



Immunogenetics

Laboratory of Immunogenetics VU University medical center Amsterdam



## EpiGenChlamydia Consortium

Laboratory of Immunogenetics, VU University Medical Center, Amsterdam, The Netherlands

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\* Reference Chlamydia trachomatis Laboratory, National Institute of the of Public Health & Environment (RIVM)

\* Co-founder and co-Director Microbiome Ltd. NL

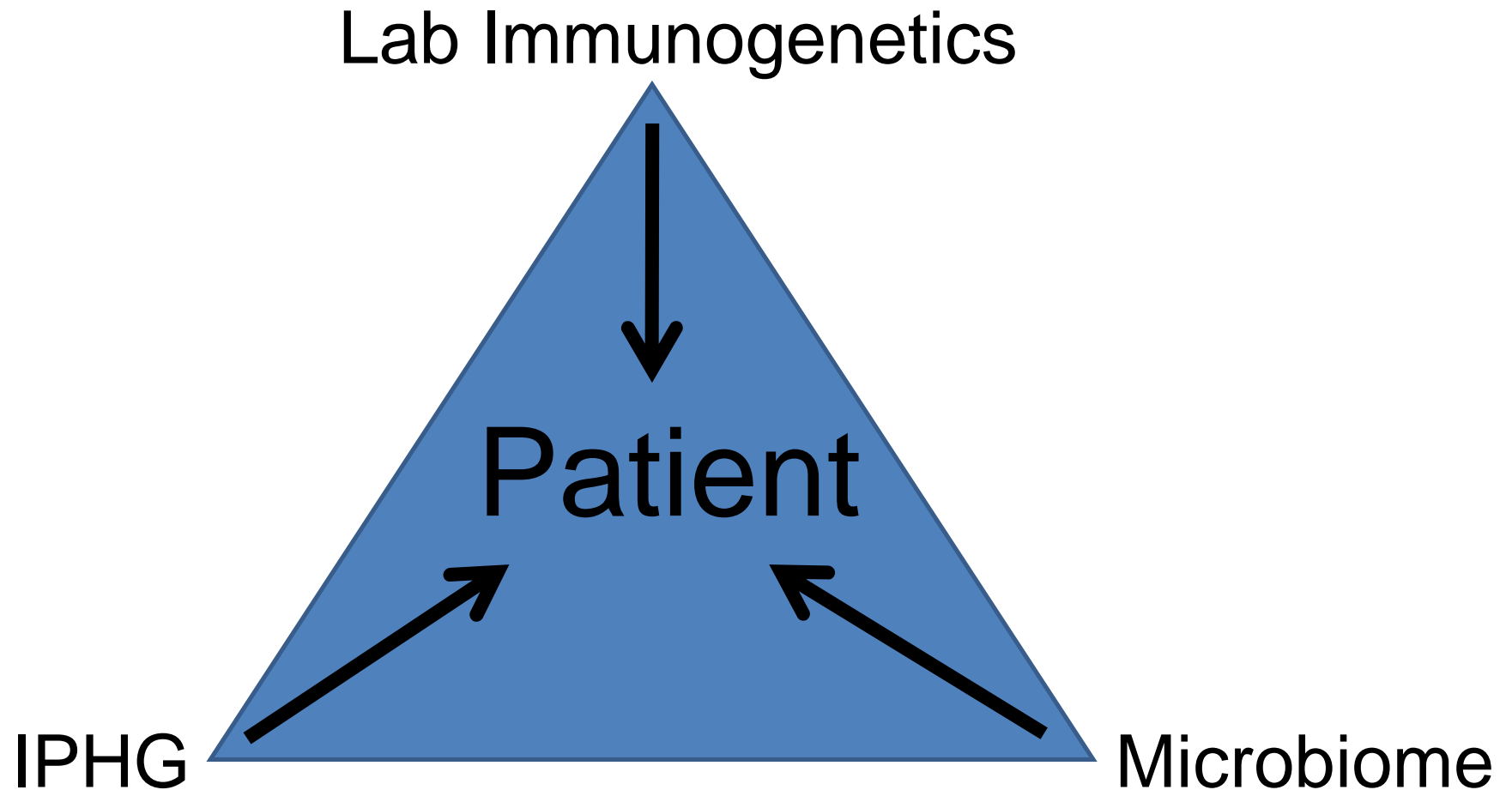
**PHGEN-II :Leuven Meeting 22-23 September 2011**



