

EPIDEMIOLOGY  
OF INFECTIOUS DISEASES

# SCIENTIFIC SEMINAR ON INFECTIOUS DISEASES

Brussels, 11 May 2023

Sciensano  
Epidemiology and public health  
Epidemiology of infectious diseases  
Rue Juliette Wytsmanstraat 14 | 1050 Brussels | Belgium

Scientific seminar on infectious diseases | 11 May 2023|  
Royal Museums of Fine Arts of Belgium, Brussels, Belgium

TABLE OF CONTENTS

Partners. ....6

Programme. ....7

Sponsors. ....8

Scientific committee. ....9

Abstracts of presentations. ....11

Charlotte Martin  
Current knowledge on monkeypox, laboratory tests, probable  
animal reservoir .....12

Sandra Van den Eynde  
Sensoa & The MPOX: A timeline of Interventions towards MSM ...13

Marc Van Ranst & Elke Wollants  
Polio eradication: a protracted endgame .....14

Emma Thomson  
Investigation into cases of hepatitis of unknown aetiology among  
young children in Scotland .....16

Isabel Leroux-Roels  
Update covid-19 vaccination .....17

Laura Van Den Borre  
Helicon project - social inequalities in COVID-related health  
outcomes .....18

Boudewijn Catry  
Impact of covid-19 on healthcare-associated infections .....20

Rosalie Sacheli  
National cartography of water points for the presence of *Vibrio*  
spp. in Belgium .....21

Eva Vanuytrecht  
Climate change as a threat to health in Europe: focus on  
infectious diseases .....22

Marie Hermy & Wim Van Bortel  
Monitoring of Exotic mosquitoes in Belgium: results of 2022 .....24

Mieke Steensels  
Zoonotic risk of the circulating highly pathogenic H5 avian  
influenza viruses .....27

## Anne Botteaux

Climate change as a threat to health in Europe: focus on infectious diseases .....	28
Abstract of posters .....	31
Human botulism in Belgium: two atypical cases in 2022 .....	33
Serotype distribution of non-invasive <i>Streptococcus pneumoniae</i> strains in Belgium, 2020-2022: a prospective, observational study	37
Performance of commercial rose bengal antigens for the diagnosis of human brucellosis .....	39
Trends of gram-negative bacteria susceptibility pattern in respiratory samples of intensive care units in the Brussels Capital Region, 2010-2021. ....	40
Comparison of Belgian COVID-19 mortality between epidemiological surveillance and death certificates for the year 2020. ....	42
A new data collection system for epilabo, the network of sentinel laboratories .....	43
Towards a new (H)ERA: Developments to strengthen infectious diseases surveillance and pandemic preparedness .....	45
Molecular typing of enterovirus positive samples for the year 2022 confirms Echovirus 9 as most prevalent genotype in Belgium	47
Surveillance of respiratory pathogens through environmental air sampling and effectiveness of air purifiers: monitoring 6 congregate settings during a respiratory season. ....	48
The highest number of rotavirus positive samples ever received at the NRC UZ/KU Leuven during the season 2021-2022. ....	49
The Sciensano biobanks before, during and after the covid-19 pandemic: challenges and opportunities .....	51
A phase 2, randomized, double-blind study to evaluate the safety, tolerability, and immunogenicity of A 21-valent pneumococcal conjugate vaccine (V116) in adults $\geq$ 50 years ....	52
PK, SNA, and Efficacy Against RSV MALRI From a Phase 1b/2a Study of the Monoclonal Antibody Clesrovimab (MK-1654) in Infants .....	53
Poliomyelitis surveillance in Belgium. ....	54
Immunogenicity and Duration of Protection After Yellow Fever Vaccine in People Living with HIV: A Systematic Review. ....	55

Monitoring of varicella trends in Belgium between 2017 and 2022 through Google Trends .....56

Age-standardized mortality rates related to viral hepatitis C in Belgium.....58

Clinical applications of rescue strategies in extensively drug-resistant HIV-1, a case report .....60

Description of the undiagnosed HIV infection in 2020 in Belgium by key populations and urbanization level.....61

Environmental detection of *Pneumocystis jirovecii* in different indoor settings highlights the potential role of children under 3 years and young adults in transmission .....63

Efficacy, durability, and tolerability of bictegravir/emtricitabine/tenofovir alafenamide for the treatment of HIV in a real-world setting in Belgium .....65

Wastewater-based epidemiology of COVID-19 in Belgium.....66

Factors underlying COVID-19 booster vaccine uptake among adults in Belgium .....67

Diphtheria re-emergence in Europe and Belgium anno 2022. ....69

Lifting disruption of invasive pneumococcal disease (IPD) cases following the covid-19 pandemic: IPD in the youngest children in Belgium after re-switch from PCV10 to PCV13.....71

Acknowledgements.....74

PARTNERS



Under the auspices of the Belgian Association of Public Health



## PROGRAMME

08:30 Registration with walking breakfast / Visit of stands

### SESSION 1

Steven Callens (UGent) & Benoit Kabamba (UCLouvain)

09:00 Welcome address

09:15 Current knowledge on monkeypox, laboratory tests, probable animal reservoir - Charlotte Martin (Saint Pierre Brussels)

09:45 Sensoa & The MPOX: A timeline of Interventions towards MSM - Sandra Van den Eynde (Sensoa)

10:15 Polio eradication: a protracted endgame – Marc Van Ranst & Elke Wollants (KU Leuven)

10:40 Investigation into cases of hepatitis of unknown aetiology among young children in Scotland – Emma Thomson, (University of Glasgow)

11:10 Coffee break / Visit of stands

### SESSION 2

Lize Cuypers (UZLeuven) & Natalia Bustos Sierra (Sciensano)

11:40 Update covid-19 vaccination – Isabel Leroux-Roels (UGent)

12:05 Climate change as a threat to health in Europe: focus on infectious diseases – Van den Borre (Sciensano)

12:35 Impact of covid-19 on healthcare-associated infections –Boudewijn Catry (Sciensano)

13:00 Lunch

### SESSION 3

Thomas Demuyser (UZBrussel) & Tinne Lernout (Sciensano)

14:10 National cartography of water points for the presence of *Vibrio* spp. in Belgium R. Sacheli (ULiège)

14:20 Climate change as a threat to health in Europe: focus on infectious diseases – Eline Vanuytrecht (European Environment Agency)

14:45 Monitoring of Exotic mosquitoes in Belgium: results of 2022 – Marie Hermy (Sciensano) & Wim Van Bortel (ITG)

15:15 Zoonotic risk of the circulating highly pathogenic H5 avian influenza viruses – Mieke Steensels (Sciensano)

15:35 Increase of invasive group A *Streptococcus* infections - Anne Botteaux (ULBruxelles)

15:45 Closing address and end of seminar

# SPONSORS





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## ABSTRACTS OF PRESENTATIONS

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## **CHARLOTTE MARTIN**

**SAINT PIERRE BRUSSELS**

### **BIOGRAPHY**

Charlotte Martin is a specialist in Internal Medicine and Infectious Diseases. She also has also trained in Tropical Medicines . She has been working since 2009 at the Department of Infectious Diseases of the CHU Saint-Pierre in Brussels, where she is Head of Department since March 2022. She is also Head of the Travel & Vaccine Clinic. She is currently finalizing her PhD thesis on the impact of HIV on yellow fever vaccination.

### **CURRENT KNOWLEDGE ON MONKEYPOX, LABORATORY TESTS, PROBABLE ANIMAL RESERVOIR**

The incidence of Mpox (formerly Monkeypox) has been steadily increasing for several decades. The largest outbreak of Mpox outside the usual endemic areas occurred in 2022. It was concentrated in a particular population, the MSM, and had different characteristics from the disease usually described so far.

Vaccination with smallpox vaccine was implemented and may have contributed to the observed decrease in new cases. However, Mpox now continues to circulate in endemic and non-endemic areas. Public health policies in terms of at-risk populations will therefore have to take into account this re-emerging pathology in the years to come.

## SANDRA VAN DEN EYNDE

### SENSOA

#### BIOGRAPHY

Sandra Van den Eynde works as a policy advisor on the prevention of HIV and STI's for Sensoa, the Flemish center of expertise on sexual health. Sandra is trained as clinical psychologist and clinical sexologist. She presides the Flemish STI Network and together with Jessika Deblonde (Sciensano) coordinates the Monitoring Committee activities for the Belgian HIV Plan. Sandra leads Sensoa's Department in which prevention interventions and communication is developed directly towards several target groups such as Men Having Sex with Men and People Living With Hiv.

#### SENSOA & THE MPOX: A TIMELINE OF INTERVENTIONS TOWARDS MSM

On May 19, we received the first report of an outbreak of Mpox in Europe. Sensoa obtained information at online expert meetings, coordinated with the Agency for Care and Health and with relevant partners in the field (business managers, Ex Aequo), participated in federal and community consultations to monitor the situation and coordinate actions. During the first phase, communication was targeted at men who have sex with men to be alert for Mpox by spreading additional messages through specific Facebook groups aimed at men who have sex with men. Sensoa also briefed our participating employees (employees and volunteers) during the Belgian Pride 2022 about Mpox and what to do in case of questions from the audience. Managers of gay venues, party organizers and fetish shops, where sex is possible on the premises, were addressed several times with specific and up-to-date information. Sensoa posted brief prevention and vaccination information on both Sensoa.be and Allesoverseks.be. Sensoa referred to the websites of the Institute of Tropical Medicine and, in a later phase, to those of the Flemish Health authorities, which provided more detailed information. An awareness campaign for Mpox symptoms was developed, modeled on the GAT (Grupo de Atavistas em Tratamentos Lisbon) handouts and posters. Sensoa kept in touch with the World Health Organization about the further development of prevention campaigns. Ex Aequo distributed our campaign material during the La D  mence cruise. In a next phase of the Mpox campaign, Sensoa sent stickers and posters to all gay catering and LGBTI+-friendly businesses and events in Flanders. An online toolkit for role models was developed to spread our campaign through their social media. Sensoa asked all gay bars with sex on site, our partner organizations and party organizers to post this campaign on their social media. Other partners such as Alias, Boysproject, Violet   and Ex Aequo also received the campaign material. Sensoa distributed 32,359 stickers and 109 posters over the entire duration of the campaign. The operators were also contacted for feedback. In response to the changed vaccination policy of the Flemish Government, Sensoa interrupted its plans for the third phase of the campaign (vaccination campaign via the dating apps for men who have sex with men).

## MARC VAN RANST & ELKE WOLLANTS

### KULEUVEN

### BIOGRAPHY

Marc Van Ranst is professor of virology at the KU Leuven, and is chairperson of the clinical department of Laboratory Medicine at the University Hospitals Leuven.

Elke Wollants is the lab manager of the laboratory of clinical & epidemiological virology at KU Leuven, and is responsible for the National Reference Center for Enteroviruses (including polio) and Parechoviruses. She is specialized in the molecular biology of emerging infectious diseases and investigates wastewater for different viruses.

### POLIO ERADICATION: A PROTRACTED ENDGAME

Poliomyelitis is a debilitating disease that primarily affects young children. When the World Health Assembly declared in 1988 its commitment to eradicate polio, there were still 350.000 cases in 125 countries. In the past twelve months, 29 polio cases were identified in Pakistan (21), Afghanistan (1) and Mozambique (7), all caused by wild poliovirus WPV1. WPV2 and WPV3 have already been eradicated. The endgame to eradicate polio is proving to be a protracted effort. When successful, polio will be the third eradication of an infectious disease, after smallpox (in humans) and rinderpest (in ruminants). If the live attenuated poliovirus vaccine strains are allowed to circulate in under- or unimmunized populations or can replicate in immunodeficient individuals, they can mutate and reacquire neurovirulence, causing illness and paralysis. These viruses are known as circulating vaccine-derived poliovirus (cVDPV), with cVDPV type 2 causing the vast majority of cases.

The two most important surveillance indicators for poliovirus are acute flaccid paralysis (AFP) surveillance and environmental surveillance. Systematic environmental sampling provides important supplementary surveillance data. Ad-hoc environment surveillance in polio-free regions provides insight into the international spread of the virus and allows the detection of the presence of poliovirus in an area before any case of paralysis appears. Wastewater surveillance has already been implemented in different countries.

According to WHO, Belgium has an intermediate risk for polio circulation because of the absence of a good AFP surveillance system. Therefore, generalized sewage testing for polio surveillance should be implemented as soon as possible. Since VDPV2 was detected in wastewater of New York and London, KU Leuven started to screen wastewater of a wastewater treatment plant (WWTP) in Leuven. Ad hoc environmental samples were also taken at places where people with a lower vaccination status live closely together.

All wastewater samples were tested for poliovirus with qPCR, and cell culture was performed on different susceptible cell lines. Some samples were positive for enterovirus but all samples were negative for poliovirus. The

initial polio screening of wastewater samples can be done with a qPCR that detects all polio variants. PCR-positive samples should be propagated in cell culture, because the viral load in the original samples is generally too low for sequencing. Genetic data analysis of polioviruses detected from sewage can show how viruses are inter-related, helping eradicators to map their paths of transmission and to determine the scope of the vaccination response.

## EMMA THOMSON

UNIVERSITY OF GLASGOW

### BIOGRAPHY

Professor Emma Thomson is Clinical Professor in Infectious Diseases and Associate Director at the MRC-University of Glasgow Centre for Virus Research and Professor of Emerging Viral Infections at the London School of Hygiene and Tropical Medicine. She runs a laboratory that uses next generation sequencing methods to investigate virus evolution and virus diversity in the UK and in Uganda. She has published more than 200 articles in the virology field.

