

**Additional Patient Outcomes and Pathways in
Evaluations of Testing**



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Additional Patient Outcomes and Pathways in Evaluations of Testing

Authors:

Patrick M. M. Bossuyt, Ph.D.^a

Kirsten McCaffery, Ph.D.^b

^a Department of Clinical Epidemiology & Biostatistics, Academic Medical Center, University of Amsterdam, the Netherlands.

^b Screening and Test Evaluation Program, School of Public Health, University of Sydney, Australia

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Abstract

Before medical tests are introduced into practice, they should be properly evaluated. Randomized trials and other comprehensive evaluations of tests and test strategies can best be designed based on an understanding of how tests can benefit or harm patients. Tests primarily affect patients' health by guiding clinical decisionmaking and downstream management, such as the decision to order more tests or to start, stop, or modify treatment. In this paper, the authors demonstrate that tests can have additional effects on patient outcome, which may be emotional, social, cognitive, or behavioral. They present a framework to help researchers and policymakers consider the emotional, social, cognitive, and behavioral effects of testing. These additional effects may be important themselves and may also influence the clinical outcomes of testing through different pathways. The authors provide examples from test evaluations in the literature to illustrate how these additional effects can be important in the evaluation of testing or, indeed, any health intervention.

Introduction

Before medical tests are introduced into practice, they should be properly evaluated, and so should tests already in use when doubts exist about their value. An essential element in evaluations of tests is the extent to which patients benefit from testing relative to undergoing other tests or no testing at all. The best way to evaluate the effects of testing on patient outcome is a randomized controlled trial, in which investigators randomly allocate patients to testing or to a control strategy and compare the aggregated outcomes in both groups.¹ Various randomized designs for evaluating tests are available.² In this White Paper series, Lord and colleagues³ show that a full randomized trial may not always be needed to evaluate test strategies and that other, simpler types of evaluations may suffice under certain conditions.

To collect evidence about the effects of testing, in primary trials or in systematic reviews, investigators have to define the primary and secondary outcome measures in randomized or other trials of testing. This requires an understanding of how tests can affect patient outcome.

In this paper, we propose a framework that researchers and policymakers can consider to ensure that a wider range of relevant effects is considered in evaluations of testing. We offer examples from the literature demonstrating that tests can have important additional effects on patients beyond the clinical ones, which may influence the overall balance of benefits and harms of testing. These examples, documented effects of testing, can also be used as reminders for future evaluations of testing to generate a list of outcomes in our framework that investigators could consider evaluating.

We also show how these additional effects can influence the primary clinical outcome of testing via different pathways than clinical management.

Emotional and social effects can mitigate or amplify the intended effects of testing on clinical outcome. We argue that comprehensive test evaluations should consider the full range of effects, focusing on the ones that are relevant for patients, clinicians, and decisionmakers.

Clinical Management Effects and Direct Effects of Testing

Trials designed to demonstrate a beneficial effect on patients from testing should have a clinical measure as the primary outcome. The primary purpose of health care is to restore or preserve health, so survival, disability, activity, and function are crucial health outcomes. Looking at the published literature is not always helpful to evaluate these effects of testing. Existing testing trials and studies do not always have a health outcome as the primary outcome measure. Researchers sometimes focus on an outcome measure for which they hope to demonstrate a benefit, such as the use of resources, length of stay, or satisfaction, or they concentrate on the results of testing, ignoring the consequences of testing.

The principal way in which testing leads to changes in a patient's health is through changes in clinical decisionmaking and management guided by these test results. Management includes selecting, starting, stopping, or modifying treatment; ordering more tests; or watchful waiting. This pathway is shown schematically in Figure 1. Assessments of the effects of testing on clinicians' diagnostic thinking and subsequent clinical decisionmaking and management feature prominently in proposals for evaluation schemes of medical tests.⁴

Clinical management is not the only pathway through which testing can affect patients' health. Some effects from testing are direct. Several forms of medical testing pose a direct health risk to patients. Colonoscopy, for example, carries a risk of perforation, and cerebral angiography can lead to permanent neurological complications.^{5,6} Yet not all direct health effects from testing are negative. A Cochrane systematic review concluded that subfertile women who received hysterosalpingography with oil-soluble contrast medium instead of water-soluble contrast medium had significantly higher pregnancy rates after testing. This was an effect from testing itself, not generated by changes in downstream decisionmaking and management.⁷

Despite the primary status of clinical outcome measures and the central role of management effects, we believe that a more comprehensive framework is needed in test evaluation. We believe that evaluations of testing should always consider including secondary outcomes measures. In the next sections, we present examples from the literature showing effects from testing on secondary, nonclinical outcomes. We do so using a framework that was informed by the illness perception theories of Leventhal and colleagues⁸ (see Figure 2). In addition to the clinical outcome, we propose consideration of potential emotional, social, cognitive, and behavioral effects of testing. These effects may represent outcomes that are relevant to clinicians, patients, or other decisionmakers. If so, they should be incorporated into test evaluation. The additional effects may accumulate to outweigh any clinical benefits observed from the test by causing emotional, social, cognitive, or behavioral harm. Alternatively, they may bring additional benefits, adding to the clinical effects of testing.