# My triangle of synergy



VU University Medical Center  
Laboratory of Immunogenetics



# CT is the most prevalent bacterial STI world-wide

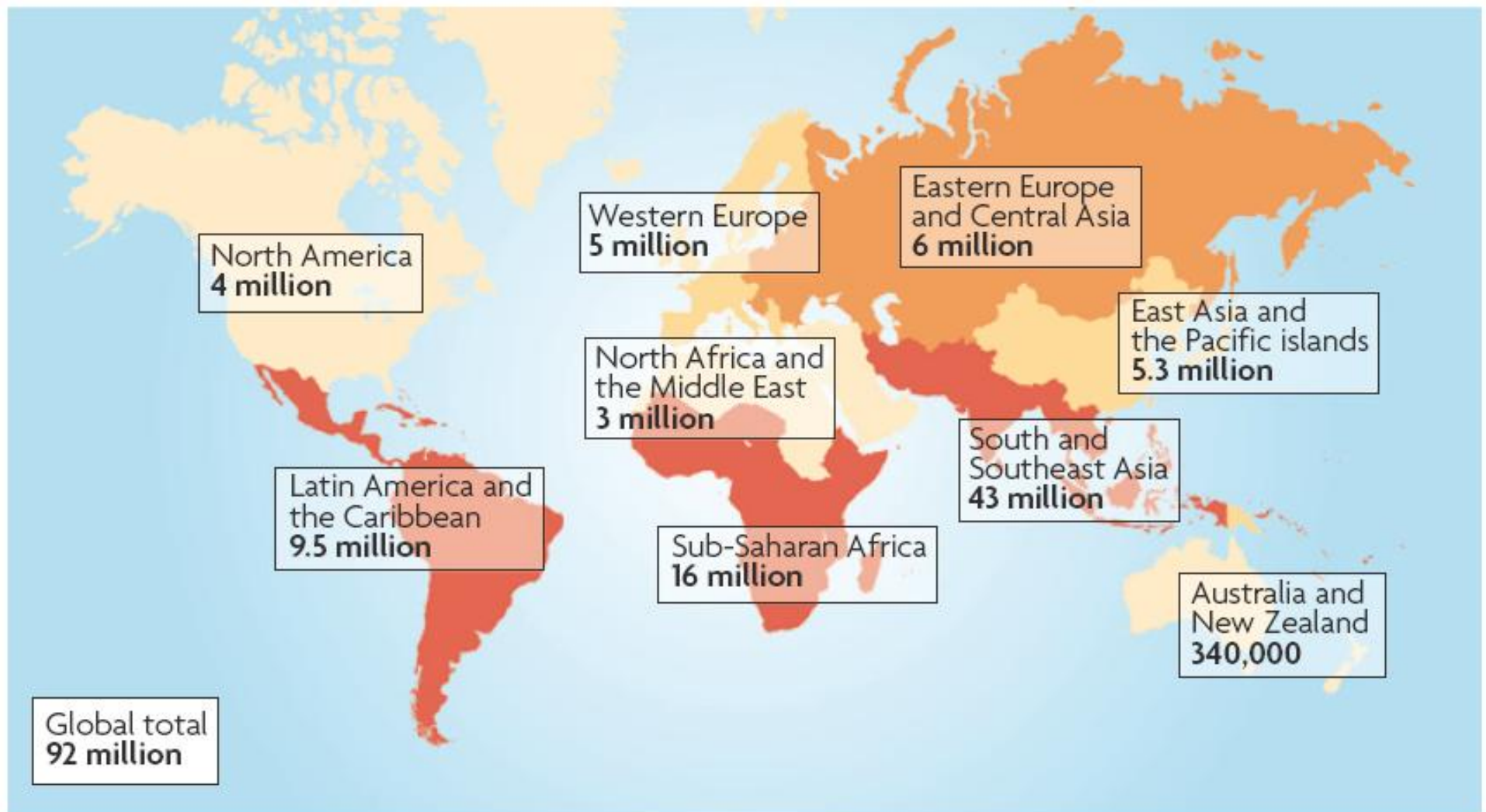


Figure 2 | Estimated number of new cases of *Chlamydia trachomatis* infections among adults

# Introduction



VU University Medical Center  
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Clear differences in the clinical course  
of *Chlamydia trachomatis* infections

- Symptomatic *vs* asymptomatic
- Transmission *vs* no transmission
- Persistence *vs* clearance
- Late complications (LC) *vs* no LC

# Immunogenetics of CT infection



VU University Medical Center

Bailey *et al.* (2009) published the most relevant study in the field of *Chlamydia* Immunogenetics:

Proliferative responses to serovar A EB antigens were estimated in monozygotic(MZ) and dizygotic(DZ) twin pairs.

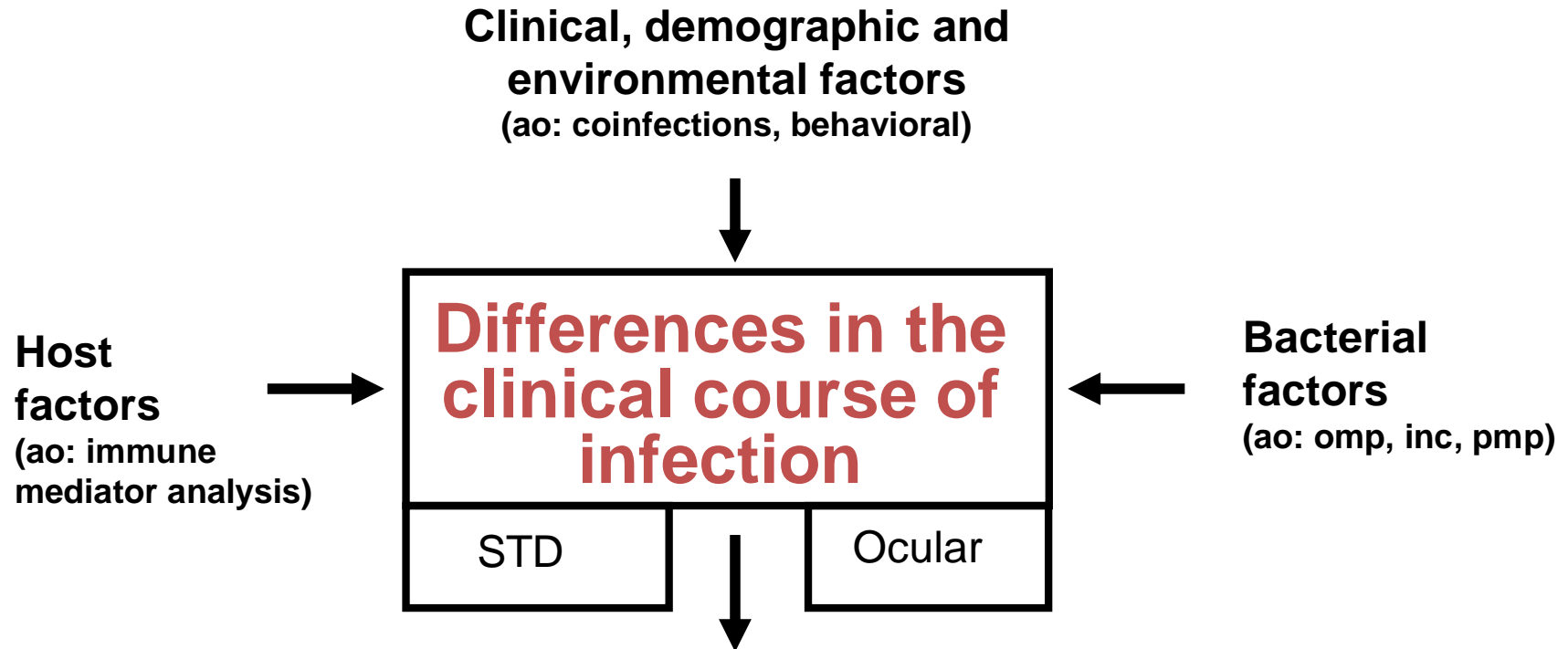
The heritability estimate was 0.39 suggesting that host genetic factors contributed almost 40% to the variation to infection.

SA Morr e et al. 2009.