### INVESTIGATION INTO CASES OF HEPATITIS OF UNKNOWN AETIOLOGY AMONG YOUNG CHILDREN IN SCOTLAND

An outbreak of acute pediatric hepatitis of unknown origin, first reported in Scotland in April 2021, spread to at least 35 countries. Recent studies have suggested that human adenovirus (HAdV) may be associated with the disease. However, this study finds a second stronger association between adeno-associated virus (AAV2) infection and host genetics in disease susceptibility. AAV2 is dependent on human adenoviruses or herpesviruses for replication. The study used advanced techniques to detect AAV2 infection in the plasma and liver samples of hepatitis cases, as well as identifying the presence of the HLA class II DRB1\*04:01 allele in affected patients. The study concludes that the outbreak of pediatric hepatitis is associated with AAV2 infection (in association with human adenovirus infection) and HLA class II-related disease susceptibility.

Ho et al (2023) Adeno-associated virus 2 infection in children with non-A-E hepatitis in press.



## ISABEL LEROUX-ROELS

### UGENT

### BIOGRAPHY

Isabel Leroux-Roels is a clinical microbiologist and infection control physician working at Ghent University Hospital since 2011. In 2017 she became the head of the Center for Vaccinology (CEVAC), a vaccine trial center with dedicated immune-monitoring laboratory. She is also the coordinating physician of the Hospital Outbreak Support Team (HOST) of the Ghent Hospital Network. Isabel is associate professor at the Department of Diagnostic Sciences of Ghent University. Her research focuses on the clinical evaluation of safety and immunogenicity of novel vaccines, with a specific emphasis on novel vaccine platforms (e.g. mRNA, viral vectors), vaccine adjuvants and vaccines against respiratory viral infections (influenza, RSV, SARS-CoV-2).

Besides many collaborations with pharmaceutical and biotech companies, Isabel and her team are also actively involved in various international consortium projects such as the Larissa project (Rift Valley fever vaccine; CEPI/ Horizon 2020), the Indigo project (effective and affordable influenza vaccines; Horizon 2020) and the Baxerna project (Mycobacterium tuberculosis mRNA vaccine; Horizon-RIA).

Isabel Leroux-Roels is a member of the Belgian NITAG (Vaccination Working Group of the Superior Health Council) and she has (co-)authored more than 60 papers in peer-reviewed journals.

### UPDATE COVID-19 VACCINATION

The large scale deployment of SARS-CoV-2 vaccines has substantially altered the course of the COVID-19 pandemic, saving millions of lives globally. Although the pandemic is now largely behind us, many questions remain on how the virus will evolve, if it will cause seasonal epidemic waves from now on, and if there is a need for an annual booster vaccination.

In this presentation the following topics and questions will be covered:

- The current SARS-CoV-2 epidemiological situation in Belgium: which VOCs are currently circulating? Has the virus become endemic yet? Which individuals are still at risk for severe disease?
- How well and how long do booster vaccines protect against (serious) disease/hospitalization caused by the currently circulating VOCs?
- Preparing for the next respiratory season: what are the booster recommendations in Belgium? Will mRNA vaccines be updated again?
- Vaccines of the future: will current spike protein-based mRNA vaccines continue to dominate the COVID-19 vaccine landscape or can we expect novel generation vaccines inducing broader and longer lasting immunity soon?

## LAURA VAN DEN BORRE

### SCIENSANO

### BIOGRAPHY

Laura Van den Borre is a postdoctoral researcher at Sciensano (Service Health information) and Vrije Universiteit Brussel (Interface Demography). Laura holds a MSC and PhD degree in Sociology (Vrije Universiteit Brussel). In her doctoral dissertation, she investigated occupational health and mortality risks for a large number of occupations including asbestos workers, cleaners and teachers. As a post-doc researcher, she gained experience in labor force mobility studies and research data infrastructures. In 2021, Laura started working on the HELICON project which aims to unravel the long-term and indirect health impact of the COVID-19 crisis in Belgium. Her current research aims to understand social inequalities with regard to COVID-19 testing, infection, hospitalization and mortality.

### HELICON PROJECT - SOCIAL INEQUALITIES IN COVID-RELATED HEALTH OUTCOMES

Belgium has been faced with unprecedented societal challenges due to the COVID-19 crisis. Although we are gaining control over the virus transmission, large uncertainties exist regarding the multidimensional impact on population health. The public health burden occurs at different time scales and is borne by different populations.

Therefore, the HELICON project aims to fulfil three research objectives:

- A. Identify sociodemographic and socioeconomic factors of risk and resilience through the assessment of the social patterning of COVID-19 testing, infection, hospitalizations and mortality.
- B. Describe the medium- and long-term direct health impact of COVID-19 infections with regard to healthcare use after COVID hospitalization.
- C. Assess the indirect health impact of the COVID-19 crisis in terms of non-COVID morbidity and mortality and the health economic impact of delayed health care use.

### 18

Throughout the project, four guiding principles are respected: valorization of administrative health data sources; evaluation of social differentials; evaluation of differentials across the epidemic waves; and knowledge translation and policy transfer.

This presentation provides insights related to social inequalities in COVID-19 related health outcomes (objective A). The COVID-19 crisis is considered to be a syndemic pandemic, meaning that the crisis interacts with and is exacerbated by social, economic and health inequalities. Risk factors and comorbidities (e.g., obesity) are expected to be intertwined, interactive and cumulative. COVID-19 severity has been clearly associated with two sociodemographic

indicators: advanced age and male sex. There is a growing body of literature recognizing the social patterned distribution of COVID- 19-related health outcomes, with indications of higher risks for exposure, infection, symptom severity, hospitalization and death among disadvantaged groups (e.g., low-income groups, people with a migrant background) and certain occupations (e.g., health care workers). The HELICON-project builds on existing and new data linkages to investigate social inequalities in COVID-related health outcomes in Belgium.

This presentation will provide insights into social inequalities in COVID-19 vaccination, COVID-19 infection and all-cause mortality. Results will be presented for different sociodemographic characteristics (e.g., sex, age, migration background, household status) and socioeconomic characteristics (e.g., educational attainment, employment status, income level).

## BOUDEWIJN CATRY

### SCIENSANO

### BIOGRAPHY

Boudewijn Catry is a researcher (°Veterinary surgeon 2000) with a particular interest in antimicrobial resistance related to both veterinary (°PhD 2005) and human medicine (°2009, Sciensano, Head of Service Healthcare-associated infections & Antimicrobial Resistance & °2018 Associated Prof Clinical Epidemiology, Faculty of Medicine, Université libre de Bruxelles).

Main aims of his projects are to reduce the use and duration of antimicrobial therapy, to provide timely feedback on microbial evolutions, and to find ways to improve hand hygiene compliance. His NSIH service at Scienano also provides outbreak support for 'difficult-to-control' germs.

### IMPACT OF COVID-19 ON HEALTHCARE-ASSOCIATED INFECTIONS

In the decade before the pandemic, the national surveillance of bloodstream infections in Belgian hospitals (Royal decree 08-01-2015) did not observe a trend or statistic significant change in healthcare-associated (HABSI) and central line-associated blood stream infection (CLABSI) incidence per 10,000 patient days. For historical reasons, the target pathogens in this project are bacteria and fungi. From 2019 to 2021, similar to what we found in 2020, the first COVID-19 year, we observed a statistical significant increase in the HABSI and CLABSI incidence and this at national and each of the regions level. At Belgian level HABSI incidence increased by 19% and CLABSI incidence by 29%. In 2021, compared to the years prior to the COVID-19 crisis, we found proportionally more HABSI with as source a pulmonary infection and an endotracheal tube and more HABSI that occurred at the intensive care unit (ICU). These findings suggest that compared with the years prior to the COVID-19 crisis there were among patients with HABSI more patients critically ill. In 2021, we did not observe a change in the trend of microorganism (MO) specific incidences of HABSI and in the antimicrobial resistance profile of selected causal MO. Also the 2021, findings on crude mortality for HABSI remained similar to the years before the COVID-19 crisis.

Estimations on the proportion of healthcare-associated SARS-cov2 infections (nosocomial COVID-19) themselves, vary widely according to the definitions applied. This currently hampers to define more in detail the substantial amount of preventable nosocomial infections in different healthcare settings

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- Duysburgh E. Surveillance of Bloodstream Infections in Belgian Hospitals: Report 2022. Brussels, Belgium: Sciensano; 2022. Depot Number: D/2022.14.440/41 ISSN: 2505-9640
- Claes J, Blot K, Serrien B, Mertens K, Catry B. Nosocomial COVID-19 infections in Belgian hospitals: a longitudinal study. 6th international conference on prevention & infection control (ICPIC), Switzerland, 2021 Antimicrobial Resistance and Infection Control. 2021.

## ROSALIE SACHELI

### ULIEGE

### BIOGRAPHY

Qualification(s): PhD, responsable et coordinatrice scientifique des centres de référence Streptocoques du groupe B, *Vibrio cholerae* et *parahaemolyticus* et mycoses au CHU de Liège.

### NATIONAL CARTOGRAPHY OF WATER POINTS FOR THE PRESENCE OF *VIBRIO* SPP. IN BELGIUM

Most *Viprio spp.* are environmental and non-pathogenic, but they can also cause illnesses such as wound infections and gastroenteritis. Invasive clinical cases of vibriosis have also been described in Belgium after water contact (De Keukeleire et al., 2018). These recent years, an universal increase occurred in the number of reports of human infections involving non-O1, non-O139 *V. cholerae* and other *Viprio spp.* Waters for recreational use such as lakes and sea water are not yet monitored for *Viprio spp.* That is why the Belgian national reference center conducted a study, by doing a cartography of Belgian water points for the presence of *Viprio spp.* to evaluate its possible impact on public health.

Sampling of waters was performed monthly between May and September 2021. These were done in different areas in Wallonia (Butchenbach, Robertville, Warfaaz lakes) and in Flanders (Blaarmeersen, Donk, Donkvijver, Boerekreek lakes) including samplings in the North Sea (Knokke). The temperature and pH of the water were systematically recorded. The collected water was then filtrated, cultured and the "most probable number" method was used for bacterial quantification. The growing colonies were identified by Maldi-Tof and multiplex PCR.

No *Viprio spp.* was found in the screened water points in Wallonia. However, several *Viprio spp.* (Non -O1, Non-O139 *Vibrio cholerae*, *Vibrio alginolyticus* and *Viprio parahaemolyticus*) were isolated at notable concentrations from different water points of Flanders (Blaarmeersen, Donkvijverand and Boerekreek) and from the North Sea. The monthly calculated concentration of *Viprio spp.* was correlated with an increase of the water temperature as in the North Sea, in June (22°C) the *Viprio cholerae* concentration was evaluated at 110 CFU/ml while in August (24.2°C), the concentration reached >11000 CFU /ml. No impact of the pH was observed.

Our study demonstrate the presence of *Viprio spp.* at concentrations able to cause human infections in different water points exclusively in the North of Belgium. This study supports the recommendation to include *Viprio spp.* in water quality controls in order to define if water recreational activities are harmless for humans in Belgium.

## EVA VANUYTRECHT

### EUROPEAN ENVIRONMENT AGENCY

#### BIOGRAPHY

Eline Vanuytrecht works at the European Environment Agency (EEA) as Climate and Health expert. She has an interest in climate impacts on human health and well-being, and the resilience of our health system in the context of climate change. Eline coordinates the European Climate and Health Observatory, a partnership that aims to support Europe to prepare for climate impacts on human health by collecting and providing access to evidence and supporting resources. Prior to joining the EEA, Eline worked as a researcher at KU Leuven, Australia's national science agency (CSIRO), the Flemish Institute for Technological Research (VITO), and the Food and Agriculture Organization of the United Nations (FAO), focusing on climate change impacts on diverse sectors. Eline holds a PhD in bio-science engineering and teaches in water productivity at KU Leuven.

#### CLIMATE CHANGE AS A THREAT TO HEALTH IN EUROPE: FOCUS ON INFECTIOUS DISEASES

Climate change is upon us and poses several threats to human health and well-being. Intensified heat, floods and extreme events directly affect human lives. As climatic conditions are becoming more suitable for the emergence and transmission of climate-sensitive infectious diseases, these are an emerging threat in Europe. Altered temperatures, precipitation and humidity contribute to the lengthening of transmission seasons and wider distribution of disease vectors like mosquitos, flies and ticks. Together with more travel, this leads to an increased likelihood for local outbreaks of diseases like dengue, malaria, West-Nile fever or tick-borne encephalitis. Infection risks amplify in regions where the diseases are endemic, and simultaneously expand to previously unaffected areas. Warming sea waters in particular stimulate the growth of *Vibrio* bacteria, especially along the Baltic Sea coastline, and increase Vibriosis infection risks. The increased incidence and geographical extent of infectious diseases are a clear threat to human health, that is corroborated by both observed trends over past decades as well as projections for the future.

While the risks are clear, impacts are not evenly distributed over the European population. Regional differences exist in the presence of threats, which require targeted strategies. Central and eastern Europe emerge as having the highest current climatic suitability for the transmission of dengue, malaria and West Nile virus. Northern and western Europe have recorded the highest increase in climatic suitability for those diseases over the past few decades and an expansion of them to previously unaffected regions. Also social inequalities determine differences in vulnerability and exposure to climate-related diseases. Vulnerable groups (e.g. children, the elderly and people with pre-existing conditions) as well as people that are more exposed to the elements

and pathogens (e.g. those working in agriculture, forestry or emergency services) face higher risks.

