Surveillance studies on infectious diseases: Evidence for action

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Introduction
General Introduction

The research in this thesis bundles several population-based surveillance studies on infectious diseases carried out by the public health service (PHS) of Amsterdam. In contrast to national surveillance systems which are designed for ongoing systematic data collection in order to monitor trends in disease prevalence in the national population, the studies in this thesis were intended to answer specific research questions generated from the actual day-to-day practice of infectious disease control by the PHS of Amsterdam. The PHS of Amsterdam has a robust reputation in producing evidence to shape and evaluate local and national public health policies and programmes. Most of the research data are routinely collected and/or locally acquired.

Since 1982 the PHS has initiated several research projects concerning infectious diseases in the Amsterdam population. Apart from an electronic database, in which data of all patients with notifiable infectious diseases are entered (as required for national surveillance), the PHS has collected supplementary information, like details of contacts of the reported patients. In addition to all routinely collected data, the PHS has established several surveillance databases bases on locally acquired data (i.e. from cross-sectional surveys, or longitudinal cohort studies), including several serum repositories. One of the reasons for performing local research in public health, and in infectious diseases in particular is the complexity of the Amsterdam population, and the presence of large risk groups for numerous infectious diseases. The PHS of Amsterdam is the biggest PHS in the Netherlands, and serves a population of approximately 800,000 residents. The urban character of the capital city is reflected in the diversity of its population. At least 35% of the population are non-Western immigrants, who are considered at risk for e.g. viral hepatitis, and import diseases. Furthermore, Amsterdam, known as one of the ‘Gay Capitals’ of Europe, is a popular residency for men who have sex with men, and hosts at least 26,000 MSM, who have a higher risk for sexually transmittable diseases. Lastly, it holds a large drug user population, and a considerable number of commercial sex workers. About 7 million foreign tourists visit Amsterdam annually.

Surveillance is defined as data collection and analysis, interpretation of these data to provide information, and dissemination of that information for action, or as its
shortest definition ‘data for action’.\textsuperscript{6,7} Surveillance studies contribute largely to the development of evidence-based public health policies in the control of infectious diseases by monitoring trends of infections and diseases in the population. They are an indispensable tool for planning and evaluation of intervention programmes as well as for establishing up-to-date practice guidelines. This thesis is about gathering evidence for action, and starts with an introductory chapter explaining how the synthesis between research and recommendations in current public health practice takes place.

**Practice guidelines**

Over the past 30 years a new trend in medicine has risen, namely the development and use of practice guidelines, also called medical guidelines, clinical protocols or clinical practice guidelines. A practice guideline in medicine may be defined as: “systematically developed statements to assist practitioners and patients in making decisions about appropriate health care for specific clinical circumstances”.\textsuperscript{8} A wide variety of international practice guidelines have been developed since, e.g. the global Guidelines International Network (GIN), founded in 2002, holds a web-based library containing (by October 2012) over 6,600 guidelines, evidence reports and related documents, developed or endorsed by 88 professional organisations from 48 countries.\textsuperscript{9} The recent surge of interest in practice guidelines can be explained by the simultaneous emergence of another phenomenon, namely the evidence-based medicine (EBM), well described as “conscientious, explicit, and judicious use of current best evidence in making decisions in health care”.\textsuperscript{10} Whereas in the past practice guidelines were mainly based on tradition and reflected expert-opinion, in the era of evidence-based medicine, modern guidelines dwell more and more on the assessment of scientific research. The premise is that the greater the strength of the evidence used, the higher the quality of the guidelines. Practice guidelines based on the best available evidence can transform practice-based medicine into evidence-based medicine and consequently improve the quality of health care.

As often is the case, notwithstanding the growing interest and attention, it is not the quantity, but the quality that counts. The enormous expansion of guidelines has given rise to a growing concern about their quality, affecting successful implementation and desired results. Several studies showed that the use of practical guidelines by the targeted user population depends on its quality and
should have a scientific base.\textsuperscript{11-13} Research on the quality of practice guidelines showed that the methodology used in the development of guidelines varied, and often was of poor quality. As a result practice guidelines lacked supporting evidence, showed inconsistency (across different guidelines), and even were biased through conflict of interest, jeopardizing its validity, acceptability, and applicability. Clearly, guidelines for practice guidelines were needed.\textsuperscript{14,15} In 2003, an international group of academics and health care practitioners from 13 countries designed a framework to appraise and compare the quality of the practice guidelines; The Appraisal of Guidelines, REsearch and Evaluation Instrument (AGREE), which can be used by both guideline designers and users to assess the key components of methodological quality of the guidelines, including the process of development, and the quality of reporting.\textsuperscript{16} Recently, a revised version, AGREE II, was developed, with improved measurement properties.\textsuperscript{17} Yet, despite the international validation and widespread dissemination of the AGREE instruments, concerns about suboptimal quality and the lack of supporting evidence persists. The greatest need for improvement is still the identification, evaluation, and synthesis of the scientific evidence.\textsuperscript{18,19}

