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Electronically available symptom data

Usefulness and feasibility of syndromic surveillance and health care service improvements

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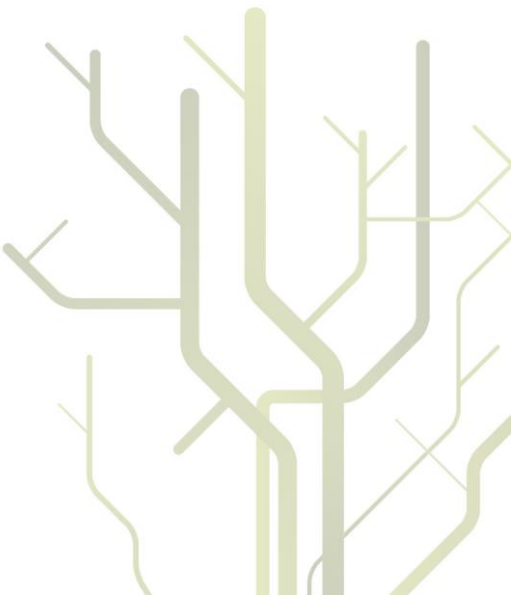

Content

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Summary

This is a thesis in the field of telemedicine and e-health. It is a cross-disciplinary field, making use of elements from information technology, medicine, and social sciences. These sciences have different traditions and are methodologically and theoretically different; therefore, it might be a challenge to choose and prioritise between methods and concepts from these fields of science. The aim with this thesis is not to develop new theories or models, but to be an empirically-based study in the field of telemedicine and e-health.

Background: The number of studies and examples of patients reporting symptoms electronically has increased greatly in recent years. This reporting of symptoms seems to be used in two main settings: to conduct *syndromic surveillance* to detect outbreaks of infectious diseases or to *improve health care service quality* through improved communication and interaction between the patient and the health care professional. Electronically available symptom data might also be extracted from the EPR or other sources for these purposes.

Objective: This thesis focuses on electronically available symptom data and its usefulness and feasibility with respect to syndromic surveillance and health care service improvements. Two main research questions are addressed:

1. Whether a new surveillance system is needed for GPs and patients, and if so, what is the most reliable and feasible data source? We consider both data extracted from EPR systems and pre-consultation symptom data reported by the patients themselves.
2. Could patients' electronic symptom reporting be feasible in health care service delivery, and if so, what impact does such reporting have on outcomes relevant to patients, health professionals, and health care systems?

Methods: Several studies were conducted, involving different methods and materials. Study 1 used individual, semi-structured interviews with five GPs. Study 2, objective 1 involves some data from the individual interviews, in addition to focus group interviews with eight additional GPs. Study 2, objective 2, involves telephone interviews of 1001 Norwegian citizens. Study 3 involves some data from the individual interviews, in addition to focus group interviews with ten additional GPs. Study 4 is based on a survey of a convenience sample of 83 respondents from Tromsø. A literature review based on a search of MedLine is conducted in study 5, and a systematic review of RCTs from several literature databases is conducted in study 6.

Results: GPs and patients would benefit from a new and better surveillance system. A combined surveillance approach, making use of both lab results and patient reported symptoms, would probably produce the best surveillance results of infectious conditions with regard to timeliness and reliability.
Patients' electronic symptom reporting seems to be feasible in health care service delivery, especially within self-management, and partly within consultation support. Electronic symptom reporting does, in general, have a positive impact on outcomes relevant to patients, and to some extent, health professionals and health care systems.

Conclusion: Possible synergies between improving health care service delivery and providing timely syndromic surveillance could be achieved through patients reporting their symptoms electronically before their GP consultations. However, further research should be carried out prior to a large-scale implementation of such a service.

List of Papers

1) Johansen MA, Scholl J, Aronsen G, Hartvigsen G, and Bellika JG. An exploratory study of disease surveillance systems in Norway. J Telemed Telecare, 2008, 14 (7): 368-71.

2) Johansen MA, Johnsen JA, Hartvigsen G, Ellingsen G, Bellika JG. Bridging the gap between patients' expectations and general practitioners' knowledge through disease surveillance. MIE, 2009, Sarajevo. Stud Health Technol Inform, 2009, 150: 423-7.

3) Johansen MA, Scholl J, Hasvold P, Ellingsen G, Bellika JG. "Garbage in, garbage out": extracting disease surveillance data from EPR systems in primary care. Proceedings of the 2008 ACM conference on computer supported cooperative work; San Diego, CA, USA: ACM; 2008.

4) Johansen MA, Berntsen G, Shrestha N, Bellika JG, Johnsen JA. An exploratory study of patient attitudes towards symptom reporting in a primary care setting. Benefits for medical consultation and syndromic surveillance? Methods Inf Med, 2011, 50 (5): 479-86.

5) Johansen MA, Henriksen E, Berntsen G, Horsch A. Electronic symptom reporting by patients: a literature review. MIE, 2011, Oslo. Stud Health Technol Inform, 2011, 169: 13-7.

6) Johansen MA, Henriksen E, Horsch A, Schuster T, Berntsen GK. Electronic symptom reporting between patient and provider for improved health care service quality: a systematic review of randomized controlled trials. Part 1: state of the art. J Med Internet Res 2012; 14(5): e118.

7) Johansen MA, Berntsen GK, Schuster T, Henriksen E, Horsch A. Electronic symptom reporting between patient and provider for improved health care service quality: a systematic review of randomized controlled trials. Part 2: methodological quality and effects. J Med Internet Res 2012; 14(5): e126.

1 Introduction

E-health can be referred to as “an emerging field in the intersection of medical informatics, public health and business, referring to health services and information delivered or enhanced through the Internet and related technologies” [1]. The intent of patient involvement and enhanced communication among health care providers is to increase efficiency, improve quality, empower patients, and encourage new relationships between patients and health professionals towards making shared decisions, as well as educating physicians [1].

Generally, patients have only reported their problems and symptoms to their health care providers orally and during a consultation. However, as traditional patient and provider roles change [2] and patients becomes more and more motivated to use electronic services [3-6], we find an increasing number of examples and trials where patients communicate their symptoms electronically to their health care providers [7-21]. In addition, patients are willing to report symptoms for the purpose of benefitting others [5, 22-24], and symptoms might also be extracted from the electronic patient record (EPR) or other sources for this purpose.

Symptom reporting seems to be used in two main settings:

- On the population/public health monitoring level, where the reported symptoms are *used or re-used for syndromic surveillance*. The collected, aggregated, and analysed symptom data can then be useful in a patient–provider setting as diagnostic support.
- On the individual level, to *improve health care service quality* through improved communication and interaction between the patient and the health care professional, so that health issues are resolved more efficiently, with higher quality, and in any way that improves the quality of life (QoL) of the patient.

In this thesis, both settings are explored. First, issues related to the use or re-use of symptoms for syndromic surveillance are investigated. Secondly, the thesis focuses on patients reporting symptoms electronically to improve the quality of health care services. Seven papers are included in the thesis. The first three focus on the syndromic surveillance setting [25-27], the fourth focuses on both settings [28], and the last three focus on the improved health care service setting [17, 29, 30]. The syndromic surveillance studies were published in 2008–2009, and the studies focusing on improved health care service in 2011–2012. Because the syndromic surveillance field has developed a great deal since 2008, more space and time has been necessary to provide “state-of-the-art” and updated references for this part.

The next two sections provide an introduction and background for 1) the syndromic surveillance setting and 2) the improved health care service quality setting. The third section presents the research questions and the corresponding study objectives and papers, while section four explains definitions used in the introduction.

1.1 Usefulness and feasibility for syndromic surveillance

Patients today report symptoms through the Internet for public health surveillance [22-24, 31], or the general physician (GP)/physician reports to the health authorities, or, most commonly, the public

health surveillance systems make use of symptom or similar data already collected for other purposes. Surveillance is recognized as "the single most important public health instrument for identifying public health events of global concern, particularly infectious diseases that are emerging" [32], p. 104. Because infectious diseases cause approximately one-quarter of all deaths worldwide [33], the detection of outbreaks is highly prioritized by the World Health Organization (WHO) [34]. Surveillance is defined by the WHO's 194 member states through the International Health Regulations as the "...systematic ongoing collection, collation and analysis of data for public health purposes and the timely dissemination of public health information for assessment and public health response as necessary" [35], p. 10. According to this international agreement, countries are required to "notify WHO of events that may constitute a public health emergency of international concern" [35].

Traditionally, reporting in disease surveillance has been based on a linear "bottom-up" process [36], p. 17, where a sick person is examined by his/her physician, followed by laboratory examinations. If the lab results identify any suspicious condition or are recognized as being unusual in trends or numbers and subject to surveillance, these findings are reported to the local health authorities. The local health authorities then inform the national health authorities of the surveillance findings, which in turn notify the WHO, and possibly other international agencies, if the findings are of global concern. The drawback with this conventional reporting process is that it takes a long time and is not efficient for initiating an intervention to reduce or stop an outbreak or attack.

The more real-time extraction and presentation of surveillance data that can be provided, the greater is the value of the systems for early disease detection and monitoring of the spread of an outbreak [37]. Syndromic surveillance, or symptom-based surveillance, refers to monitoring of symptoms or other evidence of a disease that exist at a stage before a confirmed diagnosis [37-39]. Most typically, syndromic surveillance solutions monitor sets of symptoms (fever, respiratory complaints, diarrhoea, etc.) in a geographic region without regard to the confirmed diagnoses [40]. Symptoms or syndromic surveillance systems might thus identify a disease outbreak at a much earlier stage than conventional methods. Syndromic surveillance is also considered to be useful for other health purposes. Examples here are quality improvement, epidemiology, and patient safety [37], in addition to research [37, 41]. It might also contribute to clinical medicine [37] by making clinicians aware of community trends at an early stage [42], thus enabling them to issue the right tests and improve their diagnostic accuracy.

A great deal of resources and money have been spent, especially after 9/11 and the anthrax threats in 2001, to establish new and better surveillance systems [32, 39, 43, 44]. A literature review in 2006 to determine the value of syndromic surveillance systems in identifying disease outbreaks or bioterrorism treats identified 71 articles, but only 13 contained an evaluation of one or more performance indicators [38]. Despite this vague outcome documentation, the use and popularity of syndromic surveillance is growing [32, 45, 46]. A Google search identified almost 675,000 entries for the term "syndromic surveillance", and a search in Medline (2012.09.18) for "syndromic surveillance.tw" resulted in 378 scientific publications since 2001.

Today, we have a new frontier in syndromic surveillance based on logging the symptoms that patients search for via Internet search engines or though medical websites [47-53]. We also have

other surveillance Internet solutions, not based on symptoms, but on Internet media reports [54]. These Internet solutions demonstrate a promising potential regarding timely detection of outbreaks, and they could clearly reduce costs and increase reporting transparency, both on the national level and in larger regions [47-54]. For example, Google Flu trend surveillance has demonstrated "good to excellent correlation with both the number of positive influenza tests and the number of patients presenting to the ED"[1], p. 467 [53]. In addition, the system is able to provide near-real-time surveillance data 1–2 weeks ahead of the US Centers for Disease Control and Prevention (CDC) Influenza Sentinel Provider Surveillance Network [47].

To be useful during consultations, "local data" are required

Syndromic surveillance data is suggested as useful for clinicians [37], to provide diagnostic aids, by comparing their patient's symptoms with possible disease outbreaks. However, for the physicians to make use of the surveillance information during a consultation, surveillance data must be presented for the populations where the patients live, work, or travel. This is supported by the quote by Greenlick [55] we referred to in paper 1 [25], stating that ". . .the probabilities that a physician faces with an individual patient in a given circumstance are specific to the characteristics of the population from which that patient comes. A physician who does not have data on these specific populations does not have all of the relevant knowledge necessary to treat the patient." Thus, for the syndromic surveillance information to be useful in a consultation or another diagnostic setting, there is a need for systems that extract and present timely information that is representative of local geographic areas. Timely information, in this context, is either real-time information or as close to real time that is necessary to provide a representative disease map that covers the local population.

In addition to being timely, to be useful in a clinical setting, the validity/accuracy of the syndromic surveillance system would depend on the quality of the collected and presented data [56-58]. The actual gold standard for data accuracy is described as "the true state of the patient", which is an ideal that generally is difficult or impossible to achieve [57]. However, data from a smaller area requires that the methods of detection have very high sensitivity[2], while maintaining an acceptable level of specificity[3], in order to be able to detect an outbreak.

In fact, it is a challenge to detect smaller or more localised outbreaks [38, 43, 45, 46, 59-62]. While some solutions have been demonstrated to be of high sensitivity [46, 62], others have failed [59-61], and some struggle with a considerable burden of false alarms (low specificity) [38].

Concerns regarding secondary use of data

There are two actors of special interest regarding the use or re-use of reported symptoms for syndromic surveillance in the Norwegian health care system—the patient and the GP. The patient is the one who experiences the symptoms, and as such, is the only actual real-time source for syndromic surveillance. The GP is normally the first health professional patients seek out when they do not feel well. Therefore, extracting syndromic surveillance information directly from the patient

[1] ED = emergency department

[2] Sensitivity = the proportion of actual positives which are correctly identified as such

[3] Specificity = the proportion of negatives which are correctly identified

or from the GP, or from one of the systems through which the GP reports patient data (EPR, lab referrals, other referrals), seems to be a promising and natural source.

Therefore, extracting symptom data from existing systems established for other purposes [38, 62-64] is a natural first step to investigate when establishing a new syndromic surveillance system, as information already recorded could be reused. As pointed out in paper 4, "secondary use of clinical data, for instance structured documentation from the electronic patient record (EPR), unstructured narrative text, or laboratory results, is expected to have large potential" [28, 65], at the same time as "the necessary technologies are available to extract and present surveillance data from EPRs, laboratories, and hospitals" [28, 66]. In this setting, it is important to be aware that data entered into the EPR or lab request by health professionals is produced in a totally different context and intended for purposes other than disease or syndromic surveillance. As the use of data for secondary purposes influences data quality, information should be disentangled from the context in which it is produced [67], and transformed into the new surveillance context. "This process is particularly challenging with regard to real time data" [28].

As a second step, it is natural to investigate how feasible it is to extract syndromic surveillance information directly from the patient. Self-reported symptom information from patients and families has been demonstrated at an ED waiting room of a children's hospital [68]. The patient-reported information was found to be significantly more sensitive in identifying disease categories than the data that was used by the national and regional disease surveillance systems [68]. This supports the assumption that patients reporting symptoms electronically might provide a feasible data source for syndromic surveillance, also locally.

Research challenges:
For syndromic surveillance data to be found useful in a consultation or other clinical setting, it must be near real time and have high sensitivity and an acceptable level of specificity. Thus, at present, a main challenge to the utilisation of a future surveillance system is to determine the most feasible data sources providing timely data of proper quality [69, 70], and if possible, data that is produced for the purpose of symptom-based surveillance.

However, before deciding on the most feasible sources for syndromic surveillance, it is important to investigate the actual need for a new syndromic surveillance system, and to provide a deeper understanding of the practices in which the current systems are used [67, 71], both from a GP and a patient perspective.

1.2 Usefulness and feasibility for improved health care service quality

Patient-reported symptoms are useful in the syndromic surveillance setting, but not only there. Electronic symptom reporting can be seen as a general tool for effective communication between patients and health professionals, and therefore, it could be an important contributor to the improvement of the quality of the health care service. Electronic symptom reporting could become a tool to promote patient-centred health care [2, 72] and shared decision making [73, 74], at least in countries with high e-readiness [75].

Research indicates that electronic communication supports self-disclosure [76, 77], also in pre-clinical and clinical settings [78-84]. Patients report more symptoms, more serious symptoms, and with greater precision through electronic reporting compared with oral interviews [85, 86]. As these findings indicate, there might be both qualitative and quantitative improvements if the patient reports and rates symptoms in a less stressful situation, compared to symptom reporting and symptom ratings obtained in a traditional medical setting. Therefore, health care service improvements through electronic symptom reporting should be possible to achieve for the *patient*, the *health care professional*, and *the health care system in general*.

Patients have difficulty correctly remembering symptom levels past the last few days [87], and older patients do not report most of their symptoms to health professionals [88]. This might be one explanation for why some patients receive inadequate symptom management [89, 90]. Another explanation is that pain and other symptoms are not adequately assessed [89, 90]. Therefore, a standardised method for registering and assessing pain and other symptoms is recommended [89]. Conducting this type of patient-centred care while also providing safe and efficient care supports the use of information technology [91]. These challenges point in the direction of pre-consultation electronic symptom reporting solutions. Ideally, it should be possible to report symptoms shortly after they have appeared, and under circumstances that give patients a chance to convey their problems in a less stressful situation and help them to a clear and concise understanding of their clinical problem. The reported information should then be stored in the electronic patient record.

Indeed, patients are enthusiastic about reporting symptoms electronically pre-consultation [5, 28, 92-94], and they are even positive towards using it to benefit others [5]. They believe it will improve the effectiveness and quality of care [28, 93]. For instance, when 2027 patients had the opportunity to submit symptom information before a consultation, 70% actually did so [95]. In addition, studies demonstrate that information about patient preferences affected clinicians in clinical decision making and improved patient outcomes with regard to self-care[4] [96, 97], physical functioning [96], and higher preference achievement [96, 97], where higher preference achievement correlated with greater patient satisfaction [96]. Another study refers to significantly less symptom distress and depression, as well as improved self-efficacy [98]. Reporting symptoms electronically pre-consultation makes patients feel more prepared for the visit, and they also feel that their provider has more accurate information about them [95].

As mentioned in the introduction to paper 6 [30], trials in which patients report symptoms electronically mainly divide the patients into two groups: one group for “complex conditions where it is challenging to cover all relevant issues during one short visit”, as in mental health issues [3, 7, 8], neurological disorders [9], congestive heart failure [10, 11], asthma [12, 13, 99], cancer [14], and pain [15]; and a second group for less severe problems, such as atopic eczema [16], follow-up after surgery [17-19], and general primary care settings [20, 21, 95].

For the **health care professional**, oral communication with the patient is normally crucial to determine the patient’s main problem or concern. However, this communication can be very challenging, especially when no objective parameters are presented [100]. Likewise, as pointed out in

[4] Functional performance to maintain life, health, and well-being

paper 7, “studies of interview styles show that physicians elicit only about 50% of the medical information considered important in a consultation” [29, 101]. However, results from written, paper-based pre-consultation reporting have demonstrated that pre-reporting symptoms facilitates communication and can raise physicians’ awareness of their patients’ health issues [102, 103]. Therefore, electronic symptom reporting has the potential to improve both the patient’s perceived quality of consultation and the diagnostic process.

At the **health care system** level, implementation of computerised technology suggests that more time is made available for direct patient care [104]. Computerised systems that present clinicians with relevant clinical information during the diagnostic process can contribute to a strengthened focus on key variables and implementation of a uniform care process, while at the same time avoiding information overload [105]. In addition, review of symptoms through e-consultations could reduce the number of face-to-face consultations [106]. According to trials within primary care, probably more than one-third of face-to-face consultations can be substituted [20, 21]. In addition, pre-consultation electronic collection of medical information from the patient (or the parents on behalf of a minor) has demonstrated improved documentation [12, 107] and impact on quality [108], and fewer incorrect actions for pain treatment [107].

It also should be possible to reduce the use of resources in the specialist care setting. For example, the number of surgery cancellations could be reduced [109-111] that are due to outdated, inadequate, and even wrong patient information at the time of surgery [112, 113].

Research challenges:
The field of “electronic symptom reporting” is new and unexplored. It is necessary to assemble the knowledge that already exists regarding the possible use, effect, and benefits to improving the quality of health care services from the patient, health professional, and health care system perspectives. This effort includes identifying the patient groups, technologies, health service innovations, and research targets that seem to be feasible and relevant for electronic symptom reporting to improve health care service quality in general.

1.3 Research questions and study objectives

Against the background presented in the previous sections, the purpose of this dissertation is to examine the **usefulness** and **feasibility** of electronically available symptom data, both for **syndromic surveillance** and for **health care service improvements.** To address the usefulness and feasibility of syndromic surveillance, the focus will be on Norway.

Two main research questions are addressed:

1. Whether a new surveillance system is needed for GPs and patients, and if so, what is the most reliable and feasible data source? We consider both data extracted from EPR systems and (pre-consultation) symptom data reported by the patients themselves.
2. Could patients’ electronic symptom reporting be feasible in health care service delivery, and if so, what impact does such reporting have on outcomes relevant to patients, health professionals, and health care systems?

The main research questions are translated in this thesis to the four concrete research questions presented below. The first usability question [u1] and feasibility question [f1] address aspects of the first main research question, while [f2] and [u2] address aspects of the second main research question.

- How useful do GPs find the current surveillance system, and does there seem to be a need for a new surveillance system in the GP and patient perspective? [u1]
- Which data collection procedures seem to be feasible for syndromic surveillance, and do the data hold the necessary quality? [f1]
- Which patient groups, technologies, health service innovations, and research targets have been suggested as feasible and relevant for electronic symptom reporting to improve health care service quality in general? [f2]
- What possible uses, effects, and benefits of improved health care service quality can be found in a patient, health professional, and health care system perspective? [u2]

The cross-links among the thesis research questions, the study-specific objectives, and the articles responding to the objectives are given in Table 1.

Table 1 The four research questions with regard to usefulness (u) and feasibility (f), and the corresponding study objectives and papers

Research questions	**Study specific objectives**	**Paper**
How useful do GPs find the current surveillance system, and does there seem to be a need for a new surveillance system in a GP and a patient perspective? [u1]	Gathering GPs' experiences using the current system, run by the Norwegian Institute of Public Health (NIPH), for contagious disease surveillance in Norway. Gathering GPs' high level user requirements related to future systems.	*"An exploratory study of disease surveillance systems in Norway" [25]* And partly, *"Bridging the gap" [26].* (Please see the overlap section in the method chapter.)
	Investigating to what degree patients trust their regular GPs to be fully informed about the prevalence of infectious diseases in their neighbourhood, and what GPs actually know.	*"Bridging the gap between patients' expectations and general practitioners' knowledge through disease surveillance" [26]*
Which data collection procedures seem to be feasible for syndromic surveillance, and do the data hold the necessary quality? [f1]	Investigating GPs' use of the EPR system and the effect this has on data content, such as symptoms reported by patients and diagnoses reported by GPs.	*"Garbage in, garbage out"- extracting disease surveillance data from EPR systems in primary care [27]* And partly, *"An exploratory study of disease surveillance systems in Norway" [25].* (Please see the overlap section in the method chapter.)
	Analysing whether and how health information and symptoms of satisfactory quality can be extracted, in a GP and EPR setting, to identify alternative options for extraction of surveillance data.	*"Garbage in, garbage out"- extracting disease surveillance data from EPR systems in primary care [27]*
	Investigating how and from whom GPs are informed about the prevalence of infectious diseases in their neighbourhood.	*"Bridging the gap between patients' expectations and general practitioners' knowledge through disease surveillance" [26]*
	Investigating Northern Norwegian citizens' attitudes towards providing symptom information electronically before a	*"An exploratory study of patient attitudes towards symptom reporting in a primary care setting.*

	consultation, as well as how they prefer to carry out the reporting and attitudes towards the storage, use, and presentation of symptom data in general, and in a symptom-based surveillance setting in particular.	*Benefits for medical consultation and syndromic surveillance?" [28]*
Which patient groups, technologies, health service innovations, and research targets have been suggested as feasible and relevant for electronic symptom reporting to improve health care service quality in general? [f2]	Establishing an overview of the clinical settings and technologies for which symptom reporting tools that have been examined in previous scientific studies (based on review of abstracts) might be useful	*"Electronic symptom reporting by patients: a literature review" [17]*
	Clarifying what has been investigated in RCTs so far regarding different patient groups, health service innovations, and research targets relevant for electronic symptom reporting to improve health care service quality (systematic review)	"*Electronic symptom reporting between patient and provider for improved health care service quality: a systematic review of RCTs. Part 1: State of the art" [30]*
What possible use, effect, and benefits of improved health care service quality can be found in a patient, health professional, and health care system perspective? [u2]	Assessing the methodological quality of the RCTs identified in the first part of the review. Summarizing the effects and benefits of electronic symptom reporting from data published in the methodologically best RCT articles. Benefits are presented with regards to patients, health care professionals, and health care systems.	*"Electronic symptom reporting between patient and provider for improved health care service quality: a systematic review of RCTs. Part 2: Methodological quality and effects" [29]*

1.4 Definitions

With electronic symptom reporting, we refer to text-based symptoms reported through off-line or on-line systems, on computers, or on mobile phones with Internet access, WAP, or SMS. Symptoms reported through electronic communication that require the patient and health care personnel to be present simultaneously, like video conferencing, instant messaging, or chat, are not included in our definition. Electronically available symptom data is thus defined as "Text-based symptom data that is stored on an electronic unit, either temporarily or for a longer time".