Preventing and better preparing for future outbreaks of climate-sensitive infectious diseases can lessen health implications. To this end, early warning systems, targeted vector control and vaccination are effective measures, which requires effective monitoring of vectors and disease surveillance. Also, awareness raising among the population and public health and healthcare professionals is key, as is reinforcing the resilience of healthcare facilities across Europe to withstand additional pressure on the capacity to provide patient care and diagnostics during disease outbreaks. In addition, cross-disciplinary collaboration by involving actors beyond the health sector (e.g., planning or employment sectors) and a systemic approach by involving governance levels from local to (inter)national supports a vigorous response to the emerging challenge of climate-related infectious diseases.

## MARIE HERMY & WIM VAN BORTEL

### SCIENSANO & ITG

### BIOGRAPHY

Marie Hermy works at Sciensano, at the service of Epidemiology of Infectious diseases. She has a background in vector ecology and works among others on the passive surveillance of the MEMO+ project (Monitoring of exotic mosquitoes in Belgium). Marie also supports other projects, such as 'TekenNet' and the 'Knowledge, attitude and practice' survey on mosquitoes and mosquito-borne diseases in Belgium. In the past she performed field and semi-field work in East Africa, to study the ecology of malaria vectors with an emphasis on host preference and their genetic background.

Wim Van Bortel is a medical entomologist, PhD, with more than 25 years of experience in research on vectors and vector-borne diseases in Europe, Africa and Asia. He started his career in a malaria control project in Burundi, worked at the Institute of Tropical Medicine Antwerp (ITM) and was Senior Expert vector-borne diseases at the European Centre for Disease Prevention. Currently, he is affiliated with ITM as senior Researcher in the Unit of Entomology and in the Outbreak Research Team. His research focuses on disentangling the role of arthropod vectors in transmission systems in order to improve vector-borne disease prevention and control in a public health context. For more information: <https://research.itg.be/en/persons/wim-van-bortel>

### MONITORING OF EXOTIC MOSQUITOES IN BELGIUM: RESULTS OF 2022

The invasive mosquito *Aedes albopictus*, often referred to as the tiger mosquito, continues to spread northwards in Europe. Its expansion in France and the south of Germany increases the risk of introduction and establishment of the tiger mosquito in Belgium. This mosquito species is considered to be the primary vector of several arboviruses in Europe, including the chikungunya, dengue and Zika virus. In European regions where the tiger mosquito is established, local outbreaks of these viruses have occurred in past years. In order to avoid local transmission and outbreaks of arboviruses in Belgium, it is key to monitor the introduction and spread of the tiger mosquito. This is the main task of the MEMO+ project, started in 2021 and executed by Sciensano and the Institute of Tropical Medicine (ITM). It consists of active surveillance at Points of Entry (PoEs) and since 2022, additional passive surveillance through a website where citizens can report the detection of a tiger mosquito in Belgium.

Between May and December 2022, a total of 312 notifications of potential tiger mosquitoes were made on the website. Of these, 41% of the notifications were made in Wallonia, 12% in Brussels, 31% in Flanders and another 15% without location. Of the 312 pictures, 302 were of an insect and of these, 143 showed a mosquito (Culicidae) including *Aedes*, *Culex*, and *Culiseta* mosquito species.



Twelve notifications of tiger mosquitoes were made from nine different locations in Belgium. This led to field inspections at six locations, including two (semi-) urban locations (Lebbeke and Wilrijk) where the inhabitants experienced nuisance and many tiger mosquitoes were detected. In Kallo, tiger mosquitoes were detected in a used tyre company. No additional tiger mosquitoes were detected during the three other field inspections. Active surveillance at PoEs was performed at eight parking lots along the highway. Tiger mosquitoes were found at three parking lots, in Sprimont, Wanlin and Minderhout. An extra field visit in the surroundings of Sprimont was executed, but no tiger mosquitoes were found.

In conclusion, the launch of passive surveillance in addition to the active surveillance for exotic mosquitoes was very successful. Citizens notified an unexpectedly high number of tiger mosquitoes in Belgium in 2022. The presence of tiger mosquitoes in (semi-) urban areas corroborates previous findings that the tiger mosquito also travels to Belgium by cars coming from areas in Europe where it is already established. The tiger mosquito also still enters the country via more traditional PoEs, such as used tyre trade companies. Hence the tiger mosquito can be introduced anywhere in Belgium, and if not notified, the mosquito population could become locally established and cause nuisance. If no action is taken to control the tiger mosquitoes at such locations, the population could grow and expand, which could create a potential public health risk in Belgium.

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MRG. Hermy<sup>1</sup> • I. Deblauwe<sup>2</sup> • T. Lernout<sup>1</sup> • A. Schneider<sup>2</sup> • MD. Kont<sup>3</sup> • V. Laisnez<sup>1</sup> • R. Müller<sup>2</sup> • J. Rebolledo<sup>1</sup> • W. Van Bortel<sup>2,4</sup>.

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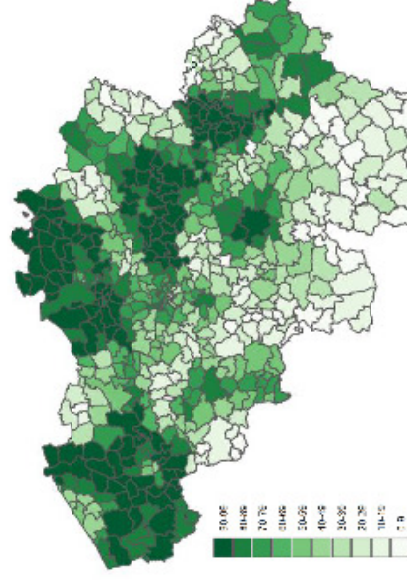
## Interested to improve healthcare in children ?



**PediSurv** is a surveillance network collecting information in children on *Measles*, *Congenital rubella syndrome*, *Acute flaccid paralysis*, *Pertussis <3y*, *Invasive pneumococcal disease* and *Mumps*.

Currently 403 physicians participate by a monthly voluntarily notification of cases or absence of disease.

Collected clinical information complement available microbiological data and informs e.g. vaccination policy. Zero-notifications are valuable for WHO elimination and eradication goals.



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**Percentage of pediatric hospitalisations covered by actively participating hospitals**

## MIEKE STEENSELS

### SCIENSANO

### BIOGRAPHY

Studies: °1998: KULeuven, Master in Bioscience engineering (Cell and Gen biotechnology/Animal Production). Thesis: "An integrated approach for the study of the effect of the probiotic *Lactobacillus rhamnosus* GG against *Salmonella typhimurium* by proteomics"; Centre of Microbial and Plant Genetics, Prof. J. Vanderleyden. PhD in Bioscience engineering, °2005: Sciensano(CODACERVA)-KULeuven. 'Novel vaccination strategies to protect birds against Asian highly pathogenic H5N1 influenza viruses' (Th. Van den Berg and B. Goddeeris)

Sciensano

- Projectleader
- Head of the AI/ND Nationale Reference Laboratory for Belgium and the Grand Duchy of Luxemburg (°2016)
- Biosafety officer avian virology and immunology service

### ZOONOTIC RISK OF THE CIRCULATING HIGHLY PATHOGENIC H5 AVIAN INFLUENZA VIRUSES

The highly pathogenic H5 clade 2.3.4.4b viruses are circulating in Europe since 2016 with variable intensity. Since 2020 the virus did not leave the continent and lost the seasonal circulation pattern in wild birds and instaurated an endemic presence within the wild bird population. The 2021-2022 was worldwide the most intense highly pathogenic AI season ever recorded.

The increased presence in the wild birds does not only pose a socio-economic threat to the poultry sector but also means an increased potential for infection of wild mammals scavenging on carcasses of wild birds. Infection of wild mammals create opportunity, and therefore increased risk, for the virus to adapt to mammalian species.

- o What is the current situation and risk-evaluation for humans?
- o How is the monitoring, surveillance and vigilance organised in regard to this topic?

Answers to these questions will be addressed.

## ANNE BOTTEAUX

### ULBRUXELLES

### BIOGRAPHY

Since 2015 Anne Botteaux is associate professor of bacteriology and PI of the Molecular Bacteriology Lab at the Free University of Brussels (ULB). After completing her PhD in Biomedical Sciences at the ULB, she spent 10 years working on deciphering the regulation and the activation mechanism of the bacterial Type 3 secretion system. After moving at GSK Vaccine, she came back to the academic world in 2015. Her actual research interests include understanding the virulence mechanisms of Group A Streptococcus, vaccination and new diagnostic tests development.

### CLIMATE CHANGE AS A THREAT TO HEALTH IN EUROPE: FOCUS ON INFECTIOUS DISEASES

Increases in invasive group A Streptococcal disease (iGAS) have recently been reported in several countries in Europe (1) but also in USA (2), mainly in children younger than 10 years. In Belgium, the same iGAS burden is observed since June 2022.

Until now, there is no evidence that the bacterium has changed in any significant way or became more resistant to antibiotics in recent months. Even if some GAS M-types have been associated with recent outbreaks, like M12 in US (3) or M1 in England (4,5), the most common M-types usually found in iGAS are identical to the prepandemic situation.

One hypothesis to explain the increase in GAS infections is concurrent high levels of circulating respiratory viruses such as RSV, Influenza or even chickenpox (6,7). Such infections can alter the balance of immune cells and microbiota in the body, potentially enabling GAS to colonize deeper tissues. Overall, outbreaks of iGAS continue to occur and emphasize the unmet need for a vaccine to prevent GAS disease. It also highlights the need of sustained coverage of chicken-pox and Influenza vaccines in susceptible population and open questions about their use in the general population. If epidemiological monitoring is mandatory, there is however no need to overreact to the current situation. WHO currently assesses that the risk of iGAS for the general population is still overall 'low'.

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## ABSTRACT OF POSTERS

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# NATIONAL CARTOGRAPHY OF WATER POINTS FOR THE PRESENCE OF *VIBRIO SPP.* IN BELGIUM.

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## Background

Most *Viprio spp.* are environmental and non-pathogenic, but they can also cause illnesses such as wound infections and gastroenteritis. Invasive clinical cases of vibriosis have also been described in Belgium after water contact (De Keukeleire et al., 2018). These recent years, an universal increase occurred in the number of reports of human infections involving non-O1, non-O139 *V. cholerae* and other *Viprio spp.* Waters for recreational use such as lakes and sea water are not yet monitored for *Viprio spp.* That is why the Belgian national reference center conducted a study, by doing a cartography of Belgian water points for the presence of *Viprio spp.* to evaluate its possible impact on public health.

## Methods

Sampling of waters was performed monthly between May and September 2021. These were done in different areas in Wallonia (Butchenbach, Robertville, Warfaaz lakes) and in Flanders (Blaarmeersen, Donk, Donkvijver, Boerekreek lakes) including samplings in the North Sea (Knokke). The temperature and pH of the water were systematically recorded. The collected water was then filtrated, cultured and the “most probable number” method was used for bacterial quantification. The growing colonies were identified by Maldi-Tof and multiplex PCR.

## Results

No *Viprio spp.* was found in the screened water points in Wallonia. However, several *Viprio spp.* (Non -O1, Non-O139 *Vibrio cholerae*, *Vibrio alginolyticus* and *Viprio parahaemolyticus*) were isolated at notable concentrations from different water points of Flanders (Blaarmeersen, Donkvijverand and Boerekreek) and from the North Sea. The monthly calculated concentration of *Viprio spp.* was correlated with an increase of the water temperature as in the North Sea, in June (22°C) the *Viprio cholerae* concentration was evaluated at 110 CFU/ml while in August (24.2°C), the concentration reached >11000 CFU /ml. No impact of the pH was observed.

## Conclusion

Our study demonstrate the presence of *Viprio spp.* at concentrations able to cause human infections in different water points exclusively in the North of Belgium. This study supports the recommendation to include *Viprio spp.* in water quality controls in order to define if water recreational activities are harmless for humans in Belgium.



## HUMAN BOTULISM IN BELGIUM: TWO ATYPICAL CASES IN 2022

J. Linussio<sup>1,2</sup>, T. Van Nieuwenhuysen<sup>1,2</sup>, L. Adams<sup>3</sup>, M. Mukovnikova<sup>1,4</sup>, A. Vodolazkaia<sup>2,4</sup>, K. Van Hoorde<sup>1,2</sup>,

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- 3 University Hospital, Ghent, Belgium.
- 4 Laboratory of Medical Microbiology, Sciensano, Brussels, Belgium.

Botulism is a paralyzing and potentially fatal disease caused by botulinum neurotoxins (BoNTs) produced by the *Clostridium botulinum* bacterium and more rarely by *C. argentinense*, *C. baratii* or *C. butyricum*. Sciensano performs the role of National Reference Center (NRC) for *C. botulinum*, *C. perfringens* and *C. tetani* with key assignments such as the diagnosis, confirmation and surveillance of human botulism. In 2022, three cases of human botulism have been confirmed by the NRC. Because of their very distinct progression, two of these cases will be presented.

Case 1 - A 67-year old woman was hospitalized with typical symptoms, including a dry mouth, diplopia, dyspnoea and general weakness. Eventually she had to be intubated. Since she consumed a 4-day old fish dish hours before the onset of symptoms, doctors suspected botulism rather quickly. Antitoxin was administered and she started to recover afterwards. Serum and faeces samples were taken before antitoxin administration and one week later. Interestingly initially only the serum sample could confirm the diagnosis, whereas for the follow-up samples, only the faeces sample was positive for the very rare type E *C. botulinum*. This is the first ever case of type E botulism that was confirmed by the NRC in Belgium. This case illustrates the importance of sending both faeces and serum for lab confirmation of the diagnosis.

