TransMID
Translational and Transdisciplinary research in Modelling Infectious Diseases

Goal: Advancing public health and epidemiology by:
- innovative methodology to address epidemiological hypotheses - *Modelling Infectious Diseases*
- basic and general research – *Translational*
- biomedical knowledge and mathematical tools - *Transdisciplinary*

Applying innovative methodology to better understand and predict the dynamics of important pathogens such as cytomegalovirus, hepatitis A, pertussis, measles-mumps-rubella, ...

Niel Hens
www.simid.be
www.simpact.org
support: 2 research managers - leading researchers
current team: 11 PhD students, 5 postdocs
TransMID team: 2 PhD students, 2 postdocs

Niel Hens, MMath, MSc, PhD
Assoc. Prof. Biostatistics
@UHasselt @UAntwerp
Scientific Chair Evidence-based Vaccinology since 2009
sponsored by a gift from Pfizer
International network
(regular collaboration)

- ECDC (Stockholm)
- LSHTM (London, UK)
- UNSW (Sydney, AUS)
- RIVM (Bilthoven, NL)
- Univ. Halle-Wittenberg (Halle, DE)
- Univ. Nottingham (Nottingham, UK)
- Vanderbilt University (Nashville, US)
- Univ. Lille2 (Lille, France)
- INSERM (Paris, France)
- Georgia State Univ. (Atlanta, US)
- ...

In advisory & collaborative capacity
- CIRN Canada,
- CRE Australia,
- Welcome Trust

National
- WIV-ISP,
- ITM,
- KU Leuven (Rega Institute)
Collecting social contact data
Mossong, Hens et al. 2008
>800 citations

Understanding transmission process

Investigating mitigation strategies: school closure, ...
MIXING: background

- Collecting social contact data
  Mossong, Hens et al. 2008
  >700 citations
- Understanding transmission process
- Investigating mitigation strategies: school closure, ...

• MIXING-ACTION
• MIXING-BEHAVE
• MIXING-CONNECT
MIXING: ACTION, BEHAVE, CONNECT – SERO: MULT, SERIAL, COMBI, DESIGN

MIXING - ACTION

frequency vs density dependent mass action (fund. hypothesis)

unique set of multi-national and serial social contact data:
- BE 2006, FL 2010
- FI
- FR
- IT
- NL
- UK
- ...

endemic equilibrium
demographic equilibrium
micro- or/and macro-level changes

(fund. hypothesis)

Modelling the impact of local reactive school closures on critical care provision during an influenza pandemic

Thomas House1,8, Marc Baguelin5,7, Albert Jan Van Hoek3,
Peter J. White4,5, Zia Sadique6, Ken Eames7, Jonathan M. Read8,
Niel Hens9,10, Alessia Melegaro11, W. John Edmunds3,7
and Matt J. Keeling1,2

De Luca et al. In prep.

A Nice Day for an Infection? Weather Conditions and Social Contact Patterns Relevant to Influenza Transmission

Lander Willem1,2, Kim Van Kerckhove3, Dennis L. Chao9, Niel Hens1,3, Philippe Beutels1,8

1Center for Health Economics Research & Modeling of Infectious Diseases, Center for the Evaluation of Vaccinations, Vaccine and Infectious Disease Institute, University of Antwerp, Antwerp, Belgium; 2Department of Mathematics and Computer Science, University of Antwerp, Antwerp, Belgium; 3Interuniversity Institute for Bioinformatics, 3-BioSoft, Hasselt University, Diepenbeek, Belgium; 4Center for Statistics and Quantitative Infectious Diseases, Vaccine and Infectious Disease Division, Fred Hutchinson Cancer Research Center, Seattle, Washington, United States of America; 5School of Public Health and Community Medicine, The University of New South Wales, Sydney, Australia
MIXING: ACTION, BEHAVE, CONNECT – SERO: MULT, SERIAL, COMBI, DESIGN

MIXING - CONNECT

– within household contact networks (fund. hypothesis)
– innovative two-level and three-level mixing models

A penalized likelihood approach to estimate within-household contact networks from egocentric data

Gail E. Potter
California Polytechnic State University, San Luis Obispo, and Fred Hutchinson Cancer Research Center, Seattle, USA

and Niels Hens
Hasselt University, Diepenbeek, and University of Antwerp, Belgium

Goeyvaerts et al. In prep.
Santerman et al. In prep.
Hens et al. (2012)

