Surveillance studies on infectious diseases: Evidence for action
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Summary
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The research in this thesis relates to a variety of practice guidelines used in the Netherlands for the control and prevention of infectious diseases. The studies presented in this thesis were intended to answer specific research questions generated from the actual day-to-day practice of infectious disease control by public health service (PHS) of Amsterdam. The outcomes were intended to serve as evidence for the national practice guidelines on the control of infectious diseases, and to support the implementation of its recommendations.

This thesis is about gathering evidence for action, and starts with an introductory chapter (chapter 1) explaining how the synthesis between research and recommendations in current public health practice takes place. Today’s medical practice, including public health, is largely dominated by practice guidelines. Practice guidelines may increase the quality of health care by improving consistency in practice and providing guidance to therapeutic, preventive, diagnostic and organisational processes. Whereas in the past practice guidelines were mainly based on tradition and reflected expert-opinion, modern guidelines aim to become more evidence-based. The premise is that the greater the strength of the evidence used, the higher the quality of the guidelines. In the Netherlands, many practice guidelines for the control of infectious diseases are still expert opinions based on practice- or knowledge, and not yet equally supported by evidence.

The first part of this thesis (chapter 2, 3 and 4) relates to the practice guidelines of the National Coordination Communicable Diseases Control (LCI) on three viral skin rash infections common in children: varicella-zoster virus; parvovirus B19; and cytomegalovirus. In addition, chapter 4 relates to the practice guideline of the Netherlands Society of Occupational Medicine (NVAB) ‘Pregnancy, Postpartum Period and Work’, in which recommendations on pregnancy and the occupational risk of infection in day care centres are made (2007). In the first part data from a cross-sectional health survey of the general Amsterdam population (the Amsterdam Health Monitor (AHM) 2004) are used. Besides the survey questionnaire, blood samples were collected from the same individuals, from which a serum repository was established. In chapter 4, only the AHM data of women of childbearing age (16 to 44 years) were used. In addition, data on child day care personnel were analysed, obtained through a cross-sectional survey among female employees of Amsterdam day care centres (2007).
In chapter 2 the seroprevalence of IgG antibodies against varicella-zoster virus (VZV) in the Amsterdam adult population was estimated. In addition, factors associated with a seronegative VZV status were identified. A total of 1341 serum samples obtained from the Amsterdam serum repository were tested for antibodies to VZV. Our findings show a rather low overall seroprevalence in the adult population of Amsterdam (94%; 95%CI 92-96%), compared to the near-total VZV seropositivity (97-100%) in the national general population. Seroprevalence among first-generation immigrants (Moroccan immigrants 90%, Surinamese or Antillean immigrants 91%, and Turkish 92%) was significantly lower than among those born in the Netherlands. In terms of health policies and the cost-effectiveness of the introduction of a universal VZV vaccination programme, the prevalence of specific risk groups for VZV seronegativity among adults, like first-generation immigrants should be taken into account. Besides improved surveillance on VZV complications in children and adults, more comprehensive research on VZV seronegativity in the general population, including the immigrant populations, is recommended.

Chapter 3 describes the seroprevalence of IgG antibodies against parvovirus B19 among various ethnic groups in the Amsterdam adult population. Serum samples obtained from 1323 participants of the AHM were tested for antibodies to parvovirus B19. The outcomes show an overall seroprevalence of 61%, which is comparable to the estimates found in neighbouring countries. No specific predictors or risk groups for seropositivity were identified. The epidemiological evidence of parvovirus B19 in the Netherlands is scarce. Also, representative data of its seroprevalence in the general Dutch population are lacking, and existing estimates are based on samples of convenience. This is the first study testing parvovirus B19 in a random sample of the Dutch adult population. Accurate estimates on the age specific risks of infection, the force of infection, and the incidence during epidemic and during non-epidemic years in the Netherlands is needed. Therefore national population-based research on parvovirus B19 seroprevalence with more emphasis on children is recommended with equal emphasis on immigrant populations. As infection with parvovirus B19 may go unnoticed, high risk groups for exposure need to be identified, especially those in occupational settings.

In Chapter 4 the association between occupation and infection in women working in child day care was assessed, by comparing the seroprevalence of IgG-class antibodies against cytomegalovirus (CMV), varicella-zoster virus (VZV) and
parvovirus B19 in female day care workers with women not working in day care. Twenty-seven percent of the day care workers were still susceptible to parvovirus B19 or CMV. Working in day care was independently associated with parvovirus B19 infection in all day care workers (prevalence ratio [PR] 1.2; 95%CI 1.1–1.3), and with CMV infection in day care workers of European origin only (PR 1.7; 95%CI 1.3–2.3). Almost all women born outside Europe tested seropositive for CMV (96%). All day care workers tested seropositive for VZV, compared to only 94% of the women not working in day care. This study confirms the clear association between employment in child day care centres and infection with CMV and parvovirus B19. Intervention policies could be improved, like screening of new employees and awareness campaigns emphasizing hygienic measures among day care workers, and reasons for not implementing current recommendations need to be explored.