Usefulness related to positive **effects on health care** refers to the evaluation of and to what extent an intervention or a system is found to be useful **for the patient, the health professional, or the health care system**. The determination of usefulness belongs to both the health care professionals and the patients [114]. Usefulness refers to what might actually be proven useful with regard to improved clinical outcomes and efficiency. It also refers to the patients' and health care professionals' personal experiences and preferences regarding what they consider useful, and why.

A health professional is a person "who has completed a course of study in a field of health, such as a registered nurse, physical therapist, or physician. The person is usually licensed by a government agency or certified by a professional organization"[5]. A **health service** is "services for the diagnosis and treatment of disease and the maintenance of health"[6].

[5] http://medical-dictionary.thefreedictionary.com/health+professional. Retrieved September, 2012
[6] MeSH definition through http://ovidsp.uk.ovid.com/sp-3.5.1a/ovidweb.cgi September, 2012

Health care system is used for "delivery of health care", the "concept concerned with all aspects of providing and distributing health services to a patient population"[7]. **Health care quality** or **quality of care** refers to "the levels of excellence which characterize the health service or health care provided based on accepted standards of quality"[8]. The Committee on Quality Health Care in America, Institute of Medicine (IOM) concludes, in their strategy "to improve the American health care delivery system as a whole, in all its quality dimensions" (p. 2), that care must be delivered by systems that are designed to be "Safe, Effective in terms of health benefits (Mortality, Morbidity and Quality of Life), Patient-centered, Timely, Efficient and Equitable" [115]. This quality concept inspired the Norwegian health ministry to develop a similar strategy[9].

The terms **contagious, communicable,** and **infectious disease** are used synonymously, referring to "*a disease whose causative agents may pass or be carried from one person to another directly or indirectly. Modes of transmission include (1) direct contact with body excreta or discharges from an ulcer, open sore, or respiratory tract; (2) indirect contact with inanimate objects such as drinking glasses, toys, or bedclothing; and (3) vectors such as flies, mosquitoes, or other insects capable of spreading the disease*." [10] While the term "contagious disease" originally referred to only points 1 and 2[11], and such represented a subset of communicable or infectious diseases, the term is often used in a broader way today to mean *any* communicable or infectious disease[12].

[7] MeSH definition through http://ovidsp.uk.ovid.com/sp-3.5.1a/ovidweb.cgi September, 2012
[8] MeSH definition through OVID September, 2012
[9] …og bedre skal det bli! http://helsedirektoratet.no/publikasjoner/nasjonal-strategi-for-kvalitetsforbedring-i-sosial--og-helsetjenesten-og-bedre-skal-det-bli-2005-2015/Publikasjoner/nasjonal-strategi-for-kvalitetsforbedring-i-sosial--og-helsetjenesten-og-bedre-skal-det-bli-2005-2015.pdf. September, 2012
[10] Miller-Keane Encyclopedia and Dictionary of Medicine, Nursing, and Allied Health, Seventh Edition, 2003 by Saunders, an imprint of Elsevier, Inc. http://medical-dictionary.thefreedictionary.com/communicable+disease Retrieved September 03, 2012
[11] Merriam-Webster dictionary definition of contagious diseases, http://www.merriam-webster.com/medical/contagious+disease Retrieved September 03, 2012
[12] contagious disease = communicable disease, A Dictionary of Nursing, 2008. Retrieved September 03, 2012 from Encyclopedia.com: http://www.encyclopedia.com/doc/1O62-contagiousdisease.html

2 Methods and Materials

An overview of the methods and main materials used, and when the studies were conducted, is presented in Table 2. The presentation in the table and the following sub-chapters are ordered according to papers; where the two last papers belong to the same study. The analysis part is not included in the table.

The next sections briefly present the interpretative study approach used in studies 1, 3, and (partly) 2, followed by how the data collection, through individual and focus group interviews, was conducted in general. Some overlap in subject, methods, and reporting is reported in a separate section; where Figure 1 illustrates the relation between study and data collection on one side and papers on the other side.

The main focus of this chapter, however, is to present briefly each study included in this thesis. The study presentations start with the objectives as they are presented in Table 1, as objectives and methods and materials are closely linked. The methods and materials presentation starts with an argumentation for *choice of method*, followed by *sample*, *data collection, and analyses* and *ethical considerations*. The *methodological strengths and limitations* are addressed in the discussion section (Chapter 4). The presentation tries not to repeat too much of the text already presented in the papers, but obviously, there will be some overlap. In addition, method and material issues not addressed previously, due to lack of space in the individual papers, will be presented.

Table 2 Overview of the methods and main materials used in each paper, and when the study was conducted.

Study	Paper (P)	Methods	Material in "Number of"	Year conducted
1	P1. An exploratory study of disease surveillance systems in Norway [25]	M[a]: Individual, semi-structured interviews. S[b]: Informal discussions and review of electronic and paper-based documents	M: 5 GPs (one of them responsible for informing GPs in their region about potentially serious outbreaks)	2007
2	P2. Bridging the gap between patients' expectations and general practitioners' knowledge through disease surveillance [26]	M1: Survey based on telephone interviews; randomised sample M2: Individual, semi-structured interviews; focus group interviews S2: Informal discussions	M1: 888 Norwegian citizens (1001 participated) M2: 13 GPs[c]; 5 individual GPs[d] and 8 additional GPs through the first interview with the two focus groups[e]	M1: 2007 M2: 2007–2008
3	P3. "Garbage in, garbage out" - extracting disease surveillance data from EPR systems in primary care [27]	M: Individual, semi-structured interviews; focus group interviews S: Informal discussions and review of electronic and paper-based documents	M: 15 GPs[c]; 5 individual GPs[f] and 10 additional GPs in two focus groups[g]. S: 10 physicians[h]; technical staff.	2007–2008
4	P4. An exploratory study of patient attitudes towards symptom reporting in a primary care setting. Benefits for medical consultation and syndromic surveillance? [28]	M: Survey based on convenience sampling	83 respondents from public locations in Tromsø, Norway	2009
5	P5. Electronic symptom reporting by patients: a literature review [17]	M: Literature review of abstracts	Search in Medline; 974 different references identified; 235 included	2010

Study	Paper (P)	Methods	Material in "Number of"	Year conducted
6	P6. Electronic symptom reporting between patient and provider for improved health care service quality: a systematic review of RCTs. Part 1: State of the art [30]	M: Systematic review of RCTs.	Search in Medline, EMBASE, PsycINFO, Cochrane Central Register of Controlled Trials, and IEEE Xplore; 642 records identified; 32 articles representing 29 studies included	2011
	P7. Electronic symptom reporting between patient and provider for improved health care service quality: a systematic review of RCTs. Part 2: Methodological quality and effects [29]	M: Systematic review to assess the methodological quality of the RCTs and summarize the effects and benefits of the methodologically best studies	32 articles representing 29 studies	2011–2012

[a] M = Main method; describes the primary data collection method is use.
[b] S = Secondary method; describes the other data collection methods in use.
[c] Please see the "Overlap" section and figure 1 under methods
[d] Some data from the interviews which mainly collected data for paper 1 [25]
[e] Which also collected data for paper 3 [27].
[f] Some data from the same interviews which collected data for paper 1 [25] and paper 2 [26].
[g] Other data from these interviews is used in paper 2 [26]. Two interview with group 1 and three with group 2.
[h] Four in depth and six only through one common meeting

An interpretative study approach

Studies 1 and 3, as well as one part of study 2, make use of an interpretative study approach. Interviews were used as the primary data collection method in studies 1 and 3 and one of the two parts of study 2. Interviews are considered to provide outside observers with the best access to the users' interpretation of their own situation [116]. Interpretive research intends to produce deep insight by focusing on human actions and interpretations regarding development and use of computer-based information systems [116, 117]. In interpretive research, knowledge is gained "through social constructions such a language, consciousness, shared meanings, documents, tools, and other artifacts" [117] p. 69, and all available data sources are taken into consideration during the interpretation process [117].

The data analysis is based on a hermeneutics approach, in which one attempts to provide an understanding of the "complex whole" through preconceptions about "parts and their interrelationships" [117] p. 71. As an interviewer, it is important to be open to the field data and to be "willing to modify initial assumptions and theories" [116] p. 76, as well as to confront "preconceptions (prejudices) which guided the original research design (i.e., the original lenses) with the data that emerge through the research process" [117] p. 76. In reality, the data collection and analysis was an iterative process with "initial theories being expanded, revised, or abandoned altogether" [116] p. 76. As an interviewer, this meant that one often had to present one's interpretation to the respondents, to check if you as the interviewer had interpreted their statements correctly. New and improved understanding in one stage was used as a starting point for the next stage in collecting and analysing the data [117]. For example, the assumption that all GPs reported all their patients' symptoms by use of the International Classification for Primary Care (ICPC) code system [118], was the reason the ICPC codes were initially suggested as the primary data

source for syndromic surveillance. This assumption had to be modified, and it went through several stages.

Data collection through individual and focus group interviews

As the individual and focus group interviews were both more or less conducted following the same principles, they are presented together. Two researchers participated in all the interviews; one was the PhD candidate. All interviews were recorded, except one of the individual interviews. Recording is recommended for interviews in general [119], and especially because it is "vital in an interpretive study to 'capture' people's interpretations" in an effective way [116] p. 78. Recommendations were followed regarding taking notes during all the interviews and writing a summary of the interviews immediately after they took place [119]. These summaries were anonymised and forwarded to the research group working with syndromic surveillance. In the focus group interviews, the researcher decided which questions to focus on, and it was the interaction among the participants that produced the research data. During these group discussions, individuals shifted opinions due to the influence of other comments or their opinions persisted. In the focus group interview, the second researcher had a special responsibility to observe whether some of the respondents dominated the debate, as well as to take notes. The recorded interviews were transcribed by a third person. However, the "representation of audible and visible data into written form is an interpretive process which involves making judgments" and therefore, is an important step in analysing the data [119] p. 130. Therefore, the PhD candidate checked the transcriptions by listening to the interviews while following the text, and strengthened it by adding missing text and adding information regarding context and body language (non-verbal dimensions of the interaction), as suggested by Bailey [119]. All verbal interactions such as laughs and interruptions were also included, even though it could clutter the text, because this information was useful to remember the situation and interpret the interview.

When transcribing the interviews, the respondents were identified by one letter. The legend identifying the actual respondents by letter was saved in a separate, secure place. This made it possible to contact two respondents by telephone to clear up statements that could be interpreted in different ways.

Overlap in topics, data sources, method, and reporting

Papers 1, 2, and 3 address some overlapping topics, and to some extent, use data from the same interviews (Figure 1). This data is mainly used to address different research questions.

Most of the results from the individual interviews (study 1) are presented in paper 1 [25], while some other results are presented in paper 2 [26], and some in paper 3 [27]. In addition, the results from these individual interviews were used as a basis for the focus group discussions in studies 2 and 3. All three studies also made use of informal discussions, which were partly overlapping, and both studies 1 and 3 included reviews of electronic and paper-based documents.

Unfortunately, there were also some overlaps in the reporting of the results. In paper 2, when investigating whether some results from the individual interviews were confirmed through the focus groups, every result from the individual interviews published in paper 1 and reported in paper 2 refers to the first/original publication. However, results based on the document reviews (that the

MSIS reports are published every second week), and information based on the informal discussions (that the MDPD informed the GPs about serious cases in the municipality) are reported in both papers 1 and 2. Paper 2 should have referred to paper 1, but the reference was omitted by mistake.

In paper 3, a general reference to paper 1 is included, saying that "Some results from these interviews [the individual interviews] have been previously reported [18]", [27] p. 527. This was done due to space limitations, but it is not a very good way to make a reference. Every result presented in paper 1 should have been referred to when presented in paper 3. It is the results presented under the paragraph "Attitudes towards the ICPC codes" in paper 1 [25] that are reported also in paper 3 [27], and then mainly in the paragraph "The ICPC-code System" in paper 3. The same quote is even presented without making a reference. The result reported in paper 3, however, is based on both the individual interviews and the focus group interviews.

There is an overlap in topic and method for the review papers (papers 5, 6, and 7) as well. The search terms used in the systematic review (papers 6 and 7) were a further development of the search terms developed for the literature review (paper 5). However, the literature review provides a simple overview in numbers of technologies and patient groups, without any limitation regarding study methodology, while the systematic review provides a thorough investigation of RCTs with regard to patient groups, health service innovations, and research targets. As the study objectives are so different, this overlap should not cause any double reporting of results, even though some of the RCTs are represented in both studies.

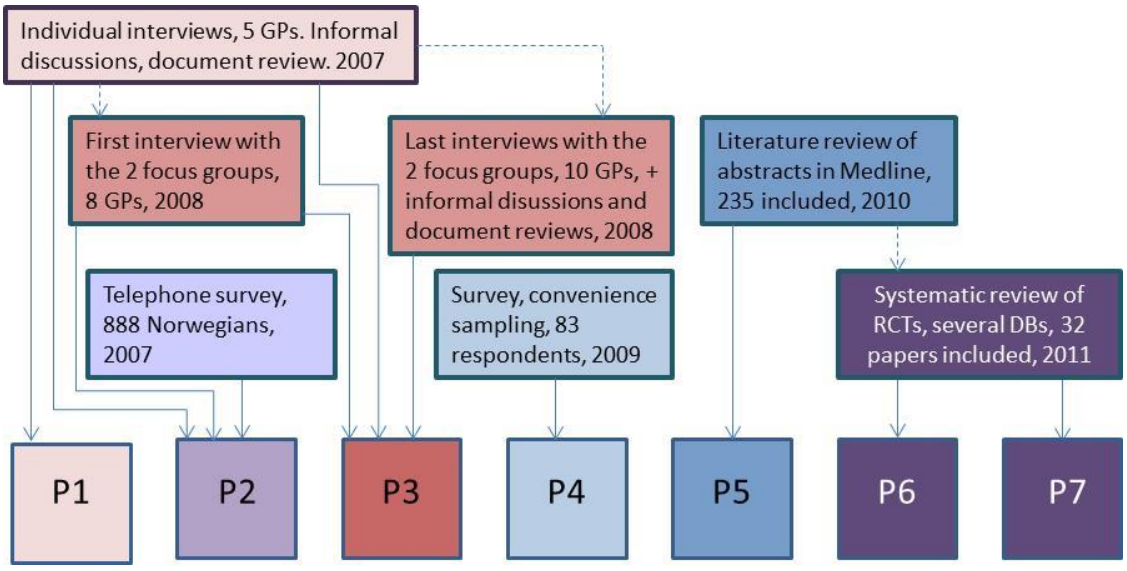


Figure 1 The relation between study and data collection on one side, and papers P1–P7 on the other side. The dotted line illustrates that results from the individual interviews were used as input for the focus group interviews, and that search terms and results from the literature review were used as input for the systematic review searches. Two boxes represent the focus groups interviews—one for the first interview with each group and one for the last. There was a total of nine GPs represented in the first interview with the two groups, and a total of 11 GPs in the last interviews; however, one person overlapped with the individual GPs, resulting in eight and ten new GPs, respectively.

In addition to the overlaps in the papers included in the thesis, there is an overlap between paper 4 [28], and a paper sent to the 13th World Congress on Medical Informatics (MedInfo), held in South Africa in September 2010 [120]. The reason for this overlap is that 18 conference papers, out of 603 submitted (see Appendix A), were invited to be extended and submitted as full papers in one of two different journals. Twelve papers were reviewed for publication in Methods of Information in Medicine, where my paper was one of five that were accepted [121].

2.1 Study 1: An Exploratory Study of Disease Surveillance Systems in Norway [25]

Objectives: 1. To gather GPs' experiences using the current system for contagious disease surveillance in Norway, which is run by the Norwegian Institute of Public Health (NIPH) 2. To gather GPs' high-level user requirements for future systems.

Comments on paper 1 [25]: The objectives in paper 1 were vaguely formulated in the introduction[13]. The last objective was presented somewhat more clearly in the paper's method[14] chapter. The first objective/research question is also missing from the paper's abstract. Therefore, the objective presented above and in the introduction of this thesis (Table 1) is based on both the formulation in the paper's introduction and the method chapter and the actual results presented.

The methodology part is not well described in the paper with regard to choice of methodology, data collection, and how the data analysis was conducted. Therefore, the methodological issues mainly relevant to this paper are now described below, while the general issues relevant to several papers have been described earlier in this chapter. In addition, neither the methodological strengths nor limitations were addressed in the paper. These issues are now addressed in the discussion section of the thesis (Chapter 4).

Choice of methodology:
To gather "human experience", and to try to understand "the world from the subjects' points of view", individual, semi-structured interviews were used [122]. In addition, electronic and paper-based documents were reviewed, and informal discussions were held with technical and medical staff.

Sample: Individual, semi-structured interviews were conducted with five strategically recruited GPs from different practices, four from the city of Tromsø and one from a rural area. The participants were two women and three men of different ages (one very young, one nearly retired), and with varying knowledge about disease surveillance. The GP responsible for the prevention of contagious diseases and for informing other GPs in the municipality about potentially serious outbreaks (named MDPD in the paper) was one of these five GPs.

[13] "to gather information about the diagnosis-based contagious disease surveillance system in Norway and to gather information that might be useful in designing a new system"
[14] "two main topics were addressed: the existing system and the GPs' views on how they wanted future systems to function"

The review of electronic and paper-based documents included reviewing the NIPH homepages regarding how the Norwegian Surveillance System for Communicable Diseases (MSIS) was intended to work and how the GPs could use the existing national system to detect possible outbreaks of infectious diseases. In addition, literature on how the ICPC codes were intended to be used during a consultation were investigated [118].
Informal discussions were conducted with medical and technical staff, including the MDPD and colleagues with former practice in primary care, system development, and security. The discussion with the MDPD was regarding how the GPs should be informed about local outbreaks of infectious diseases, and how and to whom they should report infectious diseases if identified.

Data collection and analysis: An interview guide was developed to achieve a more focused exploration of a specific topic [123]. The interview focused on the following five main questions: 1) How did they, as GPs, get information about infectious diseases, both locally and nationally? 2) How did their GP office report infectious diseases to national health authorities (NIPH)? 3) How did they use the existing national system to detect possible outbreaks of infectious diseases? 4) How did they practice the use of ICPC codes during a consultation to record the patient's symptoms and possible diagnosis in the EPR? 5) The last part focused on whether a new syndromic surveillance system could be established to present local outbreaks as well, and how it should be designed to be useful for them, especially in a consultation setting. In addition, the GPs also provided feedback to a possible user interface for receiving syndromic surveillance reports and alarms through computers or mobile phones, presented by a master student.

The interviewer (PhD candidate) posed the questions (except those regarding the user interfaces) and critically followed up on the answers from the interviewees [122]. The questions were open-ended to encourage the subjects to expand on their own experiences [124]. The interviews lasted 1.5–2 hours. The interpretative study approach and general principles used when conducting, documenting, and analysing all these data sources together were presented earlier in this chapter.

Through the course of the content analysis, the data were broken down and sorted, first according to the five main interview questions, and then according to sub-themes that emerged within these questions (relevant subjects that all GPs had commented on). These main questions were later categorised according to the subheadings presented in the results part of the paper. To conduct the content analysis, it was necessary to go through the transcribed text, the recorded interviews, and the notes several times for each interview, in order to identify all relevant issues, as some of the sub-themes first emerged after some time. When writing down the results of this content analysis, each GP was represented by a specific colour to separate them and make it readily apparent if data were missing for one of the GPs.

Ethical considerations:
Ethics permission from the Regional Medical Ethics Committee was not required, as the interview respondents were not patients in the interview setting, and no questions about their personal health were asked. Approval from the local representative of the Norwegian Data Protection Agency (Personvernombudet for forskning ved UNN) was provided. Informed consent was obtained to protect individual autonomy and rights [125]. The municipal disease preventing doctor (MDPD), the GP responsible for the prevention of contagious diseases in the municipality, approved the quotes that are used in the paper.

2.2 Study 2: Bridging the Gap between Patients' Expectations and General Practitioners' Knowledge through Disease Surveillance [26]

Objectives: 1. To investigate to what degree patients trust their regular GPs to be fully informed about the prevalence of infectious diseases in their neighbourhood, and what GPs actually know.
2. To investigate how and from whom GPs are informed about the prevalence of infectious diseases in their neighbourhood.

Comments on paper 2 [26]: The methodology part is not well described in the paper with regard to choice of methodology, data collection, and how the data analysis was conducted. This was partially due to the lack of space in a conference paper. In addition, the rationale for applying t-test and regression analysis were not included in the methodology section, nor were methodological strengths and limitations addressed.

Therefore, these methodological issues, relevant to this paper, are now described below, while the general issues relevant to several papers were described earlier in this chapter. The methodological strengths and limitations are addressed in the discussion section of the thesis (Chapter 4).

Choice of methodology: To respond to the first objective regarding trust, it was necessary to question a larger sample of possible patients, preferably in a standardised way. This requirement resulted in the choice of conducting a survey [126].

To respond to the second objective, regarding how and from whom the GPs are informed about the prevalence of infectious diseases, results from study 1 (published in paper 1, referred to in paper 2) relevant to this objective were discussed in focus groups in order to promote a broader discussion, and to learn what the GPs would agree and disagree on [127]. In other words, to explore the area in depth and cover all aspects of the subject [128]. In addition, informal discussions were used.

Sample: The survey included 888 Norwegian citizens. The interviews included 13 GPs—five individual interviews (the same interviews presented in study 1) plus eight GPs in the two focus groups (first interview with the focus groups; other results from this focus group interviews belong to study 3). The informal discussion included colleagues (former GPs) now working with e-health and a former colleague now working as a GP.

Data collection and analysis: The results from the individual interviews, which were discussed in the focus groups, corresponded to the first three questions presented in study 1. One result (from interviewing the five GPs in study 1) that needed special attention was the indication that the GPs' primary source of information regarding infectious diseases was "colleagues from their own practice" [25] p. 369. This "colleague" had to obtain this information from somewhere, which was the reason to investigate "how and from whom" further. Some new data (not published before) was also extracted from the interviews with the five GPs in study 1. This result was also discussed and confirmed in the focus groups (two last sentences p. 425 [26]).

For a complete description of the data collection through individual and focus group interviews, see the data collection section presented earlier in this chapter, as well as the presentation of study 1 in

this thesis. The interpretative study approach was used when analysing the data sources relevant to the second objective. The content analyses were conducted as described under studies 1 and 3.

Survey data collection was conducted as part of a larger study designed by others [129]. The survey data were collected through computer-assisted telephone interviews (CATI) [26], including both landline telephones and mobile phone numbers [129]. My question, aimed only at Norwegian respondents, was included in the 2007 part of the e-health consumer trends survey conducted in seven countries [129]. In Norway, 100 respondents piloted the questionnaire [129]. Stratified sampling was used to strengthen the representativeness [126]. According to theory for stratified sampling, the population is classified into strata, for example, based on age and gender, and then a sub-sample is randomly extracted from each stratum [126]. The telephone interview survey used proportional stratification to ensure that the size of the sub-sample was proportional to the stratum size in the population [126]. Six groups were constructed, based on census data, for age and gender specific to each country. For randomisation, random digit dialling within strata was conducted [130]. Kummervold (2008) [129] and Santana (2010) [130] described the EU study method and material in more detail.

A professional polling agency collected the data [129], asking the respondents "To what degree do you trust your regular doctor to be fully informed about the prevalence of infectious diseases in your neighbourhood?" [26]

SPSS 15.0 was used for the statistical data analysis [26]. The main parts of the descriptive statistics within this dissertation have been interpreted by the PhD candidate, while the analytic statistics/statistical tests were conducted by one of the co-authors. A "t-test for two independent samples" to test whether the difference between two means was significant or not [131], p. 192 and 194, was conducted. The mean of men's and women's trust, and the mean trust of respondents from villages and rural areas, were compared with the mean trust of respondents from urban areas. In addition, a linear regression analysis was originally conducted [26]. After the paper was published, more experienced statisticians concluded that for this study, an extension of the logistic regression, a proportional/cumulative odds model [132], was the most correct way to carry out the analysis. This model uses the information in the ordinal response data, without losing information by collapsing some categories of the original scale, by presenting it as binary data [132]. Therefore, a proportional odds model analysis of these data was conducted as part of finalising this thesis (see Appendix B). The statistical program R, version 2.13.2, was used for this analysis. The results from the proportional odds model analysis are consistent with those from the linear regression, with only minor differences.