- >1000 downloads in 2014
- 6 SIMID international workshops
- 6 SIMID international courses
  - Summer school
- Numerous invited talks

Unique data collection
14 datasets from 5 European countries

- SERO-MULT
- SERO-SERIAL
- SERO-COMBI
- SERO-DESIGN
SERO - MULT

- overdispersion and association/heterogeneity using mixture models
- mathematical model for multiple infections

Hens et al. (SIM, 2008)
SERO - SERIAL

- time heterogeneous mass action principle via SIR(S)-PDE
- the social contact hypothesis (*fund. hypothesis*)

\[ \lambda(a, t) = \int_{0}^{\infty} \beta(a, a', t) I(a', t) da', \]

\[ \frac{\partial S(a, t)}{\partial a} + \frac{\partial S(a, t)}{\partial t} = -\lambda(a, t)S(a, t) - \mu(a, t)S(a, t), \]

\[ \frac{\partial I(a, t)}{\partial a} + \frac{\partial I(a, t)}{\partial t} = +\lambda(a, t)S(a, t) - \sigma(a, t)I(a, t) - \mu(a, t)I(a, t), \]

\[ \frac{\partial R(a, t)}{\partial a} + \frac{\partial R(a, t)}{\partial t} = +\sigma(a, t)I(a, t) - \mu(a, t)R(a, t), \]

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MIXING: ACTION, BEHAVE, CONNECT – **SERO: MULT, SERIAL, COMBI, DESIGN**

**SERO - COMBI**

VZV-CMV-HAV-MMR-HPV
- innovatively combining SERO-MULT and SERO-SERIAL
- vaccination & vaccine uptake
  high risk – high gain

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**Epidemics** 5 (2013) 36–66

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A mathematical model for HIV and hepatitis C co-infection and its assessment from a statistical perspective
Ambaro Yovanna Castro Sanchez<sup>a</sup>, Marc Aerts<sup>a</sup>, Ziv Shked<sup>a</sup>, Peter Vickerman<sup>b</sup>,<sup>c</sup>, Fabrizio Faggiano<sup>d</sup>, Giuseppe Salamina<sup>e</sup>, Niel Hens<sup>f</sup>
The above state-of-the-art leads me to formulate the following major objectives, each of which is novel:

1. To combine the methodologies developed in Sections 2.2.1 and 2.2.2 for estimating age- and time-heterogeneous heterogeneity (in acquisition of infections).
2. To extend the SIR-PDE allowing for vaccination while modeling the dynamics explicitly.
3. To study and predict, explicitly taking into account uncertainty, the impact of increased/decreased vaccine uptake.

Innovation:
The joint analysis of multiple infectious diseases and the impact of heterogeneity on disease spread combined with the time-heterogeneous mass action principle.

Public health & epidemiology:
The development of a tool to study the dynamics of vaccine-preventable diseases relevant for the control of these diseases.

2.2.4 Designing serological studies (DESIGN)

Deciding whether or not to collect serological data is often done with a specific research question in mind as for example for determining the susceptibility to a certain pathogen in the population after risks of future outbreaks have been identified or just to see if there is considerable risk of future outbreaks.

Motivated by the mumps outbreak in Belgium in 2012, I have lead the development of a novel method to quantify the future outbreak potential for measles, mumps and rubella in Belgium [1,19, unpublished manuscript].

This simple method relies on the use of recently collected cross-sectional serological data and social contact data and it can be used to inform implementing additional catch-up vaccination campaigns. We have recently further validated our approach for the measles outbreak(s) in France as illustrated in Figure 1.

Figure 1: Observed (blue line) and predicted (red line) age-specific relative incidence of measles in Southeast France. The observed relative incidence is obtained from case notification data Sep 2010–Aug 2011 whereas the expected relative incidence is obtained from combining serological (measles, ELISA) and social contact data from France. Béraud et al. (manuscript in preparation).

The techniques, which will be developed within the context of this proposal (Sections 2.2.1–2.2.3) allow for long-term predictions and rely on time-trends inferred by the use of serial serological data. The question then arises at which moments in time should cross-sectional serological data be collected and how much benefit can be gained from serosurveillance using multiple serological surveys. Whereas in many serological surveys for childhood infections, 0–18 year olds are oversampled, there is a clear need to revisit these sampling procedures in the context of the specific research question one wants to address. In case the rate of antibody decay is of interest [12], sufficiently sampling adults is essential as illustrated in Figure 2.

