Guideline development on healthcare related testing

Summary

This thesis describes research in the field of guideline development, more specifically the development of guidelines for healthcare related testing, with the aim of facilitating and improving the process of developing guidelines recommendations about testing. This summary outlines the separate chapters of the thesis and highlights the conclusions.

Chapter 1 provides the general introduction to the thesis. It sets out the rationale for the thesis by introducing the topic and its components, emphasizing their importance and challenges, and defining the aim and research questions.

Guidelines, including clinical practice and public health guidelines, are documents that provide recommendations to enhance healthcare. The development of guidelines follows a clear process that includes systematic reviewing of available evidence and analysis of the benefits and harms of alternative care options, within a guideline panel of experts and representatives from key affected groups. Many organisations worldwide have adopted the GRADE approach, which emphasises the importance of certainty of evidence for clinically relevant differences in people-important outcomes. This approach pays specific attention to guideline development on healthcare related testing, taking into account the indirect link between testing and people-important outcomes, and emphasising the importance of consideration of false positive, false negative and inconclusive test results on people-important outcomes. Although the general competencies and knowledge required for guideline development are known, specific knowledge for creating testing guidelines has, to our knowledge, not yet been established.

The purpose of testing is to improve or prevent deterioration of people-important outcomes. People-important outcomes are components of people's (health) status following an intervention, and are used to assess effectiveness. Unlike treatment, testing usually does not have an immediate impact on people-important outcomes, although there are some exceptions. This implies that a series of steps, such as treatment, must be taken to move from testing to people-important outcomes. Testing in healthcare can serve various purposes, including screening, surveillance, risk classification, diagnosis, staging, treatment triage, prognosis, and follow-up. To assess the value of a test, various aspects should be considered. These include the analytic performance, clinical performance, clinical effectiveness, cost-effectiveness, and the broader impact of the test. Defining the role of a new test relative to existing tests, such as triage or add-on, is also critical.

In practice, both overuse and underuse of tests are common, and this can have a significant impact. For example, laboratory diagnostics accounts for approximately 2% of healthcare spending, yet it influences 64-67% of clinical decisions. Incorrect testing can result in high healthcare costs, unnecessary test burden, and anxiety.

Developing guidelines on healthcare related testing presents several challenges. These include formulating key questions that incorporate people-important outcomes, searching and synthesising evidence, interpreting test accuracy measures, and formulating recommendations. This thesis focuses on challenges and solutions in the development of guideline recommendations about healthcare related testing, with specific attention to the required knowledge for developing these recommendations and tools to facilitate this process. The aim of this thesis is to facilitate and improve guideline development concerning healthcare related testing. This has led to the following research questions:

1. What are challenges and possible solutions when assessing the certainty of evidence of a test-management pathway?
2. Which types of evidence (diagnostic accuracy, burden of the test, natural course, treatment effectiveness, link between test result and administration of treatment) are used to support guideline recommendations about testing?
3. What is the minimum knowledge required for guideline panel members involved in developing recommendations about testing?
4. Can a step-by-step guide aid guideline developers in formulating key questions about testing?

Chapter 2 addresses the first research question. This chapter analyses the added value of a test in an illustrative example. Specifically, it examines the net benefit of specific immunoglobulin E (sIgE) blood testing as an add-on test to history taking compared to history taking alone in patients suspected of having allergic rhinitis in primary care. The critical outcomes examined are relief of nasal or ocular symptoms, while the important outcomes include concentration, sleep problems, work/school absence, and quality of life. By using GRADE for diagnosis, we systematically assessed the available evidence on the elements of the test-management pathway, including test accuracy, test burden, management effectiveness, natural course, and the link between test results and management. Throughout this process, we identified challenges and proposed solutions to address them.

The lack of high certainty evidence for the various elements of the test-management pathway is a major challenge in interpreting the evidence and assessing the net benefit of a test. Another major challenge is the time required to systematically evaluate the complete test-management pathway. To save time, consulting panel members,

including patient representatives, may be a practical solution for selecting critical elements of the pathway for which a systematic review of the evidence should be undertaken. For less critical elements, the guideline panel may then refer to other guidelines, grey literature, professional expertise, and professional and consumer experience. The guideline panel can provide recommendations on the methodological approach for each element of the test-management pathway.

Chapter 3 addresses the second research question. This chapter evaluates the extent to which evidence-based guidelines on tests cover all elements of the test-management pathway. Specifically, it examines publicly accessible guidelines on three common tests: C-reactive protein (CRP) to estimate the likelihood of pneumonia, colonoscopy to detect colon cancer, and fractional exhaled nitric oxide (FeNO) to diagnose (severe) asthma in a systematic document analysis. Fifteen national and international guidelines published between 2016 and 2020 were analysed. The guidelines' methodological quality was evaluated using AGREE-II domain methodology, and it varied from poor to excellent.