Developing practice guidelines

According to current insights a guideline must include more than recommendations only; it should also contain a description of the methodology used, supporting evidence, and implementation advice.\textsuperscript{20} In summary, the process of systematic guideline development is best described by the following steps. First a topic is selected, after which a guideline development group is composed, which gathers scientific evidence, and formulates a draft. Thereafter the draft is often peer-reviewed and/or corrected by a consensus group. The final version is then ready for publication. In some cases, before publication, the final draft needs endorsement by the health authorities first.\textsuperscript{16,21} Guideline development involves both a technical process (collection of relevant evidence) and a social process (interpretation of evidence and development of recommendations). The validity of guideline recommendations can be adversely influenced if either process is biased.\textsuperscript{22} The most effective method in gathering the scientific evidence (the technical process) is to perform a systematic review to collect all available evidence, assess the quality of the selected studies and combine the results into recommendations.\textsuperscript{21} However, systematic reviews of the evidence may provide essential information, but often do not contain sufficient information for making well informed decisions,
nor lead to clear and unambiguous recommendations. Also, reviewers may draw subjective conclusions about the quality of this evidence. The interpretation of evidence and development of recommendations (the social process of guideline development) depends mostly on the composition and expertise of the guideline development group, and there is consistent empirical evidence that the composition of the guideline development group influences the resulting recommendations. It is clear that recommendations backed by scientific evidence should always take precedence over statements based on subjective judgments, yet, expert-opinion still is (especially when scientific evidence is lacking) an important brick on which practice guidelines are based. Nonetheless, practice guidelines solely based on perceived wisdom, clinical judgement and experience, and lacking an explicit decision making process (and may be biased by undeclared conflicts of interest) should best be avoided, and the undesirable methodology or GOBSAT (Good Old Boys Sat Around a Table) should no longer be valid or accepted. Therefore, when evidence is limited or absent, or when experts reach consensus that is not consistent with the evidence, practice guidelines should clearly describe the limits of the evidence or the rationale for rejecting obvious evidence.

The successful implementation of practice guidelines depends, apart from the quality of evidence and the methodology used for its development, also on the acceptance of the targeted used population and policy makers. The adherence to practice guidelines increases when future users actively participate in its development. Ideally, guideline development groups should be multidisciplinary, especially when recommendations are shaped. This ensures adequate discussion of the evidence (or its absence) as multidisciplinary groups reach different conclusions than single expert groups, even when presented with the same evidence. In guideline development groups all people involved with the subject, should be represented, that is health care professionals who directly or indirectly engage in patient care in different health care settings (for example, primary and secondary care, nurses), but also policy makers who need to make decisions about resource allocation. Evidence-based practice guidelines are a useful tool in bridging the gaps between research, health policy and practice. Research must be fed into policy in order to have any impact, whereas health policies can increase impact when implemented in practice guidelines. In public health, some practice guidelines are merely policy guidelines expressing public health intervention programmes such as screening or vaccination programmes.
Practice guidelines for control of infectious diseases

Practice guidelines are considered an essential tool for the prevention and control of infectious diseases, and most of them are primarily designed to assist medical doctors and other health care providers in the prevention, diagnosis, and management of patients infected with infectious diseases. Its main aim is the improvement of the quality of health care, by improving consistency in practice and providing guidance to therapeutic, preventive, diagnostic and organisational processes.

The control of infectious diseases is an interdisciplinary field of medicine involving hospital-based medical consultants (e.g. internal medicine, medical microbiology), public health consultants (specialised in the control of infectious diseases), and general practitioners. Furthermore, many other disciplines, such as nurses and hygienists are engaged with rendering care and advice in disease and infection control. Depending on the context in which the control of infectious diseases takes place, specific guidelines are available for e.g. hospitals, nursing care institutions, general practices, or local public health services. Depending on its purpose the guidelines’ focus may be on hygiene, treatment, infection control, prevention or outbreak management, and is accordingly developed by different organisations. It is important, especially when one subject is covered by diverse fields of medicine to attune to each other’s guidelines. The simultaneous existence of several national guidelines for one subject can cause confusion, and discouragement. All organisations responsible for guideline development should be aware, and make sure practice guidelines accommodate similar and non-conflicting recommendations. Ideally, diverse practice guidelines on a particular disease should be integrated into one.

