe symptoms (lung damage, septic shock, multiple organ failure) of COVID-19 (Coronavirus Disease-19) showed higher IL-6 levels than patients with mild and moderate COVID-19 symptoms. Since it has been proposed that elevated IL-6 levels may be associated with disease severity, it is assumed that they are also associated with worse clinical outcomes. The first anti-cytokine drug used in patients with COVID-19 was Tocilizumab (TCZ), anti-IL-6 monoclonal antibody. Tocilizumab was introduced in the early 2000s for the treatment of autoimmune diseases such as refractory rheumatoid arthritis and systemic Juvenile Idiopathic Arthritis (JIA) and has been approved by the FDA since 2017 for the treatment of Cytokine Release Syndrome (CRS). With the global outbreak of COVID-19 disease, the accumulation of evidence indicates that cytokine storm is associated to severe illness and elevated serum cytokines are the result of a complex interaction between lymphocytes and myeloid cells.

Objectives: The aim of this study is to evaluate cytokine storm in COVID-19 patients treated with TCZ. From March to June 2020, patients with COVID-19 pneumonia admitted to Goretti Hospital of Latina, were enrolled. COVID-19 related pneumonia was diagnosed by computed tomography of the chest associated with SARS-CoV-2 RNA detection from a nasopharyngeal swab through a commercial Reverse Transcription Polymerase Chain Reaction (RT-PCR) kit.

Expected results: Preliminary results showed a modulation of sCD163 plasmatic levels mediated by TCZ and support the hypothesis of a reduction in serum levels of different inflammatory cytokines after TCZ administration Therefore, TCZ therapy can be an effective method to control the heightened immune response and it has a substantial beneficial effect in majority of COVID-19 patients. We will report the development and application of an automated digital assay platform using a "next generation enzyme-linked immunosorbent assay (Ella-ELISA)" for rapid and multiplex monitoring cytokine like: IL-6, TNF-α, CCL2/MCP-1 and VEGF-A in plasma samples of COVID-19 patients.

Future perspectives: We will propose to elucidate the role of proinflammatory markers in biological fluid of TCZ group to better understand their correlation with vascular dysfunction and different COVID-19 variant like Delta and Omicron.

THE PROMOTION OF THE VACCINATION CULTURE AMONG YOUNG PEOPLE AS AN INSTRUMENT TO SAFEGUARD PUBLIC AND INDIVIDUAL HEALTH

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Background: Despite the incontrovertible power of vaccines to prevent various diseases, vaccine hesitancy remains a threat in safeguard public health. At national level, data on immunization coverage shows that young people had a generally low propensity towards free and voluntary vaccinations. The lack of knowledge about vaccines, along with doubts about their effectiveness and safety but also a low risk perception were identified as key factors of the poor attitude and the low adherence to vaccinations in this age group. Within this context, focusing on this population that is less likely to adhere to preventive strategies, but on the other hand is an ideal target for awareness-raising campaigns, since they are in a training period and therefore particularly receptive to educational interventions, could be critical to reach immunization goals.

Objectives: The aim of the research project is: 1) quantify the prevalence of vaccine hesitancy in university students and assess their knowledge, attitudes and vaccination intentions using an evidence-based tool developed ad hoc; 2) plan, implement, and evaluate a training intervention among Sapienza University students and 3) develop strategies for the promotion of vaccination adherence.

Preliminary results: In order to achieve the primary outcome, we conducted a cross-sectional survey to quantify over time the prevalence of COVID-19 vaccine hesitancy among university students, investigated its determinants, and analyzed student attitudes, risk perceptions and compliance with preventive measures. We found that vaccine hesitancy changed over time and it is negatively associated with several factors such as higher levels of perceived COVID-19 severity, concern for the emergency, confidence in vaccine safety and effectiveness, and self-reported adherence to infection prevention and control measures. Additionally, in order to investigate determinants of vaccination intentions we summarized the evidence on the role of health literacy in vaccination behaviours. Results of the systematic review showed that health literacy seems not to strongly predict vaccination uptake in the population and neither in students.

Future perspectives: The findings of the first phase will allow us to explore more in-depth factors associated with vaccine hesitancy, to understand student's perspective on vaccinations, and to identify, to plan and to implement appropriate evidence-based vaccine hesitancy response strategies in order to lastly promote vaccine culture in this population.

