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, ...



Academie

support: 2 research managers - leading researchers current team: 11 PhD students, 5 postdocs TransMID team: 2 PhD students, 2 postdocs

universiteit

►hasse

Interuniversity Institute for Biostatistics and statistical Bioinformatics

KU LEUVEN





VAXINFECTIO Vaccine & Infectious Disease Institute University of Antwerp



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)

MIXING: background

- Collecting social contact data Mossong, Hens et al. 2008
 >800 citations
- Understanding transmission process
- Investigating mitigation strategies: school closure, ...



OPEN O ACCESS Freely available online

PLOS MEDICINE

Social Contacts and Mixing Patterns Relevant to the Spread of Infectious Diseases

Joël Mossong^{1,2*}, Niel Hens³, Mark Jit⁴, Philippe Beutels⁵, Kari Auranen⁶, Rafael Mikolajczyk⁷, Marco Massari⁸, Stefania Salmaso⁸, Gianpaolo Scalia Tomba⁹, Jacco Wallinga¹⁰, Janneke Heijne¹⁰, Malgorzata Sadkowska-Todys¹¹, Magdalena Rosinska¹¹, W. John Edmunds⁴

1 Microbiology Unit, Laboratoire National de Santé, Luxembourg, Luxembourg, 2 Centre de Recherche Public Santé, Luxembourg, 3 Center for Statistics, Hasset University, Diepenbeek, Belgium, 4 Modelling and Economics Unit, Health Protection Agency Centre for Infections, London, United Kingdom, 3 Unit Health Postorian of Vaccination, Vaccine & Infectious Disease. Enstutue, University of Antwerp, Anteryn, Belgium, 4 Modelling and Coonomics Unit, Health Protection Spasse, Cantre for the Fublic Santé, Luxembourg, 3 Center for Statistics, and Modelling Infectious Disease. Native, Diseguine, Antwerp, Belgium, 6 Department of Vaccines, National Public Health, University of Antwerp, Anteryn, Belgium, 6 Department of Vaccines, National Public Health, University of Bielefeld, Bielefeld, Germany, 8 Istituto Superiore di Santia, Rome, Laly, 9 Department of Mathematics, University of Rome Tor Vergata, Rome, Italy, 10 Centre for Infectious Disease Control Netherlands, National Institute for Public Health and the Environment, Bilthoven, The Netherlands, 11 National Institute of Hygiene, Waraw, Poland

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



MIXING - BEHAVE

micro- or/and macro-level changes (fund. hypothesis)



Proc. R. Soc. B (2011) **278**, 2753–2760 doi:10.1098/rspb.2010.2688 Published online 2 February 2011

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

Thomas House^{1,*}, Marc Baguelin^{3,7}, Albert Jan Van Hoek³, Peter J. White^{4,5}, Zia Sadique⁶, Ken Eames⁷, Jonathan M. Read⁸, Niel Hens^{9,10}, Alessia Melegaro¹¹, W. John Edmunds^{3,7} and Matt J. Keeling^{1,2}

American Journal of Epidemiology © The Author 2013, Published by Oxford University Press on behal

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Practice of Epidemiology

The Impact of Illness on Social Networks: Implications for Transmission and Control of Influenza

Kim Van Kerckhove*, Niel Hens, W. John Edmunds, and Ken T. D. Eames

* Correspondence to Kim Van Kerckhove, Faculty of Science, Interuniversity Institute for Biostatistics and Statistical Bioinformatics, Hasselt University, Agoralaan–Gebouw D, 3590 Diepenbeek, Belgium (e-mail: kim.vankerckhove@uhasselt.be).



OPEN ORCESS Freely available online

PLOS ONE

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

Lander Willem^{1,2}*, Kim Van Kerckhove³, Dennis L. Chao⁴, Niel Hens^{1,3}, Philippe Beutels^{1,5}

1 Center for Health Economics Research & Modeling of Infectious Diseases, Center for the Evaluation of Vaccinations, Vaccine and Infectious Disease Institute, University of Antwerp, Antwerp, Relgium, 2 Department of Mathematics and Computer Science, University of Antwerp, Antwerp, Belgium, 3 Interuniversitary Institute for Biostatistics and Statistical Bioinformatics (I-BioStat), Hasselt University, Diepenbeek, Belgium, 4 Center for Statistics and Quantitative Infectious Diseases, Vaccine and Infectious Disease Division, Fred Hutchinson Cancer Research Center, Seattle, Washington, United States of America, 5 School of Public Health and Community Medicine, The University of New South Wales, Sydney, Australia

MIXING - CONNECT

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



Royal Statistical Societ

Appl. Statist. (2013) 62, Part 4, pp. 629–648

A penalized likelihood approach to estimate withinhousehold contact networks from egocentric data

Gail E. Potter

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

and Niel Hens

Hasselt University, Diepenbeek, and University of Antwerp, Belgium



Goeyvaerts et al. In prep. Santermans et al. In prep.