Evidence for the prevention and control of infectious diseases

Worldwide a large variety of international and national practice guidelines on infectious diseases is available. For example from 1994 to July 2009 the Infectious Disease Society in America (IDSA) has issued and endorsed over 6,500 recommendations in 63 guidelines. In 2010 a study evaluated 44 IDSA guidelines (using the US Public Health Grading System on strength of recommendation and quality of evidence), and concluded that most recommendations in IDSA guidelines are primarily based on low quality evidence derived from non-randomized studies, such as observational studies, or expert-opinion/ descriptive studies. The need for high-quality research, that is randomized clinical trials (RCT), considered the
golden standard in EBM, is high. However, in public health and the control and prevention of infectious diseases in particular, observational research may be the best evidence available. In public health RCTs are usually not feasible, or have limited external validity (generalisability).\textsuperscript{26} Observational research in infectious diseases comprises of several study designs such as cohort, case-control, and cross-sectional studies. In addition, data form surveillance systems on infectious diseases are a rich source of information contributing to the evidence in practice guidelines and policy making. Surveillance studies are used to establish baseline disease rates, to identify time trends and new and emerging epidemics, to monitor the impact of public health interventions such as vaccination programmes, to guide vaccine development and clinical management, and to help allocation of resources for disease prevention and treatment programmes.\textsuperscript{28}

**Guidelines on infectious diseases in the Netherlands**

The Netherlands has a long tradition of producing practice guidelines, and many institutes, associations and professional organizations are involved in its development. Table 1 gives an overview (although non comprehensive) of the main organisations involved in the development and dissemination of practice guidelines on infectious diseases in the Netherlands, which are used in primary care, specialist care and public health. In 1997, the Dutch Cochrane Centre and Dutch Institute for Healthcare Improvement (CBO) founded a national platform of guideline organisations with the aim to harmonise the methodology and to promote EBM guideline development. The Dutch platform (Evidence Based Richtlijn Onderzoek; EBRO) is a network that facilitates guideline development and revision. Another task is the promotion and transfer of knowledge on EBM guideline development by organising conferences and educational programmes.\textsuperscript{29} Furthermore, in 2009 the Dutch Council for Quality of Healthcare (Regieraad) was established by the Minister of Health, Welfare and Sport, also conducting research into how guidelines are developed, implemented and updated.\textsuperscript{30} In the Netherlands, there is no official system of regulation of the evaluation of practice guidelines yet, nor are there mechanisms to assess implementation assessment. However, in 2004 Burgers et al. appraised the quality of CBO and NHG guidelines using the AGREE instrument and concluded that the quality of the CBO and NHG guidelines, in particular, the reporting of the methodology could be improved, in order to determine whether the guidelines are evidence-based.\textsuperscript{31}
The following section will discuss briefly two of the organisations producing practice guidelines for the prevention of infectious diseases most relevant to the studies presented in this thesis.

**The National Coordination Communicable Diseases Control**

The National Coordination Communicable Diseases Control (Landelijke Coördinatie Infectieziektebestrijding; LCI) was founded in 1995, to coordinate and enhance the collaboration of all partners involved in the (extramural) infectious disease control in the Netherlands, e.g. local PHS (or Geneeskundige en GezondheidsDienst; GGD), local and national government and policymakers. The LCI produces and publishes the national guidelines for communicable disease control (LCI-Richtlijnen). In addition to the national guidelines for communicable disease control, the LCI also produces national guidelines concerned with health policy, health programme strategies and outbreak management (LCI-Draaiboeken). During the past 17 years, 90 disease-specific guidelines have been published, including all 42 infectious diseases notifiable by Dutch law. Upon first publication many of these guidelines were based on informal existing guidelines produced by local PHS in the 1980s, and reflected expert-opinion on local agreements between several PHS. Nowadays, LCI-guidelines are developed under supervision of the LCI board of editors, which annually evaluates the need for revision and development of new guidelines, and subsequently appoints an author. Since 2006, the author executes a systematic review in order to make the LCI-guideline evidence-based. Before publication, all new and revised guidelines must be approved by a national multidisciplinary consensus group, in which a wide range of professional organisations and governmental institutions, e.g. PHS, the National Immunisation Programme, the Dutch Inspectorate of Health Care, and the National Coordination Centre for Travellers Health Advice, are represented. The final draft is endorsed by the National Health Council. Since 2005, the LCI is part of the Centre for Infectious Disease Control (CiB), the main body for infectious disease control in the Netherlands. The CiB, as part of the National Institute of Public Health and the Environment (RIVM), is funded by the government (Ministry of Health, Welfare and Sport).