SPECIFIC CD4 AND CD8 T CELL RESPONSE OF SARS-COV-2 S EPITOPES USING TETRAMERS & MONOCYTE DYSREGULATION IN FULLY VACCINATED DONORS AND RECOVERED PATIENTS

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Background: SARS-CoV-2 is able to escape immune response, causing poor clinical outcome and reinfection. The escape is associated with development failure of T cell memory compartments. SARS-CoV-2 variants do not significantly disrupt the total SARS-CoV-2 T cells reactivity. The decrease of humoral immunity response observed, highlights the importance of active monitoring of T cell reactivity. Patients may show altered dimension of atypically activated monocytes related to immunity overactivation causing severe progression. In flow cytometry a population of bigger monocytes has been related to severe disease but clear polarization into pro-inflammatory M1 or alternatively activated, anti-inflammatory M2 macrophages hasn't been identified.

Objectives: The aim of the study is to characterize the T memory subsets testing the immune response against class I and II restricted immunodominant epitopes shared by ancestral and variants SARS-CoV-2 strains and the monocyte subsets evaluating the expression of M1 or M2 markers in classical, atypical and intermediate monocytes.

Preliminary results: 9 HDV and 14 PZ were recruited. Comparing the two cohorts of subjects, there was no statistically significant difference in the percentage of SARS-CoV-2 antigen restricted T clones in both CD4 and CD8 subsets even if there is a small increase in the PZ cohort compared to HDV. Looking at CD4 T memory subsets no difference was recorded between the two groups, whereas, in the case of CD8 T cells a significant decrease of the Tn subset (HDV 49.76±16.49% *vs* PZ 19.72±14.76%, p<0.001) is associated with a parallel significant increase of the Tem (HDV: 24.87±13.72% *vs* PZ 46.19±17.51%, p <0.007) in the PZ cohort compared to HDV. Classic Monocytes showed a significant decrease on PZ (85 ±4.44%) cohort compared to HDV (89.03±5.67%).

Future perspectives: These results suggest that, even if both vaccination and natural infection are equally able to induce the activation of T cell clones restricted for immunodominant peptides, recovered subjects display, in the case of CD8 T cells, an improved expansion of the effector memory T cell subset compared to vaccinated people. This feature probably reflects the broader T cell repertoire stimulated by the virus during the natural infection compared to the spike-restricted one activated during the vaccination schedule.

DEVELOPMENT OF AN INTEGRATIVE APPROACH FOR MONITORING SARS-COV-2 INFECTION-INDUCED VERSUS VACCINE-ACQUIRED INNATE AND T CELL IMMUNITY IN HIV-1 INFECTED PATIENTS

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Background: The ongoing outbreak of COVID-19, caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has become an emergency of international concern when thousands of people were infected around the world. Nonetheless, evidence on how HIV-1 infection affects risk of poor outcomes from COVID-19 are still poorly investigated and a clinical and immunological profile due to SARS-CoV-2 infection in patients with HIV are lacking despite about 38 million people having HIV globally. Complex immune dysregulation in both interferon and T cell responses has been observed in HIV-1 infected patients as well as in COVID-19 patients. On the light of the aforementioned considerations, further studies are urgently needed to better understand and characterize the impact of SARS-CoV-2 infection on the immunopathogenesis of HIV-1 infection. Furthermore, it is necessary to assess the effectiveness of COVID-19 vaccines, as well as their ability to modify innate and T cell associated immunity in HIV-1 positive patients.

Objectives: The first aim that will be pursued during this research project will be a comprehensive analysis of the effectiveness of SARS-CoV-2 vaccines in virologically suppressed HIV-1 infected patients, evaluating their ability to confer long-lasting humoral immune protection and their effects on interferon pathways and on T cells frequency and phenotype. As second aim of this study the impact of SARS-CoV-2 infection on the interferon and T cell response in virologically suppressed HIV-1 infected patients will be evaluated.

Expected (or preliminary) results: Preliminary results showed that humoral response following vaccination increased up to 1 month after the second dose (p<0.001). Gene expression analysis performed in 20 HIV-1 infected patients showed an overall decrease of IFNs and ISGs transcript levels after COVID-19 vaccination.