There is a second reason for considering a more comprehensive framework. Even if the clinical outcome remains pivotal in test evaluations, changes in clinical management and direct effects are not the only pathway through which testing may improve patients' health or fail to do so. The emotional, social, cognitive, and behavioral effects from undergoing the test and learning about test results are all connected and can lead to changes in patients' behavior. These changes may amplify or attenuate the intended effect on the primary clinical outcome. Measuring these additional effects could then help explain the magnitude of the clinical effects of testing. Examples follow.

Emotional Effects of Testing

Patients' emotional response to medical testing is probably the most commonly examined of the additional effects. Emotional well-being may be affected as a consequence of receiving a test result—for example, through increases in anxiety, stress, or depression. These may affect aspects of mental health and social and physical functioning. Alternatively, psychological well-being may be enhanced by testing, as it may provide reassurance and enhanced well-being for those testing negative. For patients who test positive, the result may provide information to help them make sense of their symptoms or enable them to revise future life plans in light of their test results.

Screening tests, for example, often cause short-term increases in anxiety or depression among those with positive test results.^{9,10} For some people and for some testing procedures, these negative effects may extend into the longer term.¹¹ A randomized trial of blood glucose self-monitoring among type 2 diabetes patients assessed psychological as well as health outcomes.¹² Psychological assessment included anxiety and depression components. No differences in health indicators were found at 1 year among patients who self-monitored compared to those who did not: the glycosylated hemoglobin levels, body

mass index, self-reported hypoglycemia rates, and adherence were comparable. However, patients randomized to self-monitoring had significantly higher depression scores (by 6 points out of 100) and 5.8-percent higher anxiety scores compared to controls. Whether these differences were clinically significant is not reported, but the authors call for the need to further investigate the potential psychological harms of self-monitoring.

Emotional sequelae also follow from simple aspects of the test process and care pathway. How the test is taken, how the results are delivered to patients (such as by mail or in person and with or without counseling), the type of followup examination, and the waiting period for results and followup can all affect well-being and influence the effect on patient outcome. For example, colposcopy and colonoscopy for the followup of positive cervical and colorectal cancer screening test results are well known to cause high levels of anxiety and distress among patients prior to their examination.¹³ Any test that influences the rate or method of referral to followup may have implications for patient outcome. Richardson and others¹⁴ measured women's anxiety before and after colposcopy and pre- and post-treatment for cervical dysplasia. They found sharp increases and decreases in anxiety before and after each intervention. Prenatal testing provides another useful illustration of the emotional effects of procedures following a positive test result. Pregnant women with test results indicating increased risk of fetal aneuploidy demonstrate extremely high levels of anxiety prior to amniocentesis.^{15,16} Consideration of the full care pathway following from changes to test strategies is therefore needed.

The previous examples illustrate how testing may have adverse emotional effects, and these negative effects could influence the harms-benefits balance of testing, particularly when little or no impact in the primary health outcome is observed. There may also be important beneficial emotional effects from testing. Positive emotional responses to testing include reassurance, peace of mind, and the desire to avoid regret.¹⁷ These are commonly reported by patients and often motivate individuals to participate in testing. Petrie and colleagues¹⁸ evaluated whether providing information about normal findings improved patients' reassurance and reduced anxiety about symptoms when undergoing exercise stress testing in a cardiology department. Patients who received more information from the doctor reported more reassurance on the five-item scale 1 month after the normal test, fewer had chest pain, and fewer patients were taking cardiac drugs.