*Chlamydia trachomatis*: identification of susceptibility markers for ocular and sexually transmitted infection by immunogenetics

FEMS Immunology and Medical Microbiology

# Integrated approach on *C. trachomatis*



## Insights in risk factors:

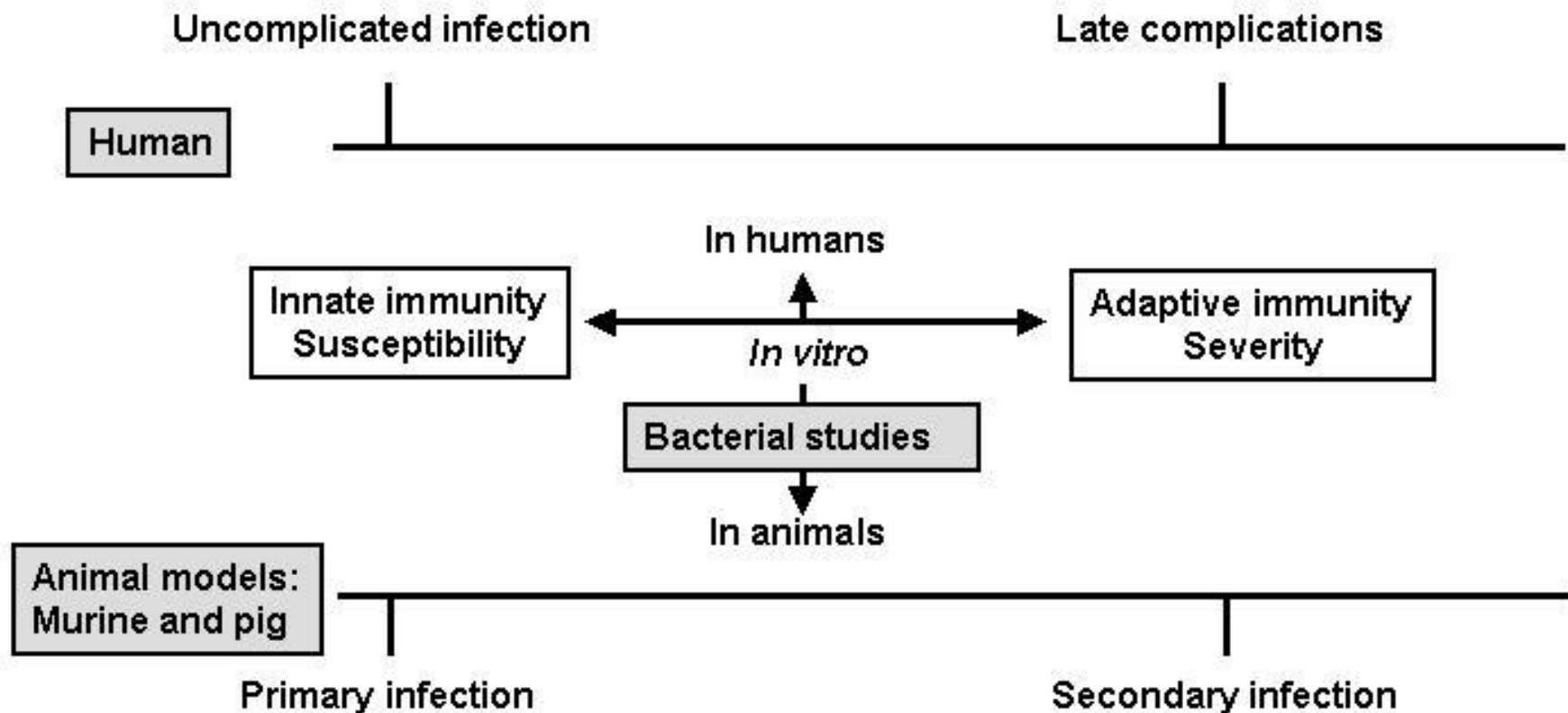
Susceptibility to disease, Severity of subsequent disease

Main immunological factors involved

→ Risk profiling, Disease etiology, Therapy, Vaccination

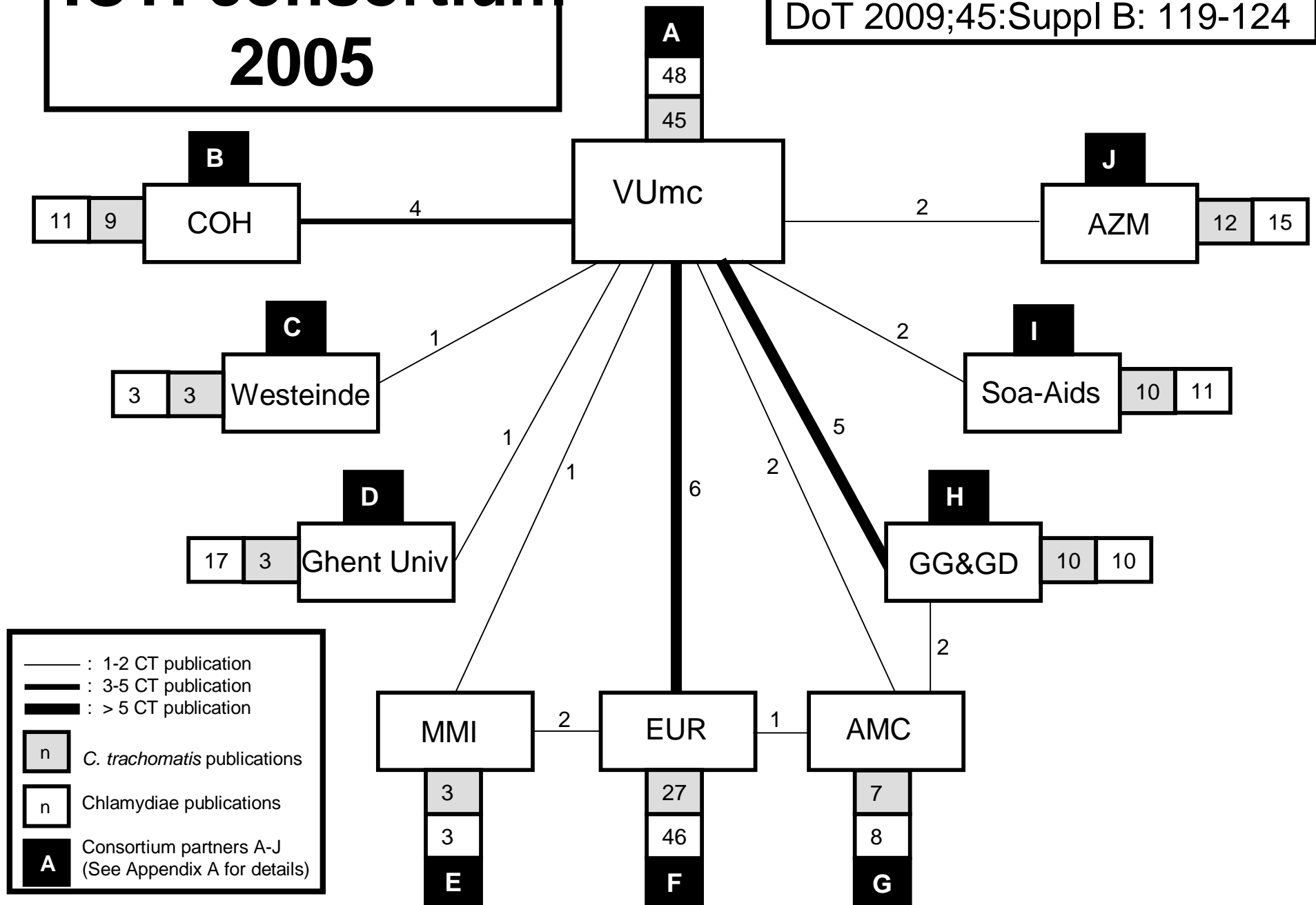
# Integrated Approach to *Chlamydia trachomatis* Infections