Case 2 - A 64-year old man was brought in at the Emergency Department after he was unable to get up after falling from the stairs. The man showed the following symptoms: a headache, vertigo, difficulty speaking and confusion. Furthermore, he showed axial rigidity, bilateral ptosis, unilateral facial weakness, uncontrolled eye movements, weakness in the limbs and diarrhea. Lots of tests were performed but remained negative. His condition worsened during the first week and he eventually needed to be intubated. After this, he started to recover slowly. As testing continued, botulism was finally suspected after an electromyography. Serum and faeces samples were sent to the NRC and botulinum neurotoxin could be detected in the faeces sample using the in vivo reference method, confirming the diagnosis. This case demonstrates the importance of the mouse bioassay, performed exclusively by the NRC. This method is considered to be the reference method and has enabled the detection of botulinum neurotoxins very long after the onset of symptoms. Unlike case 1, case 2 shows a more atypical course of disease. Aspecific symptoms such as general confusion, axial rigidity and diarrhea resulted in many differential diagnoses being considered. Botulinum neurotoxin could

ultimately be detected in stool after 7 weeks of hospitalization. Serum was negative at this point. In this case, the less obvious symptoms combined with the fact that botulism is very rare in Belgium were probably the reason for the late diagnosis.

Botulism is likely underdiagnosed in Belgium precisely because it is so rare. It is important that the doctor recognizes the symptoms at an early stage so that antitoxin can be administered as soon as possible to prevent further progression of the disease. For laboratory confirmation of the diagnosis, both a serum and stool sample should be taken before antitoxin is administered.

## BURKHOLDERIA CEPACIA COMPLEX AND OTHER GRAM NEGATIVE NONFERMENTERS IN BELGIUM: 2012-2020

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- 2 Laboratory of Microbiology (LM-UGent), Department of Biochemistry and Microbiology, Faculty of Sciences, Ghent University. National Reference Center for Burkholderia cepacia complex. K.L. Ledeganckstraat 35, 9000 Gent, Belgium.

The main task of the Belgian national reference center for Burkholderia cepacia complex (BCC) and other Gram-negative non-fermenters (GNNF) is to conduct surveillance of these microorganisms in CF patients. Belgian laboratories are asked to send up to two BCC and GNNF isolates (excluding *P. aeruginosa* and *Acinetobacter* spp.) per colonized patient each year. Each strain is first identified to the genus level by MALDI-TOF mass spectrometry at LM-UZ Brussel. Antibiotic susceptibility tests are performed on all submitted isolates. Secondly, RAPD is used if an earlier isolate of BCC and GNNF from the same patient has been identified at the NRC within the same year. All first isolates and isolates that do not match with previous ones from the same genus within a 12-month period are sent to LM-UGent for further characterization. This consists of the identification on species level by gene sequencing of appropriate genes (*recA*, *nrdA*, *rpoD* or *16SrRNA*) and performing MLST typing based on WGS data. This MLST characterization of the isolates is performed to further investigate the possible association between some subtypes and pulmonary unfavorable disease evolution in CF patients. BCC isolates from non-CF patients are also regularly sent to the NRC for confirmation of identification and antibiotic susceptibility determination. Molecular typing is also performed for isolates from non-CF patients, especially in case of cluster or outbreak suspicion.

A total of 313 BCC and other Burkholderia species were received from 2012 to 2020. *B. multivorans* represented 47% of the total number of Burkholderia isolates followed by *B. cenocepacia* (14%), *B. vietnamiensis* (12%), and the other species at lower proportions.

A total of 832 GNNF species were received from 2012 to 2020. *Achromobacter* spp. represented 48% of the total number of GNNF isolates followed by *Stenotrophomonas maltophilia* (22%) and the other GNNF species at lower proportions.

On average, 106 (mostly CF) patients, were followed up annually at the NRC with 445 patients in the whole period from 2012 to 2020. The mean age of the patients that were followed at the NRC from 2012 to 2020 was 25 years, and the number of males was slightly higher than that of females.

Regarding the geographical distribution of the patients, Antwerp, Flemish Brabant, East Flanders and Brussels-capital region are the most represented provinces. Namur Walloon Brabant and Luxembourg are the least represented. In terms of the distribution of cases according to the centers attended by the patients, the hospitals contributing the most cases are UZ Brussel, UCL Saint Luc and UZ Leuven.

The main conclusions based on the data from 2012 to 2020:

- The proportion of Burkholderia spp. isolates has been declining over the years while the proportion of other GNNF isolates has been increasing: in 2012: 59% Burkholderia, 41% GNNF and in 2020: 26% Burkholderia, 73% GNNF.
- A slight decline in the number of samples referred to the NRC was observed in 2020. This decline was due to NRC activity reduction for a few months at the beginning of the COVID-19 pandemic.
- Unfortunately, it is not possible to determine the national prevalence of BCC and GNNF among CF patients based solely on the isolates referred to the NRC, since not all Belgian centers send all their isolates. To address this issue, our NRC plans to organize a new national surveillance study and invite all Belgian CF centers to participate.

# SEROTYPE DISTRIBUTION OF NON-INVASIVE *STREPTOCOCCUS PNEUMONIAE* STRAINS IN BELGIUM, 2020-2022: A PROSPECTIVE, OBSERVATIONAL STUDY

Ioannis Passaris<sup>1</sup>, Alexandra Vodolazkaia<sup>1</sup>, Marina Mukovnikova<sup>1</sup>, Chloé Abels<sup>2</sup>, Pieter-Jan Ceysens<sup>1</sup> and the STREPTO consortium<sup>1,3</sup>

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- 2 MSD Belgium – Brussels (Belgium).

## Background

*Streptococcus pneumoniae* typically causes either invasive (IPD) or non-invasive disease (NIPD). Although IPD has been generally regarded as more severe, NIPD is by far the more common pneumococcal disease. Contrary to IPD, surveillance of NIPD is largely lacking, making it challenging to assess the full impact of PCV vaccination programs on pneumococcal disease as a whole.

## Materials/methods

During a 20-months surveillance period (September 2020 – May 2022) a total of 1025 non-invasive pneumococcal samples and related metadata were collected from the routine practices of 24 hospitals across Belgium. Capsular typing was performed by a recently validated method based on Fourier-Transform Infrared spectroscopy (IR Biotyper™, Bruker, Germany). Testing of antimicrobial resistance was performed using the broth microdilution method (Sensititre™, ThermoFisherScientific, USA) and EUCAST breakpoint tables were used to determine the proportion of antimicrobial resistance in the NIPD population.

## Results

Of the 1,025 isolates that were collected over the study period, 875 (85%) were validated as non-invasive *S. pneumoniae* isolates. ST3 was the most commonly detected serotype of the NIPD cases, 12.2% of all NIPD and >20% of otitis media/sinusitis cases. Further age stratification of the dataset revealed a significantly higher proportion of ST23B in the 0-18 years age cohort, ST8 in the 18-64 years age cohort, and ST31 in the >64 years age cohort. When comparing with published data on the serotype distribution in the IPD population in Belgium, marked differences were observed and include: serotypes ST6C, ST11A, ST15C, ST19F, ST23A, ST23B and ST35B being more common in NIPD, while ST4, ST8, ST12F, ST19A and ST22F being more common in IPD. The proportion of non-PCV20 serotypes was 20% higher in the NIPD population when compared with the IPD population. Lastly, the NIPD population was associated with higher antimicrobial resistance for the majority of tested antibiotics when compared to the IPD population.

## Conclusion

The results of this 20-months surveillance study show the persistent circulation of ST3 and ST19A (included in PCV13) and ST19F (included in PCV7 and PCV13), in the NIPD population in Belgium. Moreover, serotypes that are not included in any currently licensed PCV vaccine make up >50% of the NIPD population. The data presented in this study support the need for surveillance of NIPD along with IPD, to fully understand the contribution of each serotype to pneumococcal disease and to inform future vaccination programs.

# PERFORMANCE OF COMMERCIAL ROSE BENGAL ANTIGENS FOR THE DIAGNOSIS OF HUMAN BRUCELLOSIS

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1 Bacterial zoonoses unit, Veterinary bacteriology, Department of animal diseases, Sciensano, Brussels, Belgium.

2 National Reference Centre for *Brucella* spp.

## Background

Brucellosis is a debilitating zoonosis caused by bacterial coccobacilli of the genus *Brucella* spp. Nowadays, brucellosis is a rare disease in Europe, with few exceptions still existing in limited foci residing in the Mediterranean region (Greece, South of Italy, Portugal and Spain). In Belgium, the few yearly notified cases are associated with returning traveling from endemic countries. The Rose Bengal (RB) test is a fast, cheap, easy-to-implement and reliable buffered antigen detection method for screening the presence of *Brucella* antibodies in sera. Its use is frequent in first-line diagnostic laboratories. Lately, some companies have stopped the production of RB due to the limited market. It urged an assessment of what is still available on the Belgian market, to assure performant screening in clinical laboratories. This study compared the quality, reproducibility and diagnostic performance of four RBs from Cypress diagnostics, Vircell Microbiologists, Giesse® Diagnostics and Lorne Laboratories LTD. companies and compared the results to that obtained with a fully certified RB reagent used in veterinary medicine (IDEXX). At validation, using recommended OMS/WOAH guidelines, all companies scored as expected in terms of pH measurement, homogeneity test, sterility, and reactivity against internationally recognized positive and negative control standards (OIESSIS test). Packed Cell Volume (PCV) was, on the other hand, remarkably different between veterinary and human reagents with IDEXX scoring 9,40% and Cypress, Vircell, Giesse and Lorne scoring 4,30%, 3,15%, 2,25% and 2,05%, respectively. Reproducibility and repeatability (made by 2 technologists at two different times and 2 different days) were within the expected range (<15%) for all. Diagnostic performance, assessed on 75 human patients sera (25 confirmed and 50 negative cases), gave comparable results among all the RBs. Areas under the ROC curve were 0.9 for all kits except Giesse which is at 0.899. Overall, despite the small PCVs observed in human RB tests, the reagents from the different companies provided good performance for the human diagnosis of Brucellosis.

# TRENDS OF GRAM-NEGATIVE BACTERIA SUSCEPTIBILITY PATTERN IN RESPIRATORY SAMPLES OF INTENSIVE CARE UNITS IN THE BRUSSELS CAPITAL REGION, 2010-2021

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## Background

*Gram-negative bacteria (GNB)'s resistance complicates the management of several infections, particularly pneumonia. The effect of the Coronavirus Disease 2019 (CoViD-19) pandemic on GNB's antimicrobial non-susceptibility is unclear.*

## Objective

investigate the trends of the GNB's resistances in respiratory samples collected in the intensive care units (ICU) of the Brussels Capital Region.

## Methods

Between 01/01/2010 and 31/12/2021, the respiratory samples of ICU patients at three University Hospitals in Brussels were retrieved. Based on the non-susceptibility to antimicrobial classes, drug resistance patterns were defined as multi-drug resistant (MDR), extremely drug-resistant (XDR), and pan drug-resistant (PDR). The study time frame was divided into three periods (01/01/2010 – 31/12/2014, 01/01/2015 – 31/12/2019, and 01/01/2020 – 31/01/2021) and the impact of the CoViD-19 pandemic was assessed.

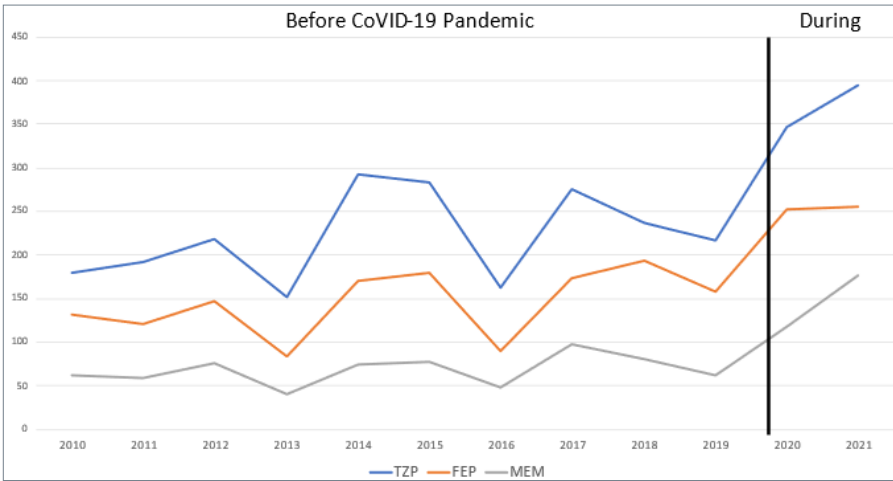
## Results

During the current study, 10577 samples were identified from 5889 patients. All three patterns of non-susceptibility significantly increased, comparing the years before and throughout the CoViD-19 pandemic. While only a significant augmentation of MDR samples was noticed between the two pre-pandemic periods. Comparing the pandemic years with the previous period, the greatest increase in antimicrobial non-susceptibility was reported for piperacillin-tazobactam (9%). During the study course, *Pseudomonas aeruginosa* was the most isolated species. This bacterium was the most involved in the appearance of resistance, with an augmentation of non-susceptibility percentage to meropenem of 22% between the pre-pandemic and the pandemic period.

## Conclusion

The CoViD-19 pandemic was associated with increasing trends of antimicrobial resistance in respiratory samples of patients admitted to the ICU in university hospitals with well-implemented antibiotic stewardship programs.