SERO: background

Statistics for Biology and Health

Niel Hens - Ziv Shkedy Marc Aerts - Christel Faes Pierre Van Damme - Philippe Beutels

Modeling Infectious Disease Parameters Based on Serological and Social Contact Data

A Modern Statistical Perspective

D Springer

EXTRA MATERIALS





- Hens et al. (2012)
 >1000 downloads in 2014
- 6 SIMID international workshops
- 6 SIMID international courses

 \rightarrow Summer school

numerous invited talks

Unique data collection 14 datasets from 5 European countries

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

SERO - MULT



Figure 5. The conditional and marginal prevalences and FOI-curves according to the monotonic spline-based BDM.

Hens et al. (SIM, 2008)

SERO - SERIAL

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

$$\begin{split} \lambda(a,t) &= \int_{0}^{+\infty} \beta(a,a',t)I(a',t)da', \\ \frac{\partial S(a,t)}{\partial a} &+ \frac{\partial S(a,t)}{\partial t} = -\lambda(a,t)S(a,t) - \mu(a,t)S(a,t), \\ \frac{\partial I(a,t)}{\partial a} &+ \frac{\partial I(a,t)}{\partial t} = +\lambda(a,t)S(a,t) - \sigma(a,t)I(a,t) - \mu(a,t)I(a,t), \\ \frac{\partial R(a,t)}{\partial a} &+ \frac{\partial R(a,t)}{\partial t} = +\sigma(a,t)I(a,t) - \mu(a,t)R(a,t), \end{split}$$



Hens et al. In Prep.

SERO - COMBI



 $\rho r_1 \sigma_{HCV}$

¥18

¥12

SERO - DESIGN

- framework for the design of serosurveys
- sampling times, sample sizes ...



Fig. 1. Illustration of the MSIRW compartmental models.



Fig. 2. Illustration of the MSIRS compartmental model.





Fig. 3. Illustration of the MSIRS-ext compartmental model.



Fig. 4. Illustration of the MSIRWS compartmental model.

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, <u>Wim Delva</u> <u>www.simpact.org</u>
- 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

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 !

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Thank You

Health Economics & Modelling Infectious Diseases Vaccine & Infectious Disease Institute University of Antwerp

VAXINFECTIO Vaccine & Infectious Disease Institute University of Antwerp www.simid.be

www.simpact.org





Interuniversity Institute for Biostatistics and statistical Bioinformatics





Backup slides

- Time schedule WPs
- Budget
- Surveys
- CV & Local Team

Time Schedule

Time Schedule WPs		2016			2017			2018				2019			2020						
		Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
MIXING-ACTION	01																				
	O2																				
	O3																				
MIXING-BEHAVE	01																				
	02																				
	03																				
MIXING-CONNECT	01																				
	02																				
	03																				
SERO-MULT	01																				
	02																				
SERO-SERIAL	01																				
	O2																				
	03																				
SERO-COMBI	01																				
	O2																				
	O3																				
SERO-DESIGN	01																				
	02																				
PROJECT-MANAGEMENT																					

Table 1: time schedule of the proposed research in work packages per quarter and for the different objectives.

Budget

Overview table followed by motivation.

	Cost category	2016	2017	2018	2019	2020	Total
Direct Costs Host	Personnel:						
Institution: Hasselt	PI*						
University	Post docs (1 FTE)**	75567,6	78622,3	81340,3	84570,2	87457,7	407558,0
	PhD Students (2 FTE)	51678,4	108576,3	120149,7	128788,7	65536,8	474729,9
	Total Personnel:	127246,0	187198,6	201490,0	213358,9	152994,5	882287,9
	Other Direct Costs						
	Equipment	3000	1500	0	0	0	4500
	Consumables	7500	6000	6000	6000	6000	31500
	Travel	6500	6500	7000	7000	8500	35500
	Publications, etc	1000	2000	2000	2000	2000	9000
	Total Other Direct Costs	18000	16000	15000	15000	16500	80500
	Total Direct Costs	145246,0	203198,6	216490,0	228358,9	169494,5	962787,9
Indirect Costs (Overhead)	25% of Direct Costs	36311,5	50799,6	54122,5	57089,7	42373,6	240697,0
Requested Grant Hasselt		181557,5	253998,2	270612,5	285448,6	211868,1	1203484,9
University							
Direct Costs Host	Personnel:						
Institution: University of	Post docs (0,8 FTE)**	60454,1	62897,8	65072,2	67656,2	69966,1	326046,4
Antwerp	Total Personnel:	60454,1	62897,8	65072,2	67656,2	69966,1	326046,4
	Other Direct Costs						
	Equipment	1500	0	0	0	0	1500
	Consumables	2000	2000	2000	2000	2000	10000
	Travel	2000	2000	2250	2250	2500	11000
	Total Other Direct Costs	5500	4000	4250	4250	4500	22500
	Total Direct Costs	65954,1	66897,8	69322,2	71906,2	74466,1	348546,4
Indirect Costs (Overhead)	25% of Direct Costs	16488,5	16724,5	17330,6	17976,5	18616,5	87136,6
Subcontracting costs at	(no overheads)	198565,0	15441,0	0	86800,0	0	300806,0
University of Antwerp							
Requested Grant		281007,6	99063,3	86652,8	176682,7	93082,7	736489,0
University of Antwerp							
Requested Grant	(by year and total)	462565,1	353061,4	357265,3	462131,3	304950,8	1939973,9