Promotes a synergism between epidemiology, immunogenetics, functional biology, and clinical studies



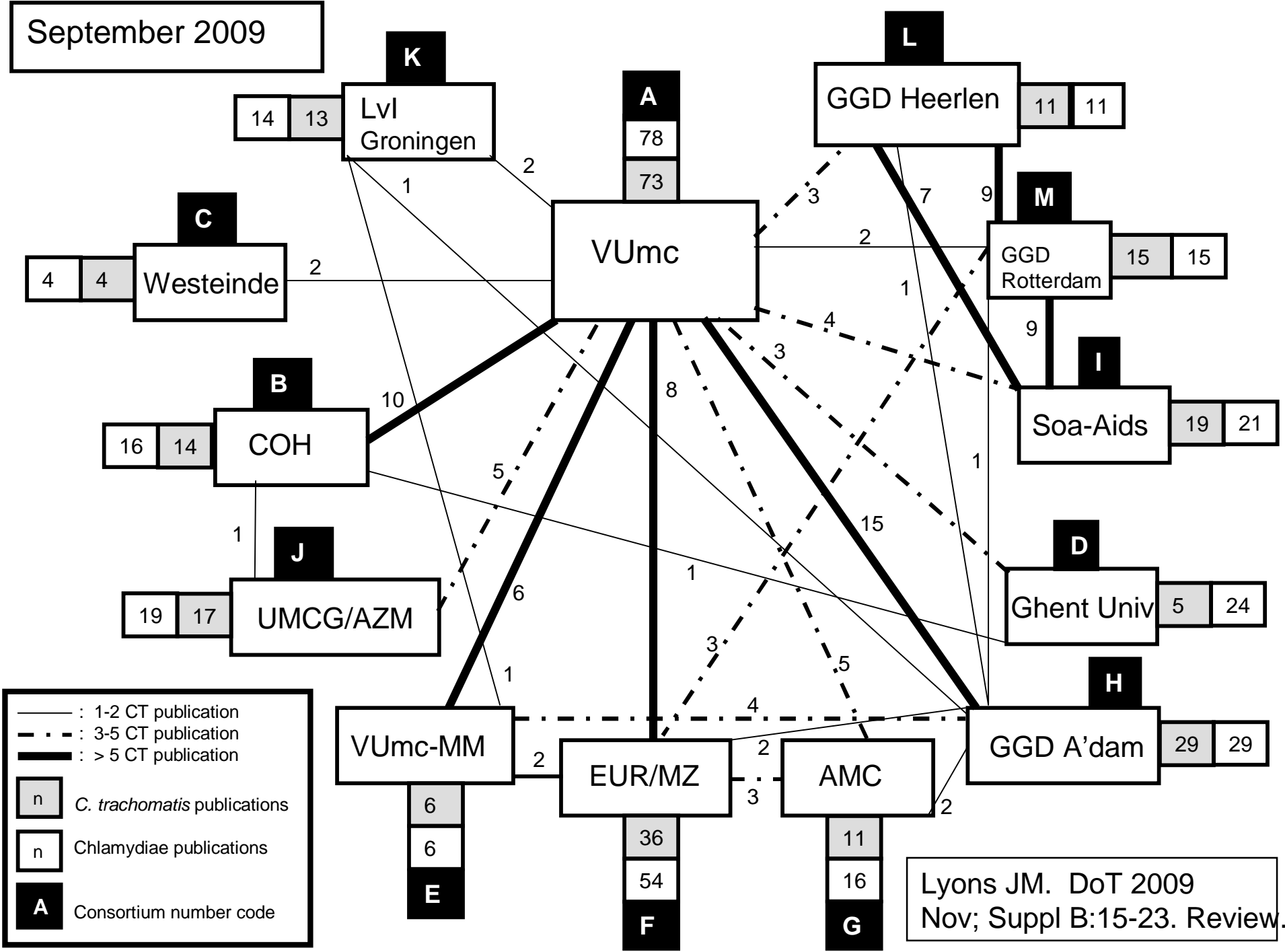
# ICTI consortium 2005

DoT 2006;42:Suppl.A:107-114  
DoT 2009;45:Suppl B: 119-124





September 2009



Lyons JM. DoT 2009  
Nov; Suppl B:15-23. Review.

2005 - Current



ICTI Consortium

2005



NWO funding for writing EU FP6 grant

2005 - 2006



EU FP6 grant application

2007-2011



EU FP6 EpiGenChlamydia Consortium





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- Chlamydia Websites
- Participants

Title:  
**Contribution of molecular epidemiology and host-pathogen genomics to understand Chlamydia trachomatis disease**

Acronym:  
**EpiGenChlamydia**

Contract N°: **037637**

Research topic addressed:  
**Framework Programme 6 (FP6)-2005-LIFESCIHEALTH-6  
LSH-2005-1.1.0-1  
« Co-ordination Actions (CA) in functional genomics research »**

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European Union

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[Participants](#)

#### Abstract:

*Chlamydia trachomatis* (CT) infections are responsible for both the world leading cause of blindness (trachoma) and the most prevalent sexually transmitted disease which is strongly associated with pelvic inflammatory disease, ectopic

**The EpiGenChlamydia Consortium aims to structure trans-national research to such a degree that comparative genomics and genetic epidemiology on large numbers of unrelated individuals can be performed.**

genetics and genetic epidemiology on large numbers of unrelated individuals can be performed. For this purpose, 6 interdependent workpackages have been defined: Epidemiology (to define suitable cohorts in Europe), Genetics & Genomics (to define a SNP-Chip, based on the complete host and bacterial genomes available), Biobanking & Datawarehouse (to built a biomedical ethically allowed central sample collection and data management system), Research integration (to streamline all European groups working on immunogenetics and chlamydial infections in general to gain synergy), Dissemination (to extend and further validate this consortium), and Project management. The collective synergy acquired in the CA will allow for the generation of scientific knowledge on the CT - host interaction, knowledge on the genetic predisposition to CT infection, development of tools for early detection of a predisposition to CT infection, and development of alternative diagnostics to detect CT infections indicative to specific treatment. Moreover, it will provide a basis for the development of effective active preventive (vaccine) and/or curative measures for CT infections.



