Diagnostic Research in Primary Care. The Marburg Declaration

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Summary

At this workshop convened at the University of Marburg (Germany) primary care researchers and methodologists discussed how research can improve diagnostic decision making. They received input from primary care research and practice, clinical epidemiology, cognitive psychology, medical decision-making and mathematics – machine learning. The shortcomings of previous research designs were identified and new approaches discussed. Novel designs will have to integrate the insights from several decades of cognitive science efforts which have largely been neglected. The specific characteristics of the primary care setting must not be forgotten which include the importance of the clinical and psychosocial context, the abundance of information and resulting cognitive load, multimorbidity and the active role of the patient. Participants outlined a research agenda of topics to be prioritised, study designs, and implementation relevant for primary care diagnosis.

Keywords

Diagnosis, cognitive science, research design, primary health care, general practice [MeSH]
Introduction: Workshop in Marburg / Germany

The Department of General Practice at the University of Marburg (Germany) convened a workshop titled “Diagnostic Research: Broadening the Perspective” (March 13-14th, 2013). This workshop received input from primary care research and practice, clinical epidemiology, cognitive psychology, medical decision-making and mathematics – machine learning. Participants from seven countries discussed recent developments and the state of the art in diagnostic research and neighbouring fields, areas of interests for future research, appropriate study designs as well as implications for primary care and related policies. The following declaration is the result of this discussion process and has been agreed upon by the participants.

Diagnostic Process in Primary Care

To have their diagnostic and prognostic uncertainty resolved is one of the main reasons why patients consult. In most countries, primary care is their main point of entry into the health care system. Physicians at this border between the professional system and the life world see unselected cases who may suffer from benign, self-limiting disease, from worries and anxieties related to their life situation, but also from severe life-threatening disease. For their diagnosis primary care physicians mainly rely on the history and the physical examination. Further investigations are only indicated after the range of possible explanations has been narrowed sufficiently.

There is generally little technical difficulty in obtaining information from visual inspection or history taking. However, this places a high cognitive burden on primary
care practitioners. While in many health care settings the patient’s context is ignored, in primary care it contains highly relevant diagnostic information. This includes previous health care utilisation, knowledge of the patient’s family, work place and wider community. A good continuous relationship with a patient helps incorporate this rich information into the diagnostic decision making process. Moreover, patients often contribute relevant insights and conclusions regarding the aetiology of their problem. They are thus active collaborators in the diagnostic process.

The complex nature of the diagnostic task in primary care requires diagnostic categorisations that may differ from pathological-anatomical or physiological definitions in other disciplines. Categories may be more general than these, and they are often oriented towards prognostic and therapeutic relevance rather than pathophysiological plausibility. ¹

While in a specialty clinic there is often a focus on one or few diseases only due to selective referral, in primary care practice a large number of possible diagnostic outcomes is commonly considered. Often these occur simultaneously in a single patient, i.e. multimorbidity is a relative issue here. Referral is mandated if specialist care is likely to resolve uncertainty further by defined investigations. Otherwise, uncertainty is managed in primary care by methods such as watchful waiting, test of time ² or safety netting.

The diagnostic process in medicine cannot be understood as a purely rational exercise. There is ample evidence that cognitive tasks require emotional intelligence. ³ Uncertainty and risk related to diagnostic decisions may result in anxiety. Regret may be felt if the actual outcome of a disease episode differs from what was
assumed at the time of a diagnostic decision. In that case patients may reproach their physicians for diagnostic error, for investigating too little or too much. Sometimes the fear of litigation leads to decisions not in the interest of the patient. The anticipation of all these may influence decisions in a way not always obvious to those concerned.

Diagnostic acts performed by health care providers always fulfil a double task: on one hand they are to estimate disease probabilities so that either relevant disease becomes sufficiently unlikely or treatment can be started. The sheer performance of tests, on the other hand, often allays patients’ and also clinicians’ anxieties. This effect has been important in all health care systems, including traditional or alternative care, but also high-tech hospital medicine. Diagnostic or prognostic validity of a test is not a necessary requirement for this to happen. This ritual function of diagnostic procedures explains the persistence of doubtful or inaccurate testing in medical care.