Future perspectives: Further analysis will be conducted on a larger HIV-1 infected population to evaluate humoral response, interferon pathways and T cells immune phenotype and frequencies in COVID-19 vaccinated patients as well as interferon and T cell response on SARS-CoV-2/HIV-1 co-infected individuals.

IMMUNOHISTOCHEMICAL AND MOLECULAR MARKERS FOR THE POST-MORTEM DIAGNOSIS OF SEPSIS

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Background: Sepsis is a common disease and has a high mortality rate, especially among older patients. An early diagnosis of sepsis is fundamental to adequately treat the patients; it is mainly based on clinical data and laboratory tests, such as the procalcitonin plasma levels. On the other hand, the post-mortem diagnosis of sepsis is a challenge for the Forensic Pathologist, because the autoptic findings usually are unspecific and there are no reliable markers to be used.

Objectives: Herein, we tested the expression of three proteins (procalcitonin, TREM1, and pro-adrenomedullin) through immunohistochemistry, as well as the expression of 10 miRNAs (miR-98, miR-218, miR-494-3p, miR181-b, miR-146, miR-122, miR-200a-3p, miR-147, miR-204-5p, miR-155) through RT-PCR, on fluids and tissues sampled during autopsies of patients who died of sepsis, and subjects who died of other causes as control.

Expected results: We'll verify if there is a differential expression of such proteins and miRNAs between the two groups.

Future perspectives: Our studies will reveal if these molecules could be used as a panel of immunohistochemical and molecular markers for the post-mortem diagnosis of sepsis. Our study would also highlight the role of such molecules in the pathophysiology of sepsis, leading the way to new therapeutic and diagnostic strategies.

"CLEAN CARE IS SAFER CARE".
POSTOPERATIVE SEPSIS: ERROR MANAGEMENT AND EVIDENCE OF NON-PREVENTABLE EVENTS

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Background: Italy is one of the few countries to have a law (No. 24/2017) that recognizes the safety of care as a fundamental right of every individual accessing health services. The primary objectives of health care safety and quality programs include preventing Healthcare-Associated Infections (HAIs), a widespread phenomenon worldwide. The most dangerous complication of infections is sepsis. Patients who develop postoperative sepsis have significantly high morbidity and mortality rate and higher costs. Moreover, it is often difficult to prove the non-preventability of this type of event, with consequent civil proceeding loss in most litigation cases, aggravating hospital costs. It means that its monitoring and prevention are critical elements for improving the quality of care, reducing health care costs, and avoiding negative repercussions on the image of the hospitals. The Agency for Healthcare Research and Quality (AHRQ) has proposed a series of quality indicators called Patient Safety Indicators (PSIs), which constitute a screening tool for identifying adverse events using codes present in the hospital discharge forms. AHRQ has included in this set of indicators one for postoperative sepsis (PSI 13). The PSIs represent the current state-of-the-art in measuring the safety of hospital care.

Objectives: To evaluate the prevalence rate of the "postoperative sepsis" event in the surgical departments of the Teaching Hospital Policlinico Umberto I of Rome; the performance and the quality of the assistance provided; the effectiveness of existing protocols for preventing post-surgical infections; to introduce any corrective measures to reduce "postoperative sepsis" and operational tools to build a defence file in case of a dispute.

Expected results: At the end of the study, the Teaching Hospital Policlinico Umberto I of Rome will have an internal report on the prevalence rate of the surgical departments. The wards will benefit from adequate preventive measures for postoperative sepsis and will be able to redesign care based on best evidence-based practices. Consequently, a reduction in this event is expected. The medico-legal team could avail of a valid defence file, helpful in case of hospital litigation.

Future perspectives: The present study proposes a methodological approach to preventing postoperative sepsis in surgical departments. Such a methodological approach could be useful in preventing additional types of adverse events frequently observed in clinical practice.