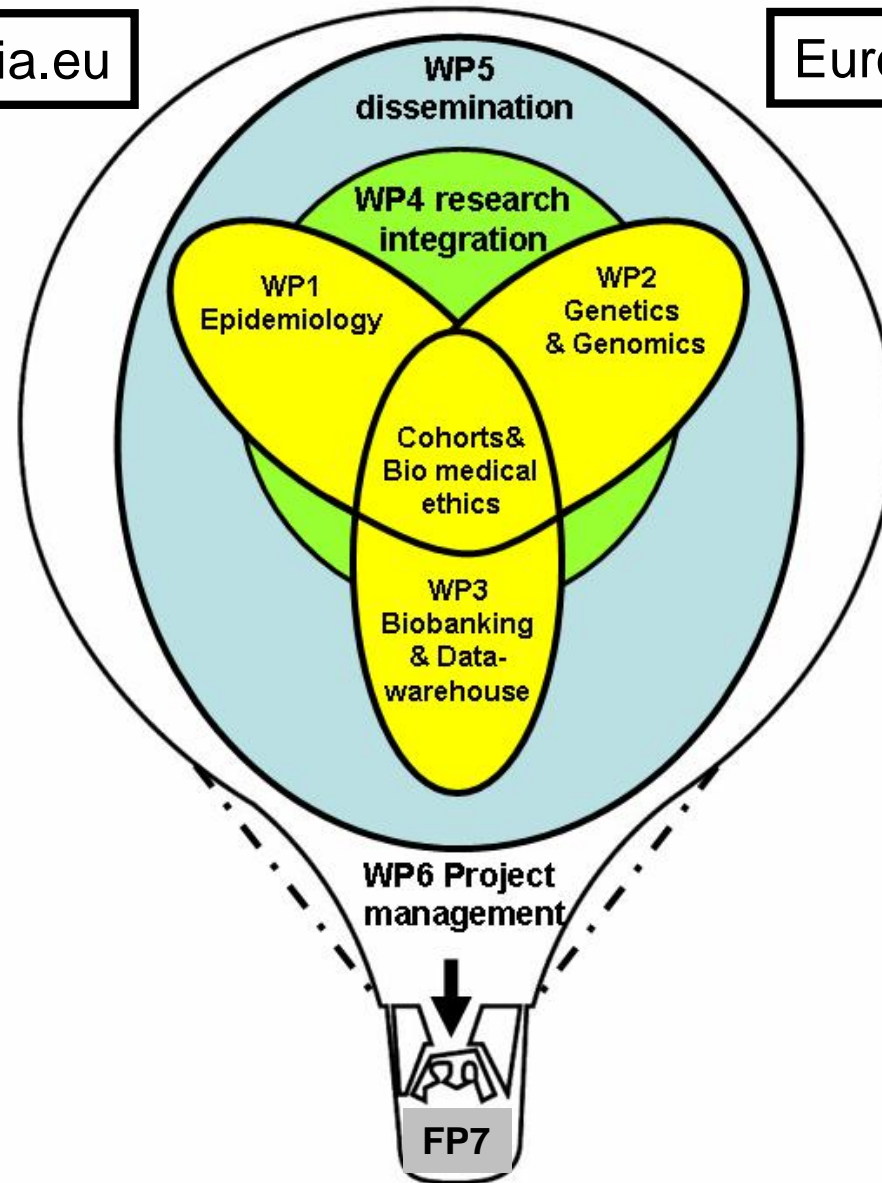
[Abstract](#)

[Home](#)

Participant no.	Participant organisation name	Participant organisation short name	Scientific team	Town
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19	Institut de Recherche pour le Développement	IRD	Jean-Francois Schemann	Dakar
20	The Gambia International Centre for Eye Health	NECP	Ansumana Sillah	Banjul

[www.EpiGenChlamydia.eu](http://www.EpiGenChlamydia.eu)

European consortium



Morré SA, Ouburg S, Peña AS, Brand A.

The EU FP6 EpiGenChlamydia Consortium: contribution of molecular epidemiology and host-pathogen genomics to understanding *Chlamydia trachomatis*-related disease.

Drugs Today. 2009 Nov;45 Suppl B:7-13.

## TubaScan:

*Improving subfertility diagnostics*

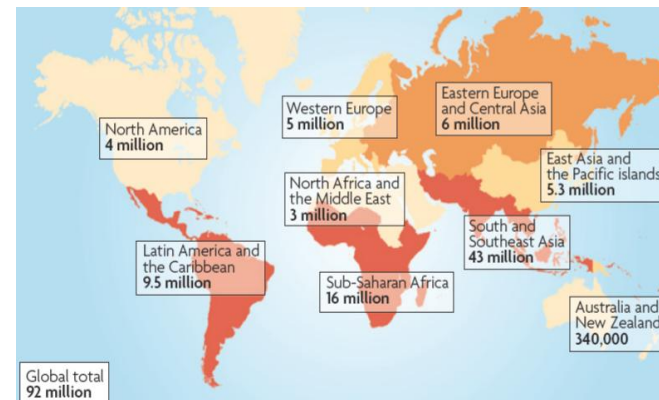
NGI Pre-Seed Grant June 2011



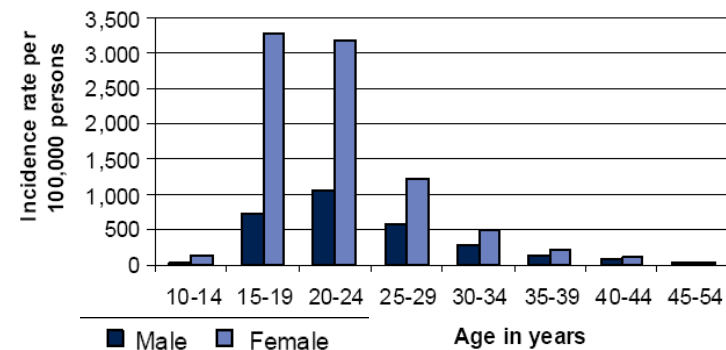
Untreated  
chlamydia  
can lead to  
infertility.