**Figure 1.** Trends of non-susceptibility for the main used anti-pseudomonal  $\beta$ -lactams over study time. Y-axis: number of non-susceptible specimens, X-axis: years. All samples together without distinction for any genus. Lines are an estimation based on the annual number of non-susceptible samples. A vertical line divided years before the CoViD-19 pandemic and during. FEP: cefepime; MEM: meropenem; TZP: piperacillin-tazobactam

**Table 1.** Trends of the pattern of non-susceptibility during the study periods. Chi-square tests were applied to estimate significant differences in the patterns of non-susceptibility between study periods. Colours are used for the second and third time spans to represent differences with the previous period. Red: significant augmentation; Orange: non-significant increase; Green significant decrease. MDR: multi drug-resistant; XDR: extensively drug-resistant; PDR: pan drug-resistant

Parameters	Total samples	1 st period 2010-2014)	2nd period (2015-2019)	3rd period (2020-2021)
	n: 10577	n: 4097	n: 4311	n: 2169
MDR	3769 (37%)	1340 (33%)	1579 (37%)	850 (39%)
XDR	894 (8%)	283 (7%)	337 (8%)	274 (13%)
PDR	41 (0%)	17 (0%)	7 (0%)	17 (1%)

# COMPARISON OF BELGIAN COVID-19 MORTALITY BETWEEN EPIDEMIOLOGICAL SURVEILLANCE AND DEATH CERTIFICATES FOR THE YEAR 2020

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Sciensano, in collaboration with health authorities, set up an ad hoc epidemiological COVID-19 mortality surveillance to monitor the severity of the epidemic in real-time, as the processing of death certificates has a 3-year delay. Epidemiological data on COVID-19 deaths was collected in hospitals [2], long-term care facilities [3], and from general practitioners. Via a one-to-one linkage, a match and mismatch analysis between the epidemiological surveillance of COVID-19 mortality (SURV) and death certificates (COD) of 2020 has been performed.

In 2020, the SURV identified globally 90% (n=19,801) of COVID-19-associated deaths from COD (n=22,015, code U07.1 and U07.2 as underlying cause of death), with high coverage via hospital (98%) and long-term care facility (90%) surveillances, but with low coverage for deaths occurring at home (5% with 1,005 missing deaths), despite a surveillance being in place. One-to-one matching revealed that 2,592 deaths collected via the SURV did not have COVID-19 as underlying cause of death according to the COD. Among these, the most frequent causes of death reported in the COD were: other ill-defined and unspecified causes (6%), pneumonia (5.5%), unspecified dementia (4.9%), heart failure (4.3%), other COPD (3.4%) or Alzheimer (2.8%).

The probability of a COVID-19 death from COD existing in the SURV, having COVID-19 as underlying cause of death, was greater for death in hospitals (85%), greater during wave 2 than in wave 1 for Flanders than for Brussels and Wallonia (using region of death), and lower during July and August 2020 (interwave period).

This comparative analysis quantifies the margin of error of the two databases and suggests future improvements in real-time cause of death surveillance for a future public health threat.

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## A NEW DATA COLLECTION SYSTEM FOR EPILABO, THE NETWORK OF SENTINEL LABORATORIES

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The Epilabo project consists of a network of sentinel clinical microbiological laboratories coordinated by Sciensano. The system has been operating since 1983 and relies upon the voluntary participation of the laboratories in the weekly submission of diagnostic data for more than 40 pathogens as of today. Epilabo contributes to improving public health by:

- monitoring epidemiological trends, and detecting potential outbreaks;
- assessing the impact of prevention programs;
- predicting the potential spread of infectious diseases;
- reporting data to international health authorities (ECDC, WHO).

The COVID-19 pandemic highlighted the importance of having a robust, digital system for timely data collection of laboratory test results at the national level, on which to rely for surveillance. Therefore, work is currently underway to set up a new data collection system based on the COVID-19 experience.

The aim is to harmonize the data collection by gathering and storing the laboratory test results in a central database on the Healthdata.be platform. The laboratories will be able to set up a system-to-system data transfer in bulk via the new HD4DP 2.0 application, developed by Healthdata.be. Additionally, the data can be transmitted in real-time to partners, such as regional health authorities. Such an infrastructure is a step forward in terms of data security and integrity, but also in terms of workability for the laboratories. Moreover, it offers the possibility of customized, automated feedback reporting towards the participating laboratories, health authorities, and the general public.

Efforts are also put in place to improve the quality of the collected data. International standards will be used for the coding of laboratory results and health conditions (LOINC and SNOMED-CT codes). This list of codes is developed in collaboration with clinical microbiologists and epidemiologists, taking into account eHealth/ReTaM initiatives. Moreover, the national registry number will be added as a mandatory variable. The availability of nominative data could enable the linkage of laboratory test results with other health databases to address relevant public health issues.

The new data collection being implemented is part of several initiatives at the European level to improve pandemic preparedness in Member States. The system has the flexibility to add additional existing or emerging pathogens, as well as to adapt the requested information by pathogen. The availability of nominative test results enables the identification of individuals who test

positive for a certain pathogen by authorized bodies, allowing contact tracing to be established if necessary. Lastly, the ability of such a system to handle large amounts of data is proven by the current comparable system set up for COVID-19.

To summarize, the revamped version of the Epilabo project will improve the data collection process in terms of data security, integrity, and quality and in workability. It will also provide new opportunities for automated tailored feedback towards the participating laboratories, contribute to pandemic preparedness and serve as a cornerstone for timely and comprehensive surveillance of infectious diseases in Belgium.

## TOWARDS A NEW (H)ERA: DEVELOPMENTS TO STRENGTHEN INFECTIOUS DISEASES SURVEILLANCE AND PANDEMIC PREPAREDNESS

By the members of the Be-HERA initiative for infectious diseases, Sciensano

In response to the COVID-19 pandemic, the HERA-Incubator-WGS project was launched in 2021 as a collaboration between the Health Emergency Preparedness and Response Authority (HERA) and the European Centre for Diseases prevention and Control (ECDC) with the main objective of **strengthening the national infrastructure and capabilities of Whole Genome Sequencing (WGS)**. During the project, a Belgian national eHealth infrastructure called Be-HERA was designed to improve the surveillance of infectious diseases. As a proof-of-concept, five study case pathogens were included: SARS-CoV-2, Influenza, *Salmonella spp.*, *Listeria monocytogenes*, and *Mycobacterium tuberculosis*. Under a new title HERA-BE-WGS-2023-2024, or HERA-BE-WGS for short, the Be-HERA infrastructure can be further developed and expanded to new pathogens. Be-HERA supports the central collection, processing and linking of these genomic, clinical and epidemiological data within the national public health information system. The data coming from National Reference Centres for human microbiology (NRCs), collected and processed by Sciensano as part of an agreement with the NRCs for epidemiological monitoring and support to public health, mainly consist of clinical and epidemiological data. Additional analyses based on the genome of a pathogen are becoming more prominent in the workflow of individual NRCs. Moreover, with a near real-time exchange of information between the various stakeholders, the project aims to improve the surveillance of infectious diseases facilitated by routine genomic analysis, both at regional, national and EU/EEA levels. This is in line with, among other things, the '*ECDC strategic framework for the integration of molecular and genomic typing into European surveillance and multi-country estate investments*'.

Within the Be-HERA infrastructure, separate databases and platforms ensure secure data gathering and processing. Each database/platform and its users only have access to the data it is allowed to process. First, a BioIT platform will function as a genomics processing environment that takes in genomic data and technical metadata. Nominative or epidemiological data will not be collected into the BioIT platform. A processing pipeline will be made available for the relevant pathogens and executed automatically to create a database of harmonized genomic indicators. Output will be validated by experts in the field within the NRC platform. The NRC platform will only be accessible for those that are mandated to review nominative data of patients. The platform can, for example, be used for linkage of genomic data to metadata for cluster analysis, resistance profiles and vaccine escape. The third platform is a pseudonymized data warehouse, hosted by Healthdata.be. This data warehouse will provide the environment to perform research on epidemiological and clinical data combined with genomic data and will be accessible for epidemiologists who are

not mandated to review nominative data. Additionally, this set-up will facilitate the reporting on the epidemiological situation concerning infectious diseases to various stakeholders at a national and international level. By connecting the databases in a secure manner, surveillance and outbreak detection can occur on a genomic, case-by-case level and on a population level, all in near real-time. Be-HERA will make it possible to support and extend the genomic surveillance which can be applied to other pathogens in a harmonized manner. Once operational, Be-HERA will further digitalize the surveillance of infectious diseases and contribute to pandemic preparedness.

# MOLECULAR TYPING OF ENTEROVIRUS POSITIVE SAMPLES FOR THE YEAR 2022 CONFIRMS ECHOVIRUS 9 AS MOST PREVALENT GENOTYPE IN BELGIUM

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## Background

*While most infections are asymptomatic, enteroviruses have been associated with a wide spectrum of both common and uncommon illnesses. Aseptic meningitis is the most commonly encountered illness associated with enterovirus infections and mainly affects very young children. Since 2014, Enterovirus D68 (EVD68) is emerging worldwide and is receiving high attention of public health authorities because of its magnitude and clinical presentation. Acute flaccid paralyse (AFP) in children under 15 years is the golden standard for polio detection.*

## Materials

In the context of epidemiological surveillance in Belgium, a selection of EV-positive samples received by the national reference centre (NRC) at UZ/KU Leuven, were genotyped. Molecular typing was done by RT-PCR using different primer sets. Enterovirus species A and B were typed by sequencing part of VP1, while for species C and D, the VP4/VP2 region and the non-coding region were used.

## Results

In 2022, 4794 samples were analysed in the context of enterovirus detection, originating from 45 Belgian laboratories (with for some >one site participating). Of those, 712 (14.9%) samples, were found to be enterovirus positive, originating from 593 cases. Overall, 550 samples were genotyped, of which the majority were respiratory samples (n=378 or 68.7%). Rhinovirus A (RVA) was the most prevalent respiratory enterovirus (42.3%) followed by RVC (32.5%) and RVB (3.4%). Overall, for all sample types, EVD68 was only detected sporadically this year (0.4%). All positive samples in cerebrospinal fluid were genotyped (n=92) with Echovirus 9 (41.3%) found to be most prevalent. Also for faeces samples that were typed (n=59), Echovirus 9 and 11 were most often detected, respectively 27.1% and 22.0%, followed by Coxsackievirus B4 (16.9%).

## Conclusions

Echovirus 9 was the most abundant enterovirus genotype in cerebrospinal fluid and faeces in the year 2022. In respiratory samples, RVA was the most prevalent enterovirus. Acute Flaccid paralyse was only reported in one case this year, and was typed as Coxsackievirus A4. No poliovirus was detected this year in Belgium.

## SURVEILLANCE OF RESPIRATORY PATHOGENS THROUGH ENVIRONMENTAL AIR SAMPLING AND EFFECTIVENESS OF AIR PURIFIERS: MONITORING 6 CONGREGATE SETTINGS DURING A RESPIRATORY SEASON.

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### Introduction

Many respiratory pathogens, including COVID-19, are transmitted by airborne aerosols and can cause outbreaks within settings such as nurseries, schools, and nursing homes. We aim to explore if environmental air sampling can complement disease surveillance in these contexts.

### Methods

An AerosolSense Sampler was used to sample indoor air in congregate settings frequented by different age groups: nursery (0-3y), kindergarten (3-6y), primary school (6-12y), secondary school (12-18y), university/pubs (18+) and nursing homes (65+). Samples were tested using an LDT multiplex respiratory qPCR panel. In the nursery, two different air filtration devices were tested in parallel with the baseline measurements.

### Results

Between October 2021 and April 2022, 335 samples were collected. Nineteen out of twenty-nine pathogens were detected at least once. In nurseries, *Streptococcus pneumoniae*, HBoV, entero-/rhinovirus, HAdV, and CMV were systematically identified, and a maximum of nine pathogens were detected concomitantly. Concurrently with a resurgence observed at the national level or documented within the setting, SARS-CoV-2 and RSV were intermittently detected. Other respiratory pathogens, *Pneumocystis jirovecii*, HPIV-3/-4, HCoV-HKU-1, HCoV-OC43, HCoV-229E, EV-D68, HMPV, *Mycoplasma pneumoniae*, IAV and *Coxiella burnettii*, were irregularly identified. Preliminary results indicate that neither the number nor the quantity of pathogens is influenced by the use of air filtration devices.

### Conclusion

We observed intense dissemination of respiratory pathogens in the indoor air of congregate settings, with the highest number of pathogens found in settings hosting children <3y. We found no evidence that air purifiers effectively reduce the number or quantity of pathogens present in indoor air in a nursery setting.



## THE HIGHEST NUMBER OF ROTAVIRUS POSITIVE SAMPLES EVER RECEIVED AT THE NRC UZ/KU LEUVEN DURING THE SEASON 2021-2022

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### Background

Rotavirus incidence and genotype distribution in Belgium have been monitored since the 1999-2000 rotavirus season at UZ Leuven. While rotavirus incidence has strongly decreased since the introduction of the Rotarix® and RotaTeg® vaccines into the Belgian childhood vaccination program in 2006 and 2007, it remains key to evaluate the effects of vaccination on the rotavirus population and to monitor the possible appearance of animal-like genotypes into the human population.

### Materials

A large number of hospitals, private laboratories and paediatricians across Belgium participate to the Rotavirus Surveillance Network Belgium, for which data for the fifteenth (2021-2022) season is presented. Rotavirus genotype was determined using reverse transcription polymerase chain reaction assays at the national reference centre (NRC).