PYRETHROID-FREE INTEGRATED MANAGEMENT OF CULICINAE VECTORS OF HUMAN AND ZOONOTIC DISEASES IN TEMPERATE AREAS

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Background: *Culex pipiens*, the native mosquito in Italy, and *Aedes albopictus*, an invasive species, are vectors of even potentially deadly human viruses such as West Nile, Dengue and Chikungunya. Until the 1990s they were considered mainly tropical arboviruses, but several human cases were reported in the last decades also in temperate regions. European and National guidelines recommend environmental and larval source management as the gold standard for reduction of mosquito abundance and related public health risks. Insecticide spraying is only recommended as an emergency tool in case of autochthonous arbovirus transmission. Nevertheless, wide-area ground and aerial spraying of pyrethroids is largely used in Italy to rapidly reduce mosquito nuisance, despite the short-term effect, negative effects on non-target species, and spread of pyrethroid resistance in target ones. Most of these interventions are focused in urban areas, whose ecosystem is affected by exposure to contamination by these pesticides. The need of innovative pyrethroid-free mosquito control approaches is thus necessary from both public health and environmental perspectives.

Objectives: Training objectives: build competences needed to develop, plan and support pyrethroid-free management of mosquitoes by conventional and innovative integrated control approaches, also through theoretical and hands-on training at ENTOSTUDIO srl (PD) and at University of Queensland (Australia). Research objectives: study of mosquito bionomics and resistance to insecticides, and development and testing of new technologies for environmentally safe surveillance and control approaches.

Expected (or preliminary) results: Training at ENTOSTUDIO and University of Queensland will provide theoretical and technical skills needed for autonomous implementation of research studies in the second part of the PhD project. These will be leveraged to achieve the following research results: i) definition of physiological (e.g. longevity, insecticide resistance) and behavioural (e.g. dispersal, multiple mating) crucial characteristics of European *Aedes* and *Culex* populations crucial for the implementation of innovative pyrethroid-free control approaches; ii) preliminary assessment of an innovative control approach in the field. Preliminary results on the assessment of resistance to Diflubenzuron in Italian populations of *Cx, pipiens* and *Ae. albopictus* show high level resistance in the former species, and first indications of possible resistance in the latter.

Future perspectives: To contribute in reducing mosquito nuisance and public health risk in urban areas in temperate regions, while decreasing the environmental impact due to widespread pyrethroid pesticide use.

THE ARTIFICIAL INTELLIGENCE AND THE RISK MANAGEMENT: A NEW MEDICO-LEGAL CHALLENGE

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Background: According to the finance report management of 2017 presented by the Court of Auditors to the Italian Parliament, there is an increase for the costs related to healthcare companies. The exponential increase of the medical claims, for real or unreal damage to patient caused by real or unreal healthcare structures or medical doctors' responsibilities represents an economic loss not only in Italy but also in European Countries that have the same degree of socio-economic development. The strategies for the reduction of Claims management's costs for Medical Malpractice are represented by an appropriate use of structural, technological and organisational resources of the healthcare system: it could help to predict the establishment of medical claims, preventing excessive economic losses and predicting also the outcome of the eventual law process.

Objectives: Our study deals with the development of an algorithm able to passively collect and analyzes the data before creating strategies of prevention and management of the medical claims through a "census" of adverse events, with a focus on the importance of judgement and highlighting the meaning of economic losses for health structures after the claims.

Material and methods: To realize our project we need for an algorithm that, starting by training information, is able to establish if there was a malpractice and to predict the Court decision. The "data training" should be extrapolated by searching on engines for case law. To establish the abilities of our software, we must use a set of tests (litigations cases of which the algorithm shall be able to predict the most probable judge's judgment): our database of tests is represented by the litigations cases of AOU of ART (Assisted Reproductive Technique) of the Teaching Hospital Policlinico Umberto I of Rome.

Future perspectives: We want to establish the real application of this algorithm to all areas of the healthcare. In fact, the aim of our study is to create a software useful for risk health manager, using Artificial Intelligence technologies. Using these technologies, could be possible to reduce management time approaching medical claims, improving costs and services for healthcare companies.

HOSPITAL - ACQUIRED PNEUMONIAE IN PATIENTS WITH SARS-COV-2 ARDS UNDERGOING NON-INVASIVE VENTILATION: PREVALENCE AND MICROBIOLOGICAL FEATURES

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Background: Non-Invasive Ventilation (NIV), compared to invasive mechanical ventilation, is able to reduce in specific patient populations risk of reintubation, mortality, length of stay and occurrence of lung infection; it is preferentially used in subintensive care Units, where intubation and invasive mechanical ventilation is at hand, or in case of Do Not Intubate (DNI) order. NIV is not the first choice of treatment in SARS-CoV2 pneumoniae, uncertain results are described in literature. Unluckily, lessons from previous viral pneumoniae are not promising. However, incidence of Hospital Acquired Pneumoniae (HAP) and sovrainfections in patients undergoing NIV is neglected.