# Chlamydia associated infertility play a major role in women's health

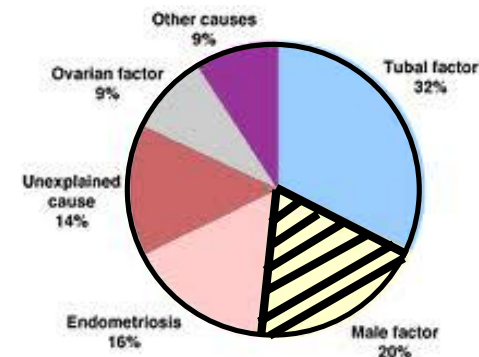
*Chlamydia trachomatis* (CT) is the most common bacterial Sexually Transmitted Disease (STD) worldwide\*



CT is most common among young women at reproductive age

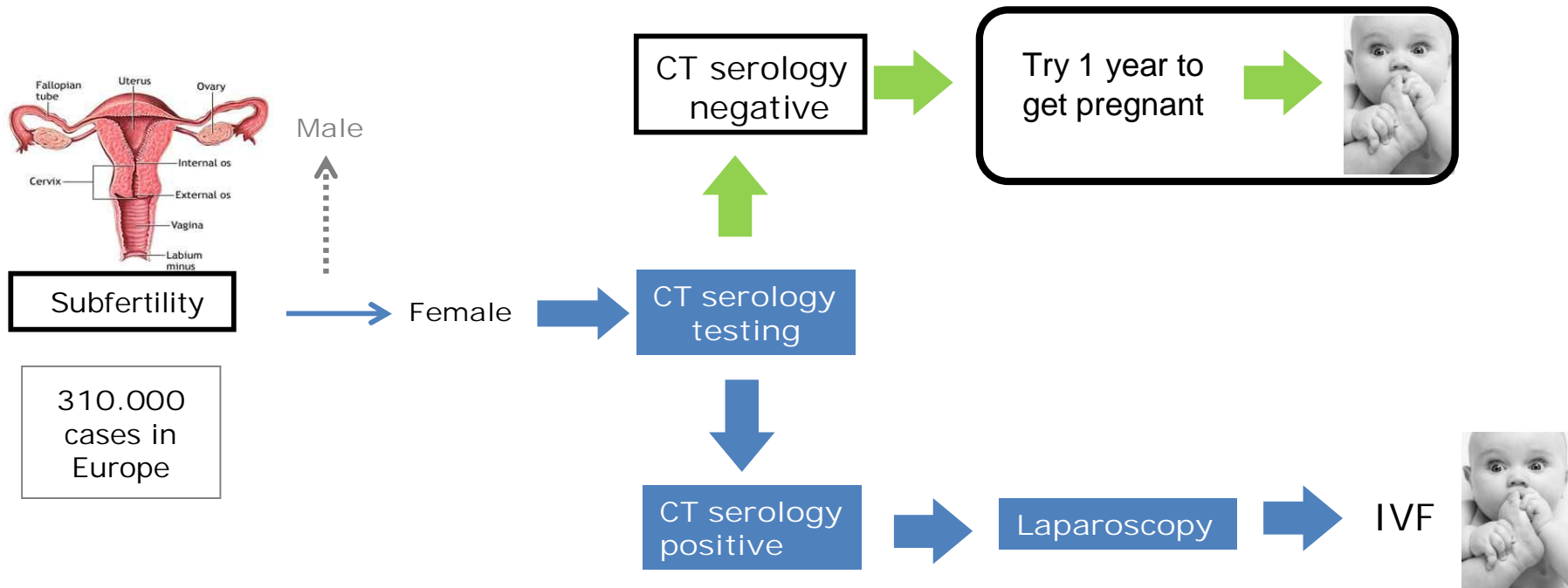


- 15% of the couples are subfertile
- CT plays a major role in subfertility





## Chlamydia associated infertility: standard of care

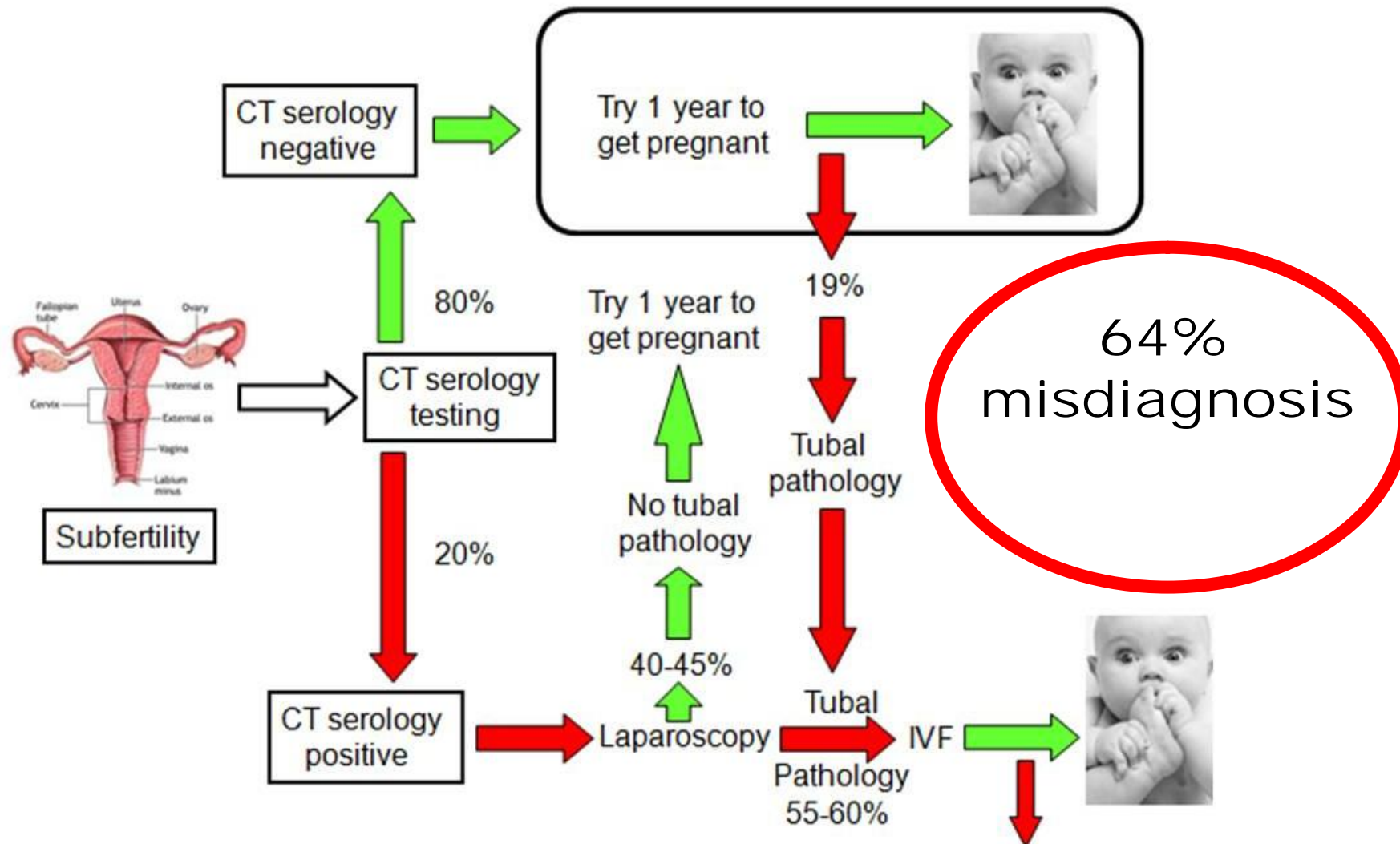


In some countries, HSG is used instead or in addition to serology  