### Results

Compared to the seasons 2019-2020 and 2020-2021 for which both a low number of samples was received at the NRC compared to pre-COVID years, a record breaking number of 1045 samples was analysed for the season 2021-2022, of which 894 (85.6%) could be (partially) genotyped. This exceptional high number of cases is also reflected in a strong rebound in the positivity rate of rotavirus gastroenteritis at UZ Leuven, from 1.5% and 1.1% for seasons 13 and 14, to 8.5% for 2021-2022. While for season 2019-2020 no clear dominant genotype was observed, a large part of the cases was classified as G2P[4] for season 2020-2021, in contrast to only 5.3% for season 2021-2022. The latter season was completely dominated by one genotype, G3P[8] (85.9%). While this genotype has been present in each of the 15 rotavirus seasons investigated since the start of the surveillance, such a large dominance has never been observed for any of the circulating genotypes. The peak of rotavirus cases was observed in March 2022.

### Conclusion

Our previous speculation that more severe rotavirus seasons are to be expected due to a decreased viral circulation and an increasing number of susceptible infants, as a consequence of the COVID-19 pandemic, has come true. The 2021-2022 rotavirus season represented the season in which

the Rotavirus Surveillance Network Belgium received the highest number of samples in its 15 years of existence. Typing of more than 85% of the 1045 samples received, demonstrated the large dominance of one particular genotype, G3P[8]. While this genotype is detected for each of the previous 15 seasons, a dominance of >85% for any genotype has never been observed.

## THE SCIENSANO BIOBANKS BEFORE, DURING AND AFTER THE COVID-19 PANDEMIC: CHALLENGES AND OPPORTUNITIES

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All Sciensano biobanks were installed conform to the biobank legislation of 2018. This in order to keep preserving and using Sciensano's existing and future collections of human body material for scientific research, mainly in the domain of infectious diseases. At the beginning of 2020, the structure of a central biobank platform has been developed to support administratively as well as operationally these different biobanks, having their specific goals and activities. At the same time, the COVID-19 pandemic broke loose, imposing several challenges.

The COVID-19 pandemic forced us to develop at a fast pace. This implied (1) giving advice to researchers throughout the entire biobanking lifecycle ; (2) installing new COVID-19 collections ; (3) ensuring adequate biobank administration for studies ; (4) supporting the registration of samples and data of importance for the biobank ; (5) providing and maintaining sample storage facilities ; and (6) providing samples to end-users. Meanwhile, the governance structure of the central biobank platform was further optimized and a biobanking software (SLIMS from Agilent) was implemented taking into account a quality system to keep guaranteeing biobanking services of high-quality.

During the COVID-19 pandemic in Belgium, when exigent sanitary measures were in place (i.e. from March 2020 until February 2022), 147.486 samples were registered in Sciensano biobanks of which 99,4% were used in COVID-19 studies and leading to the publication of 12 research articles, 11 scientific reports and other types of communication (newsletters, etc.). Compared to before the COVID-19 pandemic (cf. 26.408 samples), there was an increase of 82,1% in total amount of samples registered in Sciensano biobanks. After February 2022, 10.728 samples have been registered in Sciensano biobanks of which 89,5% were used in COVID-19 studies. This not only shows the impact of the COVID-19 pandemic on biobank activities, but also the importance of the Sciensano biobanks for research and their opportunities for the future. Indeed, the Sciensano biobanks have gathered a wealth of valuable collections that can be used in future research to study various human health problems in the domain of public health and infectious diseases.

### Conclusion

Model-based efficacy predictions aligned with the observed MK-1654 efficacy to prevent RSV MALRI in the phase 1b/2a study. The data support the continued evaluation of MK-1654 in ongoing phase 3 studies.

## A PHASE 2, RANDOMIZED, DOUBLE-BLIND STUDY TO EVALUATE THE SAFETY, TOLERABILITY, AND IMMUNOGENICITY OF A 21-VALENT PNEUMOCOCCAL CONJUGATE VACCINE (V116) IN ADULTS ≥ 50 YEARS

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### Background

V116 is an investigational 21-valent PCV containing the following pneumococcal polysaccharides: 3, 6A, 7F, 8, 9N, 10A, 11A, 12F, 15A, 16F, 17F, 19A, 20, 22F, 23A, 23B, 24F, 31, 33F, 35B, and a de-O-acetylated 15B (deOAc15B). This phase 2 study evaluated the safety, tolerability, and immunogenicity of V116 in pneumococcal vaccine-naïve adults compared with a 23-valent pneumococcal vaccine (PPSV23).

### Methods

Adults (n=508) ≥50 years were randomized 1:1 and received a single dose of V116 or PPSV23; randomization was stratified by age (50–64 years, 65–74 years, and ≥75 years). Adverse events (AEs) were collected following vaccination. Pneumococcal serotype-specific opsonophagocytic activity (OPA) and IgG were measured before and 30 days after vaccination (Day 30). Primary immunogenicity objectives were to assess the noninferiority of V116 to PPSV23 for the shared serotypes and the superiority of V116 to PPSV23 for the unique serotypes.

### Results

There were no vaccine-related serious AEs or vaccine-related deaths. V116 met noninferiority criteria compared to PPSV23 for all shared serotypes [based on the lower bound of the 95% CIs for the estimated OPA GMT ratios (V116/PPSV23) being >0.33 at Day 30] and met superiority criteria for the unique serotypes [based on the lower bound of the 95% CIs for the estimated OPA GMT ratios (V116/PPSV23) being >1.0 at Day 30].

### Conclusions

In adults ≥50 years, V116 is well tolerated with a safety profile comparable to PPSV23, elicits an immune response that is noninferior to PPSV23 for the shared serotypes and superior to PPSV23 for the unique serotypes.

Keywords (1-5): PCV, Vaccine, V116.

## PK, SNA, AND EFFICACY AGAINST RSV MALRI FROM A PHASE 1B/2A STUDY OF THE MONOCLONAL ANTIBODY CLESROVIMAB (MK-1654) IN INFANTS .

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### Background

MK-1654 is an investigational RSV-neutralizing monoclonal antibody targeting site IV of the RSV F protein currently in phase 3 development for the prevention of RSV medically attended lower respiratory tract infection (MALRI) in infants.

### Methods

This phase 1b/2a double-blind, randomized, placebo-controlled study evaluated the safety, tolerability, pharmacokinetics (PK), and serum neutralizing antibody (SNA) titers of MK-1654 in pre-term (born 29-35 weeks gestational age) and full-term infants. Participants (n=181; aged 2 weeks to 8 months) were randomized in a 4:1 ratio within five separate panels (pre-term: 20, 50, 75, or 100 mg; full term: 100 mg) to receive a single intramuscular dose of MK-1654 or placebo. Blood samples were collected to quantify MK-1654 serum concentrations and SNA titers. A preliminary population PK (popPK) model was developed to describe PK of MK-1654 in infants. The efficacy of MK-1654 was predicted using clinical trial simulations which were based on the popPK model and a published model-based meta-analysis. An exploratory efficacy analysis of observed RSV MALRI through day 150 was conducted.

### Results

Concentration data from 111 pre-term infants and 32 full-term infants through at least 150 days postadministration were available. The PK of MK-1654 was best characterized by a linear two-compartment popPK model with first-order absorption and elimination. Clearance and volume of distribution (Vd) scaled allometrically with time-varying body weight. The half-life of MK-1654 was approximately 42 days. A linear relationship was observed between increasing concentrations of MK-1654 and increasing SNA. Clinical trial simulations predict that a single 100-mg dose of MK-1654 will provide >76% efficacy for the prevention of RSV MALRI for a duration of 5 months in infants. Exploratory analysis of the phase 1b/2a study data yielded an observed efficacy of 74.2% (95% CI: -92.9%, 96.5%) for all dose groups (20-100 mg) vs. placebo and 80.6% (95% CI: -141.2%, 99.6%) for the 100-mg dose group vs. placebo.

### Conclusions

Model-based efficacy predictions aligned with the observed MK-1654 efficacy to prevent RSV MALRI in the phase 1b/2a study. The data support the continued evaluation of MK-1654 in ongoing phase 3 studies.

# POLIOMYELITIS SURVEILLANCE IN BELGIUM

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## Background

Global targets aim to eradicate polio by 2026.

No cases of poliomyelitis have been reported in Belgium since 1999 and Belgium has been polio-free since 2002. However, Belgium is classified as an intermediate-risk of transmission for poliomyelitis according to WHO because of insufficiencies in surveillance systems.

Globally, there is a risk of reintroduction of polio into polio-free areas. In 2022, new cases of polio derived Acute Flaccid Paralysis (AFP) have been identified in areas previously believed to be polio-free (USA and Indonesia). Poliovirus has also been identified in environmental surveillance in countries which are classified as polio-free (UK and Israel). Although vaccination coverage in Belgium is generally high, there may be susceptible populations where coverage is lacking.

AFP surveillance is considered the gold-standard for polio surveillance and is the primary surveillance system in Belgium. Notification of all AFP cases, regardless of cause, is mandatory across Belgium. To be considered a sufficiently sensitive surveillance system, it should be able to capture 1/100 000 cases of non-polio AFP in <15 year olds (19 cases/year in Belgium).

We evaluated current poliomyelitis surveillance systems in Belgium in relation to WHO standards.

## Methods

All reported AFP cases in <15 year olds from 2003 to 2021 were analysed. Cases were either reported via mandatory notification and/or by a network of clinicians and paediatricians (PediSurv). Additionally, PediSurv includes monthly voluntary registration of zero-cases.

## Results

82 AFP cases in children <15 years old were reported from 2003–2021, averaging 4 cases/year (~0.2/100 000). In 2019–2021, only 5 cases (~0.1/100 000) were reported, demonstrating a declining trend in reported cases.

Only 2 cases (2003–2021) underwent the required microbiological workup (2 stool samples collected 24–48h apart, within 14 days of disease onset).

## Conclusion

In 2018, AFP surveillance in Belgium was 5 times too low for WHO quality indicators. This has worsened to 10 times too low from 2019 to 2021.

Greater awareness of AFP surveillance is required, as is optimisation of registration systems.

Options for improvements include enterovirus and environmental surveillance (wastewater testing). To maximize effectiveness, these need to be supplementary to current systems. To reduce the risk of polio being reintroduced into Belgium it is necessary to improve the current surveillance systems.

# IMMUNOGENICITY AND DURATION OF PROTECTION AFTER YELLOW FEVER VACCINE IN PEOPLE LIVING WITH HIV: A SYSTEMATIC REVIEW.

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## Background

Current evidence is scarce regarding the seroconversion rate, the duration of humoral protection after yellow fever (YF) vaccine, and the impact of revaccination in people living with HIV (PLWHIV).

## Materials and Methods

MEDLINE, Google Scholar, LILACS and Cochrane CENTRAL were searched. We selected studies on PLWHIV of all ages (including perinatally HIV-infected patients) and all settings (YF endemic and non-endemic zones) vaccinated against yellow fever, at least once after the HIV diagnosis. The research questions were the seroconversion rate, duration of humoral immunity after YF vaccine and impact of revaccination in PLWHIV. Selected studies were assessed for quality using the Newcastle-Ottawa scale.

## Results

Ten, six and six studies were selected for the systematic review of each question, respectively. Only one study addressed the first question in perinatally HIV- infected children. The quality of the studies was assessed as Poor (n=16), Fair (n=2) or Good (n=4). A meta-analysis demonstrated that 97.6% (95%CI 91.6-100) of the included population seroconverted. Between 1 and 10 years after YF vaccine, reported persistence of neutralizing antibodies was 72% (95%IC53.6-91), and 62% (95%IC 45.4-78.6) more than 10 years after YF vaccine. No conclusions could currently be drawn on impact of revaccination due to small number of patients.

## Conclusion

The current evidence regarding seroconversion rate, duration of humoral protection after YF vaccine and impact of revaccination in PLWHIV is limited by the low number and quality of studies. Based on the presently available data, it is difficult to rationally develop yellow fever vaccination guidelines for PLWHIV.

# MONITORING OF VARICELLA TRENDS IN BELGIUM BETWEEN 2017 AND 2022 THROUGH GOOGLE TRENDS

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## Introduction

Varicella is a common infectious disease whose diagnosis is essentially clinical. In European countries, an annual epidemic occurs in March-May. Few data sources exist in Belgium to track trends of this disease over time, but several studies have validated the use of search queries for syndromic surveillance or trend monitoring for diseases such as varicella. We examined Varicella trends in the recent years to assess a possible influence of the covid-19 pandemic and the measures to limit its spread.

## Methods

Google Trends reflects the proportion of searches for a given keyword in a region and for a specific period, compared to the region where the rate of use of this keyword is the highest (value of 100). The numbers are standardized within each country such that values range from 0 to 100. We data-mined varicella information-seeking behavior using Google queries for the terms “varicelle”, “windpokken” and “waterpokken” for Belgium and for the 3 Belgian regions, per month, for 2017 to 2022, lockdown periods included.

## Results

We detected, as expected, significant seasonality of the Google Trends data for 2017 and 2018 (peak between March and June). Varicella seems to have been more intense in 2019 compared to previous years with an increase of queries as of February and a higher number of queries during the epidemic season. A drop in the number of queries is observed in March 2020 until June 2021 (61-81% drop in absolute search volume between April and July 2020 in comparison to the average of April to July 2017-2019) when a slight increase is visualized. The year 2022 was intense in terms of the circulation of the virus with a record number of total queries, particularly in July and Augustus with an increase of respectively 125% and 150% compared to the average absolute search volume of July and Augustus 2017-2019. Very similar trends are observed for Flanders and Wallonia. In Brussels, the trends are more variable, especially from March 2020.