Figure 2. Preliminary results of sample size calculations of the antibody decay rate informed by the results of previous analyses of parvovirus B19 in Belgium illustrated for three different age distributions: proportional to the Belgian population structure (“population”), a uniform structure and proportional to age-specific sample size of the 2002 parvovirus B19 survey in Belgium [12] in which children were oversampled.
Public Health Impact & Necessity

control strategies including vaccination schedules -> policy
– (in)validate fundamental epidemiological hypotheses
– taking into account behaviour and its impact

EU topical:
– methods applicable to: varicella, RSV, measles …
– 8th EUPHA conf 14-17 Oct. 2015: Immunization as key public health intervention: challenges and opportunities

tools:
– open science attitude
– well-documented math/stat toolbox
– workshops/courses – educate!

Ultimate goal:
– routine serological data collections in all EU countries
More recent developments

Book on **frailty models** applied to infectious disease data
- Steven Abrams
- Andreas Wienke

Following success of
- The HIV-SIMPACT project
  lead: Niel Hens, Wim Delva
  [www.simpact.org](http://www.simpact.org)
- STI scientific research community (FWO)

New collaborations:
- Gerardo Chowell:
  inference based on ODEs
- Alessia Melagaro (ERC):
  contact patterns
- Vittoria Collizza (ERC):
  meta-population models
- Jacco Wallinga:
  heterogeneity in acquisition
- Jodie McVernon:
  pertussis dynamic model

James Wood
- SERO combi
- Guest Prof. @Hasselt University

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Outlook & Thank You

• 2015: a great year ...
  – ERC Consolidator Grant
  – FWO postdoc Wim Delva
  – Marie-Curie Benny Borremans
  – ...

• Thanks to all colleagues!
• Special thanks to Sarah Vercruysse!
TransMID

Translational and Transdisciplinary research in Modelling Infectious Diseases

Thank You

www.simid.be
www.simpact.org
Backup slides

• Time schedule WPs
• Budget
• Surveys
• CV & Local Team
Table 1: time schedule of the proposed research in work packages per quarter and for the different objectives.
### Budget

Overview table followed by motivation.