Surveys

Survey	Description	Year(s)	Sample Size	Cost (incl VAT)	WP	Additional information
Social contact	3rd population-based social contact survey in					new survey part of this
survey	Flanders, Belgium (panel survey with novel	2016	2250	71765	MIXING	proposal
TransMID	longitudinal setup).					
	social contact survey on behaviour when ill	2017 2010	750	45.440		new survey part of this
	based on the Great Influenza Survey	2017-2018	/50	15440	MIXING	proposal
Serosurveys	HAV, HPV, MMR					new survey part of this
TransMID		2016	4000	128300	SERO	proposal
	pertussis, CMV	2010	1000	0.000	6500	new survey part of this
		2019	4000	86800	SERO	proposal
Social contact	1st population-based social contact survey in	2000	750			ready to use database
survey	Belgium	2006	/50		MIXING	(own portfolio)
	2nd population-based social contact survey in	2011	2250			ready to use database
	Flanders, Belgium	2011	2250		MIXING	(own portfolio)
Belgian	large residual-based surveys in Belgium either					existing collaborations
serosurveys	conducated at the University of Antwerp or at			Letter of intent		between University of
	the Scientific Institute of Public Health				SERO	Antwerp and the
	(Belgium)			attached		Scientific Institute of
						Public Health
	HAV, CMV, VZV, parvovirus B19, MMR					ready to use database
		2002	3250			(own portfolio)
	HAV. HPV. MMR. CMV					ready to use database
	·····,····, ·····, ·····	2006	3000			(own portfolio)
						(e
	Mumps, pertussis, futher tests planned	2012	2200			ready to use database
		2015	5500			(access obtained)
Dutch	large population-based surveys in the					existing collaboration:
serosurveys	Netherlands			Letter of intent	SERO	HPV serology (mixture
(RIVM)				attached		modelling)
. ,	Pienter: Pertussis, HPV, MMR, VZV, Influenza					ready to use database
	A & B, HAV, CMV (and others)	1995-1996	9973			(access obtained)
	Pienter II: Pertussis, HPV, MMR, VZV,	2006 2007	7004			ready to use database
	Influenza A & B, HAV, CMV (and others)	2006-2007	7904			(access obtained)
French	large population-based surveys in France			Letter of intent	6500	existing collaboration:
serosurveys	often restricted to specific age groups			attached	SERO	measles epidemiology
	Saturninf (hospitalized - all of France - 6mo-					ready to use database
	6y): MMR, HAV, HEV, Toxo, VZV, HSV1 &	2008-2009	1617			(access obtained)
	HSV2, CMV					· ,
	Seroinf (metropolitan, 6y-49y): MMR, HAV,					ready to use database
	VZV, HSV1 &2, CMV	2009	5300			(access obtained)
	SeroRR (blooddonors, metropolitan 18-32y):	2012	16.17			ready to use database
	Measles, Rubella	2013	4647			(access obtained)
Italian	large residual-based surveys as part of ESEN					mutual partners
serosurveys	and ESEN2 funded by the European Comission			Letter of intent	SERO	(collaboration HIV and
	(BIOMED2 and DGXII, respectively)			attached		HCV)
	part of ESEN: MMR, pertussis, diphteria					ready to use database
		1996-1997	3110			(access obtained)
	part of ESEN2: MMR. pertussis, diphteria, VZV.					(**************************************
	HAV. HBV	2003-2004	2446			
UK serosurveys	large residual-based surveys as part of ESEN			-		various collaborations
	and ESEN2 funded by the European Comission			Letter of intent	SERO	since POLYMOD study
	(BIOMED2 and DGXII, respectively)			attached		
	part of ESEN: HAV, HBV, V7V, MMR, Pertussis					ready to use database
		1996-1998	2032			(access obtained)
	nart of ESEN2: HAV HBV VZV MMP					ready to use database
	Pertussis	2000-2005	2500			(access obtained)

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, Vaxinfectio @ 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



VAXINFECTIO Vaccine & Infectious Disease Institute University of Antwerp



Health Economics & Modelling Infectious Diseases Vaccine & Infectious Disease Institute University of Antwerp

- 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