

# PhD defence Suzanne Smit

## The public health impact of congenital toxoplasmosis and cytomegalovirus infection: methods and applications.

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Dit is de omschrijving

### Supervisors:

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### Summary:

Cytomegalovirus (CMV) and *Toxoplasma gondii* are able to infect the unborn child through the placenta. Such congenital infections can be asymptomatic but can also lead to morbidity, lifelong disabilities and mortality. In combination with an assumed significant incidence, congenital toxoplasmosis (CT) and cytomegalovirus (cCMV) might have an important impact on the lives of patients and their families. There is an urgent need to boost awareness regarding both aforementioned congenital infections in the global population but also among clinicians and policy makers and for improved prevention and intervention strategies. Knowledge about the disease burden is prerequisite for every further step forward because it can boost this overall awareness and is essential for evidence-based health policy, monitoring trends, and prioritizing and evaluating the impact and cost-effectiveness of prevention and intervention strategies, including accurate diagnostic and prognostic methods and effective and safe therapeutics and vaccines. The main objective of this thesis was therefore to unravel the public health impact of both congenital infections in terms of Disability-Adjusted Life Years (DALYs). To reach this goal, we described data needs for burden assessment, focused on available evidence, identified data gaps, and developed an up-to-date methodological framework for assessing disease incidence and burden of disease, which allows routine monitoring of the public health impact of both congenital infections in time. First we assessed the epidemiology and disease burden of (congenital) CMV in Belgium. The age group weighted overall CMV seroprevalence was 32% (95% confidence interval (CI): 31%–34%) in 2002 and 31% (95% CI: 30%–32%) in 2006. We demonstrated that the CMV epidemiology differs from that of an immunizing infection such as hepatitis A virus. These data may imply that the assumption of primary infection followed by life-long immunity, including IgG positive antibody levels, may not hold and that boosting through reactivation and reinfection is likely. The public health impact of cCMV in Belgium in 2013 was 1976 (95% Uncertainty Interval (UI): 757–4067) DALYs. To our knowledge this was the first ever estimation of the public health impact of cCMV in terms of DALYs. In this context, it seemed time to stimulate awareness and public health policy by conducting similar studies for other countries. Therefore, we continued with the estimation of the public health impact of cCMV in the European Union (EU). We estimated a cCMV burden of 68 595 (UI: 22 678–162 440) DALYs in the EU, which translated to 14 (UI: 4.5–32) DALYs per 100 000 population and 133 (UI: 44–315) DALYs per 10 000 live births. This burden was comparable to Down syndrome and much higher than other important congenital infections such as CT, congenital rubella and perinatal listeriosis. Noticeable is that approximately half of the cCMV burden was due to sequelae in children that were asymptomatic at birth and a scenario analysis showed that including data on foetal losses more than doubled the DALY estimate. Overall, the data showed that cCMV is an important but potentially under-recognized and underestimated clinical and public health problem in the EU and by extension worldwide. As for cCMV, we estimated the disease burden of CT in Belgium in terms of DALYs. The estimated public health impact of CT was 188 (95%UI: 43–419) DALYs in Belgium in 2013. A scenario analysis showed important increases in years of life lost when the burden due to foetal losses was included and decreases in DALYs when comprehensive CT prevention measures were conducted. In this context, we may argue that prevention measures and focusing on the important risk factor, food contamination, might be important strategies for disease burden reduction. Since we observed a noticeable impact of primary prevention on the burden of CT, we estimated the sero-epidemiological status and risk factors of toxoplasmosis in pregnant women in Northern Vietnam, a region with an

assumed low level of awareness and lack of prevention measures. In conclusion, CT and especially cCMV infection are serious infections with an important impact on public health, although several data gaps remain resulting in a potential underestimation of the burden. The results, methodological framework, proposed applications, prioritized remaining gaps and recommendations may allow a leap forward in breaking the vicious circle of under-recognition and neglect and can support awareness, evidence based health policy and the development and evaluation of much needed prevention and intervention strategies. Similar studies in other countries may further stimulate breaking this vicious cycle.