Objectives: Evaluate incidence and prevalence of microbiological species in subjects who developed pneumonia following more than 48 h of consecutive NIV, who required subintensive care for their ARDS-SARS-COV-2 illness.

Expected results: We recruited retrospectively, from a period from March 2019 to March 2022, a population of 72 subjects who received NIV. Mortality for respiratory failure was 63.90 %. All patients underwent detailed medical history and physical examination, blood tests including C reactive and procalcitonin, complete blood count, routinary microbiological specimens such as sputum, bronchoscopic samples, blood culture, rectal and nasal swab. From our preliminary results, people with superinfections had a mortality of 100.00 %. Microbiological isolates were the following: 4 *Acinetobacter baumannii XDR, 3 Aspergillus fumigatus, 1 Psuedomonas aeurugnosa* 1 *Oxacillino-Resistant Staphylococcus aureus, 1 Klebsiella pneumoniae carbapenemase producing, 1 Escherichia coli ESBL.* We would like to extend our research by recruiting a comparison group without SARS-CoV2 infection who required for their disease a prolonged NIV for 48 hours. We would match these two groups by demographic characteristics, comorbidities and major outcomes such as death, and minor outcomes.

Future perspectives: We expect to confirm and extend literature: sideways, for its innate immunosoppressive mechanism, in SARS-CoV2 arm a higher incidence of HAP is awaited. On the other hand, from dramatic results obtained in our preliminary results about mortality, regardless coexistence of sovrainfections, a deep meditation in the choice of initiate a trial of NIV in SARS-CoV2 pneumoniae is needed. Another part of the study, about data collection of NIV parameters, is aimed to focus possible predictor of failure. We expect that these new epidemiological observations would let the physician direct his clinical management on the choice of starting NIV, by evaluating concrete risk of unfavorable infective outcomes and health care infections.

POTENTIAL ROLE OF ESTROGEN RECEPTORS IN VIRAL INFECTIONS IN THE BRAIN

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Background: Estrogens are steroid hormones that act not only on the female reproductive system, but also on the immune system and the brain, where they may exert regulatory and neuroprotective actions, respectively. These actions occur through the interaction with estrogen receptors, ERα, ERβ and GPER. ER signalling regulates cells and pathways of the immune system, contributing to the gender differences in viral infection responses. Accordingly, Selective Estrogen Receptor Modulators (SERM) have shown a therapeutic action against infectious diseases characterized by a dysregulated inflammatory response, such as those caused by respiratory viruses, like Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) and Influenza A Virus (IAV). Moreover, SERM antiviral potential occurs also in an ER-independent manner, by blocking specific steps of the replication cycle of some viruses, including Herpes Simplex Virus-1 (HSV-1), a neurotropic virus associated to Alzheimer's disease pathogenesis. Interestingly, also SARS-CoV-2 and IAV have neuroinvasive capacities since they can spread from the respiratory tract to the brain, causing severe acute damage and long-term neurological sequelae triggered by the activation of neurodegenerative processes. However, these aspects and the molecular mechanisms involved are quite unexplored.

Objectives: This study is aimed at investigating the role of ERs in respiratory virus brain infection, focusing on their possible modulation of virus-induced neurodegenerative pathways. This aim will be achieved by investigating in *in vitro* and *in vivo* experimental models of acute virus infection: a) the effects of viral infection on ERs expression/intracellular localization and signalling; b) the effects of SERM administration on viral replication and possible virus-induced neuronal damage. In addition, the effects of SERM on HSV-1-induced neurodegeneration and virus replication in neurons will be evaluated.

Expected results: This study, exploring the role of ERs in brain virus infection, will advance knowledge on the molecular mechanisms underlying neuronal damage caused by virus spreading in the brain.

Future perspectives: The overall results of this study will provide useful information for innovative therapeutic approaches to the neurological complications of infectious diseases with a strong impact on public health.