Ethical considerations: The national ethics committee had no objections to the survey study [129]. Regarding the interviews, see comments under study 1 [25].

2.3 Study 3: "Garbage In, Garbage Out" – Extracting Disease Surveillance Data from EPR Systems in Primary Care [27]

Objectives: 1. To investigate the GPs' use of the EPR system and the effect this has on data content, such as symptoms reported by patients and diagnoses reported by GPs.
2. Analyse whether and how health information and symptoms of satisfactory quality can be extracted, in GP and EPR settings, to identify alternative options for extracting surveillance data.

Comments on paper 3 [27]: The objective is not described very well in the paper's introduction ("how to extract data from the EPR that can be applied to disease surveillance"), and it is not easy to find (it is not in the last sentences of the introduction, but in the second-to-last section). The clarified objectives, as described above and in the introduction to this thesis, are based on the objectives presented in the paper's abstract. In addition, the abstract does not report findings or conclusions relevant to the results; it mainly focuses on contributions to the CSCW field. The paper also does not include a conclusion summing up the results, and it lacks a discussion of methodological strengths and limitations. The methodological strengths and limitations are now addresses in the discussion section of the thesis (Chapter 4).

There is also a mistake in the paper. In referring to around 200 ICPC codes in the Norwegian version, I misunderstood the source reference to more than 200 codes mainly used to classify reasons for encounter. In total, the Norwegian system included 698 symptoms and diagnoses in 2004, in addition to 42 process codes [133].

Choice of methodology: It was necessary to use methods that could contribute to a better understanding of the organisational culture, "explore 'taken for granted' practices within healthcare" (p. 34), and sort out whether some specific ideas sounded feasible or not [134]. We needed to achieve an in-depth understanding of people's (GPs') behaviour and the reasons they had for such behaviour [123], how the context affects outcomes [127, 128], and "how" and "why" the GP used the EPR as they did [135]. As pointed out in paper 3 [27], it is critical to understand how systems actually are used, not only how systems are designed and intended to be used, as "plans and situated action" may differ [136].

Hermeneutic interviewing was used as the primary method of data collection. This method represents "the philosophy of understanding and the science of interpretation" [137] p. 39, which means that "the hermeneutic interview seeks understanding through interpretation" [137] p. 40.

In addition, results from the individual, semi-structured interviews (in study 1) relevant to these objectives were taken into account and discussed in focus groups to promote a broader discussion [127]. Some new results (not published before) were also extracted from the individual interviews with the five GPs, and discussed and confirmed in the focus groups. Data were also collected through informal discussions and review of electronic and paper-based documents.

Sample: In total, 15 GPs were interviewed, five through individual interviews (the same interview presented in [25]) plus ten other GPs represented through two focus groups. Each focus group included all physicians in their practice and was selected to ensure that they had at least one person who was or had been involved in disease management on the municipality level. Two interviews

were conducted with group 1; group 2 could not reserve as much time to each interview, so it was necessary to conduct three interviews with them.

The questions were also discussed in depth through more informal discussions in meetings with four physicians and technical staff. There were five meetings with the syndromic surveillance project group at the Norwegian Centre for Integrated Care and Telemedicine (NST), including technologists and two former GPs, and one meeting with this project's specialist advisory group, including two physicians who were not represented in any other forum (a total of four physicians participated, but two overlapped with the focus groups, see Table 1 in paper 1). In addition, these issues were discussed, but not in depth, in a common meeting where all GPs in Tromsø were invited, including six new physicians. A total of ten participated, but four were also represented through the focus groups.

There were also other informal discussions with medical and technical persons to learn more about the field and the GPs' work practices (how and why). These discussions included medical and technical personnel in the microbiology department, involved in discussions conducted at a site visit. Further, informal discussions were conducted with the product leader and system developers working with the EPR system Profdoc, personnel involved in developing the Norwegian version of the ICPC code system [118, 133], and product leaders and system developers from Well Diagnostic (now DIPS), working with the system that makes it possible for GPs to order laboratory services from the local hospital. The electronic and paper-based document study included documents and web-based information describing the ICPC code system and the EPR system from Profdoc, used by all the interviewed GPs.

Data collection and analysis:
As suggested by Halkier (2005), results from the individual interviews were used to prepare an interview guide for the focus group interviews [127]. In addition to the GPs' practices regarding use of the ICPC code system, the GPs were engaged in discussing their use of the free-text field in the EPR system, as well as their use of records related to samples that were submitted to the microbiology laboratory. These issues had come up in the individual interviews. The GPs were also encouraged to suggest other possible data sources.

For a complete description of the data collection through the individual and focus group interviews, see the data collection section presented early in this chapter, in addition to the presentations of study 1 in this thesis, and the presentation in papers 2 and 3.

As pointed out by Pope et al., the "analytical process begins during data collection as the data already gathered are analyzed and shape the ongoing data collection" [138] p. 114. During the data analyses, all available data sources were taken into consideration during the interpretation process [117]. The interpretative study approach was used when analysing all these data sources together.

In addition, the transcribed text, the recorded interviews, and notes were explored using content analysis [138]. Content analysis refers here to exploring data through breaking it down into relevant categories and explanations [138], and/or subheadings, for examples within each question [124]. Through the content analysis, data were broken down and sorted according to the three main interview subjects, and then according to the sub-subjects that emerged within these questions. To

conduct the content analysis, it was necessary to go through the transcribed text, the recorded interviews, and the notes several times for each interview to identify all the relevant issues. When writing down the result from this analysis, the GPs were represented with specific letters to separate their statements and quotes.

Ethical considerations: As presented for study 1 [25].

2.4 Study 4: An Exploratory Study of Patient Attitudes towards Symptom Reporting in a Primary Care Setting. Benefits for Medical Consultation and Syndromic Surveillance? [28]

Objectives: To investigate Northern Norwegian citizens' attitudes towards providing symptom information electronically before a consultation and how they prefer to carry out the reporting, as well as attitudes towards the storage, use, and presentation of symptom data in general, and in a symptom-based surveillance setting in particular.

Choice of methodology: To reply to this objective, as in study 2, it was preferable to question a larger sample of people, and preferably in a standardised way. This resulted in conducting a survey [126], based on questionnaires distributed and collected through convenience sampling.

Sample: The sample consisted of 83 respondents from public locations in Tromsø.

Data collection and analysis: Data were collected during March 2009 by handing questionnaires originally containing 13 questions to the public. (Question 13 was subsequently taken out of the published survey, as it is not used in the paper [28].) Information about the types of locations and distribution of the questionnaires can be found in the paper [28]. This survey used mainly closed-ended questions, but also some open-ended ones. A master student designed the final questionnaire, mainly based on the PhD candidate's suggestions. The data collection was conducted by the master student, with some support from the PhD candidate. Because attitudes towards the use of technology for health purposes could vary based on gender, age, and education [75], the convenience sampling tried to ensure a sample with a representative distribution of those demographic variables. SPSS 16.0 was used for the statistical data analysis of the survey data collected through the questionnaires. To learn more about the relationship between the dependent variable "attitude towards providing symptom information electronically before a consultation" and one or more independent/predictor variable(s), a forward stepwise and binominal (multiple) logistic regression analysis [131] (cf. explanations p. 341) was conducted by one of the co-authors. In addition, content analysis of the free-text responses in the questionnaire was conducted to identify the dominant themes.

Ethical considerations: As for study 1, permission from the Regional Medical Ethics Committee was not required, as the respondents were not patients in the interview/survey setting, and we did not ask any questions about their personal health/illness. Written informed consent was not used; however, possible respondents were informed about the study objective, and they consented indirectly when they agreed to participate. The survey did not include personal identifiable information.

2.5 Study 5: Electronic Symptom Reporting by Patients: a Literature Review [17]

Objective: To establish an overview of the clinical settings and technologies for which symptom reporting tools might be useful that have previously been examined in scientific studies.

Choice of methodology: To establish the necessary overview within the strict time limits and resource and publication constraints, a literature review was conducted based on abstracts only. This literature review was conducted in accordance with the definition of UC Berkeley's Library Web, University of California [139]. They state that a literature review shall survey and summarise multiple primary research studies on a particular topic and represent secondary literature providing an overview of the research topic [139].

Sample: The Medline database was searched for English-language articles published from 1990 to 1 September 2010, within human medicine. The search included 115 search terms. The inclusion criterion was original studies of interventions where patients or parents reported health information electronically to health personnel or a system for health care purposes and were given feedback.

Data collection and analysis: All abstracts were independently reviewed and rated as relevant or not by the PhD candidate and the second author. Disagreements were resolved by consensus discussions. The reference to each included abstract was recorded in one Excel spread sheet, according to the study's clinical condition and use of technology. The clinical condition was first recorded according to the reported diagnosis or disease that was the focus of the study, and then classified/grouped according to the diagnosis categories of the International Classification of Primary Care (ICPC) [133], in addition to cancer and an unspecified category. This final clinical condition classification was conducted by the MD involved in the study. The technology was first recorded according to the technology specified in the abstract (text string), then categorised as defined in Table 1 in the paper [17]. A second spread sheet was used for recording reference, year of publication, country of first author, and number of patients and health care providers involved. The technology categorisation was conducted by the PhD candidate and the second author, both of whom have a technology background. Abstracts difficult to categorise were subject to consensus discussions.

Ethical considerations: None.

2.6 Study 6: Electronic Symptom Reporting Between Patient and Provider for Improved Health Care Service Quality: A Systematic Review of Randomized Controlled Trials [29, 30]

Objectives: 1. To clarify what has been investigated in RCTs thus far with regard to different patient groups, health service innovations, and research targets relevant for electronic symptom reporting to improve health care service quality. 2. To assess the methodological quality of the RCTs identified in the first part of the review. 3. To summarise the effects and benefits of electronic symptom reporting

from data published in the methodologically best RCT articles. Benefits are presented with regard to patients, health care professionals, and health care systems.

Choice of methodology: To create a comprehensive overview of what was investigated in RCTs thus far, a systematic review was considered necessary. The *systematic review* was conducted in accordance with the definition in Cochrane Handbook, 2011 [140], chapter 1.2.2, where the key characteristics are defined as: "a clearly stated set of objectives with pre-defined eligibility criteria for studies; an explicit, reproducible methodology; a systematic search that attempts to identify all studies that would meet the eligibility criteria; an assessment of the validity of the findings of the included studies, for example through the assessment of risk of bias; and a systematic presentation, and synthesis, of the characteristics and findings of the included studies."

The systematic review generally followed the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guideline, which has adopted the definitions used by the Cochrane Collaboration [141]. The systematic review resulted in two papers [29, 30].

Sample: The Medline, EMBASE, PsycINFO, Cochrane Central Register of Controlled Trials, and IEEE Xplore databases were searched for original RCT studies presented in English and published from 1990 to November 2011. The IEEE Xplore search mainly searched for RCTs, while the other searches included around 130 search terms. Included were interventions in which patients or parents reported health information electronically to the health care system for health care purposes and were given feedback.

Data collection and analysis: Abstract and full-text review was conducted independently by EH and the PhD candidate. Decisions regarding which variables to extract were guided by the Cochrane data collection checklist (Table 7.3.a in the Cochrane Handbook) [140]. In addition, study-specific variables were included. A full presentation of all the 84 variables can be found on the website of the Norwegian Centre for Integrated Care and Telemedicine [142], while a short version of the variables/items is presented in Table 3. For the full-text review of the 70 articles, the source and inclusion and exclusion variables were extracted. For the included articles, all 84 variables were extracted.

Risks of bias (based on Cochrane recommendation) were evaluated independently by MAJ, GB, and TS. MAJ and GB also extracted the effect data independently. Disagreement regarding inclusion, bias assessment, extraction, and interpretation of effects were resolved by consensus discussions.
Content analysis was used to break data into relevant health service innovation categories [138].
During this analysis, it was sometimes necessary to go back and read larger parts of the text over again in order to identify and note possible categories and then compare and contrast this with the other studies [143].

Table 3 Short versions of the 84 extracted variables/items

Source: Paper ID, Paper source (database), Reporters ID (MAJ or EH), Main author, Publication year, Title
Inclusion criteria: Randomized, Original study, Patients or parents, Reporting symptoms, Electronically, Provided with feedback, Present or last few days symptoms, Comparison of symptom reporting vs. no symptom
Exclusion criteria: Only retrospective questionnaire, Prevalence surveys, Screening, or Test of medicines; Communication requiring patient and health care provider present at same time; Only automatic biometric/signs measurements; Other reason for exclusion; (**Finally:** Included or excluded). Other reasons to look into this paper.
Methods and risk of bias: Design (Parallel, Cross-over, Cluster, Factorial, Other, Unclear), Number of arms, If multi-arm, which intervention groups are relevant, Intervention duration for each patient, What is the study about, Research question, Appropriate question, Theoretical evidence, Preclinical testing, Described design limitations, Random sequence generation + Judgement, Allocation concealment + Judgement, Blinding of participants and personnel + Judgement, Blinding of outcome assessment + Judgement, Incomplete outcome data in short-term + Judgement, Incomplete outcome data in longer-term + Judgement, Selective reporting + Judgement, Other sources of bias + Judgement.
Participants: Total number, Diagnostic criteria, Age ranges, Mean age, Recruited from, Females-total/intervention/control group, Number in intervention/control group, Start and stop of study, Country
Interventions: Name, Details, Communication conducted inside or outside health care institution, Setting for Communication, Communication technology, Comparison group description, Feasible in a real-life setting
Outcomes/Results: Outcome measures, Clinical outcome, Avoided consultation, Improved consultation/health care service for patient/ -for doctor/ -for other health care personnel, Resource utilization for patient/ - for doctor/ - for other health care personnel, Patient satisfaction, Doctor satisfaction, Other health care personnel's satisfaction, Other benefits reported, Other possible relevant results, Unintended adverse effects
Miscellaneous: Funding source, Authors' conclusions, Authors' comments, Relevant references, Reviewers' comments.

Ethical considerations: None

3 Results

This chapter presents the overall results related to each of the four research questions (italics).

How useful do GPs find the current surveillance system, and does there seem to be a need for a new surveillance system in the GP and patient perspective? [u1]

The GPs did not find the system run by the Norwegian Institute of Public Health (NIPH) for contagious disease surveillance in Norway to be very useful, and especially not in a consultation setting [25, 26]. All GPs are obliged to report to the Norwegian Surveillance System for Communicable Diseases (MSIS) in the NIPH when they diagnose specific contagious diseases, in addition to data reported by microbiology labs [144]. However, the process of collecting data from the GPs, processing the data, and producing the surveillance reports is very time consuming, resulting in data that is several weeks old when it is available to the GPs [25, 26]. In addition, the system did not provide specific information related to the local patient population, so the existing surveillance reports had very little or no value in a consultation setting [25, 26]. As reported in one of the publications, "one focus group summed up the situation as follows: 'The MSIS reports present ancient data. When we receive the reports people are dead and buried, or they have recovered.'"[26] p. 425. This feedback from the GPs indicates a need for a new surveillance system.

For a future surveillance system to be useful in a GP setting, it must present up-to-date (timely) information [25] and include information from the local patient population [25, 26]. It has to be customisable to the specific needs of the physician in order to be relevant in day-to-day practice and require minimal time for correct interpretation of data [25].

From a patient perspective, we have a situation where nearly half of the patients are confident that their GP is well informed about the prevalence of infectious diseases in their neighbourhood [26]. However, this is not the situation, as in reality, they are not well informed [26]. Therefore, there seems to be a need for a new surveillance system from the patient perspective as well, as patients trust their local GPs to have this information [26].

Which data collection procedures seem to be feasible for syndromic surveillance, and do the data hold the necessary quality? [f1]

All the discussed approaches regarding extraction of health information and symptoms from the EPR system had limitations as primary data sources for syndromic surveillance [27]. The discussed approaches were 1) extraction of ICPC codes, 2) extraction of symptoms and information from the free-text field, and 3) extraction of information from the tests ordered and the test results from the microbiology lab at the local hospital.
The most encouraging approach regarding extraction of data from the EPR system was the use of lab data [27]. Another encouraging data source was the patients [26]. The results regarding the individual sources are as follows:

1) The GPs are supposed to enter ICPC codes for all the symptoms and troubles reported by the patient [118]. The ICPC codes are standardised and could easily be extracted and serve as a good foundation for syndromic surveillance. However, the value of extracting ICPC codes alone would be very limited, as GPs do not enter all the symptoms reported by the patient [25, 27], and they usually do not enter a final diagnosis code [25, 27]. The GPs mainly enter one symptom code per consultation [25, 27], and this is only done because an ICPC code is required to receive reimbursement from the health authority for a patient visit [25, 27].

In addition, the quality of the reported symptoms and diagnoses is limited. The GPs usually entered a code that was relevant and reported by the patient, but often an appropriate code did not exist, in which case an ICPC code that had little to do with the reality was used [27]. Most of the GPs considered the ICPC code system as imprecise [25, 27]; one explanation was that the ICPC code system included few codes compared to the ICD[15] system used in Norwegian specialist health care.

2) Most of the GPs enter the patient's symptoms and a suspected diagnosis in the EPR free-text field [25, 27]. However, a system that searched the free-text field for predefined words and phrases relevant to disease surveillance was considered difficult to create, and not liable to provide sufficient data quality. The GPs' explanation of this was that there were enormous variations in what they wrote in the free-text field with regard to the overall amount of symptoms and diagnoses, the use of abbreviations, concepts, language, terminology, quality, and length [27]. In addition, creating a mapping between the phrases used by each individual GP and a language understandable by the system in order to "translate" what they wrote was considered unrealistic by most of the GPs [27]. "Only a few of the GPs believed that they would be able to specify all the abbreviations and all the terminology that they would use for the various conditions (to enable us to enter these in an individual mapping file)" [27] p. 531.

3) The most encouraging approach when evaluating extraction of information from the EPR system was the use of data exchanged with the microbiology lab. Both the tests ordered (representing the symptoms and the illnesses that the GPs suspected) and the test results (representing the diagnoses and findings) could be of use [27]. An increase in lab requests alone could be enough to detect if "something is brewing" [27]. Unfortunately, however, the lab results would not be available in real time, due to the amount of time it takes for lab results to be analysed [27], which can vary from a few days to a week [27], and due to "the timeline of when a lab request is initiated in relation to when symptoms were first presented to the GP" [27] p. 533. Another drawback is the variation in practice with regard to how often samples are submitted to the lab.

4) The results from interviewing the five GPs in study 1 indicated that the GPs' primary source of information regarding infectious diseases in their patient population was colleagues from their own practice [25]. However, this colleague had to obtain the

[15] International Classification of Diseases

information from somewhere, which was the background of why this matter was investigated further in the focus group interviews [26]. This discussion revealed that the GPs' primary source about the prevalence of infectious diseases was the patients [26]. The idea that the patient could become the primary source was taken further in a survey investigating the patients' attitudes towards electronic symptom reporting in a consultation or syndromic surveillance setting.

The results showed that the respondents generally responded positively to the idea of providing information about their symptoms to the GP's office as soon as possible after falling ill [28]. Sixty-one percent said "yes", 35% said "maybe", and only 4% said "no" [28]. Over half of the respondents preferred to use e-mail or a web interface to perform this task [28]. Sixty-one percent had already used the Internet to "Google" their symptoms prior to a consultation (41% frequently, 20% more infrequently). Eighty-four percent agreed that their symptoms could be saved in the EPR system, and 76% agreed that the GP could access the symptoms together with the prevalence of matching diseases in order to assist the diagnosing process during the next consultation [28]. Thus, this study indicates that patients could become the primary data source for symptom-based surveillance [28]. In addition, 43% of the respondents were willing to report symptoms directly into a syndromic surveillance system without passing the symptoms through the GP office or any system connected to their GP consultation; 49% had a negative response, while 9 % did not reply to this question.

Which patient groups, technologies, health service innovations, and research targets have been suggested as feasible and relevant for electronic symptom reporting to improve health care service quality in general? [f2]

The abstract review, which was not limited to RCTs, identified 235 papers within nine specific patients groups in whom electronic symptom reporting had been suggested as feasible and relevant. The following patient groups were represented: cancer (50 studies), lung disease (48, included 36 within asthma and 7 within COPD), psychiatry (18), cardiovascular disease (17), musculoskeletal disease (15, including 9 focusing on rheumatologic conditions), diabetes (12), gastrointestinal diseases (8), neurological diseases (8), HIV/AIDS (6), and a large group that was not possible to categorise based on the information in the abstract [17]. Cancer symptom reporting seems to take place inside the health care institutions, while lung disease and musculoskeletal disease reporting mainly take place at home via the Internet [17].

The systematic review of RCTs identified 32 papers [145-176], and only five different patient groups. The following patient groups were represented: "respiratory and lung diseases (12 studies), cancer (6), psychiatry (6), cardiovascular (3), and diabetes (1)", [30] p. 1. In addition to these, one study represented a mix of three groups. All of these studies, except one, focused on long-term conditions.

The technologies were investigated through the literature review. Electronic symptom reporting seemed to have been accomplished mainly by technologies such as web, e-diary,

and more advanced mobile applications, which were used much more often than “e-mail and SMS, technologies where the user interface has limited functionality” [17] p. 16.

Health service innovations and research targets were investigated through the systematic review of RCTs. Health service innovations were categorised into four groups: “consultation support (7 studies), monitoring with clinician support (12), self-management with clinician support (9), and therapy (1)”, [30] p. 1. “Most of the research (21/29, 72%) was conducted within four combinations: consultation support innovation in the cancer group (5/29, 17%), monitoring innovation in the respiratory and lung diseases group (8/29, 28%), and self-management innovations in psychiatry (4/29, 14%) and in the respiratory and lung diseases group (4/29, 14%)” [30] p. 1.

The “most common research target was disease-specific health benefits at the patient level; and, second, to provide patient-centered care” [30] p. 21. “Research targets in the consultation support studies focused on increased patient centeredness, while monitoring and self-management mainly aimed at documenting health benefits” [30] p. 1. “The studies aiming for reduced health care costs were all in the subgroup of monitoring articles, except for 1 study on self-management” [30] p. 21.

What possible uses, effects, and benefits of improved health care services quality can be found in a patient, health professional, and health care system perspective? [u2]

Of the 32 RCT papers identified in the systematic review, 12 were excluded due to high risk or unclear risk of selective reporting and blinding of outcome assessment, leaving 20 papers for the effect assessment [29]. The self-management papers were generally of higher methodological quality [29]. The authors’ hypothesis was confirmed in 13 (65%) of the 20 remaining articles.

“Overall, articles on self-management support were of a higher quality, allowing a larger proportion of studies to be assessed with respect to effects” [29] p. 12. Benefits for “patients, and partly also for health professionals and the health care system, have been documented in this area” [29] p. 12.

Within monitoring, health benefits were identified for asthmatic patients, both children and adults [29] p. 13. “Both of these interventions included self-management elements with computer-tailored feedback. Of the 6 monitoring studies, 5 also addressed health care costs, but with one small exception, no cost benefits were identified.” [29] p. 13.

“The cancer studies in consultation support are encouraging, since it was found to provide patient-centered care, ensuring that patient-reported symptoms guided the clinical decisions.” [29] p. 13.

4 Discussion

The first part of the discussion will for each paper address its main contributions, strengths, and limitations. Then, the main findings will be discussed in relation to the two main research questions, and finally, the possible synergies between syndromic surveillance and improved health care service will be addressed.

Because the papers responding to main research question 1, syndromic surveillance, were published some years ago (2008–2009) and more or less lack discussion of literature relevant to the findings, this research question will be discussed thoroughly here. In contrast to these loose bonds making a full discussion in this chapter mandatory, there is a very close match among main research question 2, improved health care service, and the research questions addressed in papers 5–7, where the findings are more recent and thoroughly discussed within those papers. Therefore, research question 2 and the related findings will mainly be discussed with regard to new literature after October 2011 that has not been included in the review papers.