**Multidisciplinary Contributions**

Clinical epidemiologists have developed study designs and statistical methods to evaluate the accuracy of diagnostic tests or their combinations. The accuracy of a particular test cannot be considered in isolation but depends on the clinical context, the patient population and the results of other tests. The latter may include demographic and psychosocial data. Novel tests must therefore show that they add in terms of accuracy and impact.
From cognitive psychology we have learnt that fast and frugal heuristics are useful to reduce uncertainty. In some areas heuristics have been shown not only to be fast and easy to use but also valid because they make smart use of some features of the environment. Most cognitive psychologists, however, have shied away from what they call ill-defined settings. Paradoxically, these are the occasions causing most anxiety for clinical decision-makers, such as front-line physicians.

In the fields of machine learning, data mining or artificial intelligence strategies and tools have been developed to make sense of vast amounts of data. Theoretically, diagnosis in primary care is a setting where these methods would help us understand the diagnostic process, develop and test new strategies. There are similarities regarding the learning from cases, the definition of prototypes, the development of efficient algorithms and the understanding of uncertainty. However, primary care and medicine in general have been slow to embrace this kind of research.

Cognitive science is the intersection of philosophy, psychology, artificial intelligence, neuroscience, linguistics, and anthropology for the study of human cognition. We think that there is huge potential in this interdisciplinary field to improve our understanding of medical diagnosis.

**Need for research**

There seems to be an inverse care law operating: while the simple means, i.e. the history and physical examination, are the most frequently used by clinicians to reduce uncertainty, this is at the same time the least researched area. This discrepancy is most apparent in generalist primary care. For the evaluation of expensive and
invasive tests, however, test evaluation studies are common and sufficient funding is available for obvious commercial and regulatory reasons. As a result, the evidence base for the accuracy of the history and clinical findings is poorly developed and biased towards secondary and tertiary care.

Ultrasound, ECG and large number of biochemical tests are available to GPs in many European countries. Our current knowledge regarding their contribution to the diagnostic process is limited. Neither is their actual role in diagnostic decision making clear nor do we have recommendations regarding their use based on comprehensive evidence. While diagnostic studies are essentially observational, more interventional studies comparing study arms using a test against control without the test are needed. 13

The use of biomarkers is often suggested to individualise treatments. 14 Although in theory this should improve the effectiveness and safety of treatments, there are only very few situations where biomarkers or profiles of individual patients have become relevant for the management of disease. 15 The development of biomarkers is disease driven, i.e. it originates from insights into the biological mechanisms of diseases and their treatments. Most of these diseases, however, are very rare in primary care. Even if biomarkers are shown to accurately distinguish between groups that differ regarding prognosis, treatment effectiveness and/or safety, they are unlikely to reduce overall uncertainty to a relevant degree. Genetic profiles of common diseases, to name an example, have contributed little to diagnostic or prognostic assessment. Although valid and relevant biomarkers will have a larger impact on
primary care than previously, their contribution to the overall diagnostic task will presumably be small.

**A Research Agenda**

In order to prioritise research in diagnostics in primary care, areas of existing uncertainty should be identified systematically. Surveys with practitioners\textsuperscript{16}, such as interviews or focus groups based on case vignettes, may serve that purpose, but also reviews of previously published work. Data obtained by systematic research (diagnostic studies) and the knowledge accumulated by experienced practitioners will be interesting to compare and to combine.

Mathematical models have reached a level of considerable sophistication. Over the last 30 years there has been a research tradition to model cognitive processes by computer based learning algorithms. However, this work has hardly had an impact on the study of medical diagnosis or on medical practitioners. We expect an improved understanding of clinical reasoning and the development of decision support technologies once this tradition is acknowledged and used within collaborative projects.