Testing may also offer the patient the opportunity to get further emotional support, encouragement, and information from a health care provider.¹⁹ A study of the uptake of colorectal cancer screening found perceived benefits, which included the desire for reassurance, positively predicted interest, and attendance at screening.^{20,21} Similarly, the desire to avoid regret has been found to be an important determinant of a range of health behaviors of screening and testing.^{22,23}

Social Effects of Testing

Social dimensions of testing include the areas of social relationships, social function, sexual relationships, and the impact on an individual's actual and perceived social role and position within his or her community. A study of genetic testing for BRCA1 and BRCA2 found that women testing positive for a mutation reported disrupted family relationships and feelings of guilt about passing on the faulty gene to their offspring.²⁴ Similar issues may occur in thrombophilia testing.²⁵

Patients may feel stigmatized and socially isolated as a consequence of testing positive.²⁶ Patients with a negative test result may also experience adverse social and

emotional effects. Genetic screening studies have shown that some women still feel at elevated risk of disease despite their negative test results and report feelings of anxiety and guilt when other family members test positive.²⁷⁻²⁹ Notably, the worst psychological effects are often reported among women who are offered testing but decline.³⁰

Other reported additional effects of testing include legal and ethical issues, which may affect patients' lives. These include discrimination in employment, difficulty in obtaining health insurance, and the ethical duty to report test results once the result is known.³¹⁻³⁴ Many HIV-positive patients encounter legal problems associated with their health status and occasionally face discrimination in employment, housing, and medical care. Genetic testing research represents one area of testing in which this broader range of additional effects and pathways has been considered.³⁵

Cognitive Effects of Testing

Cognitive effects include patients' beliefs, perceptions, and understanding about their test result and condition. The way in which people think about their illness or diagnosis will influence their emotional, social, and behavioral response to it, which may have downstream consequences for health outcomes.³⁶

Patient cognitions include perceptions about the risk of disease, as well as its severity, cause, consequences, duration, and symptomatology.⁸ All may be influenced by testing.

Test results may help patients make sense of their symptoms and lead them to make future life plans in light of their condition. A positive diagnosis of thrombophilia may be beneficial to patients having experienced an episode of venous thromboembolism by providing an explanation as to why they developed thrombosis.²⁵ This is mentioned as a potential beneficial effect from testing, in the absence of solid evidence of positive effects on clinical outcome through changes in management.

A patient's response to test results will depend on his or her prior knowledge and experience of an illness or condition and on his or her current understanding and beliefs. These illness perceptions or illness cognitions have been shown to affect adherence behavior among patients with HIV, diabetes, hypertension, and asthma.³⁶⁻³⁸ Certain beliefs have been associated with greater distress, less adaptive illness behavior with slower recovery, and increased use of health care services.³⁶ Patient beliefs will be influenced by the doctor-patient relationship and by how health information is communicated by health care providers.

Behavioral Effects of Testing

The emotional, social, and cognitive effects of testing may also affect patients' behavior. One of the most obvious pathways between testing and patients' health runs through patient adherence to followup tests and examinations and treatment. Tests that are more inconvenient, unpleasant, uncomfortable, or anxiety inducing may result in lower levels of adherence at the initial test and followup, which may affect the net benefit of the test on health outcomes.

Risk perceptions and anxiety about cancer influence patients' screening behavior following testing, leading to unnecessary overscreening or underscreening. For example, changes in mammography screening have been observed among women with both positive and negative genetic test results.^{39,40} Unnecessary early rescreening among women with low-grade Pap test results is also observed.⁴¹ Qualitative data indicate that these women often overestimate the severity of their low-grade Pap test result and incorrectly believe time is critical in their followup to prevent disease progression.^{42,43}

Testing may also influence people's engagement in other health behaviors, such as following a healthy diet, participating in exercise, and smoking behavior. Such effects can function both positively and negatively. One study examined the unintended effects of colorectal cancer screening on health behaviors and found exercise rates to be lower among the screened group compared to those who were unscreened.⁴⁴ Apparently, the "certificate of health effect" made screening participants persist in existing, adverse health behavior patterns after negative test results.

Alternatively, a positive test result may act as an early warning and trigger perceptions of vulnerability, which in turn stimulate positive behavior change such as adopting a more healthy diet.⁴⁵ The Family Heart Study Group found reduced smoking prevalence in people screened compared to those unscreened in a cardiovascular screening trial (18 percent vs. 23 percent, $P < 0:001$).⁴⁶ This was an intended effect of testing on patients' behavior.

Some patients use medical tests as a way of testing out their own hypotheses and theory about their illness and its determinants. This is described as "naive scientist" behavior.^{47,48} Like the certificate of health effect, it can reinforce unhelpful illness belief structures and negative behavior patterns, as well as lead to unintended consequences.