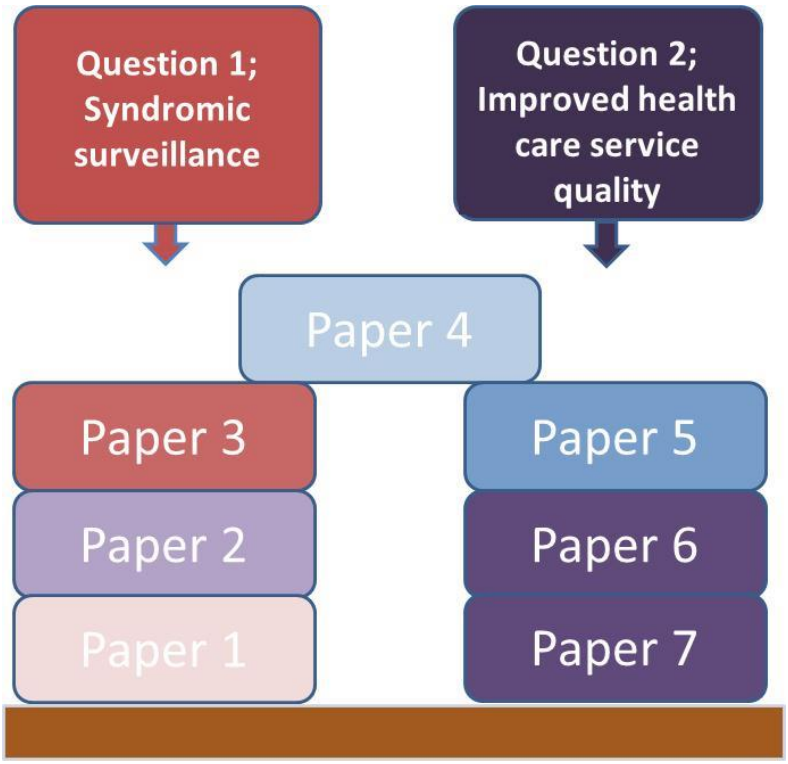


Figure 2 The first three papers focus on syndromic surveillance, paper 4 focuses on the connection between syndromic surveillance and improved health care services, and papers 5–7 focus on improved health care services.

4.1 Papers 1–7: Main contributions, strengths and limitations

This section will present the main contributions, strengths, and limitations for each of the papers.

It is a drawback of the syndromic surveillance papers that the presented results and conclusions are not in 100 % accordance with the objectives/research questions. The objectives are answered, but so are other questions, without being presented as objectives/research questions. Papers 1 and 2, and to some extent, paper 3, also lack discussion of relevant literature (relevant to the findings).

Paper 1: The main contribution of paper 1 [25] is the valuable input with regard to how disease surveillance should—and should not—be conducted in general, if surveillance information is to be useful in a consultation setting. It is a strength that even though the responding GPs had different backgrounds and knowledge about disease surveillance, they agreed on all the important issues. This supports the result from this sample, even though the sample is small. We were working under strict time constraints, which is why only five GPs were included in these individual interviews. Ideally, we should have included more GPs, to be more confident that no new information of significance was obtained and that we had reached saturation [177].

Paper 2: The main contribution of paper 2 [26] is that, to my knowledge at that time, this was the first paper (proceeding) addressing the possibility that the patient could become the primary data source for syndromic surveillance. During the presentation of this paper at the MIE conference in Sarajevo in 2009, I learned about Gripenet [22-24], which collects influenza-like symptoms directly from the patients to predict the flu. However, to my knowledge, this paper is still the first to address the possibility that collection of syndromic surveillance information could be combined with reporting symptoms before consultation, and that, as such, both could improve the quality of the consultation and provide real-time syndromic surveillance data at the local level.

Regarding the interviews, it is a strength that the focus groups were strategically selected so that they included at least one person who was or had been involved in disease management on the municipality level (named MDPD in paper 1). A future syndromic surveillance system is likely to have a broad impact on their work practice, and they have more knowledge than regular GPs regarding the type of information that is available through the current system. However, this might also be considered a limitation, as the presence of an MDPD in a GP practice could influence the other GPs. They might be more mindful of and focused on the advantages of syndromic surveillance than GPs in a practice without an MDPD, and as such, might express a stronger need for an improved surveillance system. It may also appear as a limitation that both focus groups came from a single city—Tromsø. Focus group interviews could have been conducted in other places as well, but this would have raised the study cost.

The questions regarding what the GPs actually knew about infectious diseases in their neighbourhood were first investigated through the individual interviews, and then in the first focus group interview with each group. This required quite standardised questions, and because no new information of significance regarding this matter emerged through the focus groups, compared with the individual interviews, saturation seems to be reached [177, 178]. However, it is not possible to be 100% sure that saturation is reached, as the literature lacks clear “advice regarding the number of

interviews with no new information that is required before the researcher can be reasonably certain that saturation has been reached" [178] p. 2.

The survey's strongest point is that it was well designed. However, the survey was not primarily designed to investigate my research question. It would have been preferable to include more questions to investigate whether there was a need for a new surveillance system in a patient perspective, but it was not possible to include more questions in this survey. On the other hand, it would not have been possible for me to request so many respondents if I had had to bear the cost of the survey.

All the respondents answered almost all the questions, with a few exceptions. On two questions, 99% answered, 98% answered three questions, 97% answered two questions, and 88% answered one question. In addition, "only" 89% of those respondents answered my "trust" question. The fact that this question had the second lowest number of answers indicates that the respondents found the "trust" question a bit difficult to answer. However, investigating 888 respondents' trust with proportional stratified sampling through a standardised way of questioning a sample [126] should provide a quite representative result.

Paper 3: Paper 3 contributed to an important understanding regarding GPs' use of the EPR system and the effect this had on data content, such as symptoms reported by patients and diagnoses reported by GPs [27]. The paper revealed serious limitations regarding the suggested approach using ICPC codes as a primary data source for syndromic surveillance. The paper also revealed limitations regarding extracting data from the free-text field and information from lab tests and results, as well as adaptations that could be made to overcome some of the limitations of the three approaches. The use of lab data appeared to be the most encouraging approach [27].

This knowledge was used as input for the syndromic surveillance project at the Norwegian Centre for Telemedicine and Integrated Care, regarding how to design a new and improved surveillance system. Today, a pilot system is established, based on extracting test results from the microbiology lab at the University Hospital of North Norway, representing the counties of Troms and Finnmark [179]. This pilot shows the number of patients who provided positive or negative tests in each county or municipality [180], and is thus a surveillance system; however, it is not a syndromic surveillance system.

In addition, the NIPH, department for contagious disease surveillance in Norway, referred to the paper's result in their 2010 annual meeting[16].

Paper 3 also contributes to the understanding "of sociotechnical issues related to disease surveillance", and to "issues important to CSCW", such as "how data collected in one context may be applied to a different context, and the delicate interplay between organizational and technical design challenges", p. 525 [27].

[16] Presentation by Rønning

The strengths and limitations in terms of strategically selecting focus groups, including one person that was or had been involved in disease management on the municipality level, are addressed in the discussion of paper 2, above. However, in relation to the study objective, it is also a strength that these key persons have more knowledge than regular GPs regarding the type of information that is necessary to extract.

The number of focus groups was actually not determined by data saturation, but by the fact that we only identified two GP practices in Tromsø with a person that was or had been involved in disease management on the municipality level. To define if saturation is reached, an iterative process of concurrent data collection and analysis is necessary [178]. Therefore, the PhD candidate reviewed transcripts or tapes to analyse and reflect on the findings before conducting the next interview. These findings were summed up and presented in the beginning of the next interview to enable the focus group to correct the interpretation, and to enable the examination of newly identified concepts. As the concepts and the information of significance that emerged during interviews with one group were consistent with the other group, and (when looking at both groups) no new information of significance was obtained under the last of the focus groups interviews, saturation seems to have been reached [177, 178]. However, as commented under paper 2, it is not possible to be 100% sure that saturation is reached, as clear "advice regarding the number of interviews with no new information" is lacking in the literature [178] p. 2. One may consider it both a strength and a limitation in this matter that the GPs discussed the different research objectives in the time between the interviews. At least one view that had come up in a group in the first interview had totally changed between meetings, when the GPs had had "more time to think it through", as they explained themselves. No dominance was observed from any particular individuals. In addition, findings from the individual interviews were confirmed in the focus groups discussions, which also strengthen the results.

Paper 4: The main contribution of paper 4 [28] is that it reveals that people seems to have a positive attitude towards providing symptom information electronically before a consultation, and to use this symptom reporting both for an improved consultation and for syndromic surveillance purposes. To my knowledge, this paper is the first journal paper to address that the same electronically patient-reported symptoms could be used both to improve the quality of the consultation and to provide real-time syndromic surveillance data at a local level.

It is a strength that a questionnaire from another study was used as a starting template [75], and that the final questionnaire was piloted and validated. Due to strict time constraints, convenience sampling was chosen. The limitations of such an approach are discussed in the paper. The fact that the sample was small, and that the questionnaires were distributed only to people in one city, Tromsø, also limit the representativeness. However, as described in the paper [28], comparing the sample with statistics representing the population of Tromsø reveals an approximate representation, except for respondents 16–22 years of age, who were a bit overrepresented [181], and the lowest education group, which was a bit underrepresented [182]. In addition, the highest education group (in percentages) was approximately in accordance with data from Norway and ten other high-income countries [183]. We also found that the sample reflected data from the Norwegian population very closely with regard to visits to the GP during the last 12 months [184], use of the Internet to

"Google" symptoms [75], and the fact that more females than males had visited the GP during the previous 12 months [184]. These findings should allow for generalisation to a certain extent.

Paper 5: The main contribution of paper 5 [17] is that it provides an overview of patient groups and technologies in which electronic symptom reporting has been suggested as feasible and relevant to improve health care service quality. It also revealed that the number of studies within electronic symptom reporting had increased heavily over the last two decades [17].

It can be considered as both a strength and a limitation that we only reviewed abstracts. It is a strength because reviewing abstracts made it possible to obtain a wide overview within strict time and resource constraints. However, for some abstracts, it was impossible to categorise the clinical conditions (total of 53) or the technology (total of 87), due to limited information. A full text review would have improved this categorisation work.

Conducting a systematic review instead of a general literature review is a stronger methodology, but it can be characterised as overkill in answering this objective. It is also a limitation that only one database, Medline, was searched; searching more databases would clearly have provided additional information. Another limitation is that the technology categories are not optimal, as they partially overlap. However, no good example of categorising this type of technology was found, and there is still no obvious way to categorise them.

Therefore, to sum up, this study has some methodological limitations. However, it is reasonable to argue that the abstract reviews that were conducted provided the required overview of the field, and as such, replied to the study objective in a sufficient way.

Papers 6 and 7: The main contribution of paper 6 is that it provides an overview of patient groups, health service innovations, and research targets from RCTs relevant for electronic symptom reporting to improve health care service quality. The main contributions of paper 7 are the summarised effects and benefits of electronic symptom reporting from the methodologically best RCT papers, and that the paper identified that the methods for conducting and reporting RCTs within the field need to be improved. To my knowledge, this is the first systematic review to address these topics.

It is an important strength that this review conducted a comprehensive search using many search terms, and that search terms were adapted to the individual databases. Another important strength is that Cochrane Handbook recommendations were used [140] to decide which databases to search and which data/variables to extract (through their data collection checklist) for selection of studies (full-text review by two independent reviewers), as well as warning regarding citation bias (not hand-search reference lists), minimum requirements for describing characteristics of included studies, and assessment of methodological quality through their risk of bias judgment. The risk assessment was conducted by three independent authors. In addition, Cochrane's recommendation regarding identifying the types of bias that were of most importance for the review were followed, in addition to the warning regarding not to present effects for low-quality studies [140]. Effects were extracted by two independent authors.

Limiting the searches to only RCTs can both be a strength and a limitation. The strength is that RCTs are considered the most mature stage of developing a complex intervention, i.e. the last step before taking the service into ordinary use [185, 186]. However, this might have resulted in missing interventions that were relatively mature, but not tested in an RCT.
It is a limitation that articles might have been lost in the adaptation of the search strategies between the databases. Search words might have been overlooked, and the psychiatry field does not seem to have been covered adequately.

It is also a limitation that "blinding of participant and personnel" was evaluated as one single risk of bias; participants and personnel could have been evaluated separately. The experiences from this review imply that it is much harder to blind health care personnel than to blind patients within e-health and telemedicine projects.

In the second systematic review paper (paper 7), studies were defined as either superiority or equivalence studies. Equivalence studies are loosely defined as studies where "authors hypothesized that the study arms would be equivalent in terms of the effect measure" [29] p. 4. We considered four of the studies to be equivalence studies, and the authors' hypotheses were confirmed in all four of them. The definition and evaluation of the studies were in line with our idea of equivalence at the time. However, we later discovered literature that takes the equivalence term further and provides more precise definitions and requirements regarding proper testing for equivalence [187-190]. Ideally, this literature should have been used to support our evaluation of the equivalence studies. The main definitions from this literature are presented in Appendix C.

Although some limitations were identified, the methodological strength of this study should benefit that the objectives were sufficiently answered.

4.2 Main research question 1: Syndromic surveillance

Main findings for the overall research question focusing on syndromic surveillance will be briefly presented and then discussed more thoroughly in the light of related literature.

Main research question 1:

> *Whether a new surveillance system is needed for GPs and patients, and if so, what is the most reliable and feasible data source? We consider data extracted from both EPR systems and (pre-consultation) symptom data reported by the patients themselves.*

To reply to main research question 1, it is necessary to go into the two sub-research questions, u1 and f1.

4.2.1 How useful do GPs find the current surveillance system, and does there seem to be a need for a new surveillance system in the GP and patient perspective? (u1)

The individual GPs expressed that the existing surveillance system was more or less "useless" when it came to providing information about the local patient population in a consultation setting [25]. These results were confirmed in the focus group interviews and in the informal discussions [25, 26]. The

individual GPs also agreed on the most important requirement for a possible new system [25], and all GPs involved in these studies expressed that if the surveillance information is to be useful in a consultation setting, real-time information about the local population must be provided [25, 26]. This agreement, as well as the knowledge that nearly half of the patients are confident that their GPs are well informed about the prevalence of infectious diseases in their neighbourhood, while the GPs actually are not well informed [26], provides a reason to believe that both the GPs and the patients need a new surveillance system — a more real-time system that also provides surveillance information regarding the local patient population.

However, it is not possible to say that the question "whether a new surveillance system is needed for GPs and patients" is finally answered by this, due to the uncertainty connected to 1) the limitations of papers 1 and 2 that already have been addressed, 2) the GP sample, and 3) the understanding of what a "need" is.

Looking at the GP sample, we realize that even if all GPs agree, only 14 of the 60[17] GPs in the municipality of Tromsø were interviewed, and with one exception, only GPs from Tromsø. In addition, the understanding of the word *need* is important to define. The dictionary[18] refers to *need* as both something "wanted" and something "deemed necessary". There is no doubt that the GPs wanted a new and better surveillance system that could provide information relevant for local cases, but there is still an unanswered question regarding how "deemed necessary" it is. A discussion that came up in the second focus group meeting with group 1 illustrates this point (not published before): Some of the doctors pointed out that a surveillance system would not be used very often. One of the doctors, who had been very enthusiastic regarding a new and improved syndromic surveillance system in the first interview, commented that in the month between the first and second interviews, he had counted exactly how many patients he had in whom he suspected a contagious disease. That number was two. The group discussed this and agreed that "it would be rather rarely" that they really could make use of a new surveillance system. They also expressed that they did not see a surveillance system as an important tool to detect the flu that they knew would come, but an important tool if some unusual or rare contagious disease should arrive in their patient population.

However, it is always difficult to consider an effect before one has experienced it himself, or convincing documentation is provided, so maybe this attitude would have been totally different if they had had experience with a more timely syndromic surveillance system, or with using other epidemiological data under the diagnostic reasoning process. For instance, it is interesting to learn that Fine, through several retrospective studies, emphasised the benefit of integrating state-wide [191] or more local incidence data (local epidemiologic context data) [192-194] into the clinical decision model, in order to improve diagnostic accuracy. The evaluations involved in these studies have focused on diseases that have seasonal variations or are communicable, such as correctly identifying aseptic from bacterial meningitis [193], pertussis in infants [191], and facial palsy in children [192]. Fine also demonstrated that the diagnostic accuracy for as common a disease as streptococcal pharyngitis could be improved based on local disease incidence data [194]. The study was conducted by incorporating real-time incidence data and using the incidence data to estimate the disease risk in 54,981 symptomatic patient visits [194]. The editors concluded that these results

[17] https://tjenester.nav.no/minfastlege/innbygger/fastlegesokikkepalogget.do
[18] http://dictionary.reference.com/browse/need

implicated that incorporation of surveillance data can "improve clinical decision making for a common infectious disease and reduce unnecessary use of antibiotics", p. 346 [194].

Therefore, to sum up, one might say that if we want GPs to carry out the most accurate diagnoses when it comes to unusual and rare contagious diseases, and possibly also for more common cases, a new and better surveillance system is needed. Whether this surveillance system should be based on symptoms or diagnoses, or both, remains to be discussed.

As reported earlier, a pilot disease surveillance system has been developed and made available to GPs in Tromsø [179, 180]. The system's effects are under investigation.

4.2.2 Which data collection procedures seem to be feasible for syndromic surveillance, and do the data hold the necessary quality? (f1)

Regarding possible data sources, both data extracted from EPR systems and symptom data reported by the patients themselves were considered.

Extraction of ICPC codes

Medical classifications, such as the International Classification for Primary Care (ICPC), have been developed to support both primary and secondary use of clinical data [195]. However, the results showing that GPs mainly enter only one ICPC code into the EPJ system for each patient consultation, and not all the symptoms the patient reports, lead to the conclusion that conducting syndromic surveillance based on ICPC codes alone is not recommendable. Other studies support this conclusion. A retrospective study looking at 12 primary care sites in Norway, for the period from when the use of ICPC codes became compulsory in 1992 [196] until 2008, revealed that "Codes were missing in 6.2% of the problem events; incorrect codes were observed in 4.0% of the problem events and text mismatch between the diagnoses and the expected ICPC-2 diagnoses text in 53.8% of the problem events", [197] p. 1. In addition, the investigation of EPRs from 82 GPs over three months in Norway reveals that GPs, on average, only report 1.3 ICPC codes per patient consultation [198]. This supports that the use of ICPC codes is not feasible for syndromic surveillance without changing the reporting practice.

In addition, in the UK, the data quality varies enormously in the EPRs in primary care [199, 200]. The coding completeness for seven primary care practices ranged from 5% to 97% [200] before a program to improve quality was established. It was also demonstrated that clinicians reported many more symptoms through the free-text field than by using codes [201]. Some of these challenges might possibly be explained by the fact that nurses and GPs struggle with the motivation to code symptoms and diagnoses in a consultation [202]. They report that it is sometimes difficult to find an appropriate diagnosis, and that they fear assigning a wrong diagnostic label and have concerns about stigmatising the patient (whether the code is correct or not). They also feel that coding takes away the attention from the patient, and they worry that the use of codes might damage the doctor–patient relationship [202]. Possibilities and limitations regarding providing more codes and changing the GPs work practice are addressed in paper 3 [27].

In sum, several findings support that extraction of ICPC codes alone is a weak tool to identify patient-reported symptoms, and that conducting syndromic surveillance based on ICPC codes alone is not recommendable.

Extracting symptoms and suspected diagnoses from free-text

Most GPs did enter both the patient's symptoms and a suspected diagnosis in the EPR free-text field [25, 27]. However, symptoms reported in the free-text field were not considered an appropriate primary data source for syndromic surveillance, due to the variation in what they wrote in the free-text field and how this would challenge the extraction of relevant data.

Even if the GPs' use of the EPR has not changed since 2008–2009, the field regarding natural language processing has moved forward in recent years, making it relevant to look more into this possibility.

Natural language processing (NLP) is a field of computer science in which programs search, index, and extract relevant information from text [203]. Within health care, the results could be used for "decision support, outbreak detection and quality review" [204]. However, there are many challenges linked to NLP development in the clinical domain [205], and it is not a big surprise that research making use of NLP focuses more on specialist care than primary care, as it is more challenging to search within "all possible diseases" than within a few.

Several studies have worked on these challenges to extract information from clinical notes [206, 207]. A 2012 study revealing that NLP can be useful to measure and report on the quality of care also reported that the "accuracy of the tool compared with physician abstraction decreased as the complexity of the data and language increased", and that NLP-based tools will have more difficulty with documents that are less limited in scope [208] p. 1238. Further, the use of NLP in clinical text is complicated, as "clinical texts are ungrammatical and composed of short, telegraphic phrases", and include "abbreviations, acronyms, and local dialectal shorthand phrases", included misspelling and the fact that "clinical narratives can contain any characters that can be typed" [209] p. 129, in addition to the frequent use of negation phrases in clinical reports [210, 211]. The same set of letters can be highly ambiguous, even in context. A study of abbreviations in medical reports revealed that 33.1% of abbreviations with six characters or less had multiple meanings [212, 213]. These challenges with the medical language make it necessary to "develop narrowly domain-specific analytical tools for medical natural language processing" [214] p. 28. However, Meystre's 2008 review reveals that NLP in clinical data has been demonstrated successfully, but that the solutions are mainly used within the laboratory where they are developed, and mainly for one specific purpose or disease category [209]. Today, open-source solutions, also intended to be less domain/disease specific, are under development and evaluation [215].

NLP, to some extent, is also tested for syndromic surveillance. The information relevant for syndromic surveillance is often present in a variety of clinical documents. Chapman (2004) suggests that as chief complaints are available at an earlier time than emergency department reports, a

combined application that extracts free-text to classify patients based on their chief complaint (CC),[19] followed by classification based on their emergency department (ED) report, may provide an effective method for surveillance of febrile illness [216]. Niiranen (2008) and Yli-Hietanen (2009) "lab-tested" NLP for automatic classification of CC for potential identification of syndrome peaks [214, 217]. For the algorithm to be accurate in terms of classification correctness, the variety in the free-text CC had to be reduced through the training of end-users [214, 217] and through new writing rules [214]. South's 2008 study compared the performance of a simple text classifier applied to different document sources from the electronic medical record, with the purpose of detecting influenza-like illness [218]. The best results were achieved "when the text classifier was applied to chief complaints ED and combined[20] surveillance document sources" [218] p. 694.

Hripcsak suggested that it was feasible to use electronic health records as a source for syndromic surveillance [219]. The structured data extraction (ICD-9 codes) performed best, while the system based on extraction of EPR free-text data correlated well with influenza-like illness, but less well with gastrointestinal infectious disease [219].

To an extent, NLP has been practiced for "real-life" syndromic surveillance. Chapman (2005) demonstrated that a trainable NLP system could successfully classify free-text triage chief complaints into syndromic categories [220], using this system to monitor the 2002 Winter Olympic Games [220, 221], as one additional surveillance source along with other systems [221].

In sum, the reported examples and findings support that extraction of symptoms from the free-text fields is still a bit premature or experimental; however, the field is moving forward and can already be a possible contributor to syndromic surveillance when used together with other sources. This is a promising area for future research.

Extraction of test orders and test results from the lab

The most encouraging data source based on extraction of data from the EPR was the use of lab test orders and results. Lab test orders have been demonstrated as a promising source of surveillance data [222]. Other studies have evaluated the use of confirmed lab results against syndromic surveillance [53, 223, 224]. Whereas some have ended up using the lab results as the primary data source (laboratory surveillance), others have used them together with syndromic surveillance data [39, 45]. As the lab data represent confirmed infections, it is not surprising that lab data is perceived as more reliable and accurate by the end-users than syndromic data, which is pre-diagnostic [45]. In addition, it is confirmed that the local incidence of a specific disease, available through lab results, could be used as part of the clinical decision process to predict the risk of this disease and improve the diagnostic process [191-194]. However, even if lab data is encouraging, as it represents confirmed diagnoses and can be used in decision support, it could be a challenge that the lab data does not include patients who have not contacted a physician, or when tests have not been requested. In addition, the time delay is a challenge. A study comparing laboratory influenza test results with ED visits that were assigned a provisional diagnosis through an ICD code in 49 public hospitals over five years found that the ED-based information could provide a warning at least three

[19] the reason for encounter, usually in free-text

[20] combined surveillance document sources, including a CC string, nursing or nurse triage note, and emergency department notes

days sooner compared with the laboratory-confirmed information [225]. If the laboratory processing and reporting delays are taken into account, this time advantage is even greater. However, laboratory delays could probably be reduced in the future, either through greater use of point-of-care tests or through systems that conduct lab result reporting more automatically.

In sum, there seems to be little experience using lab test orders as a syndromic surveillance source; therefore, this is a possibility that requires much more research before it can be established. On the other hand, the use of lab results does seem to be considered the most reliable and accurate surveillance source, but the current time delay is a challenge, preventing it from representing the disease map in real time or close to real time.

Symptom data reported by the patients themselves

There are several arguments to support that patient-reported symptoms could represent a primary real-time data source for symptom-based surveillance in Norway. First of all, the GPs' primary source of information about the prevalence of infectious diseases seems to be the patients [26]. Second, patients in primary care seem willing and motivated to report symptoms, especially if they are reported to their GP before a consultation [28]. Third, in 2005, 80% of persons 15–80 years of age in Norway were Internet users [75], a number we can expect to be much higher today.