<table>
<thead>
<tr>
<th>Cost category</th>
<th>2016</th>
<th>2017</th>
<th>2018</th>
<th>2019</th>
<th>2020</th>
<th>Total</th>
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<tr>
<td><strong>Direct Costs Host</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Institution: Hasselt University</td>
<td></td>
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<tr>
<td>Personnel:</td>
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<tr>
<td>PI*</td>
<td></td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Post docs (1 FTE)**</td>
<td>75567,6</td>
<td>78622,3</td>
<td>81340,3</td>
<td>84570,2</td>
<td>87457,7</td>
<td>407558,0</td>
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<tr>
<td>PhD Students (2 FTE)</td>
<td>51678,4</td>
<td>108576,3</td>
<td>120149,7</td>
<td>128788,7</td>
<td>65536,8</td>
<td>474729,9</td>
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<td>Total Personnel:</td>
<td>127246,0</td>
<td>187198,6</td>
<td>201490,0</td>
<td>213358,9</td>
<td>152994,5</td>
<td>882287,9</td>
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<td><strong>Other Direct Costs</strong></td>
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<tr>
<td>Equipment</td>
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<td>1500</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>4500</td>
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<td>Consumables</td>
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<td>6000</td>
<td>6000</td>
<td>6000</td>
<td>6000</td>
<td>31500</td>
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<td>Travel</td>
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<td>6500</td>
<td>7000</td>
<td>7000</td>
<td>8500</td>
<td>35500</td>
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<tr>
<td>Total Other Direct Costs</td>
<td>18000</td>
<td>16000</td>
<td>15000</td>
<td>15000</td>
<td>16500</td>
<td>80500</td>
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<td><strong>Total Direct Costs</strong></td>
<td>145246,0</td>
<td>203198,6</td>
<td>216490,0</td>
<td>228358,9</td>
<td>169494,5</td>
<td>962787,9</td>
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<td>Indirect Costs (Overhead)</td>
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<tr>
<td>25% of Direct Costs</td>
<td>36311,5</td>
<td>50799,6</td>
<td>54122,5</td>
<td>57089,7</td>
<td>42373,6</td>
<td>240697,0</td>
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<td>Requested Grant Hasselt University</td>
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<td><strong>Direct Costs Host</strong></td>
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<tr>
<td>Institution: University of Antwerp</td>
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<tr>
<td>Personnel:</td>
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<td>Post docs (0.8 FTE)**</td>
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<td>62897,8</td>
<td>65072,2</td>
<td>67656,2</td>
<td>69966,1</td>
<td>320464,4</td>
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<tr>
<td>Total Personnel:</td>
<td>60454,1</td>
<td>62897,8</td>
<td>65072,2</td>
<td>67656,2</td>
<td>69966,1</td>
<td>320464,4</td>
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<tr>
<td><strong>Other Direct Costs</strong></td>
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<td></td>
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</tr>
<tr>
<td>Equipment</td>
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<td>Travel</td>
<td>2000</td>
<td>2000</td>
<td>2250</td>
<td>2250</td>
<td>2500</td>
<td>11000</td>
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<tr>
<td>Total Other Direct Costs</td>
<td>5500</td>
<td>4000</td>
<td>4250</td>
<td>4250</td>
<td>4500</td>
<td>22500</td>
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<tr>
<td><strong>Total Direct Costs</strong></td>
<td>65954,1</td>
<td>66897,8</td>
<td>69322,2</td>
<td>71906,2</td>
<td>74466,1</td>
<td>348546,4</td>
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<tr>
<td>Indirect Costs (Overhead)</td>
<td></td>
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<td></td>
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<tr>
<td>25% of Direct Costs</td>
<td>16488,5</td>
<td>16724,5</td>
<td>17330,6</td>
<td>17976,5</td>
<td>18616,5</td>
<td>87136,6</td>
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<td>Subcontracting costs at University of Antwerp</td>
<td>(no overheads)</td>
<td>198565,0</td>
<td>15441,0</td>
<td>86800,0</td>
<td>0</td>
<td>300806,0</td>
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<td>176682,7</td>
<td>93082,7</td>
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<td>353061,4</td>
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<tr>
<td>Survey</td>
<td>Description</td>
<td>Year(s)</td>
<td>Sample Size</td>
<td>Cost (incl VAT)</td>
<td>WP</td>
<td>Additional information</td>
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<td>----------------------------</td>
<td>------------------------------------------------------------------------------</td>
<td>---------</td>
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<td>----------------------------------------------------------------------------------------</td>
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<tr>
<td>Social contact survey</td>
<td>3rd population-based social contact survey in Flanders, Belgium (panel survey with novel longitudinal setup).</td>
<td>2016</td>
<td>2250</td>
<td>71765</td>
<td>MIXING</td>
<td>new survey part of this proposal</td>
</tr>
<tr>
<td>TransMID</td>
<td>social contact survey on behaviour when ill based on the Great Influenza Survey</td>
<td>2017-2018</td>
<td>750</td>
<td>15440</td>
<td>MIXING</td>
<td>new survey part of this proposal</td>
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<td>Serosurveys</td>
<td>HAV, HPV, MMR</td>
<td>2016</td>
<td>4000</td>
<td>128300</td>