**The National Coordination Centre for Travellers Health Advice**

In 1996, the Dutch National Coordination Centre for Travellers Health Advice (Landelijk Coördinatiecentrum Reizigersadvisering; LCR) was established to improve the uniformity of travellers' health advice and to increase the quality of
national vaccination centres. To reach the first objective, in 1996, the LCR published national guidelines for vaccinations and malaria prophylaxis for travellers (LCR-Protocollen). To reach the second objective, the improvement of the quality of national vaccination centres, the LCR published criteria for the quality of care in travel clinics and general practices. Most LCR-guidelines are disease-specific (most vaccine-preventable diseases), problem-based (e.g. the pregnant or immune-deficient traveller), or informative (e.g. on international health regulations). LCR-guidelines are developed, depending on its subject, e.g. by a working group on vaccination; on malaria; on nursing issues, or on quality of care issues. The working groups consist of a range of medical consultants and/ or nurses considered experts in the field of tropical medicine, epidemiology, and travellers’ medicine. In practice, the working group decides on the need for revision or development of a new guideline, and appoints an author, who writes a draft proposal. In quarterly meetings draft proposals are reviewed and discussed. Before publication, the final proposal has to be approved and accepted by a national LCR consensus group, whose members represent all professional organizations (e.g. PHS, travel clinics, academic hospitals, occupational health organisations, general practitioners, and Ministry of Health) involved with travel medicine in the Netherlands. The Dutch Inspectorate of Healthcare (IGZ), part of the Ministry of Health, Welfare and Sport, regards the LCR guidelines as professional standards. The LCR is a non-governmental organisation. The secretariat is a trust, and it does not receive public funding, nor sponsorship from the pharmaceutical industry. Expenses are covered by membership fees paid by travel health advisors. LCR-guidelines are available for paying members only, who have access to the guidelines in writing and online.
<table>
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<th>Organisation (year)</th>
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<th>Focus</th>
<th>Examples</th>
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<tr>
<td>Dutch Institute for Healthcare Improvement (Centraal BegeleidingsOrgaan; CBO) 1979</td>
<td>Department of TNO management consultants</td>
<td>Assist professional societies in development of EBM guideline and enhances appraisal. Dissemination of guidelines for guidelines Practice guidelines (NHG standaarden) for general practitioners (and partners in primary care)</td>
<td>Lyme borreliosis (2012) Varicella (2011) (with NVMM and NVDV)</td>
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<td>National Coordination Communicable Diseases Control (Landelijke Coördinatie Infectieziektebestrijding; LCI) 1995</td>
<td>Governmental</td>
<td>Practice guidelines and policies on infection control in Public Health</td>
<td>Health risks in child day care (2011) Requirements ship sanitation (2011))</td>
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<tr>
<td>National Coordination Centre for Travellers Health Advice (Landelijk Coördinatiecentrum Reizigersadviesing; LCR) 1996</td>
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Aim of this thesis

The research in this thesis aims to contribute to more evidence-based guidelines on the control of infectious diseases. In the Netherlands, most national guidelines for the prevention of infectious diseases are comprehensive and based on solid knowledge of the disease and its consequences. Yet many recommendations are still expert opinions based on practice- or knowledge, and not equally supported by evidence. Therefore the need for scientific evidence to support the recommendations in national guidelines remains high.

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 the PHS of Amsterdam. Most research questions arose from a lack of guidance in the national practice guidelines, others serve as evaluations of the effectiveness of existing recommendations. The outcomes are intended to improve the national practice guidelines, and to support the evidence and implementation of its recommendations.

Outline of this thesis

This thesis is divided in three parts, each relating to specific national practice guidelines or policy programmes.

Seroprevalence of varicella-zoster virus, parvovirus B19, and cytomegalovirus

The first part of this thesis (chapter 2, 3 and 4) relate to the LCI-guidelines on three viral skin rash infections common in children: varicella-zoster virus; parvovirus B19; and cytomegalovirus. In addition, chapter 4 relates to the NVAB practice guideline “Pregnancy, Postpartum Period and Work”, in which recommendations on pregnancy and the occupational risk of infection in day care centres are made. According to Dutch law, schools and child day care centres need to report all outbreaks of skin rash illness to the PHS. Depending on the diagnosis (or most likely diagnosis, and often case ascertainment is required), the PHS advises school- and child day care management on control measures, and gives health education on hygiene measures to control further spread of the pathogen. Although most skin rash infections in children are benign and self-limiting, risk groups for
complications, such as immune-compromised persons or pregnant women, need to be identified for disease specific investigation and management. In daily practice, the PHS is regularly consulted by pregnant women, who have been exposed to a child with a skin rash disease. In order to assess the risk of infections after exposure, sound epidemiological data on the presence of antibodies against these infections within the population, and knowledge about special risk groups without immunity is needed. However, for many infections, these data are rare or lacking completely.