Thus, the question about representativeness of the data is a primary question regarding who would actively participate. Patients even seemed quite motivated to report symptoms directly into a syndromic surveillance system, without passing the symptoms through the GP office or any systems connected to their GP consultation. Of course, Norwegian citizens' actual willingness to report symptoms remains to be tested, as what people say and actually do can vary significantly [226].

However, some instances of patients voluntarily reporting symptoms for disease surveillance have been identified over the last years. Influenzanet, an internet-based surveillance system to monitor influenza-like illness (ILI), is now established in several countries in Europe. It started as a project in the Netherlands and Belgium in 2003 [227], then in Portugal in 2005 [228], Italy in 2007 [229], and the UK in 2009 [230]. Since 2011, Germany [231], Austria [232], Switzerland [233], France [234], and Sweden [235] also have used Influenzanet.

Influenzanet has been evaluated in the Netherlands, Belgium, Portugal, and the UK [22-24, 236, 237]. Of these, the UK system was established last and was able to learn from the others. Here, 5000 participants were recruited during the first week through a "publicity campaign involving television, radio, and newspaper coverage and word of mouth", [236] p. 2. Participants registered on a website, received a password-protected account, and completed a background questionnaire regarding "age, gender, household size and composition, occupation, location of home and workplace", in addition to whether they had received an influenza vaccine or not, and if they were members of a defined high-risk group [236]. The participants were then asked to complete a symptoms and social contacts questionnaire every week to report whether they had symptoms or not. The symptoms were selected from a list, where "no symptoms" was one option. The questionnaire was "intended to take no more than a couple of minutes to complete", [236] p. 2. Participants could also record data on behalf of other members of their family, such as their children. An e-mail reminder was sent to

participants each week, including a summary of the latest influenza facts. The flu survey website was updated daily. These information initiatives were to keep up the participants' interest in the survey.

In total, 5738 subjects took part, of which 3370 reported only once. To reduce the effect of individuals who only reported their current symptoms when they were recruited, only "reports made by participants who participated more than once" were included [236] p. 3. This resulted in 2369 participants contributing to 17,532 reports over 5.5 months [236]. Obviously, the participants did not report every week. They were probably "more motivated to complete the surveys on those weeks when they experienced symptoms" [236] p. 4. The resulting sample was not demographically or geographically representative, but the participants' risk statuses were similar to those of the general population, except for the children [236]. To sum up the results, Influenzanet provides relative size and timing of the peaks that are close to traditional systems, although the rates are mainly higher [22-24, 236], and it seems to capture a wider range of cases than traditional (GP-based) surveillance. For example, Influenzanet represents people who have not contacted health care [236], and it tracks changes in health care attendance patterns in real time [236].

The Flutracking system in Australia is very similar to Influenzanet [238-243], and the number of participants has more than doubled between 2008 and 2010 [238]. Flutracking is also used to estimate influenza vaccine effectiveness [238, 242] by comparing "ILI syndrome rates between vaccinated and unvaccinated participants to detect inter-pandemic and pandemic influenza and provide early confirmation of vaccine effectiveness or failure" [238] p. 288. The survey takes less than 15 seconds to complete [238]. Flutracking demonstrates a correlation with other, more traditional surveillance systems, such as lab results [240, 243] and data reported by GPs [240], in terms of timing and scale of seasonal influenza epidemics, as well as accurately detecting the timing and peak of the 2009 influenza pandemic and being less biased than other systems using treatment-seeking behaviour and protocols for laboratory testing [241].

There is also a FluTracker website in Maryland, USA, which aims to investigate infectious diseases internationally through "contributors from around the world including journals, news sources, and citizens" [244].

In Japan, health observations via the Internet through self-reporting by respondents have been validated and found suitable for syndromic surveillance [245, 246]. Also in this case, although response rates were quite high, participants seemed to prefer reporting when symptoms were present [245].

Overall, there are many good examples today indicating that patient-reported symptoms might be a feasible and inexpensive real-time source for surveillance of infectious diseases in both local and national populations. However, the absolute level of incidence in the community needs to be investigated further.

4.2.3 Conclusion: Main research question 1: Syndromic surveillance

Both GPs and patients would benefit from a new and better surveillance system. Lab results are usually considered the most reliable data source, but labs struggle with time delays and may be

biased by testing activity and humans' treatment-seeking behaviour. In recent years, several systems based on patients who report their symptoms have provided very encouraging results. Thus, a combined surveillance approach that uses both lab results and patient-reported symptoms would probably produce the best results with regard to timeliness and reliability.

4.3 Main research question 2: Health care service improvements

Main findings for the overall research question focusing on health care service improvements will be presented briefly and then discussed in the light of related literature.

Main research question 2:

> *Could patients' electronic symptom reporting be feasible in health care service delivery, and what impact does it have on patients, health professionals, and health care systems?*

To reply to main research question 2, it is necessary to go into the two sub-research questions, f2 and u2.

4.3.1 Relevant patient groups, technologies, health service innovations, and research targets (f2)

In order not to repeat the discussions already presented in papers 5–7, but to discuss the findings of these papers in relation to new literature, the Medline search from the systematic review [30] was updated on 1 February, 2013. Possible relevant RCTs were identified by reviewing titles and abstracts, according to the same inclusion and exclusion criteria applied in paper 6. It was considered sufficient to search Medline only, as approximately 70% of the full-text articles assessed for eligibility, and 75% of the articles that were ultimately included in the systematic review, came from Medline.

While the Medline search in the systematic review identified 185 records over nearly 22 years, this new search identified 30 new records for the period November 2011 to 1 February, 2013. Twenty-nine of these studies were published in 2012. Twelve studies were rated as potentially relevant after abstract review, and seven were found to be relevant after full-text review. These figures underline that the area is a growing field of research.

Only five **patient groups** were identified through the systematic review of RCTs [30], while the literature review of abstracts [17], not limited to any trial methodology, identified four additional patient groups as relevant for electronic symptom reporting. The patient groups common to both reviews were respiratory and lung diseases (12 studies identified through the review of RCTs and 48 studies identified in the review of abstracts), cancer (6 RCTs/50 abstracts), psychiatry (6 RCTs/18 abstracts), cardiovascular (3 RCTs/17 abstracts), and diabetes (1 RCT/12 abstracts). Of the seven RCTs found in the updated search, six were added to three of the patient groups: respiratory and lung diseases (1), cardiovascular disease (1), and psychiatry (4) (see Table 4). One of the psychiatry RCTs investigated the effect on anxiety and depression in diabetes patients, and therefore, could also have been placed in the diabetes group [247].

This update confirms that the RCTs within this field still focus mainly on the same patient groups. However, there was one exception—an RCT that did not focus on a specific diagnosis, but on a health

service for multiple health issues [248]. This is a new approach (see Table 4). All RCTs from the updated search focused on long-term conditions, which is in accordance with the findings of the systematic review [30].

Table 4 RCT articles identified in an updated search of Medline, November 2011 to 1 February, 2013, by health service innovation and patient groups

Health service innovation -> Patient group	Monitoring with clinical support	Self-management with clinical support
Respiratory and lung diseases: Asthma		Gustafsson [249]
Cardiovascular disease	Seto [250]	
Psychiatry	Bauer [251] Kauer [252] (recommended as consultation support)	Andersson [253] Van Bastelaar [247]
Multiple health issues	Takahashi [248]	

The literature review mainly identified **technologies** as web, e-diary, and more advanced mobile applications used for electronic symptom reporting, instead of "e-mail and SMS, technologies where the user interface has limited functionality" [17]. The technologies were not investigated in the systematic review, but the updated search from the end of 2011 to the beginning of 2013 supports that the main user interface, both for the patient and the health professional, is through web-based services and advanced mobile phones (see Table 5). The web-based services may include e-mail functionality as well. These are technologies with which most patients are already familiar.

Table 5 Main user interface for patients and health professionals.

User / Main Interface	Patient	Health professional
Web	van Bastelaar [247] Andersson [253] Gustafson [249]	van Bastelaar [247] Andersson [253] Gustafson [249] Takahashi [248]
Advanced mobile phone	Kauer [252] Seto [250]	Kauer [252] Seto [250]
SMS	Baur [251]	
Computer program		Baur [251]
Video conference	Takahashi [248]	

All three monitoring services from the updated search, which make use of mobile phone technology, were found to be feasible and useful by the authors [250-252]. Seto's mobile phone monitoring of heart failure patients had high adherence and was reported as feasible for elderly patients and those with no experience with mobile phones as well [250]. In addition to providing immediate feedback to the patients if something goes wrong, "easy and quick to use" was reported as an important factor of successful monitoring and for the patient to integrate the service into daily life [250].

The one monitoring service that made use of video conference technology on the patient's side had the opposite results. This was Takahashi's study using telemonitoring accomplished by daily

biometrics, symptom reporting, and videoconference downloaded to a website tested on adults older than 60 years and at high risk for rehospitalisation [248]. The system did not result in fewer hospitalisations or ED visits, and mortality was actually higher in the telemonitoring group (cause unknown) [248]. One explanation for the lack of positive effect could be that they did not focus on a specific disease. Another explanation could be that they made use of technology with which patients are not familiar and perhaps found too challenging and resource demanding to use, especially for older people.

The **health service innovations** represented in the update were only within "monitoring with clinical support" (4) and "self-management with clinical support" (3). These two groups were also the largest groups in the systematic review. There were no new studies within "consultation support", except one of the monitoring trials was also recommended as a consultation support solution [252], but was not tested for this purpose. Whereas the combination of monitoring and respiratory and lung diseases formed the largest group (28%) in the systematic review [30], no such combinations were identified in the updated search. Four of seven (4/7) studies are within psychiatry, a number that was only 6/29 in the systematic review. We now find studies within both monitoring and self-management for the psychiatry patient group, while there were no studies within the combination monitoring and psychiatry in the systematic review. This confirms our assumption from paper 6 [30] that new patient groups (we found one: "Multiple health issues") and new combinations of patient groups and health service innovations (we found one, again: psychiatry and monitoring) could be expected.

The most common research target in the update according to the IOM quality areas [115], as in the systematic review, was disease-specific health benefits at the patient level; the second most common target was patient-centred care [30]. Only two of the studies in the update aimed for reduced health care costs: the monitoring study focusing on multiple health issues [248] and the guided internet-delivered cognitive behaviour therapy study for social anxiety disorder (SAD) that compared effects of using inexperienced therapists [253]. This confirms that the research focuses on the same issues, and mainly on outcomes benefitting the patients.

4.3.2 Possible use and effects for patients, health professionals, and the health care system (u2)

Of the 32 RCT papers identified in the systematic review, 12 were excluded due to low methodological quality [29]. The self-management studies were generally of higher methodological quality than the consultation support and monitoring studies [29].

In the systematic review, effects and health benefits were presented according to health service innovations [29]. In the following, I will summarize these effects and benefits with regard to patients, health professionals, and the health care system. Then, I will do the same for the studies from the update. Finally, I will briefly discuss benefits for patients, health professionals, and the health care system, in light of both searches, while remembering the relevant literature presented in the introduction.

In the **systematic review,** health benefits for **patients** were identified within consultation support, monitoring, self-management, and therapy [29].
Cancer studies in consultation support were found to provide patient centeredness[21] and positive health benefits for the patients [29, 148, 149]. Most interesting, however, is the fact that the symptom summary made available to the physician was found to be useful for focusing the conversation on the symptoms and other issues patients found troublesome and needed help to solve, as well as to guide both the consultation and the clinical decisions [147-149].

While only two monitoring studies reported patient health benefits [155, 158], all studies in self-management reported health benefits [166-174], and satisfaction was also documented [167, 169, 170]. In addition, the one study within therapy reported health benefits for the patient and satisfaction with the treatment [176]. "Only 20% missed face-to-face contact with a therapist, and 85% had positive attitudes to being treated via the Internet instead of face-to-face" [29, 176].

The seven studies identified within the **updated** search also mainly focused on **health benefits** at the **patient** level, and six of these studies supported electronic symptom reporting as a feasible and useful service for the patient: three within monitoring [250-252] and three within self-management [247, 249, 253].

In the **systematic review**, only a few benefits for **health professionals** were identified. These were within consultation support and self-management, with none within monitoring. Consultation support studies reported usefulness of the summaries during a consultation [149] and a reduced need for symptom management [148]. Within self-management, some reduction in number of consultations was reported [167, 168], in addition to less therapist time for Internet-delivered treatment [171]. On the other hand, one e-mail based study resulted in longer therapist time when it was compared with guided self-help [172].

In the **systematic review**, very few benefits for the **health care system** were identified. Identified benefits were within consultation support and partly within self-management. Although nearly all studies within monitoring aimed to reduce health care costs, such benefits were not identified [155, 160, 163, 165, 254], except for in one study [160]. In consultation support, visit duration was found to be the same, whether a summary was used or not [149]; in self-management, one Internet treatment was reported as nearly four times cheaper than group treatment [171].

Two of the studies in the **updated search** aimed for reduced health care costs: no positive effect was found in the monitoring study [248], and possible health care cost reduction when using inexperienced therapists was identified in the self-management study [253].

Looking at the literature review, the systematic review, the updated search, and other literature presented in the introduction, they all point in the same direction. First of all, most of the research within this field focuses on patients' benefits, and many of these trials confirm that electronic

[21] Patient centeredness is according to Crossing the Quality Chasm: "providing care that is respectful of and responsive to individual patient preferences, needs, and values and ensuring that patient values guide all clinical decision", and includes education of the patient.

symptom reporting has a positive impact on patients' disease and patients' feeling of self-management of their disease.
Second, we found little research that focused on usefulness for health professionals. On the other hand, for many of these trials, the fact that patients experienced fewer or less severe symptoms is also a result of the health professionals' use of the information. Thus, indirectly, it might be possible to say that electronic symptom reporting is also proven useful for health professionals in their work, to identify and solve patients' problems.

Third, the monitoring studies mainly have not proven any reduction in health care costs. As mentioned in paper 6, none of the studies from the systematic review, using computer tailored feedback, investigated possible health care cost reduction, even though the potential should have been much better in these studies than in the monitoring or self-management ones which mainly used human resources [30]. However, the economical aspect seems more promising for consultation support and self-management.

4.3.3 Conclusion: Main research question 2: Health care service improvements

Results produced within this thesis support that patient electronic symptom reporting could be feasible in health care service delivery, especially within self-management, and partly within consultation support. Electronic symptom reporting, in general, does have a positive impact on outcomes relevant to patients, and to some extent, to health professionals and health care systems

4.4 Synergy between syndromic surveillance and health care service improvements

Synergy between improved health care service and the syndromic surveillance strategies, as illustrated in Figure 3, can be exemplified through a primary care scenario where all patients are encouraged or required to report their symptoms electronically before their GP consultation.

As already mentioned, electronic symptom reporting could be useful in many health care settings, such as in self-management and consultation support. It is important to be aware that both of these settings might also include reporting of symptoms relevant to infectious diseases.

In addition, syndromic surveillance is not only interesting in the context of infectious diseases; it could be used for general epidemiological surveillance as well. Therefore, in the suggested scenario, patients report symptoms electronically for various purposes, even though, in the following, we mainly discuss synergy in the context of infectious diseases.

The reporting system can be based on today's positive examples of e-consultations in primary care [20, 21, 95, 255-259]. The process of pre-reporting and grading importance and severity would most probably help patients to clarify their symptoms—for themselves as well—and, as reported earlier, would probably make it easier for the patients to report more symptoms, and more sensitive and serious symptoms. Applications for electronic symptom reporting should also be developed for mobile devices (smart phones, tablets), thereby enabling greater scalability, due to their relatively

low cost compared to traditional systems, and because they provide portability and freedom for the patient.

Symptom information should be made available for syndromic surveillance purposes at the time that the reporting is completed. Then, real-time syndromic surveillance information could be produced at the local, regional, national, and even international levels. To achieve the best "symptom quality" possible, both for syndromic surveillance purposes and for consultation purposes, patients should use a template that structures the reporting [255-257], or a combination of template and free text. In Norway, this template could be based on the ICPC codes "translated" to a symptom description that is easily understandable by the patient. However, the template should probably include more symptoms than the ICPC code system does, and these should be defined by health professionals, including GPs, as the GPs we interviewed found the ICPC codes imprecise [25]. Other examples of template concepts that could be investigated further are the symptom checkers presented at WebMD [260] and the Mayo Clinic [261]. It is also necessary to investigate which symptoms are relevant for international syndromic surveillance, so that data from the Norwegian system could be aggregated to an international level.

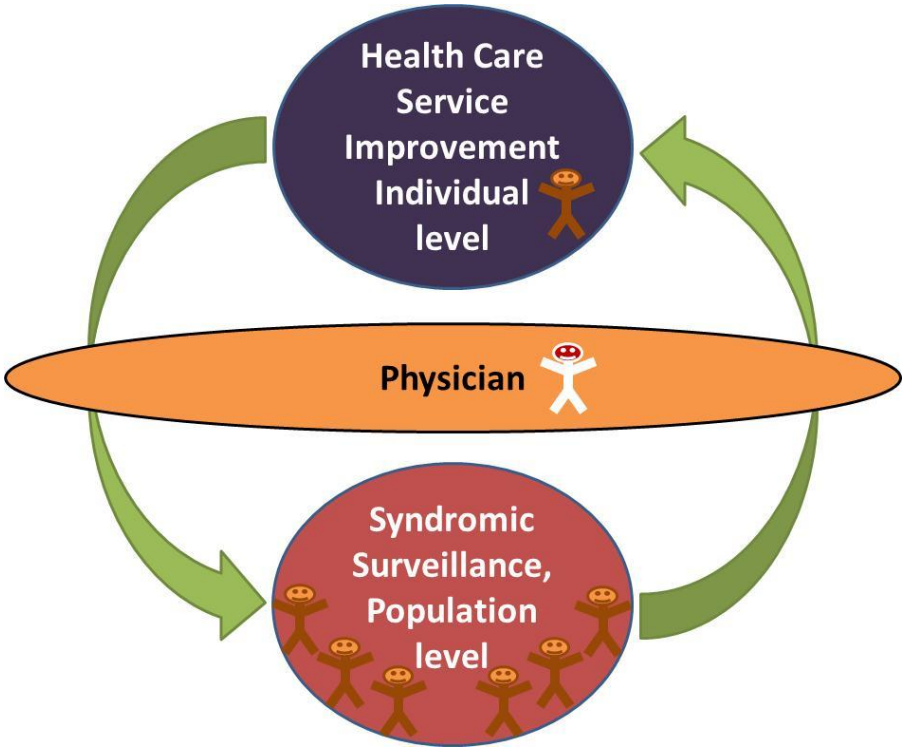


Figure 3 On the individual level, patients report symptoms electronically to their physician before their consultations. A depersonalised copy of these symptoms is made available on the population/public level at the time the reporting is completed, to produce syndromic surveillance reports in an aggregated form. The surveillance reports can be used as a diagnostic aid by the physician during the consultation.

Risk of communicable disease depends on the incidence rate in the communities where the patients have recently spent time [262, 263], which is data that physicians rarely can access at the point of care. As already exemplified, local epidemiological context through local incidence data in real time could be used to predict the risk for a specific communicable disease and improve the diagnostic process and health care service delivery [191-194]. In addition, it has been demonstrated that alerts about disease outbreaks incorporated into the electronic health record system affect clinical behaviour (through providing local situational awareness and timely point-of-care decision support) [264, 265] and result in a significant increase in laboratory testing [265]. Similarly, computer-assisted decision support, notified through electronic health records, has demonstrated a significant positive impact on prescribing behaviour when making use of context-relevant information [266], in addition to a positive effect on the delivery of preventive care [267, 268]. In addition, detection of adverse vaccine events and the rate of reporting these events to public health authorities have been improved though the use of context-sensitive alarms integrated into the health record [269]. One systematic review assessing the effect of computerised clinical decision support systems (CDSSs) found that of 97 controlled trials, 64% improved practitioner performance (improved diagnosis, preventive care, disease management, drug dosing, or drug prescribing) [270]. Another systematic review found that of 32 computer-based decision support systems, in which decision support was provided automatically as part of the clinician workflow and delivered at the time and location of decision-making, and which included actionable recommendations, 30 (94%) significantly improved their clinical practice [271].

In a presentation in December 2012, Fine [272] suggested having the patients to conduct the decision support, as it will save time and money for both the patients and the health care system. The idea is that individuals report and score their own symptoms from home, and that the system automatically compares their symptoms with the actual incidences derived from patients who have tested positive for these symptoms, in order to estimate the risk of specific diseases and suggest whether or not a visit is necessary. Patients with less than 10% risk were given the recommendation not to contact a physician. Fine's study involving 48,000 individuals demonstrated a very good correlation between the home score for predicting strep throat and the actual risk of strep throat, which clearly would reduce the number of medical consultations, time, and costs for the health care system [272].

Yardley's 2010 study supports the suggestion that patients could benefit from conducting the decision support themselves [167]. Patients with minor respiratory problems who used a web-based decision support system provided a "higher level of enablement, higher satisfaction, better understanding of the illness, and a modest effect on reduced consultation rates" [30, 167].

In our anticipated future scenario, the patient might first choose to use a computerised system to "evaluate" the symptoms to determine the actual need for a consultation, and receive tailored advice on self-management of the symptoms. This tailored advice, of course, should make use of the local incidence rate of communicable diseases. Complementarily, symptoms the patients choose to report to the GP will result in tailored computerised advice on self-management, if suitable.

Patient-reported symptoms should be made available to the GP through the EPR system when the consultation starts, as a part of the documentation related to the patient's problem. These pre-

reported and graded symptoms should then be used as a tool to help the GP and the patient focus their conversation on the problems that are most troublesome for the patient. If the problem needs further investigation after this consultation, the reported symptoms could be repeatedly accessed by the GP. In cases where the GP suspects an infectious disease, the patient's symptoms should be matched with the local syndromic surveillance results from places the patient has visited recently, in order to assist the GP in the medical decision making. In addition, the GP could receive advice though the EPR system regarding recommended actions [273] and tests [264, 265], solutions and differential diagnoses [90, 274, 275], and medication and management guidance, if necessary [264, 265]. However, care must be taken not to overload the GP with information, even if it is context-based.

The primary care scenario described above would certainly also be relevant for various settings within specialist care.

Future research

In the following suggestion for future research, points 1–3 are meant to be relevant for patients reporting symptoms electronically for various purposes, while point 4 focuses on additional research questions if reported symptoms are also to be used for syndromic surveillance, and point 5 focuses on additional research questions in the case of established e-consultations.

Before the suggested system is implemented, in addition to the possible future research that is suggested in the papers, it would be feasible and useful to design studies that focus on:

1) **How symptoms should be reported:** What kind of structure or template should be used? Should the reported symptoms be linked to or derived from a standardised code system, such as ICPC or ICD, the WebMD or Mayo Clinic symptom checkers [260, 261], or a mix? The success of others with regard to the use of templates/structure or lack of structure should be investigated as part of this research [20, 21, 95, 255-259].

2) **If patients are able to report and rate symptoms:** Determine how many patients a) are able to complete the computer-based symptom registration and rating when presented with a user-friendly symptom checklist/tool; b) need assistance, and what kind; and c) drop out because of complicated procedures. Further, it is interesting to determine d) the length of time patients spend on registering the symptoms; e) whether there is a correlation between education and the patient being able to report and rate symptoms, as patient education has been reported to be strongly related to patient disclosure of medical information to the physician [101]; f) whether the proportion of patients requiring assistance increases with increasing age (these findings were revealed in a study where patients responded to 60 symptom items on the computer) [276]; and g) whether the impact of an available resource person among the GPs to keep motivation high and provide user support, training, and teaching [277] influenced their adoption of the system.