Patient Outcome After Testing: The Big Picture

Figure 2 summarizes all of the effects discussed so far. In addition to effects on clinical outcome through management changes and the direct health effects, the framework includes the emotional, social, cognitive, and behavioral changes on the patient's side. We would like to emphasize that the examples in this article show that these emotional, social, cognitive, and behavioral effects do not always have to be negative. In many cases, they may be positive and intentional.

Including multiple outcomes in evaluations is not uncommon in medicine, as randomized trials of interventions often collect additional outcomes.⁴⁹ Although primary outcome measures represent the principal focus of the study and have a pivotal role in sample size calculations and statistical testing, most trials will also collect data on secondary outcome measures. The role of analyses carried out on these secondary outcomes is to provide support for—or attenuate—conclusions drawn from the trial's primary outcome measures. By demonstrating mechanisms and elucidating pathways, analyses of these secondary outcomes can add persuasive force—or nuance—to the argument for the beneficial effects of the intervention evaluated. In this, testing is no exception.

Other authors have used alternative frameworks to consider testing, such as the health belief model, the theory of planned behavior, the common-sense model of self-regulation, and the transactional model of stress and coping. Gooding and colleagues³⁵ used these frameworks to understand the uptake of genetic testing for Huntington's disease, Alzheimer's disease, hereditary breast cancer, and hereditary colorectal cancer. Most of these frameworks look at determinants of testing, however, not at the effects of testing.

Whether the additional patient effects of testing negate or amplify the beneficial management effects on clinical outcome will depend on the magnitude of the latter. In situations where the intended clinical benefit from testing is small, variable, and accrued over a long period, smaller negative effects on emotion, social life, cognition, and behavior may outweigh the effect on the primary clinical outcome. Where there is a large and clear benefit in mortality or morbidity from testing, alternative negative effects, such as increases in anxiety and distress, may more readily be tolerated.

Yet differences in the use of tests—between testing and no testing or between alternative test strategies—rarely lead to major clinical changes. The benefits for the individual may sometimes be substantial, but the aggregated outcomes may not be that different. One of the explanations is that management changes will only apply to those with discordant results (i.e., those whose results differ from the old test compared to the new test), which constitute a minority of all tested.⁵⁰ Many of the examples in our paper have been derived from screening, where many have to be invited to achieve a large health effect in some. Screening does not lead to major changes in clinical outcome on a population level, and small negative effects in a large number of participants may offset the beneficial effects, tipping the balance in policymaking against screening. The UK National Screening Committee and the U.S. Preventive Services Task Force explicitly use as one of their criteria that the benefits from the screening program should outweigh the physical and psychological harm caused by the test, diagnostic procedures, and treatment.

The range of effects presented here is very wide. Deciding which outcomes are potentially relevant and have to be measured will depend on the claim of the new test relative to existing tests and current management, and on the additional outcomes as identified by the patients themselves. Health care providers are poor at knowing what outcomes are important to patients unless they explicitly ask.⁵¹ The range of potential outcomes should be explored through existing literature on patient experiences and, if that is not available, through qualitative interviews or patient surveys, with expertise from social or behavioral scientists to protect against bias. The perceived importance of various effects may differ between the patient and the health care provider. Decisions about whether benefits outweigh harms in any new testing strategy should include consumers and patients, either as part of a formal consultative process or as an individual informed or shared decision between the patient and clinician.⁵²

The existence of additional effects and pathways has consequences for the types of studies to evaluate the effects of testing. If such additional pathways exist, evaluating the management effects alone can never be sufficient for estimating the net health effects of testing. Furthermore, evaluating test accuracy in isolation can never be decisive, even if the benefits of treatment are clear for those who test positive and the downsides of treatment are known for those who test negative. Only a randomized trial of testing will then be able to capture all of the intended and unintended effects of testing on the primary clinical outcome and the additional outcomes.

Many studies now include quality-of-life measures to document additional effects of the medical interventions on patients, beyond the primary clinical outcome measures. The construct is variously defined and measured but typically includes measures of social, emotional, and physical functioning. In recent years, more emphasis has been placed on subjective perspectives compared to objective ones such as functional status.⁵³ The more recent World Health Organization quality-of-life instrument also includes the additional dimensions of environment, independence, and spiritual health.^{54,55} Although potentially useful, health-related quality-of-life measures rarely capture all the possible effects of testing discussed here, and they may miss other issues such as stigma, reassurance, or ease of procedure. For evaluating some of the emotional, social, cognitive, and behavioral effects discussed earlier, more specific instruments have to be considered alongside any measure of quality of life.