## Conclusion

The circulation of the varicella zoster virus has been strongly impacted by the covid-19 pandemic related measures. Already validated tools such as Google trends represent an interesting alternative to conventional surveillance systems and have the advantage of being inexpensive, accessible to all, and of monitoring in real time certain diseases whose symptoms are easily recognizable by the population.



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# AGE-STANDARDIZED MORTALITY RATES RELATED TO VIRAL HEPATITIS C IN BELGIUM

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## Background

Following the United Nations Sustainable Development Goals target to combat hepatitis, the World Health Organization (WHO) has set up specific targets to eliminate viral hepatitis as a public health threat in 2016. In particular, it aimed to reduce hepatitis C virus (HCV) attributable mortality by 10% by 2020 and 65% by 2030 compared to 2015 levels. Few data have been published on the subject in Belgium, mainly modelling studies. We aimed to assess age-standardised mortality rates from HCV in Belgium and evaluate our progress towards the WHO targets.

## Methods

Mortality and population data were obtained through Statistics Belgium, the national statistical office. We analysed the Belgian national causes of death registry data from year 2000 to year 2019 (latest available data). The ICD-10 codes used to identify HCV related deaths were B17.1 and B18.2. Deaths were included if HCV was considered as the underlying cause of death or present in any other cause of death. We calculated crude and age-standardized mortality rates, expressed per 100,000 inhabitants, using the Belgian mid-year 2010 population as reference population.

## Results

During these 20 years, 3,793 deaths had HCV mentioned in their death certificate. Nearly half of them (47.5%) belonged to the age group 60-79 years, and 51.3% were females. The age-adjusted HCV-related mortality rate in Belgium seemed stable between 2000 and 2008, ranging between 2.17 and 2.65 per 100,000 population, and began to decline from there. The highest rate was always observed in Brussels capital city, followed by Wallonia and Flanders. In 2015, the age-adjusted HCV-related mortality rate in Belgium was 1.18 per 100,000 population, while it was 0.85 in 2019. This represented a decline of nearly 30%, much more than the WHO target for 2020. The steepest decline was observed in Brussels (52%), while it was about 4% in Flanders and 28% in Wallonia.

## Conclusion

While HCV related mortality remains an issue in Belgium, our findings suggest that Belgium is well on track to meet the specific WHO mortality target by 2030. Regional differences in mortality rates must be further investigated. Since 2019, HCV treatment is reimbursed for all patients in Belgium, which is expected to help further in achieving these objectives. However, access to

testing and treatment must still be strengthened for persons living with HCV, and particularly hard-to-reach populations. A national surveillance system for HCV infections is also highly needed to tackle viral hepatitis, in order to support tailoring the public health measures.

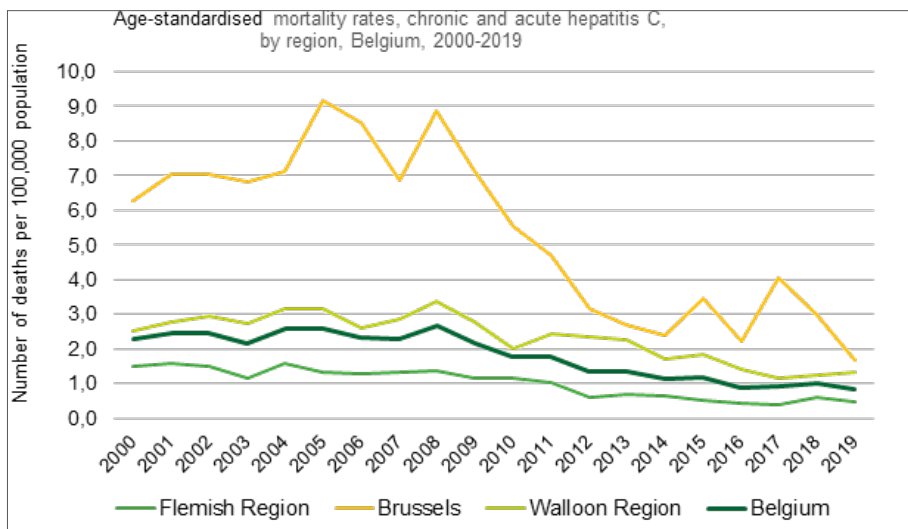


Figure 1. Causes of death registry, codes ICD10: B17.1 and B18.2 as underlying or other cause of death. Direct standardisation using the Belgian mid-year 2010 population as reference population, according to five age groups (0-19, 20-39, 40-59, 60-79, 80+). Deaths are registered according to place of residence and not place of death.

# CLINICAL APPLICATIONS OF RESCUE STRATEGIES IN EXTENSIVELY DRUG-RESISTANT HIV-1, A CASE REPORT

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## Background

The availability of antiretroviral therapy for people living with HIV is increasing worldwide. However, limited therapeutic options are available for patients with multi-drug resistant HIV.

## Purpose

To describe the clinical management and potential rescue strategies for a patient with extensively drug-resistant HIV-1 strains. Virological failures were followed by serial genotyping analyses showing the evolution of mutations and resistances.

## Methods

Genotyping analyses were performed with Sanger sequencing followed by resistance prediction using Stanford HIV Drug Resistance Database. Phenotypic drug susceptibility was defined using PhenoSense® (Monogram Biosciences Inc.). Tropism analyses were conducted using Trofile® (Monogram Biosciences Inc.).

## Results

A 38-years old female, perinatally HIV-1 infected, was treated with 14 different antiretroviral regimens over 27 years, gradually leading to four-class drug-resistance. Various attempts were made to obtain sustained viral suppression including administration of intravenous Foscarnet and Enfuvirtide. Recently, reinforcement of the maintenance regimen with Fostemsavir and Lenacapavir combined with strategies to improve treatment adherence resulted in complete viral suppression.

## Conclusions

The described patient evolved to a four-class drug-resistance HIV-1 infection due to suboptimal virological control. Induction regimen with off-label intravenous Foscarnet and Enfuvirtide, but mostly the new first-in-class drugs Fostemsavir and Lenacapavir might be a game-changer for patients without alternative treatment options.

# DESCRIPTION OF THE UNDIAGNOSED HIV INFECTION IN 2020 IN BELGIUM BY KEY POPULATIONS AND URBANIZATION LEVEL.

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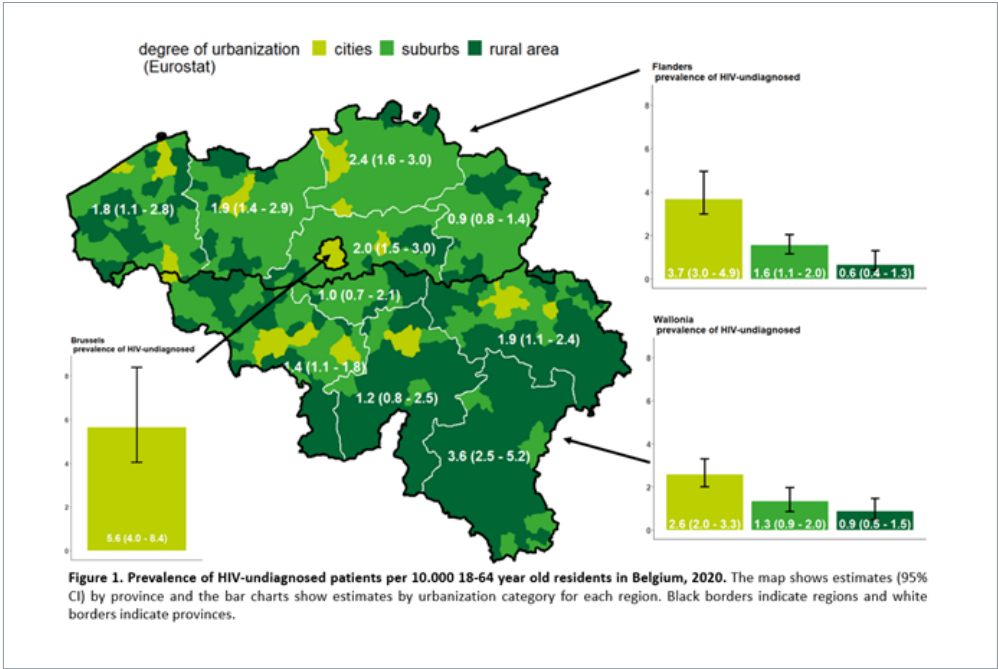
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## Background

Early diagnosis and initiation of treatment for PLWH are key to control their viral load and hence inhibit disease progression and onward HIV transmission. The objective of this study is to provide a description of the undiagnosed population in Belgium by the end of 2020 in terms of key subpopulations and urbanization level.

## Methods

A CD4-based back-calculation method developed by ECDC (the HIV modelling tool) was applied on the Belgian HIV surveillance data to estimate the size of the undiagnosed population, by subpopulation and urbanization category, at national and regional level. 95%CI's were obtained using parametric bootstrapping with 100 iterations. Ten-fold multiple imputation of missing variables was performed in R before applying the back-calculation model. All prevalence estimates are given per 10.000 in the 18-64 year old subpopulation.



In each region, the prevalence of undiagnosed people is the highest among men-having-sex-with-men (MSM) of non-European nationality (434 [338-560] at national level). MSM of Belgian and European nationalities also contribute significantly to the undiagnosed HIV population but the prevalence of undiagnosed infection is lower in these subpopulations (16.9 [14.4-28.6] and 49.9 [37.4-64.4] respectively). Within heterosexuals, the undiagnosed prevalence is low and approximately equal for both sexes (1.5 [1.2-1.8]). Among heterosexuals of Belgian nationality, the HIV-undiagnosed prevalence is very low, particularly among women (0.3 [0.2-0.4]) compared to men (0.7 [0.5-0.9]). Among heterosexuals of Sub-Saharan African nationality, the prevalence of undiagnosed people is much higher among women (81 [70-110]) compared to men (51 [41-85]). In persons-who-inject-drugs (PWID) actively in the last 12 months, the undiagnosed prevalence was 62 ([28-150]). In the Brussels Capital Region, the prevalence of HIV-undiagnosed PWID was higher (142 [43-640]) than at the national level.

## Conclusions

Undiagnosed HIV infection remains a substantial public health problem in certain key populations in Belgium in 2020: MSM (especially MSM of non-European nationality), heterosexuals of Sub-Saharan African nationality and PWID. Prevalence of undiagnosed HIV people is higher in cities compared to towns/suburbs and rural areas. This is probably related to larger MSM and migrant communities in large cities and particularly in Brussels. As the COVID-19 pandemic and related social restrictions have strongly impacted HIV testing activities and HIV transmission in 2020, the impact of COVID-19 on the evolution of the (undiagnosed) HIV epidemic will need to be followed carefully in the next years. These findings on the undiagnosed HIV population contribute to a more granular understanding of the epidemic for targeting awareness and testing campaigns.

# ENVIRONMENTAL DETECTION OF PNEUMOCYSTIS JIROVECI IN DIFFERENT INDOOR SETTINGS HIGHLIGHTS THE POTENTIAL ROLE OF CHILDREN UNDER 3 YEARS AND YOUNG ADULTS IN TRANSMISSION

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## Background

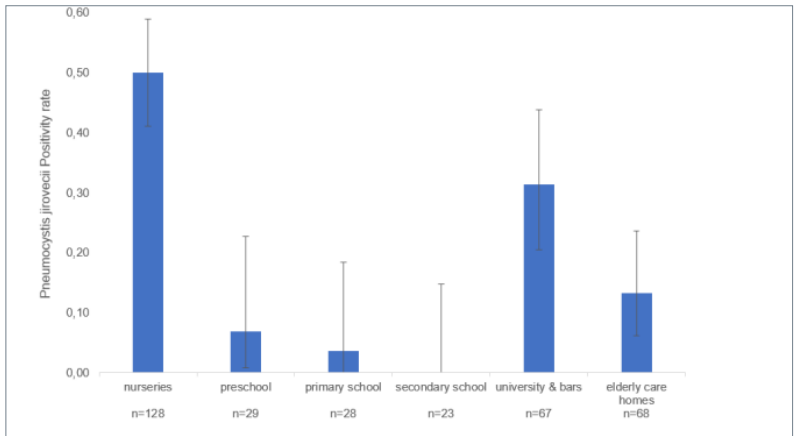
*Pneumocystis jirovecii* (PJ) is an opportunistic pathogen. Most humans develop antibodies against PJ at an early age. However, it remains uncertain whether PJ tends to colonize immunocompetent hosts long-term or if re-infections occur. Research in this field is hampered by subclinical presentations of PJ secondary infections, invasive sampling procedures required for diagnosis, and the inability of serological tests to capture reinfections. We here explore environmental air sampling to gather evidence of PJ shedding by asymptomatic carriers as a way to assess exposure.