3) **What are the possible positive effects on health care service:** Some of the effects on health care will be related to quality of consultations. As it is believed that the current intervention will influence the communication process, focusing on measurements and findings that reflect changes in communication is of importance. Increased quality might then be defined

as a set of variables or constructs, measureable by quantitative and qualitative methods. Consequently, positive effects on health and health care might be measured with regard to a) the degree to which the patient remembered everything he/she planned to discuss with the GP (patient after consultation); b) the degree to which the patient discussed/brought up all the problems he/she came for (both GPs and patients); and c) the degree to which the problem the patient came for was solved during the consultation (patient after consultation, possibly also the GP). Further, with regard to symptom usefulness, it would be interesting to determine d) the degree to which the symptoms (initially) brought up by the patient indicated the final diagnosis or problem description provided by the GP; e) if the GP received written information, did he/she actively use the written information in the consultation (GP and patients in intervention group), and if so, how useful was the information; and f) how easy was it to understand the patient's needs; to what degree was the information from the patient clear and to the point (ask GP for patients in both groups). It might also be interesting to investigate g) how and if the use of pre-reported symptoms affects length of consultation/time per consultation, and h) whether pre-consultation symptom reporting has an effect on lab analysis requests and prescriptions. In addition, with regard to consultation quality and general satisfaction, we would want to know i) if pre-consultation symptom reporting leads to higher satisfaction and quality for GPs; j) if pre-consultation symptom reporting leads to higher satisfaction and quality for patients; k) if patient satisfaction differs with regard to age, sex, and educational background, and i) the degree to which satisfaction for patients who visit the GP often differs compared to patients who only visit the GP once in a while. Established instruments should be used as the basis for usability[22] tests [278] and patient satisfaction with the consultation [279-284].

4) **Issues around syndromic surveillance:** If reported symptoms are also to be used for syndromic surveillance, then it will be necessary to thoroughly investigate a number of additional issues, including: a) reliability, timeliness, and accuracy compared to other surveillance sources; b) threats to information security in real-time surveillance systems [285, 286]; and c) the usefulness of surveillance information from the local population as a decision tool to estimate the level of risk for a disease during a consultation.

5) **Issues around e-consultations:** If e-consultations have been established, studies should investigate, for example: a) possible resource utilisation of health professionals; as mentioned in the introduction, other studies suggest that as many as one-third or more of face-to-face consultations in primary care could be substituted with e-consultations [20, 21]; b) improved access to clinical care in the form of reduced waiting time or timeliness for patients [115]; c) the effect of using or not using reimbursement of the physician's time and patients paying fees for the consultation [257].

[22] The extent to which a product can be used by specified users to achieve specified goals with effectiveness, efficiency, and satisfaction in a specified use context.

5 Conclusion

GPs and patients would benefit from a new and better surveillance system. To overcome the time delay associated with using lab results and the possible biases introduced by testing patterns and humans' treatment-seeking behaviour, a combined surveillance approach that uses both lab results and patient-reported symptoms is suggested. The symptom reporting part of the system would be able to provide timely data that would most probably be reliable enough to detect outbreaks of infectious diseases affecting the population, both locally and nationally. The lab result part of the system would provide confirmations of alerts, with a delay of some days. This lab information would also be useful for improving and correcting the design of the self-learning system based on patients' reported symptoms.

In addition, patients' electronic symptom reporting seems to be feasible in health care service delivery, especially within self-management, and partly within consultation support. The electronic symptom reporting, in general, does have a positive impact on outcomes relevant to patients, and to some extent, health professionals and health care systems.

Therefore, my recommendation is to capitalise on the possible synergy between improving the health care service and providing timely syndromic surveillance, as illustrated in Figure 3, through patients reporting their symptoms electronically before their GP consultations. However, further research should be carried out prior to a large-scale implementation of such a service. In addition, I recommend that health care providers promote future self-management services based on best practices.

6 Appendix A: Reason for overlap between paper 4 and the MedInfo 2010 proceeding.

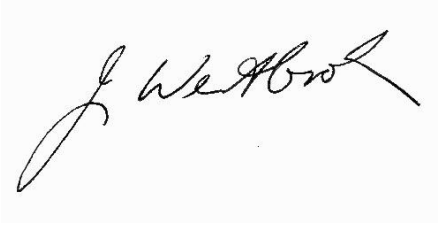
Ms Monika Alise Johansen

Norwegian Centre for Integrated Care and Telemedicine
University Hospital of North Norway
WHO Collaborating Centre for Telemedicine

Dear Ms Johansen

I am writing to confirm that your paper *"Patients as the Primary Information Source for Real-time Surveillance"* was selected for consideration as one of the best papers for the 13th World Congress on Medical Informatics, held in South Africa in September 2010. Your paper was one of 18 papers (out of a total 603 submitted to the Congress) which received the highest scores from the reviewers. You are to be congratulated for this achievement.

Yours Sincerely



Professor Johanna Westbrook and Professor Riccardo Belazzi

Co-Chairs, Scientific Program Committee

7 Appendix B: The proportional odds model

Table 6 A logistic regression with the proportional odds model, based on the same data as that presented in "Bridging the Gap between Patients' Expectations and General Practitioners' Knowledge through Disease Surveillance" [26]

Model	Variable	Coef.	SE	t	P>|t|
1	Gender (female 1, male 0)	0.25	0.12	2.12	0.034
2	Gender (female)	0.24	0.12	1.95	0.051
	Medical visits (0/1)	0.32	0.15	2.16	0.031
	Location (numeric)	0.20	0.055	3.63	0.00028
3	Gender (female)	0.23	0.12	1.91	0.056
	Medical visits (0/1)	0.33	0.15	2.16	0.031
	Location: minor city (ref. city)	0.23	0.16	1.41	0.16
	Location: village (ref. city)	0.55	0.17	3.35	0.00082
	Location: rural (ref. city)	0.53	0.17	3.06	0.0022

Coef.: regression coefficient; SE: standard error of coefficient; SE = standard derivation (SD)/√(sample size); t: t-value; P >|t|: p-value of a z-test comparing t to a standard normal distribution

Stein Olav Skrøvseth performed a logistic regression with the proportional odds model. According to him, the proportional odds assumption was checked and found to be reasonable.

In model 2, location is coded as 0 (city), 1 (minor city), 2 (village), 3 (rural). In model 3, these are treated as unordered categories, and each is compared to the category "city".

The results are consistent with those in [26], with only minor differences. Notably, the relation with gender is now marginally non-significant, while location is consistently highly significant. Note that the updated regression coefficients in the logistic regression model are not directly comparable to the linear model in [26]. The regression coefficient here is the log-odds for each cumulative step of confidence level for the given covariate. For example, in model 1, a regression coefficient on gender of 0.25 means that the odds ratio is exp(0.25)=1.28, such that women have 1.28 times the odds of "high confidence" relative to all lower categories combined.

In addition, the signs/directions of all relations are unchanged and positive. Positive signs indicate that women have a higher degree of confidence than men, albeit non-significant. In addition, those having visited their GP have higher confidence, and those in rural locations have a higher degree of confidence.

For the full model (model 3) with categorised location, it is now clear that the difference between minor and major city is not significant, and the substantial distinction is between urban areas (city, minor city) and rural areas (village, rural).

8 Appendix C: Definitions and requirements regarding proper testing for equivalence

According to Julious (2004), a trial can demonstrate superiority, equivalence, non-inferiority, "as good as or better" or bioequivalence [188]. Both non-inferiority trials and equivalence trials usually "compare the investigative therapy to an active control" [188] p. 1946. In addition, "1. One must be confident that the active control would have been different from placebo had one been employed. 2. One should be able to determine that there is no clinically meaningful difference between investigative treatment and the control. 3. Through comparing the investigative treatment to control one should indirectly be able to determine that it is superior to placebo" [188] p. 1938. These requirements are based on several authors' definitions, including D'Agostino (2003) [190].

Equivalence means to "demonstrate that two treatments have no clinically meaningful difference, i.e. that they are clinically equivalent" in terms of clinical difference *d* [188] p. 1935, Jones (1996) suggests predefining the range of equivalence as an interval from -Δ to +Δ, and "then simply check whether the confidence interval centred on the observed difference lies entirely between -Δ and +Δ. If it does, equivalence is demonstrated; if it does not, there is still room for doubt"[189] p. 36.

Non-inferiority means to "demonstrate that a given treatment is clinically not inferior compared to another" [188] p. 1946, which requires the authors to "define a margin for when the test group is worse than the control group" [187] p. 2. The margin should be related to what experts find clinically relevant [187]. "Technically, a non-inferiority test is nothing other than a one-sided equivalence test, requiring fewer participants to obtain the same power" [187], p. 2. A non-inferiority test shall test "that the target effect was larger than the non-inferiority margin" [187] p. 4.

"*As good as or better*" trials first test whether the treatment is clinically not inferior, and if so, they test whether it is clinically superior compared to the control [188] p. 1954.

In *bioequivalence* trials, "the null and alternative hypotheses are similar to those for equivalence studies" [188] p. 1957. However, bioequivalence studies are "conducted to demonstrate that two formulations of a drug have similar bioavailability i.e. that the same amount of drug gets into the body for each formulation" [188] p. 1957.

9 References

1. Eysenbach G. What is e-health? J Med Internet Res 2001; 3(2): E20. PMID:11720962
2. Kaplan B, Brennan PF. Consumer informatics supporting patients as co-producers of quality. J Am Med Inform Assoc 2001; 8(4): 309-16. PMID:11418537
3. Kummervold PE, Gammon D, Bergvik S, Johnsen JA, Hasvold T, Rosenvinge JH. Social support in a wired world: use of online mental health forums in Norway. Nord J Psychiatry 2002; 56(1): 59-65. PMID:11869468
4. Webb PM, Zimet GD, Fortenberry JD, Blythe MJ. Comparability of a computer-assisted versus written method for collecting health behavior information from adolescent patients. J Adolesc Health 1999; 24(6): 383-8. PMID:10401965
5. Millsopp L, Frackleton S, Lowe D, Rogers SN. A feasibility study of computer-assisted health-related quality of life data collection in patients with oral and oropharyngeal cancer. Int J Oral Maxillofac Surg 2006; 35(8): 761-4. PMID:16697148
6. Nijland N, van Gemert-Pijnen JE, Boer H, Steehouder MF, Seydel ER. Increasing the use of e-consultation in primary care: results of an online survey among non-users of e-consultation. Int J Med Inform 2009; 78(10): 688-703. PMID:19625210
7. Lieberman DZ, Kelly TF, Douglas L, Goodwin FK. A randomized comparison of online and paper mood charts for people with bipolar disorder. Journal of Affective Disorders 2010; 124(1-2): 85-9. PMID:19896202
8. Ljotsson B, Hedman E, Andersson E, Hesser H, Lindfors P, Hursti T, Rydh S, Ruck C, Lindefors N, Andersson G. Internet-delivered exposure-based treatment vs. Stress management for irritable bowel syndrome: A randomized trial. American Journal of Gastroenterology 2011 Aug; 106(8): 1481-1491. PMID:21537360
9. Miller DM, Moore SM, Fox RJ, Atreja A, Fu AZ, Lee J-C, Saupe W, Stadtler M, Chakraborty S, Harris CM, Rudick RA. Web-based self-management for patients with multiple sclerosis: a practical, randomized trial. Telemedicine Journal & E-Health 2011; 17(1): 5-13. PMID:21214498
10. Artinian NT, Harden JK, Kronenberg MW, Vander Wal JS, Daher E, Stephens Q, Bazzi RI. Pilot study of a Web-based compliance monitoring device for patients with congestive heart failure. Heart & Lung 2003; 32(4): 226-33. PMID:12891162
11. Ross SE, Moore LA, Earnest MA, Wittevrongel L, Lin C-T. Providing a web-based online medical record with electronic communication capabilities to patients with congestive heart failure: randomized trial. Journal of Medical Internet Research 2004; 6(2): e12. PMID:15249261
12. Porter SC, Kohane IS, Goldmann DA. Parents as partners in obtaining the medication history. J Am Med Inform Assoc 2005; 12(3): 299-305. PMID:15684127
13. de Jongste JC, Carraro S, Hop WC, Group CS, Baraldi E. Daily telemonitoring of exhaled nitric oxide and symptoms in the treatment of childhood asthma. American Journal of Respiratory & Critical Care Medicine 2009; 179(2): 93-7. PMID:18931330
14. Head BA, Keeney C, Studts JL, Khayat M, Bumpous J, Pfeifer M. Feasibility and Acceptance of a Telehealth Intervention to Promote Symptom Management during Treatment for Head and Neck Cancer. Journal of Supportive Oncology 2011 Jan; 9(1): e1-e11. PMID:21499540
15. Gaertner J, Elsner F, Pollmann-Dahmen K, Radbruch L, Sabatowski R. Electronic pain diary: a randomized crossover study.[Erratum appears in J Pain Symptom Manage. 2004 Dec;28(6):626]. Journal of Pain & Symptom Management 2004; 28(3): 259-67. PMID:15336338
16. Eysenbach G, Diepgen TL. Epidemiological data can be gathered with world wide web. Bmj 1998; 316(7124): 72. PMID:9451290
17. Johansen MA, Henriksen E, Berntsen G, Horsch A. Electronic symptom reporting by patients: a literature review. Stud Health Technol Inform 2011; 169: 13-7. PMID:21893705

18. Barnason S, Zimmerman L, Nieveen J, Schulz P, Miller C, Hertzog M, Tu C. Influence of a symptom management telehealth intervention on older adults' early recovery outcomes after coronary artery bypass surgery. Heart & Lung 2009; 38(5): 364-76. PMID:19755186
19. Zimmerman L, Barnason S, Hertzog M, Young L, Nieveen J, Schulz P, Tu C. Gender differences in recovery outcomes after an early recovery symptom management intervention. Heart and Lung: Journal of Acute and Critical Care 2011 Sep-Oct; 40(5): 429-439. PMID:21501872
20. Adamson SC, Bachman JW. Pilot study of providing online care in a primary care setting. Mayo Clin Proc 2010; 85(8): 704-10. PMID:20516427
21. Kummervold PE, Trondsen M, Andreassen H, Gammon D, Hjortdahl P. Erfaringer med lege-pasient-kontakt over Internett [Patient-physician interaction over the internet]. Tidsskr Nor Laegeforen 2004; 124(20): 2633-6. PMID:15534640
22. van Noort SP, Muehlen M, Rebelo de Andrade H, Koppeschaar C, Lima Lourenco JM, Gomes MG. Gripenet: an internet-based system to monitor influenza-like illness uniformly across Europe. Euro Surveill 2007; 12(7): E5-6. PMID:17991409
23. Friesema IH, Koppeschaar CE, Donker GA, Dijkstra F, van Noort SP, Smallenburg R, van der Hoek W, van der Sande MA. Internet-based monitoring of influenza-like illness in the general population: experience of five influenza seasons in The Netherlands. Vaccine 2009; 27(45): 6353-7. PMID:19840672
24. Marquet RL, Bartelds AI, van Noort SP, Koppeschaar CE, Paget J, Schellevis FG, van der Zee J. Internet-based monitoring of influenza-like illness (ILI) in the general population of the Netherlands during the 2003-2004 influenza season. BMC Public Health 2006; 6: 242. PMID:17018161
25. Johansen MA, Scholl J, Aronsen G, Hartvigsen G, Bellika JG. An exploratory study of disease surveillance systems in Norway. J Telemed Telecare 2008; 14(7): 368-71. PMID:18852319
26. Johansen MA, Johnsen JA, Hartvigsen G, Ellingsen G, Bellika JG. Bridging the gap between patients' expectations and general practitioners' knowledge through disease surveillance. Stud Health Technol Inform 2009; 150: 423-7. PMID:19745346
27. Johansen MA, Scholl J, Hasvold P, Ellingsen G, Bellika JG. "Garbage in, garbage out": extracting disease surveillance data from epr systems in primary care. in CSCW '08 Proceedings of the 2008 ACM conference on Computer supported cooperative work. 2008 San Diego, CA, USA: ACM.
28. Johansen MA, Berntsen G, Shrestha N, Bellika JG, Johnsen JA. An exploratory study of patient attitudes towards symptom reporting in a primary care setting. Benefits for medical consultation and syndromic surveillance? Methods Inf Med 2011; 50(5): 479-86. PMID:21897995
29. Johansen MA, Berntsen GK, Schuster T, Henriksen E, Horsch A. Electronic symptom reporting between patient and provider for improved health care service quality: a systematic review of randomized controlled trials. Part 2: methodological quality and effects. J Med Internet Res 2012; 14(5): e126. PMID:23032363
30. Johansen MA, Henriksen E, Horsch A, Schuster T, Berntsen GK. Electronic symptom reporting between patient and provider for improved health care service quality: a systematic review of randomized controlled trials. Part 1: state of the art. J Med Internet Res 2012; 14(5): e118. PMID:23032300
31. Eysenbach G. Infodemiology and infoveillance: framework for an emerging set of public health informatics methods to analyze search, communication and publication behavior on the Internet. J Med Internet Res 2009; 11(1): e11. PMID:19329408
32. Castillo-Salgado C. Trends and directions of global public health surveillance. Epidemiol Rev 2010; 32(1): 93-109. PMID:20534776
33. WHO. 1999. World Health Organization. Report on infectious diseases: Removing Obstacles to Healthy Development. . http://www.who.int/infectious-disease-report/index-rpt99.html

34. WHO, World Health Organization. The world health report 2007: a safer future: global public health security in the 21st century, 2007.
35. WHO. 2008. International Health Regulations (IHR-2005). http://whqlibdoc.who.int/publications/2008/9789241580410_eng.pdf Accessed: 2012-09-18. Archived by WebCite® at http://www.webcitation.org/6AlryNYnp
36. IOM, Lemon SM, Hamburg MA, Sparling PF, Choffnes ER, Mack A, Global Infectious Disease Surveillance and Detection: Assessing the Challenges - Finding Solutions, Workshop Summary, Institute of Medicine 2007, National Academies Press: Washington, D.C. p. 284.
37. Mandl KD, Overhage JM, Wagner MM, Lober WB, Sebastiani P, Mostashari F, Pavlin JA, Gesteland PH, Treadwell T, Koski E, Hutwagner L, Buckeridge DL, Aller RD, Grannis S. Implementing syndromic surveillance: a practical guide informed by the early experience. J Am Med Inform Assoc 2004; 11(2): 141-50. PMID:14633933
38. Hope K, Durrheim DN, d'Espaignet ET, Dalton C. Syndromic Surveillance: is it a useful tool for local outbreak detection? J Epidemiol Community Health 2006; 60(5): 374-5. PMID:16680907
39. Kman NE, Bachmann DJ. Biosurveillance: a review and update. Adv Prev Med 2012; 2012: 301408. PMID:22242207
40. Reingold A. If syndromic surveillance is the answer, what is the question? Biosecur Bioterror 2003; 1(2): 77-81. PMID:15040185
41. Buehler JW. Review of the 2003 National Syndromic Surveillance Conference--lessons learned and questions to be answered. MMWR Morb Mortal Wkly Rep 2004; 53 Suppl: 18-22. PMID:15714621
42. Foldy SL. Linking better surveillance to better outcomes. MMWR Morb Mortal Wkly Rep 2004; 53 Suppl: 12-7. PMID:15717406
43. Kirkwood A, Guenther E, Fleischauer AT, Gunn J, Hutwagner L, Barry MA. Direct cost associated with the development and implementation of a local syndromic surveillance system. J Public Health Manag Pract 2007; 13(2): 194-9. PMID:17299325
44. General" DoHSOoI. 2007 Report. . Better Management Needed for the National Bio-Surveillance Integration System Program. http://www.oig.dhs.gov/assets/Mgmt/OIG_07-61_Jul07.pdf. Accessed: 2012-09-18. (Archived by WebCite® at http://www.webcitation.org/6Alp5pAK7)
45. Savage R, Chu A, Rosella LC, Crowcroft NS, Varia M, Policarpio ME, Vinson NG, Winter AL, Hay K, Davies RF, Gemmill I, Willison D, Johnson I. Perceived usefulness of syndromic surveillance in Ontario during the H1N1 pandemic. J Public Health (Oxf) 2012; 34(2): 195-202. PMID:22194318
46. van den Wijngaard CC, van Asten L, van Pelt W, Doornbos G, Nagelkerke NJ, Donker GA, van der Hoek W, Koopmans MP. Syndromic surveillance for local outbreaks of lower-respiratory infections: would it work? PLoS One 2010; 5(4): e10406. PMID:20454449
47. Ginsberg J, Mohebbi MH, Patel RS, Brammer L, Smolinski MS, Brilliant L. Detecting influenza epidemics using search engine query data. Nature 2009; 457(7232): 1012-4. PMID:19020500
48. Hulth A, Rydevik G, Linde A. Web queries as a source for syndromic surveillance. PLoS One 2009; 4(2): e4378. PMID:19197389
49. Johnson HA, Wagner MM, Hogan WR, Chapman W, Olszewski RT, Dowling J, Barnas G. Analysis of Web access logs for surveillance of influenza. Stud Health Technol Inform 2004; 107(Pt 2): 1202-6. PMID:15361003
50. Polgreen PM, Chen Y, Pennock DM, Nelson FD. Using internet searches for influenza surveillance. Clin Infect Dis 2008; 47(11): 1443-8. PMID:18954267
51. Wilson K, Brownstein JS. Early detection of disease outbreaks using the Internet. CMAJ 2009; 180(8): 829-31. PMID:19364791
52. Eysenbach G. Infodemiology: tracking flu-related searches on the web for syndromic surveillance. AMIA Annu Symp Proc 2006: 244-8. PMID:17238340

53. Dugas AF, Hsieh YH, Levin SR, Pines JM, Mareiniss DP, Mohareb A, Gaydos CA, Perl TM, Rothman RE. Google Flu Trends: correlation with emergency department influenza rates and crowding metrics. Clin Infect Dis 2012; 54(4): 463-9. PMID:22230244
54. Freifeld CC, Mandl KD, Reis BY, Brownstein JS. HealthMap: global infectious disease monitoring through automated classification and visualization of Internet media reports. J Am Med Inform Assoc 2008; 15(2): 150-7. PMID:18096908
55. Greenlick MR. Educating physicians for population-based clinical practice. Jama 1992; 267(12): 1645-8. PMID:1542174
56. Buehler JW, Hopkins RS, Overhage JM, Sosin DM, Tong V. Framework for evaluating public health surveillance systems for early detection of outbreaks: recommendations from the CDC Working Group. MMWR Recomm Rep 2004; 53(RR-5): 1-11. PMID:15129191
57. Hogan WR, Wagner MM. Accuracy of data in computer-based patient records. J Am Med Inform Assoc 1997; 4(5): 342-55. PMID:9292840
58. Dixon BE, McGowan JJ, Grannis SJ. Electronic laboratory data quality and the value of a health information exchange to support public health reporting processes. AMIA Annu Symp Proc 2011; 2011: 322-30. PMID:22195084
59. Balter S, Weiss D, Hanson H, Reddy V, Das D, Heffernan R. Three years of emergency department gastrointestinal syndromic surveillance in New York City: what have we found? MMWR Morb Mortal Wkly Rep 2005; 54 Suppl: 175-80. PMID:16177711
60. Cooper DL, Verlander NQ, Smith GE, Charlett A, Gerard E, Willocks L, O'Brien S. Can syndromic surveillance data detect local outbreaks of communicable disease? A model using a historical cryptosporidiosis outbreak. Epidemiol Infect 2006; 134(1): 13-20. PMID:16409646
61. Dembek ZF, Carley K, Siniscalchi A, Hadler J. Hospital admissions syndromic surveillance--Connecticut, September 200-November 2003. MMWR Morb Mortal Wkly Rep 2004; 53 Suppl: 50-2. PMID:15714628
62. Smith S, Elliot AJ, Mallaghan C, Modha D, Hippisley-Cox J, Large S, Regan M, Smith GE. Value of syndromic surveillance in monitoring a focal waterborne outbreak due to an unusual Cryptosporidium genotype in Northamptonshire, United Kingdom, June - July 2008. Euro Surveill 2010; 15(33): 19643. PMID:20738999
63. Pavlin JA, Mostashari F, Kortepeter MG, Hynes NA, Chotani RA, Mikol YB, Ryan MA, Neville JS, Gantz DT, Writer JV, Florance JE, Culpepper RC, Henretig FM, Kelley PW. Innovative surveillance methods for rapid detection of disease outbreaks and bioterrorism: results of an interagency workshop on health indicator surveillance. Am J Public Health 2003; 93(8): 1230-5. PMID:12893601
64. Centers for Disease Control and Prevention, Syndromic surveillance: reports from a national conference, 2004, in Morb Mortal Wkly Rep2005.
65. Einbinder JS, Bates DW. Leveraging Information Technology to Improve Quality and Safety. IMIA Yearbook of Medical Informatics 2007. Methods Inf Med. 2007; 46 (Suppl. 1): 22-29
66. Bellika JG, Sue H, Bird L, Goodchild A, Hasvold T, Hartvigsen G. Properties of a federated epidemiology query system. Int J Med Inform 2007; 76(9): 664-76. PMID:16949338
67. Berg M, Goorman E. The contextual nature of medical information. Int J Med Inform 1999; 56(1-3): 51-60. PMID:10659934
68. Bourgeois FT, Porter SC, Valim C, Jackson T, Cook EF, Mandl KD. The value of patient self-report for disease surveillance. J Am Med Inform Assoc 2007; 14(6): 765-71. PMID:17712092
69. Henning KJ. Overwiew of Syndromic Surveillance: What is syndromic surveillance? MMWR Morb Mortal Wkly Rep 2004; 53 Suppl: 5-11. PMID:15714620
70. Osemek P, Kocik J, Pasnik K. [Syndromic surveillance in circumstances of bioterrorism threat--the essence, application abilities and superiority over a traditional epidemiological surveillance]. Pol Merkur Lekarski 2009; 27(162): 535-40. PMID:20120725