Chapter 5 describes the epidemiology and trends of all imported malaria in the Netherlands from 2000 to 2008. Using national surveillance data on all reported infections of imported malaria, the annual incidence of Plasmodium falciparum infections was estimated with the annual number of travellers to malaria-endemic regions as denominator. In addition, data from Dutch pharmacies regarding annual prescriptions for malaria chemoprophylaxis were used to describe the trend in use, as well as to estimate the number of travellers visiting malaria-endemic regions without prophylaxis. Despite increasing travel to malaria-endemic countries, the estimated incidence of imported P. falciparum infections per 10,000 travellers declined from 10.0 in 2000 to 3.4 in 2007. The causes for this decrease are likely multi-factorial, and not readily explained by more (or better use) of malaria chemoprophylaxis alone, but may reflect a reduced risk of infection due to decreasing local malaria transmission in some malaria endemic areas. Nevertheless, the increasing number of unprotected travellers remains worrisome. The percentage of unprotected travellers rose from 47% to 52% of all travellers. The drop in incidence of imported P. falciparum infections is greatest in travellers returning from Middle and West Africa. The import of malaria from this region by immigrants visiting friends and relatives (VFR) decreased from 138 infections in 2000, to 69 infections in 2007. VFR from West-Africa remain the highest risk group for acquiring import malaria as many West Africans are not consulting pre-travel preventive health services. Further research on the social and cultural aspects of health seeking behaviour for, and/or compliance to malaria chemoprophylaxis is
needed, enabling subsequent recommendations for targeted risk-group interventions.

Chapter 6 studied the incidence and risk factors for acute hepatitis B (HBV) infection in returning travellers. All reported acute HBV patients in Amsterdam, the Netherlands, from 1992 till 2003, were analysed. The estimated incidence in travellers from Amsterdam to HBV-endemic countries is 4.5/100,000 travellers, and was much lower than was expected from the estimated potential risk of infection from behavioural studies, and the increasing number of travellers in the past decades. Two thirds of these patients were immigrants who lived in Amsterdam and who had visited their friends and relatives in their country of origin. In 12 years, only three Dutch short-term tourists contracted HBV while travelling, all by heterosexual contacts. Based on these findings, the working group of the Dutch National Coordination Centre for Travellers Health (LCR) decided to change the guideline in 2009 and recommended that all immigrants from HBV-endemic countries were eligible for HBV vaccination, irrespective of the duration of travel. Also, as the risk of infection in Dutch short-term travellers is low, and probably similar to the low risk of infection in Dutch-born persons in the Netherlands, it was decided not to target all travellers for hepatitis B vaccination.

In chapter 7 trends in hepatitis A (HAV) acute hepatitis B (HBV) and shigellosis are compared with the trends of gonorrhea and infectious syphilis in Amsterdam men who have sex with men (MSM) over a period of 15 years (1992-2006). Since the mid-1990s, sexually transmitted infections (STI) among MSM have increased and appear to be related to more risky sexual behaviour. Data of all reported HAV, acute HBV, and shigellosis, and from all patients newly diagnosed with gonorrhea and infectious syphilis who visited the PHS STI outpatient department in Amsterdam were used. Both gonorrhea and infectious syphilis in MSM show a steep increase, mainly after 1998, yet the incidence of HAV (0.97/1000 MSM) and acute HBV (0.47/1000 MSM) remained unchanged. The incidence of shigellosis (0.41/1000 MSM) also remained stable, but showed large fluctuations, with two distinct peaks in 1995 and in 2001, and patients varying from 0 to 25 per year. Our results show that HAV, acute HBV, and shigellosis do not follow the rising trends of conventional STI in MSM, which are believed to result from increased risky sexual behaviour. This disparity in trends implies differences in transmission dynamics. Recent molecular epidemiological studies suggest that clustered transmission in social MSM networks plays a major role. The trend of acute HBV needs more
careful exploration as the negative effects of increased risky sexual behaviour among MSM have been counterbalanced by the positive effects of the targeted vaccination campaign for this group that started in 1998.

Chapter 8 describes incidence trends of all reported acute hepatitis B (HBV) in the Amsterdam MSM population from 1992 to 2012, and the impact of the targeted HBV vaccination campaign that began in 1998. A mathematical model, using the Amsterdam data from the national database of the vaccination programme for high risk groups, population data from the Research and Statistics department of Amsterdam, and estimates of changes in sexual risk behaviour from the Amsterdam Cohort Studies, explores potential explanations for trends described. Our findings show a strongly declining incidence of acute HBV from 2005 onwards. At the end of 2011, the vaccination coverage was estimated to be 30-38%. Most participants (67%) were high-risk MSM recruited at the outpatient department for sexually transmitted infections (STI), and outreach locations such as saunas and gay bars. The scenario of the mathematical model in which MSM who engage most in high-risk sex are vaccinated, best explained the decline in incidence. This is the first time that a targeted HBV vaccination programme has proven to be effective. HBV transmission among Amsterdam MSM, despite ongoing sexual risk behaviour, has decreased. Vaccination programmes targeting MSM do not require full coverage, but are effective when MSM who engage most in high-risk sex (i.e. clients of STI-clinics) are reached.

Chapter 9 describes the major findings of the studies presented in this thesis, and consequently discusses the 'evidence for action'. The evidence generated from these studies proves to be more than 'local' evidence alone, but has led to amendments in national practice guidelines, or may have raised the discussion to do so. In addition, some outcomes have generated specific new research questions, as evidence supporting some recommendations appears to be lacking, which need urgent investigation. This thesis emphasises the potentials and advantages of local research, as evidence acquired from local research has proven additional value, and can improve and shape future practice guidelines and health policy programmes. Evidence-based practice guidelines bridge the gaps between research, health policy and practice, and health policies have more impact when implemented in practice guidelines. Practice guidelines based on the best available evidence may transform practice-based health care into evidence-based health care and consequently improve the quality of its outcome.