<td>SERO</td>
<td>new survey part of this proposal</td>
</tr>
<tr>
<td>TransMID</td>
<td>pertussis, CMV</td>
<td>2019</td>
<td>4000</td>
<td>86800</td>
<td>SERO</td>
<td>new survey part of this proposal</td>
</tr>
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<td>Social contact survey</td>
<td>1st population-based social contact survey in Belgium</td>
<td>2006</td>
<td>750</td>
<td></td>
<td>MIXING</td>
<td>ready to use database (own portfolio)</td>
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<tr>
<td></td>
<td>2nd population-based social contact survey in Flanders, Belgium</td>
<td>2011</td>
<td>2250</td>
<td></td>
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<td>ready to use database (own portfolio)</td>
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<td>Belgian serosurveys</td>
<td>large residual-based surveys in Belgium either conducted at the University of Antwerp or at the Scientific Institute of Public Health (Belgium)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>existing collaborations between University of Antwerp and the Scientific Institute of Public Health</td>
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<tr>
<td></td>
<td>HAV, CMV, VZV, parvovirus B19, MMR</td>
<td>2002</td>
<td>3250</td>
<td></td>
<td>SERO</td>
<td>ready to use database (own portfolio)</td>
</tr>
<tr>
<td></td>
<td>HAV, HPV, MMR, CMV</td>
<td>2006</td>
<td>3000</td>
<td></td>
<td></td>
<td>ready to use database (own portfolio)</td>
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<tr>
<td></td>
<td>Mumps, pertussis, futher tests planned</td>
<td>2013</td>
<td>3300</td>
<td></td>
<td></td>
<td>ready to use database (access obtained)</td>
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<tr>
<td>Dutch serosurveys (RIVM)</td>
<td>large population-based surveys in the Netherlands</td>
<td></td>
<td></td>
<td></td>
<td>SERO</td>
<td>existing collaboration: HPV serology (mixture modelling)</td>
</tr>
<tr>
<td></td>
<td>Pienter: Pertussis, HPV, MMR, VZV, Influenza A &amp; B, HAV, CMV (and others)</td>
<td>1995-1996</td>
<td>9973</td>
<td></td>
<td></td>
<td>ready to use database (access obtained)</td>
</tr>
<tr>
<td></td>
<td>Pienter II: Pertussis, HPV, MMR, VZV, Influenza A &amp; B, HAV, CMV (and others)</td>
<td>2006-2007</td>
<td>7904</td>
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<td>ready to use database (access obtained)</td>
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<tr>
<td>French serosurveys</td>
<td>large population-based surveys in France often restricted to specific age groups</td>
<td></td>
<td></td>
<td></td>
<td>SERO</td>
<td>existing collaboration: measles epidemiology</td>
</tr>
<tr>
<td></td>
<td>Saturninf (hospitalized - all of France - 6mo-6y): MMR, HAV, HEV, Toxo, VZV, HSV1 &amp; HSV2, CMV</td>
<td>2008-2009</td>
<td>1617</td>
<td></td>
<td></td>
<td>ready to use database (access obtained)</td>
</tr>
<tr>
<td></td>
<td>Seroinf (metropolitan, 6y-49y): MMR, HAV, VZV, HSV1 &amp;2, CMV</td>
<td>2009</td>
<td>5300</td>
<td></td>
<td></td>
<td>ready to use database (access obtained)</td>
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<tr>
<td></td>
<td>Serorr (blooddonors, metropolitan 18-32y): Measles, Rubella</td>
<td>2013</td>
<td>4647</td>
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<td>ready to use database (access obtained)</td>
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<td>Italian serosurveys</td>
<td>large residual-based surveys as part of ESEN and ESEN2 funded by the European Comission (BIOMED2 and DGXII, respectively)</td>
<td></td>
<td></td>
<td></td>
<td>SERO</td>
<td>mutual partners (collaboration HIV and HCV)</td>
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<tr>
<td></td>
<td>part of ESEN: MMR, pertussis, diphtheria</td>
<td>1996-1997</td>
<td>3110</td>
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<td>ready to use database (access obtained)</td>
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<td></td>
<td>part of ESEN2: MMR, pertussis, diphtheria, VZV, HAV, HBV</td>
<td>2003-2004</td>
<td>2446</td>
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<td>ready to use database (access obtained)</td>
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<td></td>
<td>SERO</td>
<td>various collaborations since POLYMOD study</td>
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<td></td>
<td>part of ESEN: HAV, HBV, VZV, MMR, Pertussis</td>
<td>1996-1998</td>
<td>2032</td>
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<td></td>
<td>ready to use database (access obtained)</td>
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<tr>
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<td>part of ESEN2: HAV, HBV, VZV, MMR, Pertussis</td>
<td>2000-2005</td>
<td>2500</td>
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<td>ready to use database (access obtained)</td>
</tr>
</tbody>
</table>

Table 2: survey overview with description, year, sample size, costs in case of a new survey, WP and additional information.
CV & Local Team

- MMath, MSc BioStat, PhD in Stats
- Associate professor
  - CenStat, I-BioStat @ Hasselt University
  - Chermid, Vaxinfec7o @ University of Antwerp
- Chair evidence-based vaccinology @ Chermid
- Member of the Young Academy of Belgium
- Heading the MID group @ CenStat
- Co-heading the SIMID group @ Chermid & CenStat
- h-index (WoK,scholar): 20, 27,
  #A1 publications > 125,
  #Citations > 3000,
  1 monograph as lead author
- 5(+4) former PhD students
- 11(+6) PhD students
- 5 postdocs
- Interdisciplinary research: mathematics, statistics, medicine, biomedical sciences, biology, health economics, computer scientists, ...
- Support 2 research managers
- Support leading researchers (H. Goossens, P. Van Damme, Z. Berneman, P. Beutels, G. Molenberghs)
- EU projects: e.g. FP6 POLYMOD
- Experience with projects for the federal government
- WHO collaborating center