71. Coiera E. Four rules for the reinvention of health care. Bmj 2004; 328(7449): 1197-9. PMID:15142933
72. Randeree E, Whetstone M. Personal health records: Patients in control. In: Wilson EV, editors. Patient-Centered E-Health. Hershey, PA: IGI Global; 2009. p.47-59.
73. Drake RE, Deegan PE, Woltmann E, Haslett W, Drake T, Rapp CA. Comprehensive electronic decision support systems. Psychiatr Serv 2010; 61(7): 714-7. PMID:20592007
74. Drake RE, Cimpean D, Torrey WC. Shared decision making in mental health: prospects for personalized medicine. Dialogues Clin Neurosci 2009; 11(4): 455-63. PMID:20135903
75. Andreassen HK, Bujnowska-Fedak MM, Chronaki CE, Dumitru RC, Pudule I, Santana S, Voss H, Wynn R. European citizens' use of E-health services: a study of seven countries. BMC Public Health 2007; 7: 53. PMID:17425798
76. Joinson AN. Self-disclosure in computer-mediated communication: The role of self-awareness and visual anonymity. European Journal of Social Psychology 2001; 31: 177-192.
77. Joinson AN. Knowing me, knowing you: Reciprocal self-disclosure on the Internet. CyberPsychology & Behavior 2001; 4: 587-591.
78. Greist JH, Klein MH, VanCura L. A computer interview by psychiatric patient target symptoms. Archives of General Psychiatry 1973; 29: 247-253.
79. Robinson R, West R. A comparison of computer and questionnaire methods of history-taking in a genito-urinary clinic. Psychology and Health 1992; 6: 77-84.
80. Ferriter M. Computer aided interviewing and the psychiatric social history. Social Work and Social Sciences Review 1993; 4: 255-263.
81. Webb PM, Zimet GD, Fortenberry JD, Blythe MJ. Comparability of a computer-assisted versus written method for collecting health behavior information from adolescent patients. Journal of Adolescent Health 1999; 24: 383-388.
82. Jarlais DD, Paone DC, Milliken J, Turner CF, Miller H, Gribble J, Shi Q, Hagan H, Friedman SR. Audio-computer interviewing to measure risk behavior for HIV among injecting drug users: A quasi-randomized trial. The Lancet 1999; 353: 1657-1661.
83. Hasley S. A comparison of computer-based and personal interviews for gynecologic history update. Obstetrics and Gynecology 1995; 85(4): 494-498.
84. Michaud P-A, Narring F, Ferron C. Alternative methods in the investigation of adolescent's sexual life. Journal of Adolescent Health 1999; 25: 84-90.
85. Ruland C, Roslien J, Bakken S, Kristiansen J. Comparing tailored computerized symptom assessments to interviews and questionnaires. AMIA Annu Symp Proc 2006: 1081. PMID:17238700
86. Johnsen J-AK, Gammon D. Connecting with Ourselves and Others Online: Psychological Aspects of Online Health Communication. In: Wilson E, editors. Patient-Centered E-Health. New York: Medical Information Science Reference; 2009. p.26-46.
87. Broderick JE, Schwartz JE, Vikingstad G, Pribbernow M, Grossman S, Stone AA. The accuracy of pain and fatigue items across different reporting periods. Pain 2008; 139(1): 146-57. PMID:18455312
88. Brody EM, Kleban MH. Physical and mental health symptoms of older people: who do they tell? J Am Geriatr Soc 1981; 29(10): 442-9. PMID:7276408
89. Seland M, Kaasa S, Klepstad P. [Symptoms assessment in cancer patients on admission to a hospital]. Tidsskr Nor Laegeforen 2005; 125(18): 2500-3. PMID:16186872
90. Elvidge K. Improving pain & symptom management for advanced cancer patients with a clinical decision support system. Stud Health Technol Inform 2008; 136: 169-74. PMID:18487726
91. Bates DW, Gawande AA. Improving safety with information technology. N Engl J Med 2003; 348(25): 2526-34. PMID:12815139

92. Sciamanna CN, Diaz J, Myne P. Patient attitudes toward using computers to improve health services delivery. BMC Health Serv Res 2002; 2(1): 19. PMID:12225617
93. Benoit A, Dykes P, Chang F, Gertman P, Vandever W, Li Q, Wald J. Using electronic questionnaires to collect patient reported history. AMIA Annu Symp Proc 2007: 871. PMID:18693972
94. Buzaglo JS, Millard JL, Ridgway CG, Ross EA, Antaramian SP, Miller SM, Meropol NJ. An Internet method to assess cancer patient information needs and enhance doctor-patient communication: a pilot study. J Cancer Educ 2007; 22(4): 233-40. PMID:18067435
95. Wald JS, Businger A, Gandhi TK, Grant RW, Poon EG, Schnipper JL, Volk LA, Middleton B. Implementing practice-linked pre-visit electronic journals in primary care: patient and physician use and satisfaction. J Am Med Inform Assoc 2010; 17(5): 502-6. PMID:20819852
96. Ruland CM. Decision support for patient preference-based care planning: effects on nursing care and patient outcomes. J Am Med Inform Assoc 1999; 6(4): 304-12. PMID:10428003
97. Ruland CM. Handheld technology to improve patient care: evaluating a support system for preference-based care planning at the bedside. J Am Med Inform Assoc 2002; 9(2): 192-201. PMID:11861634
98. Ruland CM, Andersen T, Krahn A. Cancer Patients' Patterns of Use of an Internet System to Support them in Illness Management. AMIA 2009 Proceedings 2009: p. 247.
99. Porter SC, Cai Z, Gribbons W, Goldmann DA, Kohane IS. The asthma kiosk: a patient-centered technology for collaborative decision support in the emergency department. J Am Med Inform Assoc 2004; 11(6): 458-67. PMID:15298999
100. Haugli L, Finset A. [Physician-patient relations in functional disorders]. Tidsskr Nor Laegeforen 2002; 122(11): 1123-5. PMID:12043058
101. Roter DL, Hall JA. Physician's interviewing styles and medical information obtained from patients. J Gen Intern Med 1987; 2(5): 325-9. PMID:3655958
102. Detmar SB, Muller MJ, Schornagel JH, Wever LD, Aaronson NK. Health-related quality-of-life assessments and patient-physician communication: a randomized controlled trial. Jama 2002; 288(23): 3027-34. PMID:12479768
103. Detmar SB. Use of HRQOL questionnaires to facilitate patient-physician communication. Expert Rev Pharmacoecon Outcomes Res 2003; 3(3): 215-7. PMID:19807368
104. Andre B, Ringdal GI, Loge JH, Rannestad T, Kaasa S. Implementation of computerized technology in a palliative care unit. Palliat Support Care 2009; 7(1): 57-63. PMID:19619375
105. Sucher JF, Moore FA, Todd SR, Sailors RM, McKinley BA. Computerized clinical decision support: a technology to implement and validate evidence based guidelines. J Trauma 2008; 64(2): 520-37. PMID:18301226
106. Bergmo TS, Kummervold PE, Gammon D, Dahl LB. Electronic patient-provider communication: will it offset office visits and telephone consultations in primary care? Int J Med Inform 2005; 74(9): 705-10. PMID:16095961
107. Fine AM, Kalish LA, Forbes P, Goldmann D, Mandl KD, Porter SC. Parent-driven technology for decision support in pediatric emergency care. Jt Comm J Qual Patient Saf 2009; 35(6): 307-15. PMID:19565690
108. Porter SC, Forbes P, Feldman HA, Goldmann DA. Impact of patient-centered decision support on quality of asthma care in the emergency department. Pediatrics 2006; 117(1): e33-42. PMID:16396846
109. Aguirre-Cordova JF, Chavez-Vazquez G, Huitron-Aguilar GA, Cortes-Jimenez N. [Why is surgery cancelled? causes, implications, and bibliographic antecedents]. Gac Med Mex 2003; 139(6): 545-51. PMID:14723050
110. Trentman TL, Mueller JT, Fassett SL, Dormer CL, Weinmeister KP. Day of Surgery Cancellations in a Tertiary Care Hospital: A One Year Review. J Anesthe Clinic Res 2010; 1(109): doi:10.4172/2155-6148.1000109.

111. Yoon SZ, Lee SI, Lee HW, Lim HJ, Yoon SM, Chang SH. The effect of increasing operating room capacity on day-of-surgery cancellation. Anaesth Intensive Care 2009; 37(2): 261-6. PMID:19400490
112. Gonzalez-Arevalo A, Gomez-Arnau JI, delaCruz FJ, Marzal JM, Ramirez S, Corral EM, Garcia-del-Valle S. Causes for cancellation of elective surgical procedures in a Spanish general hospital. Anaesthesia 2009; 64(5): 487-93. PMID:19413817
113. Schofield WN, Rubin GL, Piza M, Lai YY, Sindhusake D, Fearnside MR, Klineberg PL. Cancellation of operations on the day of intended surgery at a major Australian referral hospital. Med J Aust 2005; 182(12): 612-5. PMID:15963016
114. Nelson LJ. Primum utilis esse: the primacy of usefulness in medicine. Yale J Biol Med 1978; 51(6): 655-67. PMID:752199
115. IOM. Committee on Quality of Health Care in America, Institute of Medicine. Crossing the Quality Chasm: A New Health System for the 21st Century. Washington, D.C.: The National Academies Press; 2001, 364. ISBN:0309072808
116. Walsham G. Interpretive case studies in IS research: nature and method. European Journal of Information Systems 1995; 4: 74-81.
117. Klein HK, Myers MD. A Set of Principles for Conducting and Evaluating Interpretive Field Studies in Information Systems MIS Quarterly 1999; Vol. 23 No. 1: 67-93.
118. KITH. 2004. ICPC-2.The International Classification of Primary Care (Description), Norwegian version. Translated and adapted to Norwegian conditions by KITH (Norwegian Centre for Informatics in Health and Social Care) in cooperation with "Norsk selskap for allemennmedisin". [Only in Norwegian]. http://www.kith.no/sokeverktoy/icpc-2/bok/kontaktarsak.html
119. Bailey J. First steps in qualitaive data analysis: transcribing. Family Practice 2008; 25: 127-131.
120. Johansen MA, Johnsen JA, Shrestha N, Bellika JG. Symptoms from patients as the primary information source for real-time surveillance. Stud Health Technol Inform 2010; 160(Pt 1): 427-31. PMID:20841722
121. Hasman A. Highlights of Medinfo 2010. Methods Inf Med 2011(50): 445-6.
122. Kvale S. Dominance Through Interviews and Dialogues. Qualitative Inquiry 2006; 12(3): 480-500.
123. Hewitt J. Ethical components of researcher researched relationships in qualitative interviewing. Qual Health Res 2007; 17(8): 1149-59. PMID:17928485
124. Appelton JV. Analysing qualitative interview data: adressing issues of validity and rehability. Journal of Advanced Nursing 1995; 22: 993-997.
125. Smith LJ. How ethical is ethical research? Recruiting marginalized, vulnerable groups into health services research. J Adv Nurs 2008; 62(2): 248-57. PMID:18394037
126. Ringdal K. Enhet og mangfold. Samfunnsvitenskapelig forskning og kvantitativ metode. [Unity and diversity. Social science research and quantitative methods]. Fagbokforlaget; 2001. ISBN:82-7674-569-5
127. Halkier B. Fokusgrupper. Samfundslitteratur & Roskilde Universitetsforlag; 2005. ISBN:87-593-0912-1
128. Bojlén S, Fokusgruppe - hvad, hvorfor, hvordan?, in Månedskrift for praktisk lægegerning.2001. p. 9 pages.
129. Kummervold PE, Chronaki CE, Lausen B, Prokosch HU, Rasmussen J, Santana S, Staniszewski A, Wangberg SC. eHealth trends in Europe 2005-2007: a population-based survey. J Med Internet Res 2008; 10(4): e42. PMID:19017584
130. Santana S, Lausen B, Bujnowska-Fedak M, Chronaki C, Kummervold PE, Rasmussen J, Sorensen T. Online communication between doctors and patients in Europe: status and perspectives. J Med Internet Res 2010; 12(2): e20. PMID:20551011

131. Altman DG. Practical statistics for medical research. London: Chapman & Hall; 1991. ISBN:0 412 27630 5
132. Armstrong BG, Sloan M. Ordinal regression models for epidemiologic data. Am J Epidemiol 1989; 129(1): 191-204. PMID:2910061
133. KITH. 2004. ICPC-2e International Classification of Primary Care- Coding, Norwegian version. Translated and adapted to Norwegian conditions by KITH (Norwegian Centre for Informatics in Health and Social Care) in cooperation with "Norsk selskap for allemennmedisin". [Only in Norwegian]. http://www.kith.no/upload/1895/ICPC-2-kodekort_fastsatt-04.2004.pdf Archieved at: http://www.webcitation.org/6815fPfhJ
134. Popay J, Williams G. Qualitative research and evidence-based healthcare. J R Soc Med 1998; 91 Suppl 35: 32-7. PMID:9797748
135. Wikipedia. 2009. Qualitative research. http://en.wikipedia.org/wiki/Qualitative_research
136. Suchman LA. Plans and Situated Actions: The Problem of Human-Machine Communication (Learning in Doing: Social, Cognitive and Computational Perspectives). Cambridge University Press; 1987.
137. Geanellos R. Hermeneutic interviewing: An example of its development and use as research metod. Contemporary Nurse 1999; 8: 39-45.
138. Pope C, Ziebland S, Mays N. Qualitative research in health care. Analysing qualitative data. Bmj 2000; 320(7227): 114-6. PMID:10625273
139. California" TRotUo. Scientific literature. UC Berkeley Library Web. Marian Koshland Bioscience & Natural Resources Library. http://www.lib.berkeley.edu/BIOS/bio1bscholcomm.html
140. Higgins J, Green S, The Cochrane Collaboration. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. Available from www.cochrane-handbook.org. , 2011.
141. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA Statement. Open Med 2009; 3(3): e123-e130. PMID:21603045
142. Johansen MA. 2012. List of variables. http://telemed.custompublish.com/getfile.php/1936271.357.dvtfsvvepq/Variabelliste.pdf Archived at: http://www.webcitation.org/67VZUbsga
143. Evans D, Pearson A. Systematic reviews of qualitative research. Clinical Effectiveness in Nursing 2001; 5: 111-119
144. NIPH. MSIS-Statistikk [The Norwegian Surveillance System for Communicable Diseases (MSIS) statistics]. http://www.msis.no/
145. Berry DL, Blumenstein BA, Halpenny B, Wolpin S, Fann JR, Austin-Seymour M, Bush N, Karras BT, Lober WB, McCorkle R. Enhancing patient-provider communication with the electronic self-report assessment for cancer: A randomized trial. Journal of Clinical Oncology 2011 Mar; 29(8): 1029-1035. PMID:21282548
146. Boyes A, Newell S, Girgis A, McElduff P, Sanson-Fisher R. Does routine assessment and real-time feedback improve cancer patients' psychosocial well-being? European Journal of Cancer Care 2006; 15(2): 163-71. PMID:16643264
147. Ruland CM, White T, Stevens M, Fanciullo G, Khilani SM. Effects of a computerized system to support shared decision making in symptom management of cancer patients: preliminary results. Journal of the American Medical Informatics Association 2003; 10(6): 573-9. PMID:12925545
148. Ruland CM, Holte HH, Roislien J, Heaven C, Hamilton GA, Kristiansen J, Sandbaek H, Kvaloy SO, Hasund L, Ellison MC. Effects of a computer-supported interactive tailored patient assessment tool on patient care, symptom distress, and patients' need for symptom

management support: a randomized clinical trial. Journal of the American Medical Informatics Association 2010; 17(4): 403-10. PMID:20595307
149. Velikova G, Booth L, Smith AB, Brown PM, Lynch P, Brown JM, Selby PJ. Measuring quality of life in routine oncology practice improves communication and patient well-being: a randomized controlled trial. Journal of Clinical Oncology 2004; 22(4): 714-24. PMID:14966096
150. Stevens J, Kelleher KJ, Gardner W, Chisolm D, McGeehan J, Pajer K, Buchanan L. Trial of computerized screening for adolescent behavioral concerns. Pediatrics 2008; 121(6): 1099-105. PMID:18519478
151. Leveille SG, Huang A, Tsai SB, Allen M, Weingart SN, Iezzoni LI. Health coaching via an internet portal for primary care patients with chronic conditions: a randomized controlled trial. Medical Care 2009; 47(1): 41-7. PMID:19106729
152. Kearney N, McCann L, Norrie J, Taylor L, Gray P, McGee-Lennon M, Sage M, Miller M, Maguire R. Evaluation of a mobile phone-based, advanced symptom management system (ASyMS) in the management of chemotherapy-related toxicity. Supportive Care in Cancer 2009; 17(4): 437-44. PMID:18953579
153. Chan DS, Callahan CW, Sheets SJ, Moreno CN, Malone FJ. An Internet-based store-and-forward video home telehealth system for improving asthma outcomes in children. American Journal of Health-System Pharmacy 2003; 60(19): 1976-81. PMID:14531243
154. Chan DS, Callahan CW, Hatch-Pigott VB, Lawless A, Proffitt HL, Manning NE, Schweikert M, Malone FJ. Internet-based home monitoring and education of children with asthma is comparable to ideal office-based care: results of a 1-year asthma in-home monitoring trial. Pediatrics 2007; 119(3): 569-78. PMID:17332210
155. Guendelman S, Meade K, Benson M, Chen YQ, Samuels S. Improving asthma outcomes and self-management behaviors of inner-city children: a randomized trial of the Health Buddy interactive device and an asthma diary. Archives of pediatrics & adolescent medicine 2002 Feb; 156(2): 114-20. PMID:11814370
156. Jan R-L, Wang J-Y, Huang M-C, Tseng S-M, Su H-J, Liu L-F. An internet-based interactive telemonitoring system for improving childhood asthma outcomes in Taiwan. Telemedicine Journal & E-Health 2007; 13(3): 257-68. PMID:17603828
157. Prabhakaran L, Chee WY, Chua KC, Abisheganaden J, Wong WM. The use of text messaging to improve asthma control: a pilot study using the mobile phone short messaging service (SMS). Journal of telemedicine and telecare 2010 Jul; 16(5): 286-90. PMID:20576744
158. Rasmussen LM, Phanareth K, Nolte H, Backer V. Internet-based monitoring of asthma: a long-term, randomized clinical study of 300 asthmatic subjects. Journal of Allergy & Clinical Immunology 2005; 115(6): 1137-42. PMID:15940125
159. Willems DCM, Joore MA, Hendriks JJE, Nieman FHM, Severens JL, Wouters EFM. The effectiveness of nurse-led telemonitoring of asthma: results of a randomized controlled trial. Journal of Evaluation in Clinical Practice 2008; 14(4): 600-9. PMID:19126178
160. Lewis KE, Annandale JA, Warm DL, Rees SE, Hurlin C, Blyth H, Syed Y, Lewis L. Does home telemonitoring after pulmonary rehabilitation reduce healthcare use in optimized COPD? A pilot randomized trial. Copd: Journal of Chronic Obstructive Pulmonary Disease 2010; 7(1): 44-50. PMID:20214462
161. Lewis KE, Annandale JA, Warm DL, Hurlin C, Lewis MJ, Lewis L. Home telemonitoring and quality of life in stable, optimised chronic obstructive pulmonary disease. Journal of Telemedicine & Telecare 2010; 16(5): 253-9. PMID:20483881
162. Nguyen HQ, Gill DP, Wolpin S, Steele BG, Benditt JO. Pilot study of a cell phone-based exercise persistence intervention post-rehabilitation for COPD. International Journal of Copd 2009; 4: 301-13. PMID:19750190

163. Carrasco MP, Salvador CH, Sagredo PG, Marquez-Montes J, Gonzalez de Mingo MA, Fragua JA, Rodriguez MC, Garcia-Olmos LM, Garcia-Lopez F, Carrero AM, Monteagudo JL. Impact of patient-general practitioner short-messages-based interaction on the control of hypertension in a follow-up service for low-to-medium risk hypertensive patients: a randomized controlled trial. IEEE Trans Inf Technol Biomed 2008; 12(6): 780-91. PMID:19000959
164. Santamore WP, Homko CJ, Kashem A, McConnell TR, Bove AA. Using a telemedicine system to decrease cardiovascular disease risk in an underserved population: design, use, and interim results. Conf Proc IEEE Eng Med Biol Soc 2007; 2007: 3701-4. PMID:18002801
165. Schwarz KA, Mion LC, Hudock D, Litman G. Telemonitoring of heart failure patients and their caregivers: a pilot randomized controlled trial. Progress in Cardiovascular Nursing 2008; 23(1): 18-26. PMID:18326990
166. DeVito Dabbs A, Dew MA, Myers B, Begey A, Hawkins R, Ren D, Dunbar-Jacob J, Oconnell E, McCurry KR. Evaluation of a hand-held, computer-based intervention to promote early self-care behaviors after lung transplant. Clinical Transplantation 2009; 23(4): 537-45. PMID:19473201
167. Yardley L, Joseph J, Michie S, Weal M, Wills G, Little P. Evaluation of a Web-based intervention providing tailored advice for self-management of minor respiratory symptoms: exploratory randomized controlled trial. Journal of Medical Internet Research 2010; 12(4): e66. PMID:21159599
168. van der Meer V, Bakker MJ, van den Hout WB, Rabe KF, Sterk PJ, Kievit J, Assendelft WJJ, Sont JK, Group SS. Internet-based self-management plus education compared with usual care in asthma: a randomized trial.[Summary for patients in Ann Intern Med. 2009 Jul 21;151(2):I-42; PMID: 19620146]. Annals of Internal Medicine 2009; 151(2): 110-20. PMID:19620163
169. Nguyen HQ, Donesky-Cuenco D, Wolpin S, Reinke LF, Benditt JO, Paul SM, Carrieri-Kohlman V. Randomized controlled trial of an internet-based versus face-to-face dyspnea self-management program for patients with chronic obstructive pulmonary disease: pilot study. Journal of Medical Internet Research 2008; 10(2): e9. PMID:18417444
170. Berger T, Caspar F, Richardson R, Kneubuhler B, Sutter D, Andersson G. Internet-based treatment of social phobia: A randomized controlled trial comparing unguided with two types of guided self-help. Behaviour Research and Therapy 2011 Mar; 49(3): 158-169. PMID:21255767
171. Bergstrom J, Andersson G, Ljotsson B, Ruck C, Andreewitch S, Karlsson A, Carlbring P, Andersson E, Lindefors N. Internet-versus group-administered cognitive behaviour therapy for panic disorder in a psychiatric setting: a randomised trial. BMC Psychiatry 2010; 10: 54. PMID:20598127
172. Vernmark K, Lenndin J, Bjärehed J, Carlsson M, Karlsson J, Oberg J, Carlbring P, Eriksson T, Andersson G. Internet administered guided self-help versus individualized e-mail therapy: A randomized trial of two versions of CBT for major depression. Behaviour research and therapy 2010 May; 48(5): 368-76. PMID:20152960
173. Oerlemans S, van Cranenburgh O, Herremans P-J, Spreeuwenberg P, van Dulmen S. Intervening on cognitions and behavior in irritable bowel syndrome: A feasibility trial using PDAs. Journal of Psychosomatic Research 2011; 70(3): 267-77. PMID:21334498
174. Glasgow RE, Nutting PA, King DK, Nelson CC, Cutter G, Gaglio B, Rahm AK, Whitesides H. Randomized effectiveness trial of a computer-assisted intervention to improve diabetes care. Diabetes Care 2005; 28(1): 33-9. PMID:15616230
175. Williams GC, Lynch M, Glasgow RE. Computer-assisted intervention improves patient-centered diabetes care by increasing autonomy support. Health Psychology 2007; 26(6): 728-34. PMID:18020845