DEVELOPING AN INTEGRATED ANTICIPATORY WARNING SYSTEM FOR ARBOVIRUSES BASED ON PARTICIPATORY ACTION AND DATA INNOVATIONS

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Background: The past five decades have seen an unprecedented emergence of epidemic arboviral diseases, a type of Vector-Borne Diseases (VBDs) caused by viruses transmitted to people by the bite of an infected arthropod. Unfortunately, Early Warning Systems (EWS) for VBDs, including arboviral diseases, are generally able to detect the infectious agents once they reach the human or the animal population. To strengthen prevention and preparedness strategies, EWS should work to anticipate the emergence of threats, by monitoring the arboviruses drivers, like rapid urbanization, deforestation, globalization of travel and trade, climate change and behavioural practices. However, creating Anticipatory Warning Systems (AWS) requires extensive data collection and an integrated approach, that promotes the collaboration among different disciplines, such as the One Health approach, to tackle the arboviruses determinants which lie within human, animal, ecological and social systems. Communities are a rich source of information regarding these systems; however, they are routinely left out of monitoring activities and decision-making, resulting in the failure of surveillance systems. Bottom-up approaches, such as community-based AWS paired with data innovations, could monitor arboviruses drivers across different sectors, and support formal surveillance systems with up to date and readily accessible information. To this end a study would be performed in a selected country of the MediLabSecure Network, which aims to promote integrated surveillance of emerging arboviruses, to support the development of a prototype of an innovative community-based AWS for arboviral diseases.

Objectives: The objective of this PhD thesis is to support a knowledge building process involving different disciplines and stakeholders at country level to co-create a prototype of an integrated community-based AWS for arboviruses drivers and test its feasibility.

Expected results: The expected results of the study are the knowledge co-production process that will involve the stakeholders in the co-creation of a prototype of a community-based AWS paired with data innovations (i.e., remote sensing and computer vision), and assess its feasibility (acceptability, practicality, integration, sustainability). A capacity building curriculum for all the involved stakeholders and a toolkit for communities for implementing the AWS, would also be developed with a participatory process.

Future perspectives: The prototype could be piloted during a next stage of the research within selected communities and, after evaluation, scaled-up to the whole country under the guidance of the engaged stakeholders. The lessons learnt could be shared with other countries of the MediLabSecure Network and the prototype piloted to standardise its features and replicability.

THE IMPACT OF DSM-5 ON THE DIAGNOSIS OF AUTISM SPECTRUM DISORDER AND GENDER DIFFERENCES IN AUTISM DIAGNOSIS

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Background: Autism is a neurodevelopmental disorder characterized by restricted interests and repetitive behaviors or activities along with disabilities in social communication and interaction, namely stereotyped and restricted language, inability to understand abstract, equivocal, and picturesque language, or figures of speech like metaphor and irony. Once considered a rare condition, ASD has gone through a shift in terms of diagnosis, with a prominent increase over time. Compared to males, females are at substantially elevated risk of their ASC going undiagnosed: their difficulties are frequently mislabelled or missed entirely.

Objectives: Our work aims at investigating the hypothesis of a diagnosis dropout between the DSM-IV-TR and the new classification in DSM-5, which would result in social consequences for the newly excluded patients. great attention will be given to females diagnosed with autism, in an attempt to make a contribution to the construct of female autistic phenotype.

Expected (or preliminary) results: One explanation is the 'female protective effect': there is something inherent in being female which reduces the likelihood of developing autism. However, evidence suggests that the condition is underdiagnosed in females, perhaps because females express their autism in ways which do not meet current diagnostic criteria. This project explores evidence for a female-typical autism presentation, the Female Autism Phenotype (FAP) and the component of camouflaging (compensating for and masking autistic characteristics) in particular.

Future perspectives: The evidence supports the existence of a female-typical autism presentation, although further examination of the characteristics and their impact across all genders and ages is needed.

INCREASED ACCESS TO VACCINATION FOR NEWLY ARRIVED MIGRANTS (ACTOVAX4NAM)

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Background: Migrants within the European Union and European Economic Area may be under immunized or lack documentation on previous vaccinations. Ensuring high levels of vaccination coverage for all is a key priority for the European Union (EU); yet both external and internal migration in the region poses an additional challenge to achieving this. "Access to Vaccination for Newly Arrived Migrants (NAM) - AcToVax4NAM project" aims to improve vaccination access for NAMs making access conditions equitable and guaranteed. The project responded to a specific call under 3rd EU Health Programme for "Increased access to vaccination for disadvantaged, isolated and difficult to reach groups of population" (Grant n 101018349, 3rd EU Health Programme).