Test accuracy was considered in the development of ten out of fifteen guideline recommendations, with four of them being based on a systematic review and rating of the certainty in the evidence. None of the guidelines included an evaluation of all steps of the test-treatment pathway. Three guidelines included consideration of test burden and two of natural course, but without a systematic review of the evidence. Of the three guideline recommendations that included consideration of management effectiveness, one based this on a systematic review and rating of the certainty in the evidence. The link between test results and management was not considered in any of the guidelines. Reporting issues and challenging methodology may explain the lack of transparent consideration of all elements of the test-management pathway.

Chapter 4 addresses the third research question. This is a developmental study, in which we determined the minimum knowledge required for guideline panel members involved in developing recommendations on healthcare related testing. We determined a draft set of knowledge components based on literature review. Subsequently, semi-structured interviews were conducted with nine internationally respected experts in testing in healthcare, test evaluation, guideline development including GRADE for tests, public involvement in guideline development, and training in guideline development on healthcare testing. The knowledge components were modified based on feedback from the interviewees and approved by all study participants.

The list of knowledge components required for guideline panel members to adequately develop recommendations on healthcare related testing consists of 26 items. These

items cover the topics health question, test-management pathway, target population, test, test result, interpretation of test results & subsequent management, and impact on people-important outcomes. The required level of knowledge for each component is also defined. Understanding the test-management pathway concept appears to be the key knowledge component, linking all other essential knowledge components.

Chapter 5 provides four practical examples of test-management pathways for test scenarios in various settings, purposes, and roles. For each test-management pathway example concrete details are meticulously described, for educational purpose. The need for such examples became apparent during the interviews in chapter 4 and in academic presentations on this topic. The scenarios include various types of tests: self-testing, screening, diagnostic testing, and follow-up testing. These examples can be used by guideline methodologists, guideline panel chairs, and trainers to help guideline panel members understand and adopt the test-management pathway concept.

Chapter 6 addresses the fourth research question. In this developmental study, we created a step-by-step guide for guideline developers to specify a test-management pathway using a co-creative design. The draft guide underwent user testing in a workshop with nineteen healthcare professionals and researchers who have expertise and/or interest in guideline development. The adjusted step-by-step guide was subsequently user-tested in a before-after approach. Seven guideline panel members were asked to formulate a guideline question on testing, first without and subsequently with the use of the step-by-step guide.

The step-by-step guide for specifying a test-management pathway consists of five blocks with signalling questions, which emphasise people (including setting and timing), the index test, outcomes of interest, linking outcomes to testing, and comparator. The user can change the order of the steps and questions. Participants found the step-by-step guide helpful for structuring questions and defining the purpose and impact of the test of interest, and were intended to use the guide in a guideline panel setting. The guide should facilitate guideline developers in defining guideline questions on healthcare related testing by identifying relevant elements, which is an essential step in guideline development.

Chapter 7 provides an overview of the results presented in this thesis and a general discussion based on these findings, including a general reflection on methodological strengths and limitations. The thesis highlights the challenges of developing guideline recommendations on healthcare related testing, including the frequent lack of evidence for critical elements of a test-management pathway, and the time required to adequately evaluate the evidence. The thesis highlights the significance of the test-

management pathway concept in guideline development on healthcare related testing. This is crucial to understand for guideline panel members when developing guideline recommendations on healthcare related testing. The thesis also provides examples of test-management pathways and a step-by-step guide for specifying such pathways. These can help to understand the importance of the test-management pathway concept and facilitate the formulation of key questions about healthcare related tests. The research focuses on evaluating the evidence and facilitating guideline panel members in the guideline development process. It does not cover the process of moving from evidence to decision and the roles of guideline methodologists and guideline panel chairs.

In addition to the previous described results, the research has prompted reflections on the concept of test-management pathways. These include the use of more inclusive language over time, as well as a recurring debate regarding the definition of test burden. Furthermore, in published evidence, there is a great focus on diagnostic tests and dichotomous test results, whereas other purposes and test results are less discussed. It is acknowledged that test evaluation in guideline development occurs in a simplified version of reality. Guideline developers should be aware of these insights. Additionally, it is important to raise awareness about the potential downsides of testing, not only in scientific and guideline development environments, but also in the context of shared decision-making. Implementing the test-management pathway in healthcare policymaking could potentially reduce overtesting, overdiagnosis (including overdetection and overdefinition), and subsequent overtreatment. This involves evaluating the net benefit of testing on people-important outcomes in guideline development.

Recommendations for practice include emphasising the importance of the test-management pathway concept when updating guidance on guideline development, incorporating this concept into training of guideline panel members and methodologists, and creating an online tool to specify the test-management pathway by guideline panels. Recommendations for research include identifying the required knowledge for guideline methodologists and guideline panel chairs to develop recommendations on testing, evaluating the step-by-step guide for specifying the test-management pathway in guideline panel settings, and developing and testing educational strategies and tools to facilitate guideline development on healthcare related testing.