The first two chapters describe two sero-epidemiological studies on the presence of IgG antibodies against varicella-zoster virus (chapter 2), and parvovirus B19 (chapter 3) among various ethnic groups in the Amsterdam adult population. Knowing that immunity may depend on the country of birth, the researchers anticipated to find differences in seroprevalence between people born in the Netherlands and immigrants. In chapter 4 the seroprevalence rates of IgG antibodies against varicella-zoster virus, parvovirus B19, and cytomegalovirus in women working in Amsterdam child day care centres in Amsterdam were estimated. By comparing these seroprevalence rates with data from Amsterdam women not working in day care, the association between occupation and infection in women working in child day care was assessed. Additionally, other likely determinants of seropositivity for varicella-zoster virus, parvovirus B19, and cytomegalovirus, such as age and ethnic origin, were investigated.

**Travel related diseases**

The second part comprises of two chapters relate to travel medicine, and the recommendations made in the LCR-guidelines on malaria and hepatitis B. Travel medicine practice guidelines offer guidance to the interdisciplinary range of health care workers practising travel medicine (consultants of internal and tropical medicine; public health consultants; occupational health consultants, general practitioners and specialised nurses). As a young discipline, however, the evidence base of many topic areas is still feeble, and the guideline development process is often dominated by expert opinion and experience, highlighting the need for more research and evaluation to support current recommendations.

**Chapter 5** describes the epidemiology and trends of all imported malaria in the Netherlands from 2000 to 2008.
In the Netherlands, the Malaria Working Group writes the LCR-guideline on malaria chemoprophylaxis for travellers. The recommendations in the practice guideline are based on the most actual epidemiology of malaria available, which needs regular updating as the epidemiology and drug resistance in parasites worldwide is ever changing. Surveillance of import malaria is specifically important to evaluate the effectiveness of the current recommendations, to identify trends, and guide the development of new strategies for prevention of import malaria. In this study travel statistics, and data on the use of malaria chemoprophylaxis are taken into account as well. In the Netherlands, despite the availability of adequate chemoprophylactic drugs in the Netherlands, imported malaria continues to cause considerable morbidity and mortality among returning travellers.

Chapter 6 evaluates whether the LCR-guideline (version 2008) on hepatitis B vaccination for travellers was adequate. All notified acute hepatitis B cases in Amsterdam between 1992 and 2003 were analyzed in order to answer the following questions: which proportion of acute hepatitis B infections is travel-related and imported from endemic countries? Is hepatitis B vaccination for all travellers necessary, or are particular groups more at risk of hepatitis B than others while travelling?

Sexually transmitted diseases in men having sex with men
The last part presents two chapters on the trends of sexually transmitted diseases among approximate 26,000 men who have sex with men (MSM) living in Amsterdam, and relate to the national HBV vaccination programme targeted at behavioural high risk groups. Amsterdam - about 800 000 inhabitants - is a popular residency for MSM from all over the world and hosts at least 26,000 MSM. Among Amsterdam MSM the incidence of sexually transmitted disease (STI) is much higher than in the general population and largely depending on changes in sexual risk-behaviour. After the introduction of combination antiretroviral therapy (cART) for human immunodeficiency virus (HIV) infected patients in the mid-1990s, the sexual risk-behaviour among MSM increased, followed by an increase of STI. In 2002, a hepatitis B vaccination programme targeting these behavioural high risk-groups was implemented nationally, following a pilot programme from 1998-2000 in several regions including Amsterdam.
In Chapter 7 data of all Amsterdam notifications of hepatitis A, acute hepatitis B, and shigellosis from 1992 to 2007, were compared with data from all patients newly diagnosed with gonorrhoea and infectious syphilis at the STI outpatient department of the PHS in Amsterdam. Though hepatitis A, acute hepatitis B, and shigellosis are not considered conventional STIs, their transmission within groups of MSM is known to be linked to sexual activities. Yet it is not known whether more risky sexual behaviour affects their incidence as it affects the conventional STIs like syphilis.

In chapter 8, the same data on notified acute hepatitis B in MSM were used, but supplemented with the notifications until 2011. In this study, incidence trends of acute hepatitis B in the Amsterdam MSM population are used to evaluate the impact of the hepatitis B vaccination programme targeted at MSM that began in 1998.
References