Selecting measurement instruments requires some additional consideration, one of the questions being whether the aim is to detect a major effect on the clinical outcome or to explain an additional pathway. If one feels that testing may lead to clinically relevant anxiety,

one of the existing anxiety scales can be used. These scales are probably not sensitive enough to detect more subtle changes, which could help to explain changes in patients' behavior that interact with the intended clinical effects of testing.

Conclusion

Our description of the additional outcomes of testing is necessarily incomplete. We have included only emotional, social, cognitive, and behavioral outcomes and pathways on the patient's side, whereas tests also have effects on the health care professional's side beyond the direct health effects and the clinical management effects. Surgeons may use imaging tests to monitor the effectiveness of their interventions and to improve their own performance. Clinicians use tests to increase their diagnostic and therapeutic confidence. Family practitioners can order tests to assist the patient-physician relationship. A full exploration of these effects is beyond the scope of this paper. We feel that the clinician side of effects and pathways is rarely looked at but all important for understanding what happens in practice and may help explain why tests are and are not taken up. Learning, psychological health, and personal satisfaction are important for health care professionals and for quality health care. We will describe these provider effects and these additional pathways in more detail in a followup article paper.

Including the full range of effects that testing may have on patient outcome, as described in this paper, broadens data collection. It renders evaluations of tests and testing strategies inherently multidimensional, and therefore inevitably more complex. We feel that integrating these multiple outcomes into test evaluation is challenging but achievable and should lead to better evaluations of the effects of tests. Ultimately, we hope that it will help improve the delivery of quality health care.

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Figure 1. Direct and management effects on patient outcome

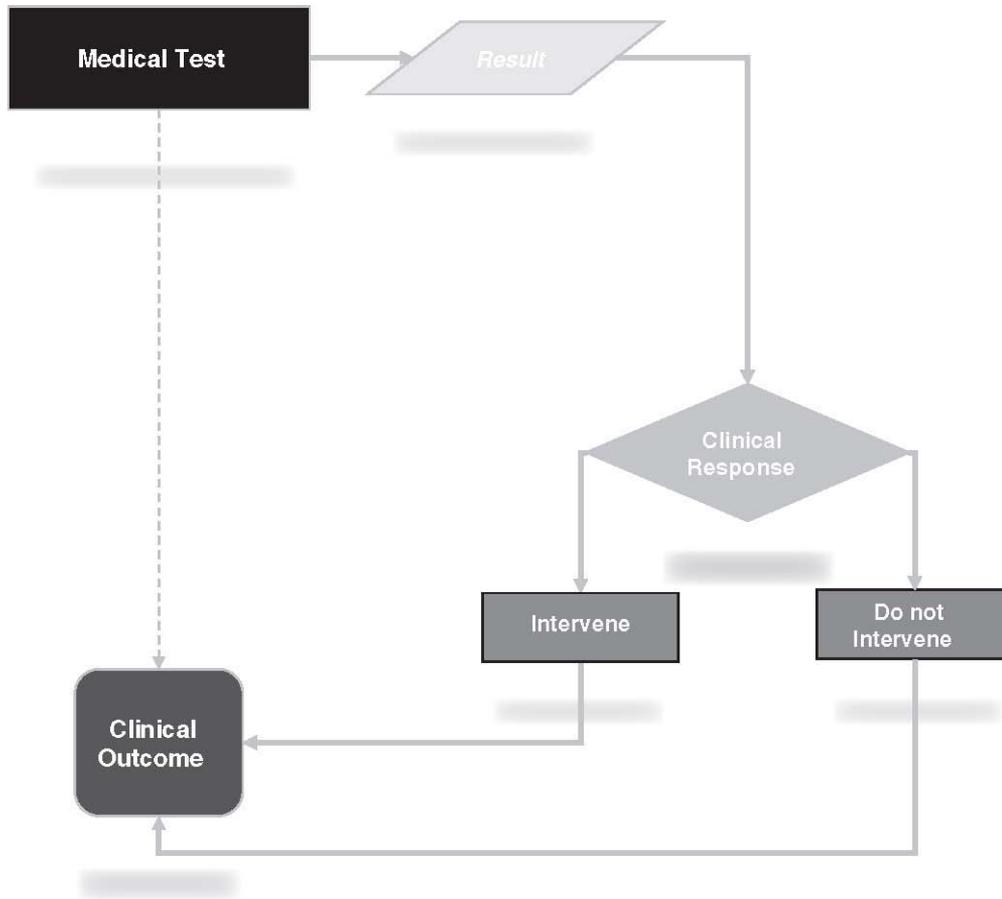


Figure 2. Full range of effects of testing on patient outcome