- Limited added value of HSG compared to serology

The main hurdle is that many CT+ women undergo laparoscopy while they do not have disease

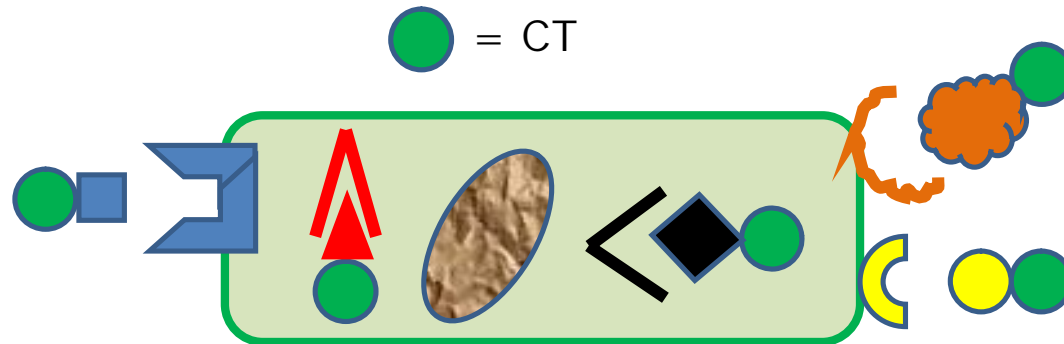
This results in many unnecessary laparoscopies with high burden (both costs and psychosocial)

# The problem: misdiagnosis

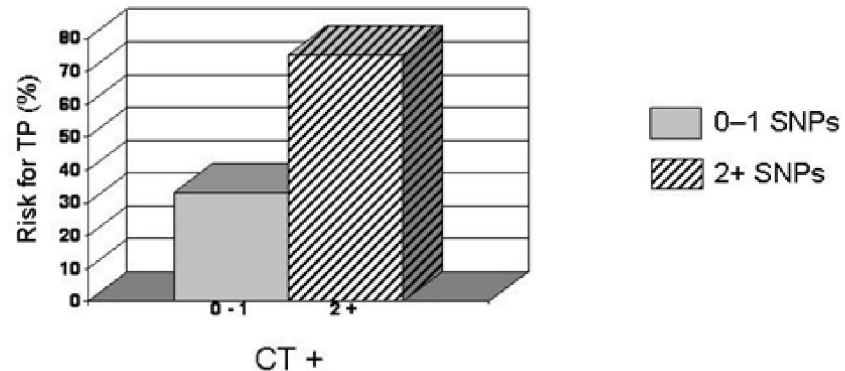


## Proof of Concepts

Current state-of-the-art



What are our findings



Innovative steps and goal

- To develop a human genetic trait for ID diagnostics
- 10-50 SNPs trait: define a cut-off SNP load
- New diagnostic approach: combine serology and genetics