Objectives: 1) To describe existing immunisation guidance, reception and vaccination offer systems for NAMs in Consortium Countries; 2) To characterise system barriers that hinder the immunisation of NAMs and to identify possible solutions; 3) To reinforce networking capacity among institutional and non-institutional organisations and actors to address Vaccination Literacy (VL) and migrant-sensitivity of the health care system with respect to the immunisation of NAMs; 4) To strengthen the healthcare system VL and responsiveness among health care professionals and other health operators ("Professional FOR health") in order to increase the capacity building skills and cultural sensitivity of the healthcare system in promoting active immunisation of NAMs; 5) To develop country specific action-oriented flow-charts to improve access to immunisation for NAMs including identified barriers, proposed solutions and relevant tools specific for each country situation and validated by the professionals FOR health (target group); 6) to pilot test and evaluate country-specific solutions to overcome system barrier and increase vaccination uptake with emphasis on a life course approach, on the immunisation of NAMs and to produce final recommendations.

Expected (or preliminary) results: 1) Updated knowledge on reception and vaccination systems/conceptual framework; 2) Country-specific information on system barriers and relevant solutions/logic flow-charts/Database with tools; 3) Capacity building to strengthen health literacy perspectives among target groups/related activities and training; 4) Pilot testing solutions to overcome system barriers and demonstrate concrete and effective practices to increase coverage/Recommendations.

Future perspectives: Positive impact on vaccination uptake in NAMs. Supporting health systems in overcoming barriers that pose difficulties in the vaccination of NAM. Making tools and solutions to improve vaccination uptake among NAM readily available also at an EU level.

CHARACTERIZATION OF HUMORAL AND T CELL RESPONSE TO COVID-19 MRNA-BASED VACCINE IN A COHORT OF PLWH ON ART

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Background: Since December 2019 the Severe Acute Respiratory Syndrome CoronaVirus-2 (SARS-CoV-2) has spread globally, causing a devastating pandemic. mRNA-based vaccines have been widely used in Italy, also for the immunization of frail and immunosuppressed subjects, included People Living With HIV (PLWH). Many studies demonstrate that mRNA-based vaccines are able to induce a protective humoral and cellular response against SARS-CoV-2 Spike protein (S). In particular, there is an increasing evidence of the importance of vaccine-induced S-specific T-cells in conferring protection against COVID-19, as observed for those induced by natural infection. In fact, vaccine-induced S-specific T cells can recognize different regions of S protein, contributing to vaccine efficacy against viral variants. In PLWH, despite the effective control of viremia with ART is correlated with an improvement of responsiveness to routine vaccines, some immune defects might alter vaccine-induced immune response to SARS-CoV-2, evidencing the need to investigate it in this population.

Objectives: The main aim of the project is to investigate specific B and T cell response to COVID-19 mRNA-based vaccines in a cohort of PLWH on ART by intracellular cytokine staining upon S peptide libraries stimulation, with a focus on the quality of the response.

Preliminary results: Our preliminary results showed that a specific antibody response was present in most of the participants already after the second dose, but the third dose increased both the rate of response and its magnitude. The vaccine was able to induce a cell-mediated immune response in most of PLWH. Stratifying the population according to CD4 cell count, we found that this immune response was significantly poorer in those with a lower current CD4T cell count compared to those with a higher CD4T cell count, but the third dose improved the responsiveness to vaccination.

Future perspectives: Clarify the knowledge gaps in the understanding of the magnitude, duration and quality of immunity to COVID-19 vaccination in PLWH is critical for the proper application of mitigation strategies against the SARS-CoV-2 pandemic, as well as for vaccine design. Therefore, we will continue to characterize the immune response at different time-points from the administration of the third dose, including in the analysis the response against viral variants. Moreover, we will correlate the data to CMV serostatus, in order to establish if CMV infection could represent a risk factor involved in a lower responsiveness to vaccination, since its association with pathological events and chronic immune activation in PLWH is already known.