176. Wagner B, Knaevelsrud C, Maercker A. Internet-based cognitive-behavioral therapy for complicated grief: a randomized controlled trial. Death Studies 2006; 30(5): 429-53. PMID:16610157
177. Tuckett AG. Qualitative research sampling: the very real complexities. Nurse Res 2004; 12(1): 47-61. PMID:15493214
178. Carlsen B, Glenton C. What about N? A methodological study of sample-size reporting in focus group studies. BMC Med Res Methodol 2011; 11: 26. PMID:21396104
179. Bellika JG. 2012. The SNOW disease surveillance homepage. http://telemed.custompublish.com/the-snow-agent-system.312475.html
180. Bellika JG. 2012. SNOW sykdomsovervåkning [The SNOW disease surveillance pilot system]. http://snow.cs.uit.no/#/Home
181. Statistics-Norway-1. Befolkningen etter kjønn og alder. Tromsø. 1.1. 2010. Prosent. [The population of Tromsø presented according to gender and age]. Available from http://www.ssb.no/kommuner/region.cgi?nr=19. Last downloaded: 16. March 2011.
182. Statistics-Norway-2. Personer 16 år og over, etter utdanningsnivå og bostedskommune, 2009. [Persons, 16 years or older in accordance with education level and municipality of residence, 2009]. Available from http://www.ssb.no/utniv/tab-2010-06-25-02.html. Last downloaded: 16. March 2011
183. Statistics-Norway-3. Fakta om utdanning 2011 - nøkkeltall fra 2009. [Facts about education 2011- key figures from 2009]. Page 21. Available from http://www.ssb.no/emner/04/02/fakta/fakta2011.pdf. Last downloaded: 16. March 2011
184. Nossen JP, Hva foregår på legekontorene? Ny statistikk fra NAV [What happen at the primary care offices? New statistics from The Norwegian Labour and Welfare Service (NAV)], welfare] A-ovDola, Editor 2007.
185. Campbell NC, Murray E, Darbyshire J, Emery J, Farmer A, Griffiths F, Guthrie B, Lester H, Wilson P, Kinmonth AL. Designing and evaluating complex interventions to improve health care. Bmj 2007; 334(7591): 455-9. PMID:17332585
186. Campbell M, Fitzpatrick R, Haines A, Kinmonth AL, Sandercock P, Spiegelhalter D, Tyrer P. Framework for design and evaluation of complex interventions to improve health. Bmj 2000; 321(7262): 694-6. PMID:10987780
187. Kummervold PE, Johnsen JA, Skrovseth SO, Wynn R. Using noninferiority tests to evaluate telemedicine and e-health services: systematic review. J Med Internet Res 2012; 14(5): e132. PMID:23022989
188. Julious SA. Sample sizes for clinical trials with normal data. Stat Med 2004; 23(12): 1921-86. PMID:15195324
189. Jones B, Jarvis P, Lewis JA, Ebbutt AF. Trials to assess equivalence: the importance of rigorous methods. Bmj 1996; 313(7048): 36-9. PMID:8664772
190. D'Agostino RB, Sr., Massaro JM, Sullivan LM. Non-inferiority trials: design concepts and issues - the encounters of academic consultants in statistics. Stat Med 2003; 22(2): 169-86. PMID:12520555
191. Fine AM, Reis BY, Nigrovic LE, Goldmann DA, Laporte TN, Olson KL, Mandl KD. Use of population health data to refine diagnostic decision-making for pertussis. J Am Med Inform Assoc 2010; 17(1): 85-90. PMID:20064807
192. Fine AM, Brownstein JS, Nigrovic LE, Kimia AA, Olson KL, Thompson AD, Mandl KD. Integrating spatial epidemiology into a decision model for evaluation of facial palsy in children. Arch Pediatr Adolesc Med 2011; 165(1): 61-7. PMID:21199982
193. Fine AM, Nigrovic LE, Reis BY, Cook EF, Mandl KD. Linking surveillance to action: incorporation of real-time regional data into a medical decision rule. J Am Med Inform Assoc 2007; 14(2): 206-11. PMID:17213492

194. Fine AM, Nizet V, Mandl KD. Improved diagnostic accuracy of group A streptococcal pharyngitis with use of real-time biosurveillance. Ann Intern Med 2011; 155(6): 345-52. PMID:21930851
195. Gardner M. Why clinical information standards matter. Bmj 2003; 326(7399): 1101-2. PMID:12763958
196. Brage S, Bentsen BG, Bjerkedal T, Nygard JF, Tellnes G. ICPC as a standard classification in Norway. Fam Pract 1996; 13(4): 391-6. PMID:8872099
197. Botsis T, Bassoe CF, Hartvigsen G. Sixteen years of ICPC use in Norwegian primary care: looking through the facts. BMC Med Inform Decis Mak 2010; 10: 11. PMID:20181271
198. Brøyn N, Lunde ES, Kvalstad I. SEDA- Sentrale data fra allmennlegetjenesten 2004-2006. Ny statistikk fra allmennlegetjenesten? [SEDA- Key data from general practitioners 2004-2006. New statistics from general practitioners?] Reports 2007/15.: Statistics Norway; 2007. ISBN:978-82-537-7171-7
199. Thiru K, De Lusignan S, Sullivan F, Brew S, Cooper A. Three steps to data quality. Inform Prim Care 2003; 11(2): 95-102. PMID:14567876
200. Porcheret M, Hughes R, Evans D, Jordan K, Whitehurst T, Ogden H, Croft P, North Staffordshire General Practice Research N. Data quality of general practice electronic health records: the impact of a program of assessments, feedback, and training. J Am Med Inform Assoc 2004; 11(1): 78-86. PMID:14527973
201. Koeling R, Tate AR, Carroll JA, Automatically Estimating the Incidence of Symptoms Recorded in GP Free Text Notes, in First International Workshop on Managing Interoperability and compleXity in Health Systems (MIXHS'11)2011, ACM: Glasgow, Scotland, UK.
202. de Lusignan S, Wells SE, Hague NJ, Thiru K. Managers see the problems associated with coding clinical data as a technical issue whilst clinicians also see cultural barriers. Methods Inf Med 2003; 42(4): 416-22. PMID:14534643
203. Nadkarni PM, Ohno-Machado L, Chapman WW. Natural language processing: an introduction. J Am Med Inform Assoc 2011; 18(5): 544-51. PMID:21846786
204. Bleeker T. 2012. Open Health Natural Language Processing (OHNLP) Consortium. https://wiki.nci.nih.gov/display/VKC/Open+Health+Natural+Language+Processing+(OHNLP)+Consortium
205. Chapman WW, Nadkarni PM, Hirschman L, D'Avolio LW, Savova GK, Uzuner O. Overcoming barriers to NLP for clinical text: the role of shared tasks and the need for additional creative solutions. J Am Med Inform Assoc 2011; 18(5): 540-3. PMID:21846785
206. Xu H, Stenner SP, Doan S, Johnson KB, Waitman LR, Denny JC. MedEx: a medication information extraction system for clinical narratives. J Am Med Inform Assoc 2010; 17(1): 19-24. PMID:20064797
207. Li L, Chase HS, Patel CO, Friedman C, Weng C. Comparing ICD9-encoded diagnoses and NLP-processed discharge summaries for clinical trials pre-screening: a case study. AMIA Annu Symp Proc 2008: 404-8. PMID:18999285
208. Mehrotra A, Dellon ES, Schoen RE, Saul M, Bishehsari F, Farmer C, Harkema H. Applying a natural language processing tool to electronic health records to assess performance on colonoscopy quality measures. Gastrointest Endosc 2012; 75(6): 1233-9 e14. PMID:22482913
209. Meystre SM, Savova GK, Kipper-Schuler KC, Hurdle JF. Extracting information from textual documents in the electronic health record: a review of recent research. Yearb Med Inform 2008: 128-44. PMID:18660887
210. Chapman WW, Bridewell W, Hanbury P, Cooper GF, Buchanan BG. Evaluation of negation phrases in narrative clinical reports. Proc AMIA Symp 2001: 105-9. PMID:11825163
211. Matheny ME, Fitzhenry F, Speroff T, Green JK, Griffith ML, Vasilevskis EE, Fielstein EM, Elkin PL, Brown SH. Detection of infectious symptoms from VA emergency department and primary care clinical documentation. Int J Med Inform 2012; 81(3): 143-56. PMID:22244191

212. Liu H, Lussier YA, Friedman C. A study of abbreviations in the UMLS. Proc AMIA Symp 2001: 393-7. PMID:11825217
213. Liu H, Lussier YA, Friedman C. Disambiguating ambiguous biomedical terms in biomedical narrative text: an unsupervised method. J Biomed Inform 2001; 34(4): 249-61. PMID:11977807
214. Yli-Hietanen J, Niiranen S, Aswell M, Nathanson L. Domain-specific analytical language modeling--the chief complaint as a case study. Int J Med Inform 2009; 78(12): e27-30. PMID:19307149
215. Savova GK, Masanz JJ, Ogren PV, Zheng J, Sohn S, Kipper-Schuler KC, Chute CG. Mayo clinical Text Analysis and Knowledge Extraction System (cTAKES): architecture, component evaluation and applications. J Am Med Inform Assoc 2010; 17(5): 507-13. PMID:20819853
216. Chapman WW, Dowling JN, Wagner MM. Fever detection from free-text clinical records for biosurveillance. J Biomed Inform 2004; 37(2): 120-7. PMID:15120658
217. Niiranen ST, Yli-Hietanen JM, Nathanson LA. Toward reflective management of emergency department chief complaint information. IEEE Trans Inf Technol Biomed 2008; 12(6): 763-7. PMID:19000956
218. South BR, Chapman WW, Delisle S, Shen S, Kalp E, Perl T, Samore MH, Gundlapalli AV. Optimizing A syndromic surveillance text classifier for influenza-like illness: Does document source matter? AMIA Annu Symp Proc 2008: 692-6. PMID:18999051
219. Hripcsak G, Soulakis ND, Li L, Morrison FP, Lai AM, Friedman C, Calman NS, Mostashari F. Syndromic surveillance using ambulatory electronic health records. J Am Med Inform Assoc 2009; 16(3): 354-61. PMID:19261941
220. Chapman WW, Christensen LM, Wagner MM, Haug PJ, Ivanov O, Dowling JN, Olszewski RT. Classifying free-text triage chief complaints into syndromic categories with natural language processing. Artif Intell Med 2005; 33(1): 31-40. PMID:15617980
221. Gesteland PH, Gardner RM, Tsui FC, Espino JU, Rolfs RT, James BC, Chapman WW, Moore AW, Wagner MM. Automated syndromic surveillance for the 2002 Winter Olympics. J Am Med Inform Assoc 2003; 10(6): 547-54. PMID:12925547
222. Kimia A, Brownstein JS, Olson KL, Zak V, Bourgeois FT, Mandl KD. Lumbar puncture ordering and results in the pediatric population: a promising data source for surveillance systems. Acad Emerg Med 2006; 13(7): 767-73. PMID:16690814
223. Marsden-Haug N, Foster VB, Gould PL, Elbert E, Wang H, Pavlin JA. Code-based syndromic surveillance for influenzalike illness by International Classification of Diseases, Ninth Revision. Emerg Infect Dis 2007; 13(2): 207-16. PMID:17479881
224. Bourgeois FT, Olson KL, Brownstein JS, McAdam AJ, Mandl KD. Validation of syndromic surveillance for respiratory infections. Ann Emerg Med 2006; 47(3): 265 e1. PMID:16492494
225. Zheng W, Aitken R, Muscatello DJ, Churches T. Potential for early warning of viral influenza activity in the community by monitoring clinical diagnoses of influenza in hospital emergency departments. BMC Public Health 2007; 7: 250. PMID:17877836
226. Blomberg J, Burell M, Guest G. An ethnographic approach to design. In: Jacko JA Sears A, editors. The Human-Computer Interaction Handbook. Lawrence Erlbaum Associates; 2003. p.964-986.
227. De-Grote-Griep-Meting. Influenzanet Netherlands and Belgium. https://www.degrotegriepmeting.nl/
228. Gripenet. Influenzanet Portugal. http://www.gripenet.pt/
229. Influweb. Influenzanet Italy. https://www.influweb.it/
230. Flusurvey. Influenzanet UK. http://flusurvey.org.uk/
231. Aktivgegengrippe. Influenzanet Germany. http://www.aktivgegengrippe.de/
232. Aktivgegengrippe. Influenzanet Austria. http://www.aktivgegengrippe.at/
233. Aktivgegengrippe. Influenzanet Switzerland. http://www.aktivgegengrippe.ch/

234. Grippenet. Influenzanet France. https://www.grippenet.fr/
235. Influensakoll. Influenzanet Sweden. https://www.influensakoll.se/
236. Tilston NL, Eames KT, Paolotti D, Ealden T, Edmunds WJ. Internet-based surveillance of Influenza-like-illness in the UK during the 2009 H1N1 influenza pandemic. BMC Public Health 2010; 10: 650. PMID:20979640
237. van Noort SP, Aguas R, Ballesteros S, Gomes MG. The role of weather on the relation between influenza and influenza-like illness. J Theor Biol 2012; 298: 131-7. PMID:22214751
238. Dalton CB, Carlson SJ, Butler MT, Feisa J, Elvidge E, Durrheim DN. Flutracking weekly online community survey of influenza-like illness annual report, 2010. Commun Dis Intell 2011; 35(4): 288-93. PMID:22624489
239. Dalton C, Durrheim D, Fejsa J, Francis L, Carlson S, d'Espaignet ET, Tuyl F. Flutracking: a weekly Australian community online survey of influenza-like illness in 2006, 2007 and 2008. Commun Dis Intell 2009; 33(3): 316-22. PMID:20043602
240. Parrella A, Dalton CB, Pearce R, Litt JC, Stocks N. ASPREN surveillance system for influenza-like illness - A comparison with FluTracking and the National Notifiable Diseases Surveillance System. Aust Fam Physician 2009; 38(11): 932-6. PMID:19893847
241. Carlson SJ, Dalton CB, Durrheim DN, Fejsa J. Online Flutracking survey of influenza-like illness during pandemic (H1N1) 2009, Australia. Emerg Infect Dis 2010; 16(12): 1960-2. PMID:21122231
242. Carlson SJ, Durrheim DN, Dalton CB. Flutracking provides a measure of field influenza vaccine effectiveness, Australia, 2007-2009. Vaccine 2010; 28(42): 6809-10. PMID:20732464
243. Carlson SJ, Dalton CB, Tuyl FA, Durrheim DN, Fejsa J, Muscatello DJ, Francis JL, d'Espaignet ET. Flutracking surveillance: comparing 2007 New South Wales results with laboratory confirmed influenza notifications. Commun Dis Intell 2009; 33(3): 323-7. PMID:20043603
244. Flutrackers. International Flutrackers - Organized from Maryland USA http://www.flutrackers.com/forum/
245. Sugiura H, Ohkusa Y, Akahane M, Sano T, Okabe N, Imamura T. Development of a web-based survey for monitoring daily health and its application in an epidemiological survey. J Med Internet Res 2011; 13(3): e66. PMID:21946004
246. Sugiura H, Ohkusa Y, Akahane M, Sugahara T, Okabe N, Imamura T. Construction of syndromic surveillance using a web-based daily questionnaire for health and its application at the G8 Hokkaido Toyako Summit meeting. Epidemiol Infect 2010; 138(10): 1493-502. PMID:20067657
247. van Bastelaar KM, Pouwer F, Cuijpers P, Riper H, Snoek FJ. Web-based depression treatment for type 1 and type 2 diabetic patients: a randomized, controlled trial. Diabetes Care 2011; 34(2): 320-5. PMID:21216855
248. Takahashi PY, Pecina JL, Upatising B, Chaudhry R, Shah ND, Van Houten H, Cha S, Croghan I, Naessens JM, Hanson GJ. A randomized controlled trial of telemonitoring in older adults with multiple health issues to prevent hospitalizations and emergency department visits. Archives of Internal Medicine 2012; 172(10): 773-9. PMID:22507696
249. Gustafson D, Wise M, Bhattacharya A, Pulvermacher A, Shanovich K, Phillips B, Lehman E, Chinchilli V, Hawkins R, Kim J-S. The effects of combining Web-based eHealth with telephone nurse case management for pediatric asthma control: a randomized controlled trial. Journal of Medical Internet Research 2012; 14(4): e101. PMID:22835804
250. Seto E, Leonard KJ, Cafazzo JA, Barnsley J, Masino C, Ross HJ. Mobile phone-based telemonitoring for heart failure management: a randomized controlled trial. Journal of Medical Internet Research 2012; 14(1): e31. PMID:22356799
251. Bauer S, Okon E, Meermann R, Kordy H. Technology-enhanced maintenance of treatment gains in eating disorders: efficacy of an intervention delivered via text messaging. Journal of Consulting & Clinical Psychology 2012; 80(4): 700-6. PMID:22545736

252. Kauer SD, Reid SC, Crooke AHD, Khor A, Hearps SJC, Jorm AF, Sanci L, Patton G. Self-monitoring using mobile phones in the early stages of adolescent depression: randomized controlled trial. Journal of Medical Internet Research 2012; 14(3): e67. PMID:22732135
253. Andersson G, Carlbring P, Furmark T, Group SOFIER. Therapist experience and knowledge acquisition in internet-delivered CBT for social anxiety disorder: a randomized controlled trial. PLoS ONE [Electronic Resource] 2012; 7(5): e37411. PMID:22649526
254. Willems DCM, Joore MA, Hendriks JJE, Wouters EFM, Severens JL. Cost-effectiveness of a nurse-led telemonitoring intervention based on peak expiratory flow measurements in asthmatics: Results of a randomised controlled trial. Cost Effectiveness and Resource Allocation 2007 Jul; 27(5): 10. PMID:17662113
255. Albert SM, Shevchik GJ, Paone S, Martich GD. Internet-based medical visit and diagnosis for common medical problems: experience of first user cohort. Telemedicine Journal & E-Health 2011; 17(4): 304-8. PMID:21457013
256. Horner K, Wagner E, Tufano J. Electronic consultations between primary and specialty care clinicians: early insights. Issue Brief (Commonw Fund) 2011; 23: 1-14. PMID:22059281
257. Jung C, Padman R, Shevchik G, Paone S. Who are portal users vs. early e-Visit adopters? A preliminary analysis. AMIA Annu Symp Proc 2011; 2011: 1070-9. PMID:22195168
258. Zhou YY, Garrido T, Chin HL, Wiesenthal AM, Liang LL. Patient access to an electronic health record with secure messaging: impact on primary care utilization. Am J Manag Care 2007; 13(7): 418-24. PMID:17620037
259. Padman R, Shevchik G, Paone S, Dolezal C, Cervenak J. eVisit: a pilot study of a new kind of healthcare delivery. Stud Health Technol Inform 2010; 160(Pt 1): 262-6. PMID:20841690
260. WebMD. 2013. Better Information. Better Health. http://www.webmd.com/
261. MayoClinic. 2013. Symptom Checker. http://www.mayoclinic.com/health/symptom-checker/DS00671
262. Fisman DN. Seasonality of infectious diseases. Annu Rev Public Health 2007; 28: 127-43. PMID:17222079
263. Wallinga J, Teunis P, Kretzschmar M. Using data on social contacts to estimate age-specific transmission parameters for respiratory-spread infectious agents. Am J Epidemiol 2006; 164(10): 936-44. PMID:16968863
264. Lurio J, Morrison FP, Pichardo M, Berg R, Buck MD, Wu W, Kitson K, Mostashari F, Calman N. Using electronic health record alerts to provide public health situational awareness to clinicians. J Am Med Inform Assoc 2010; 17(2): 217-9. PMID:20190067
265. Wu WY, Hripcsak G, Lurio J, Pichardo M, Berg R, Buck MD, Morrison FP, Kitson K, Calman N, Mostashari F. Impact of integrating public health clinical decision support alerts into electronic health records on testing for gastrointestinal illness. J Public Health Manag Pract 2012; 18(3): 224-7. PMID:22473114
266. Terrell KM, Perkins AJ, Dexter PR, Hui SL, Callahan CM, Miller DK. Computerized decision support to reduce potentially inappropriate prescribing to older emergency department patients: a randomized, controlled trial. J Am Geriatr Soc 2009; 57(8): 1388-94. PMID:19549022
267. Dexheimer JW, Talbot TR, Sanders DL, Rosenbloom ST, Aronsky D. Prompting clinicians about preventive care measures: a systematic review of randomized controlled trials. J Am Med Inform Assoc 2008; 15(3): 311-20. PMID:18308989
268. Frank O, Litt J, Beilby J. Opportunistic electronic reminders. Improving performance of preventive care in general practice. Aust Fam Physician 2004; 33(1-2): 87-90. PMID:14988972
269. Hinrichsen VL, Kruskal B, O'Brien MA, Lieu TA, Platt R. Using electronic medical records to enhance detection and reporting of vaccine adverse events. J Am Med Inform Assoc 2007; 14(6): 731-5. PMID:17712091

270. Garg AX, Adhikari NK, McDonald H, Rosas-Arellano MP, Devereaux PJ, Beyene J, Sam J, Haynes RB. Effects of computerized clinical decision support systems on practitioner performance and patient outcomes: a systematic review. Jama 2005; 293(10): 1223-38. PMID:15755945
271. Kawamoto K, Houlihan CA, Balas EA, Lobach DF. Improving clinical practice using clinical decision support systems: a systematic review of trials to identify features critical to success. Bmj 2005; 330(7494): 765. PMID:15767266
272. Fine AM. 2012. How Real-time Biosurveillance can Help Clinical practice. http://webcast.jhu.edu/Mediasite/Play/9f8768ab64164ceab7da24435dae16211d
273. Tanaka Y, Shibata S, Ohtuka Y, Hattori M, Aoshima T, Tohyama S, Uchiyama A, Kashihara H, Tamura M, Tsuchiya A, Yoshida K, Sasamori N. Subjective symptoms acquisition system in a health promotion system for the elderly. Committee of System Development, Council of Japan AMHTS Institutions. Methods Inf Med 2000; 39(3): 238-40. PMID:10992751
274. Hunt D, Haynes R, Hanna S, Smith K. Effects of computer-based clinical decision support systems on physician performance and patient outcomes: a systematic review. JAMA. 1998; 280(15): 1339-46. PMID:9794315
275. Johnston ME, Langton KB, Haynes RB, Mathieu A. Effects of computer-based clinical decision support systems on clinician performance and patient outcome. A critical appraisal of research. Ann Intern Med 1994; 120(2): 135-42. PMID:8256973
276. Fyllingen EH, Oldervoll LM, Loge JH, Hjermstad MJ, Haugen DF, Sigurdardottir KR, Paulsen O, Kaasa S. Computer-based assessment of symptoms and mobility in palliative care: feasibility and challenges. J Pain Symptom Manage 2009; 38(6): 827-36. PMID:19833476
277. Andre B, Ringdal GI, Loge JH, Rannestad T, Kaasa S. The importance of key personnel and active management for successful implementation of computer-based technology in palliative care: results from a qualitative study. Comput Inform Nurs 2008; 26(4): 183-9. PMID:18600124
278. ISO/IEC25062, Common Industry Format for Usability Test Reports, 2006.
279. Wolf MH, Putnam SM, James SA, Stiles WB. The Medical Interview Satisfaction Scale: Development of a scale to measure patient perceptions of physician behavior. Journal of Behavioral Medicine 1978; 1(4): 391-401.
280. Mercer SW, Maxwell M, Heaney D, Watt GC. The consultation and relational empathy (CARE) measure: development and preliminary validation and reliability of an empathy-based consultation process measure. Fam Pract 2004; 21(6): 699-705. PMID:15528286
281. Fung CS, Mercer SW. A qualitative study of patients' views on quality of primary care consultations in Hong Kong and comparison with the UK CARE Measure. BMC Fam Pract 2009; 10: 10. PMID:19173724
282. Mercer SW, McConnachie A, Maxwell M, Heaney D, Watt GC. Relevance and practical use of the Consultation and Relational Empathy (CARE) Measure in general practice. Fam Pract 2005; 22(3): 328-34. PMID:15772120
283. Mercer SW, Reynolds WJ. Empathy and quality of care. Br J Gen Pract 2002; 52 Suppl: S9-12. PMID:12389763
284. Mercer SW, Howie JG. CQI-2--a new measure of holistic interpersonal care in primary care consultations. Br J Gen Pract 2006; 56(525): 262-8. PMID:16611514
285. Henriksen E, Johansen MA, Baardsgaard A, Bellika JG. Threats to information security of real-time disease surveillance systems. Stud Health Technol Inform 2009; 150: 710-4. PMID:19745403
286. Bellika JG, Ilebrekke L, Bakkevoll PA, Johansen H, Scholl J, Johansen MA. Authentication and encryption in the Snow disease surveillance network. Stud Health Technol Inform 2009; 150: 725-9. PMID:19745406

Paper I

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Paper VII

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