# The diagnostic development plan



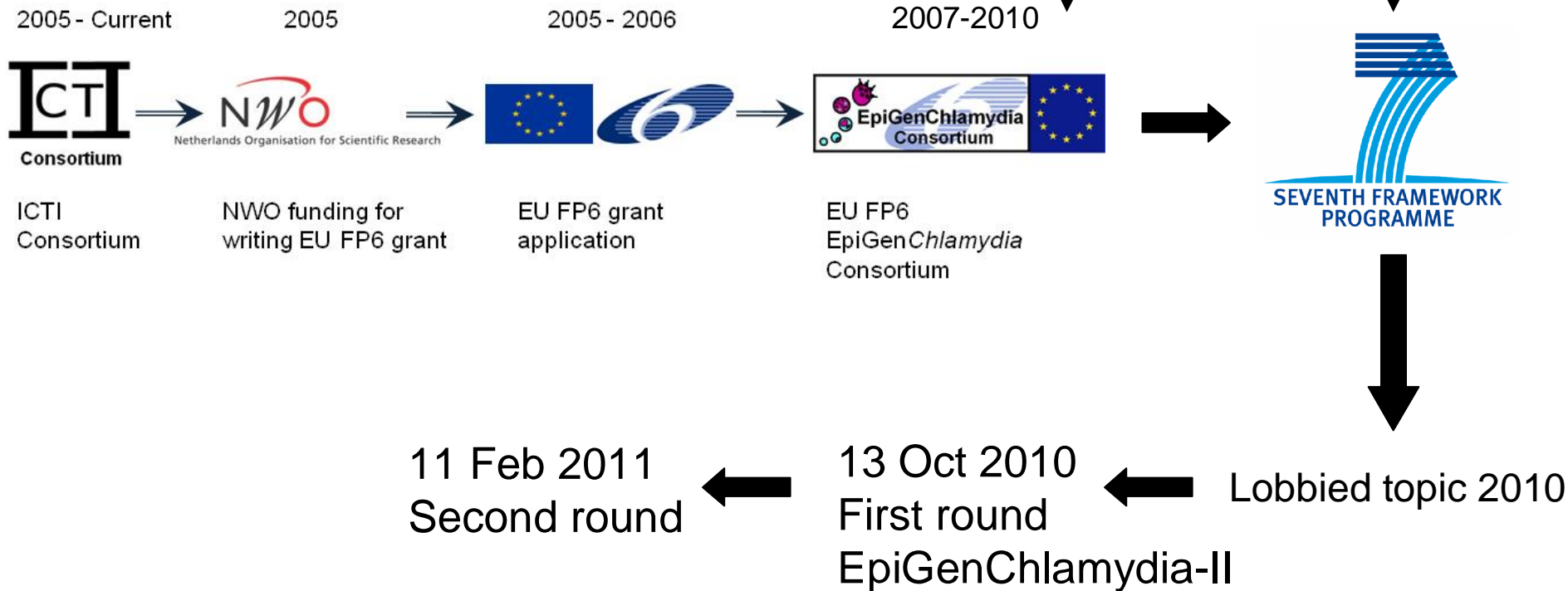
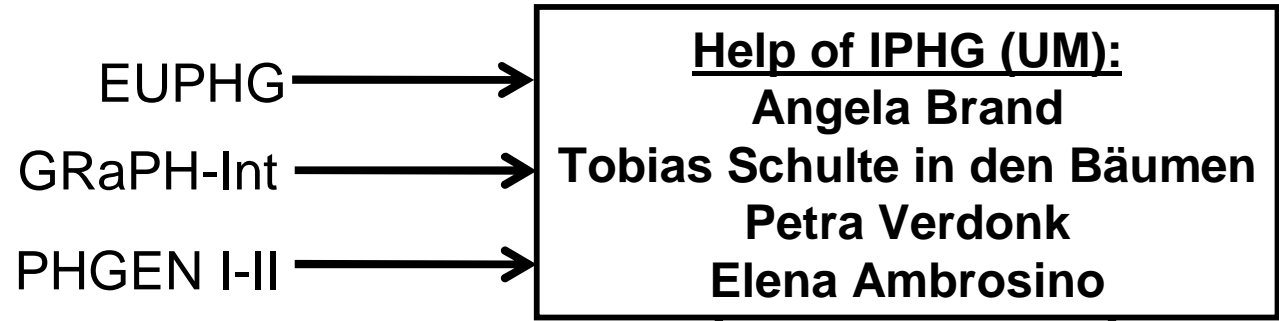
## Summary of Tuba-scan

- A clear unmet medical need
- A well-defined approach to reduce the 64% misdiagnosis in subfertility
- Access to large European cohorts
- Potential solid IP position
- Highly skilled team to launch **Tuba-scan** and its **CE IVD certified diagnostic kit**



# PHG aspects





Submission to the ETB-Office  
Deadline: 1<sup>st</sup> February 2011, 1 pm CET  
Please see ETB Guidelines  
and national funding rules

Please save file as  
COORDINATING COUNTRY\_ACRONYM

*e.g. : ITALY\_BIOBIO10*

And submit to

[www.etbsubmission.eu](http://www.etbsubmission.eu)

For help on submitting your proposal please  
contact ETB-Office, [etboffice@innomedica.fi](mailto:etboffice@innomedica.fi)

## EUROTRANS-BIO: 6<sup>th</sup> transnational call for proposals

### PROPOSAL FORM PART A - Overview



**Project Title (may be  
published)**

*Max. 120 characters*

Development of a diagnostic test to assess Chlamydia trachomatis-associated tubal damage in subfertile women



# Summary



VU University Medical Center  
Laboratory of Immunogenetics

- 40% of the responses to CT infection are host based
  - Well defined Biobanks and datawarehouses essential
  - Innate immune system plays a key role: SNPs identified
    - TLRs, cytokines and chemokines
  - PH: SNP profiling for prediction of tubal pathology
  - Large scale SNP profiling needed
- Ultimate goal: personalized healthcare approach based on host genetics for subfertility patients**



Consortium

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VU University Medical Center

# Acknowledgements

## Laboratory of Immunogenetics

### VU University MC Amsterdam, NL

Servaas A. Morré, PhD

Sander Ouburg, PhD

Ouafae Karimi, MD

Jolein Pleijster

### STD Outpatient Clinic & Public Health

### Services Amsterdam, NL

Han S.A. Fennema, MD, PhD

Henry J.C. de Vries, MD, PhD

### CDC, Atlanta, USA

Joseph Igietseme, Carolyn Black, F. Eko

## Kathleen A. Kelly, PhD Lab (UCLA)

Cheryl Champion, Amanda Freed, Raymond Moniz  
Bo Wei, Maria King.

## Martin Lipp, PhD Lab (Germany)

Uta Hoepken (KO mice: CXCR5<sup>-/-</sup>)

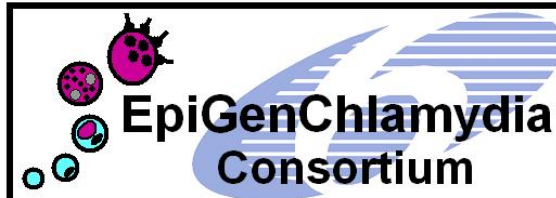
## Academic Hospital Groningen, NL

Prof. Jolande A. Land, MD, PhD

## City of Hope, Dept. Of Infectious Diseases, Duarte CA, USA

Joseph M. Lyons, PhD

James I. Ito, MD



# Acknowledgements PHG

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Angela Brand, Tobias Schulte in den Bäumen, Elena Ambrosino

All other team members

## Public Health Agency of Canada

Mohamed Karmali, Suneil Malik, Ross Duncan

## Networks and consortia

[www. ecphg.eu](http://www.ecphg.eu), [www. phgen.eu](http://www.phgen.eu), [www. graphint.org](http://www.graphint.org),

[www. cdc.gov](http://www.cdc.gov), [www. ecdc.eu](http://www.ecdc.eu), [www. PHAC.org](http://www.PHAC.org)

[www. EpiGenChlamydia.eu](http://www.EpiGenChlamydia.eu)