Given the large number of possible diseases and the diversity in consequences, accuracy is not sufficient. As soon as several diagnostic outcomes are considered simultaneously, some weighting of outcomes is required for the understanding and the prioritisation of diagnostic processes. Missing an acute coronary syndrome differs from missing oesophageal reflux, to name an example. Weights, however, are ultimately based on values, which we assume to vary between individuals but also
between groups (patients, health professionals). Surveys can help explore these issues. Future decision support systems should incorporate values held by patients and clinicians for a particular decision and related outcomes.

**Objectives and questions for future research**

1. Exploratory – explanatory research
   - Understanding of cognitive processes in primary care diagnosis, their context and related constraints,
   - Understanding of emotions (“gut feelings”, “regret”, “risk as feeling”) and values related to the diagnostic process felt by both clinicians and patients

2. Confirmatory research
   - Evaluation of single tests
   - Derivation and validation of heuristics and diagnostic prediction rules including combinations of tests
   - Studies of impact of diagnostic tests on management, subsequent health outcomes and cost

Study objectives mentioned under 1) are descriptive and analytical. Those under 2) have rather a normative character because they ultimately aim at clinical recommendations.
Research design and methods

Given the breadth and complexity of primary care research, the whole array of research designs and methods can potentially be applied. This includes qualitative and quantitative research, observational and interventional studies, explorative and confirmatory objectives. Among these we regard the following studies as particularly promising.

Qualitative surveys of diagnostic decision making in practice: these may include interviews and focus groups.\textsuperscript{16,17} These studies will allow insights into diagnostic thinking and deciding, information search principles and stopping rules as well as epistemological beliefs. They will help elicit values and emotions regarding particular diseases or scenarios, identify areas of uncertainty and lack of evidence.

Observation of diagnostic work in practice: direct observation and video/audio recording of real consultations or with standardised patients allow insights into actual diagnostic processes. Prospective data collection avoids bias arising from retrospective designs and/or self report.

Experimental simulation studies with human subjects: Case scenarios (vignettes) or, more rarely, standardised patients are used in this kind of study frequently conducted by cognitive psychologists. Ill-defined, complex inferential tasks, however, have not been investigated very often. Regarding the application to primary care decision making, these studies are hypothesis generating at best. Whether they actually reflect in vivo decision making, must be shown in appropriate studies.
Computer modelling: Machine learning provides an opportunity to model diagnostic reasoning, preferably it should to be based on real-life data. Isomorphic models claim to reflect the architecture of cognitive reasoning, whereas paramorphic models are understood as a black box providing valid prediction. Computer based models may serve a descriptive or analytic purpose in that they help understand actual decisions made by clinicians. Computer based modelling may also result in tools supporting and improving diagnostic decision making by clinicians. This kind of intervention has to be evaluated with adequate studies.

Comprehensive diagnostic study design: In this kind of study, patients with a defined clinical problem, such as chest or abdominal pain, are recruited and evaluated for relevant diagnostic outcomes. Data on diagnostic tests potentially modifying the likelihood of outcomes are gathered from each participant. These form a data set which can serve the evaluation of individual tests regarding more than one outcome, the development and validation of diagnostic prediction rules or heuristics. In order to produce understandable and applicable results, analytical strategies should reflect clinical decision making. These data may also help develop computerised decision support systems.

Intervention studies: Controlled trials are the ultimate tests to evaluate the impact of individual tests, diagnostic prediction rules, testing strategies, decision support systems and/or educational interventions. Studies with patient-relevant clinical
endpoints are often not feasible. Clinician behaviour (change in management) can be a useful surrogate measure.

Evidence for Patients, Clinicians and the Health Care System

The main objective of diagnostic research is to improve the evidence base of clinical recommendations for health professionals. While clinicians often have strong opinions regarding the value of diagnostic tests in their practice, there are different kinds of bias associated with tests (“wicked environments”, “illusionary correlations”).

Evidence from systematic studies can provide a more objective view to correct for misconceptions and bias. We should, on the other hand, regard clinical experience as source of wisdom and insight to be explored systematically by appropriate study designs.