## Methods

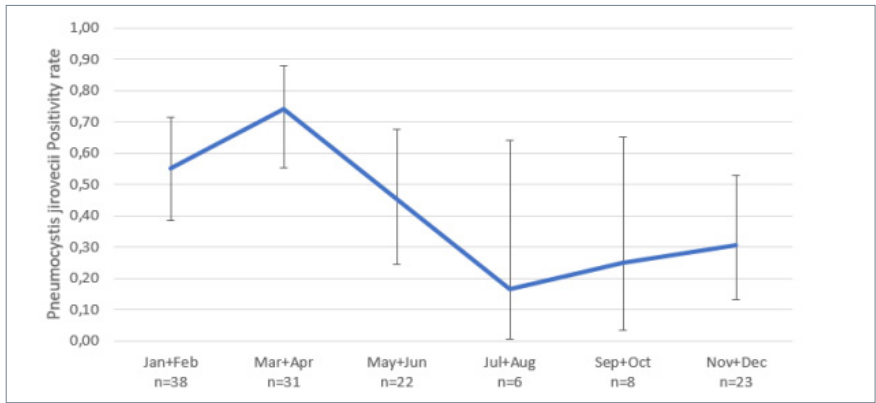
Between October 2021 and January 2023, we collected 391 air samples in congregate settings frequented by different age groups: nursery (0-3y), kindergarten (3-6y), primary school (6-12y), secondary school (12-18y), university/bar (18+) and nursing homes (65+)(Table 1). Indoor air was sampled at a rate of 200 L/min for two hours using an AerosolSense Sampler (Thermo Fisher Scientific). AerosolSense cartridges were transferred to Universal Transport Medium (Copan). Samples were tested with multiplex qPCR for the detection of 29 respiratory pathogens, including PJ.

## Conclusions

Our results highlight the importance of PJ shedding by minimally symptomatic or asymptomatic carriers, particularly infants, toddlers, and young adults. Our findings suggest that immunocompromised patients may be exposed to PJ in daily life more frequently than expected encouraging the use of face masks and sufficient ventilation. Further, we seek to open the debate on monitoring exposure to respiratory pathogens in specific medical settings, such as intensive care units or haematology wards. Environmental air sampling may be a suitable tool for this purpose.



**Figure 1.** Overall positivity rate of PJ in air samples per setting. Vertical lines indicate 95% confidence intervals. We calculated positivity rates independent of the exact threshold cycle (Ct)



**Figure2.** PJ year-round positivity rate in air samples from nurseries. We collected data from November 2021 to Januari 2023. Vertical lines indicate 95% confidence intervals.



## EFFICACY, DURABILITY, AND TOLERABILITY OF BICTEGRAVIR/EMTRICITABINE/TENOFOVIR ALAFENAMIDE FOR THE TREATMENT OF HIV IN A REAL-WORLD SETTING IN BELGIUM

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### Objectives

To evaluate the efficacy, durability, and tolerability of BIC/FTC/TAF in a real-world setting in Belgium.

### Methods

A retrospective, multicenter cohort study involving adult treatment-naïve (TN) and -experienced (TE) PLWH on BIC/FTC/TAF between January 1, 2019 and September 30, 2020. Primary outcome was rate of virologic suppression (plasma HIV-1 viral load [VL] <50 copies/mL; on-treatment analysis) at weeks 24 and 48. Main secondary outcomes included loss of virologic suppression (LVS; 2 consecutive VLs of >200 copies/mL after being virologically suppressed) by week 48 and analysis of resistance-associated mutations (RAMs) at time of LVS; tolerability of BIC/FTC/TAF over the 48-week study period; and change in weight and proportion of participants reporting a >10% weight gain at week 48.

### Results

Overall, 2,001 participants were included. Through 48 weeks, overall rate of virologic suppression was 93.5% with similar results observed in the following sub-groups: age  $\geq 50$  (92.7%), women (92.8%), black sub-Saharan African (91%), TN (94%), TE (93.2%), and non-suppressed at baseline (86.6%). LVS was observed in 0.7% ( $n = 14$ ) of participants with one participant developing RAMs to NRTIs (184V) and INSTIs (263KR). Of the 131 (6.5%) treatment discontinuations, the most common cause was an adverse event (2.4%) with the most frequent being CNS/psychiatric (0.4%) and gastrointestinal (0.4%) toxicity. Median (IQR) weight gain at week 48 was 2kg (-1 – 5) and >10% weight increase was observed in 11.6% of participants.

### Conclusions

In this large real-world cohort, BIC/FTC/TAF showed excellent virologic efficacy in a diverse population of HIV patients. Rare occurrence of emergent drug resistance was observed and treatment was well tolerated.

## WASTEWATER-BASED EPIDEMIOLOGY OF COVID-19 IN BELGIUM

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### Background

In this work, the correlations between the SARS-CoV-2 concentrations measured in wastewater, the positive cases and the hospital admissions are investigated. Several COVID-19 waves are studied with different contexts between February 2021 and March 2023: variants in circulation, vaccination coverages, non-pharmaceutical interventions, testing strategies, etc. Additionally, the pertinence of three wastewater alerting indicators to assess the epidemiology situation is presented.

### Methods

Over 5 million inhabitants representing 45% of the Belgian population are monitoring in routine throughout 42 wastewater treatment plants since September 2020. Spearman correlation coefficients of the SARS-CoV-2 concentration are computed for several waves against case incidences and hospital admissions. Three alerting indicators are computed on normalized concentrations per individual treatment plant to allow for a comparison with a reference period as well as between analyses performed by distinct laboratories.

### Results

The alerting indicators effectively monitor the evolution of the waves. High correlation levels are observed between the daily new COVID-19 cases, the daily hospital admission and the SARS-CoV-2 concentration in wastewater corrected for rain impact and covered population size. Since the first waves, the testing strategy has evolved in a way that test are recently performed only for clinical reasons, as it is the case for the other respiratory diseases. The modification of this testing strategy has a negative impact on the correlation with the case incidence.

### Conclusions

The high correlation levels obtained in this work, together with the valuable information provided by the wastewater alerting indicators proved that wastewater-based epidemiology played an important role in the management of the COVID-19 crisis in Belgium, alongside with other conventional epidemiological indicators.

# FACTORS UNDERLYING COVID-19 BOOSTER VACCINE UPTAKE AMONG ADULTS IN BELGIUM

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## Background

To tackle waning protection against severe COVID-19 infection, booster doses of the COVID-19 vaccines were recommended among individuals who received their primary course. A first COVID-19 vaccine booster campaign was performed in winter of 2021 (age  $\geq 18$  years) and a second campaign (age  $\geq 50$  years) in autumn of 2022. During these campaigns, persons were actively invited to get a booster dose against COVID-19. We aimed to explore (first and second) booster uptake among adults who completed a full primary course in Belgium and investigate demographic (age, region of residence and sex) and COVID-19 related (having had a documented COVID-19 infection) factors associated with the first and second booster uptake.

## Methods

We used individually-linked data from the Belgian COVID-19 vaccine registry and the COVID-19 test database to determine booster uptake among the 18+ Belgian population having completed the primary vaccination course (PC). We reported coverage by demographics (age, region of residence and sex) and confirmed COVID-19 infection (based on PCR tests) history before or after completion PC (first booster uptake) or receiving the first booster (second booster uptake). We used a quasibinomial logistic regression model to determine influential factors on the booster uptake.

## Results

Among the Belgian adult population, the coverages reached on the 31st January 2023 were 72.65% and 40.85% for the first and second booster respectively. The highest coverage (number of individuals boosted over the ones who completed a PC) was observed in the 75-84 age group (96.73%) and 85+ age group (82.30%) for the first and second booster respectively and the lowest for both boosters in the 18-24 age group (69.86% and 17.85%, respectively). Individuals who had previous infections were significantly less likely to receive the first booster dose compared to individuals with no infection, especially when the infection occurred after completion of PC and with multiple infections (COVID-naïve reference, minimum 1 infection before PC: OR=0.73, 95%CI 0.67-0.79, 1 infection after PC: OR=0.29, 95%CI 0.27-0.31; multiple infections before and after; OR=0.15, 95%CI 0.12-0.18; multiple infections after, none before: OR=0.09, 95%CI 0.03-0.29). Older age and living in Flanders were positively associated with uptake in both boostersd

## Conclusions

We report a high booster uptake among the 18+ Belgian population (first booster: 72.65%, second booster: 40.85%) compared to the European average (first booster: 57.54%  $\pm$  21.71%, second booster: 14.61%  $\pm$  11.91%). Individuals previously infected were less likely to receive the first booster dose while older individuals were more likely to receive any booster dose. These results offer important insights for future booster campaigns for COVID-19 vaccines.

## DIPHTHERIA RE-EMERGENCE IN EUROPE AND BELGIUM ANNO 2022.

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### Background

Thanks to an effective vaccine and high vaccination coverage, diphtheria has been a rare disease in Europe for over two decades. However, the second half of 2022 saw a strong increase in *C. diphtheriae* infections in migrants in several European countries, including Belgium. Most of these cases were cutaneous infections, but some severe respiratory infections have been reported as well. The ECDC reports 371 diphtheria cases in migrants from 2022 to February 2nd 2023.<sup>1</sup>

The Belgian National Reference Centre (NRC) for toxigenic corynebacteria confirmed 25 such cases in Belgium in 2022. Two of these were respiratory, one being severe and necessitating diphtheria antitoxin (DAT) administration. Additionally, one non-migrant-related *C. diphtheriae* case and 5 cases caused by *C. ulcerans* were reported, bringing the total number in Belgium in 2022 to 31. This represents a major increase compared to previous years: less than 30 cases of diphtheria have been reported in Belgium over the whole period ranging from 2010 to 2021. Moreover, most of these were caused by *C. ulcerans*, only five by *C. diphtheriae*.

National and international measures were taken in response to this emergence in order to limit the spread of disease. Screening and vaccination efforts are still ongoing and seem to have been effective based on data from the first months of 2023, which show a decrease of cases in Belgium and internationally. It is, however, too early to tell if this decrease represents a return to the baseline or a temporary downswing. Heightened awareness and screening remain necessary, especially considering the vulnerability of the affected migrant population, who live in conditions that favor rapid transmission.

This public health emergency also highlighted the ongoing need for DAT availability, which remains difficult to access in many European countries, and for an optimal antibiotic treatment and prophylaxis policy. Penicillin and erythromycin are recommended for the eradication of *C. diphtheriae* and *C. ulcerans*. However, the occurrence of antimicrobial resistance is becoming an issue,<sup>2</sup> and among the 2022 cases, two strains resistant to erythromycin and clindamycin were found. This warrants concern and further investigation, as azithromycin treatment is highly preferred for patients that are homeless or residing in overcrowded shelters, given its shorter duration and better compliance.

Close surveillance is needed to monitor the situation, so that any diphtheria re-emergence can be noticed and responded to swiftly, and so that appropriate measures can be taken should resistant strains become more prevalent.

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# LIFTING DISTRUPTION OF INVASIVE PNEUMOCOCCAL DISEASE (IPD) CASES FOLLOWING THE COVID-19 PANDEMIC: IPD IN THE YOUNGEST CHILDREN IN BELGIUM AFTER RE-SWITCH FORM PCV10 TO PCV13

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## Background

Due to the restrictive measures to contain the COVID-19 pandemic, a significant and sustained reduction in invasive pneumococcal disease (IPD) cases in children (<2 years) was observed in 2020-2021. The 13-valent pneumococcal conjugate vaccine (PCV13) was reinstalled in 2019 in the childhood vaccination programme, after a re-emergence of serotype 19A IPD in children following the switch from PCV13 to PCV10 in 2015-2016 in Belgium.

## Materials

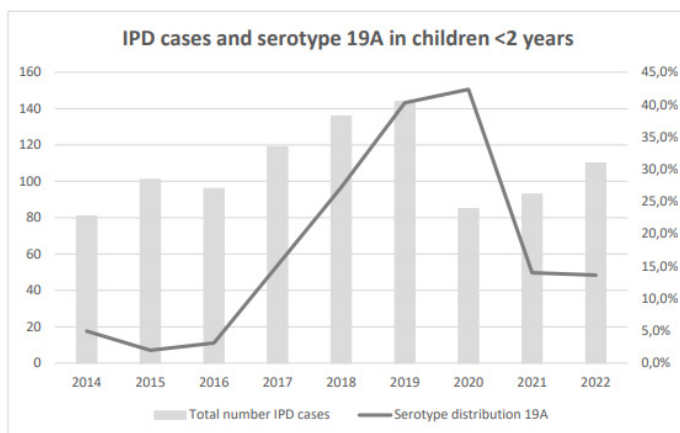
Surveillance of IPD in Belgium is based on a stable laboratory-based system involving yearly around 100 laboratories, evenly spread over the country, sending their strains to the National Reference Centre for Invasive Pneumococci, for capsular typing by Quellung reaction.

## Results

While the total of 107 IPD cases in children for 2022 is a reduction of 24.6% compared to the preCOVID year 2019, numbers have increased compared to 2020 and 2021 (respectively +25.2% and +13.1%), and exceeded cases of the years 2014 to 2016. Although capsular typing determined 19A as most prevalent serotype (14.0%) in young children for 2022, equal to 2021, this entails a continued reduction of 19A cases following the re-switch from PCV10 to PCV13 in 2019 as serotype 19A accounted for 40.3% and 42.4% of cases in children in 2019 and 2020. Serotypes 33F (10.3%), 10A (9.3%), 11A (8.4%) and 23B (7.5%) complete the top 5 of most frequently detected serotypes in 2022. Serotype coverage of pneumococcal vaccines PCV13, PCV15 and PCV20 based on IPD cases is 19.7%, 31.8% and 58.0%, respectively.

## Conclusions

For 2022, IPD epidemiology is no longer heavily disturbed by the COVID-19 pandemic, characterized by increasing cases, although still lower compared to 2019. Furthermore, three years post PCV10 to PCV13 switch, a further reduction of the proportion of serotype 19A was observed.



**Figure 1.** The number of IPD cases and the distribution of serotype 19A in children (<2 years old) was evaluated over time (2014 to 2022). Although the overall number of 107 cases in 2022 is still lower compared to the pre-COVID years 2018 and 2019, it exceeds the case numbers for 2014 to 2016. Following the switch from PCV10 to PCV13 in 2019, the distribution of serotype 19A has continued to decrease compared to the years 2019 and 2020.





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