PROFESSIONAL RESPONSABILITY PROFILES FOLLOWING COVID-19 PANDEMIC

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Background: Health is a right constitutionally guaranteed by Italian Constitution in Article 32, where to health is raised a fundamental right due to the importance and essentiality that this legal good has for the individual, whether it is considered as single or as part of a community. The state, in fact, has an obligation to protect this right considered as a "perfect subjective right": COVID-19 pandemic breakdown opens up new medical and legal scenarios in professional liability. Among the dramatic aspects that were highlighted during the pandemic there was also the fear that this emergency could turn into a real accusation against health personnel, already put to the test by the unpredictable extent of this phenomenon. There is no doubt that the COVID-19 pandemic represents a health emergency, difficult to solve and understand. For these reasons, in our country, during the initial phase of the emergency, we discussed about some possible changes to be made to the regulations on medical liability in order to guarantee them to operate with greater serenity in an already critical period. In the criminal field it should be noted that with the L. 76/2021 excludes the punishment of health professionals in cases of: "Criminal liability for administration of the anti-SARS-CoV-2 vaccine" and the non-punishable clause, the so-called "Criminal shield", of health workers in cases of negligent liability.

Objectives: The aim of the project is to prepare an analysis of the evolution of professional health responsibility based on the peculiarities of the pandemic in progress and the jurisprudential innovations made.

Expected results: the trend of complaints is still low, but most of the COVID-19 related clinical cases concern fragile subjects with multiple morbidities.

Future perspectives: The goal aims to standardize a working methodology capable of implementing risk management clinical in reference to the pandemic emergency and, at the same time, aims to analyze the evolution and revolution that COVID-19 will bring in the legal field, to evaluate the effects of pandemic on the over-growing phenomenon of medico-legal litigation.

AUTHOR'S INDEX

Migliara G.; 15
Milanese A.; 61
Milano A.; 48; 81
Miles A.; 64
Minardi V.; 69
Miteva M.T.; 49
Modiano D.; 5; 18
Mongiovì R.; 73
Montesano C.; 50; 62
Montesano M.; 43
Negro F.; 78
Novello F.; 7
Ogenchuk M.; 16
Okechukwu C.E.; 16
Oliva A.; 14; 36; 45
Olmati F.; 79
Onesti M.G.; 17
Orlandi S.; 34
Orsi G.B.; 43
Ouédraogo I.N.; 18
Ouédraogo M.; 18
Padovano M.; 22
Pagano F.; 50
Palamara A.T.; 4; 49; 80
Palange P.; 45; 79
Parente A.; 73
Parente P.; 32
Pasquali F.; 49; 80
Piaggi S.; 52
Pichler V.; 64; 77
Pietrantoni A.; 70
Pietropaolo V.; 19
Pinto B.; 52
Pizzarelli A.; 4
Poleggi A.; 61
Pombi M.; 5; 13; 35
Ponzi M.; 18
Porreca F.; 61
Prezioso C.; 19
Protto V.; 49
Provenzano M.; 11
Puopolo M.; 61
Radocchia G.; 20
Raffone A.; 65
Raponi G.; 14
Reali M.; 10

Regini F.M.; 9
Renzi E.; 51
Ricci S.; 82
Robbiati C.; 48; 81
Rodriguez Fernandez V.; 52
Romeo G.; 73
Rondón S.; 21
Rossino M.G.; 52
Ruggeri G.; 17
Ruotolo I.; 68
Salciccia C.; 61
Saliaj A.; 44
Santinelli L.; 74
Sarsha M.; 4
Sbriccoli M.; 61
Scagnolari C.; 74
Scarso S.; 83
Schilirò T.; 7
Schippa S.; 20
Sciurti A.; 34
Scopetti M.; 22
Scordio M.; 74
Scribano D.; 4
Sellitto G.; 68
Sergi M.; 50; 62
Serra R.; 11
Serraino G.F.; 11
Sgroi G.; 35
Shaholli D.; 65
Siccardi G.; 45
Siciliano G.; 37
Simione L.; 65
Soulama I.; 37
Spagnolello O.; 23
Sparano M.; 7
Spartà A.; 34
Spataro P.; 65
Straccamore M.; 78
Tennessen J.; 64
Tieghi T.; 73
Tiple D.; 61
Tofani M.; 24
Torcia G.; 18
Tortellini E.; 84
Tramontano A.; 45
Trampuz A.; 14