Clinicians will appreciate recommendations regarding the use of particular tests, test combinations, heuristics and decision rules. Not having to use invalid tests anymore, saves time and financial resources. Still systems will have to be in place to translate knowledge from research into practice. Clinical practice guidelines, the formulation of simple diagnostic rules, reminders and decision support built into practice software will facilitate the dissemination in practice.

30 years ago there was a wave of enthusiasm regarding expert systems. It was then expected that the computer would replace the clinician with his cognitive limitations. Despite the advancements in this area, expert systems have hardly had an impact on medical care. Today, thresholds to use computers in clinical settings are much lower than previously. Health professionals and increasingly patients routinely interact with
computers during episodes of care. We therefore expect computerised support for diagnostic decision-making to become more relevant. What will the evidence base of these software systems look like? How are they designed to fit smoothly into the process of care? In which kind of scenarios will they be used? How can these systems learn from experience? Will they affect the communication between patients and health care professionals? Will they change or even threaten the roles and the self-image of professions that regard diagnosis as their core task? These are important questions for future research in this area.

Computerised diagnostic support systems well suited to provide feedback for medical education. In real patients, feedback on a diagnostic hypothesis will take days or weeks, until definite investigations have performed and/or the disease run its course. A diagnostic support system can, like a simulator, provide immediate feedback regarding the optimal choice of tests and their interpretation.

While researchers and policy makers discuss the value of point of care tests in clinical decision-making, manufacturers are increasingly advertising diagnostic tests to lay persons. The border between the professional and the lay system becomes thus blurred. However, the majority of symptoms felt by individuals are assessed and managed within the lay sector without consulting a health professional. In other words: most diagnostic assessments have always been performed by lay persons (“folk sector”). More than 200 years ago with the invention of the stethoscope physicians systematically started to use diagnostic technology. Now it is consumer-patients who have access to point-of-care-testing. This will create new challenges for primary care, the border between the professional and the lay sector will have to be
defined differently. How and under which circumstances will consumer-patients use novel tests? Will their uncertainties be reduced or increased? Which behaviours result from testing? What impact will they have on the utilisation of the professional sector? Future research will have to address these questions.

The division of labour in general practice is changing. Nurses, nurse practitioners and physician assistants take over parts of the work previously in the hand of physicians. The implications of these changes will have to be researched.

We should not pretend to eliminate diagnostic uncertainty. Sophisticated models and empirical data show how large residual uncertainty often is even after extensive testing. Professional culture and the communication with patients will have to face this. Future research can help to develop and evaluate means to communicate diagnostic and prognostic uncertainty to patients. Here a balance will have to be struck between transparent communication of uncertainty and the wish of the patient perhaps not to know. Communication of uncertainty should also include the impact, i.e. expected reduction of uncertainty, of possible diagnostic tests. Transparency in this regard will help the wish for further testing entertained by clinicians and patients to be reconciled with the requirements of the wider health care system. This is especially important with expensive and/or invasive advanced technology.

Researchers planning to investigate the validity of symptoms, signs and contextual information have difficulty obtaining funding. Given the rarity of many relevant diseases in primary care, study samples have to be large.\(^{21}\) Obviously, there is little commercial interest in this field. For governments wanting to improve the competitiveness of their respective economies there is hardly an incentive to invest in
this area. Moreover, the public may assume that this is a topic where no new insights can be gained. Against this background clinicians and researchers interested in the topic will have to show the relevance and expected benefit from this kind of investigation. By making optimal use of easy to obtain clinical data, costly and/or invasive investigations can be avoided. Skilful diagnosis is thus not only patient-centred but often improves the cost-effectiveness of health care.

**Conclusion**

Diagnostic research has often been criticised for being overly reductionist in nature. The framework outlined above, with an emphasis on primary care, will reconcile a clear focus on precisely formulated research objectives and sufficient attention to the context in which patients and clinicians live.

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