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Title

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Permalink

<https://escholarship.org/uc/item/2tb780p3>

Journal

Personalized Medicine, 16(5)

ISSN

1741-0541

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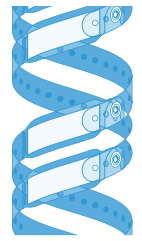
Publication Date

2019-09-01

DOI

10.2217/pme-2019-0045

Peer reviewed



Can precision medicine help achieve the goal of reducing care when the risks exceed the benefits?

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“Precision medicine could improve not only patient outcomes but also outcomes for healthcare systems and society as part of a larger agenda for US healthcare. However, to date there has been a greater focus on the ability of precision medicine to *increase* the use of more effective treatment than its ability to decrease care when the risks exceed the benefits”

First draft submitted: 18 April 2019; Accepted for publication: 2 May 2019; Published online: 25 September 2019

Keywords: economics • evidence-based medicine • precision medicine • preferences

It is widely understood that more healthcare does not always result in better outcomes for patients, and there is ample evidence that many healthcare interventions in the USA are unnecessary and thus drive up costs as well as cause harm [1]. Thus there is a growing movement to develop approaches to reduce care when the risks exceed the benefits, for example, the ‘Choosing Wisely’ program, which aims to facilitate choosing care that is supported by evidence, not duplicative, free from harm and truly necessary [2].

Precision medicine could improve not only patient outcomes but also outcomes for healthcare systems and society as part of a larger agenda for US healthcare. However, to date there has been a greater focus on the ability of precision medicine to *increase* the use of more effective treatment than its ability to decrease care when the risks exceed the benefits [3]. We discuss opportunities for precision medicine to facilitate the goal of decreasing unnecessary care – but also assert that this potential benefit is largely understudied and untapped. We discuss how precision medicine illustrates both the opportunities and challenges to achieving the overarching goal of reducing care when the risks exceed the benefits. We focus particularly on the ubiquitous challenge that actively choosing to forgo treatment is typically more difficult for patients and clinicians than choosing to obtain treatment [4,5].

Early studies suggested that precision medicine was not more likely to facilitate willingness to forgo treatment than other interventions [6]. For example, our nationally representative 2013 study found that many individuals stated that they would not change decisions based on precision medicine test results: when asked if genetic testing indicated that they are not candidates for oncology therapies, most (84%) would seek a second opinion or want therapy anyway [6].

In contrast to the early findings, there is now some evidence suggesting that precision medicine might facilitate the willingness of patients and clinicians to forgo treatment. We use the example of gene expression profiling (GEP) for patients with early-stage breast cancer, which predicts whether patients are likely to benefit from chemotherapy, to illustrate both the opportunities and challenges. There is now widely accepted evidence, including results from a pivotal trial, that GEP testing can identify patients who can safely forgo chemotherapy [7]. There is also strong evidence that the actual use of chemotherapy among these patients has decreased because of GEP testing and other factors [8]. In addition to these clinical studies, there is evidence from consumer and physician surveys that individuals value the information provided by GEP and are willing to use it to make a decision to forgo treatment. For example, a quantitative preferences study found that women state that GEP scores would highly influence their

willingness to forgo chemotherapy [9] and a qualitative study found that GEP would be the ‘deciding factor.’ [10] Similar results were found in a study of physicians: 79% of physicians reported greater confidence in their treatment recommendations (including forgoing chemotherapy) as a result of GEP [11].

Thus, GEP testing provides an example of how precision medicine might contribute to reduction of unnecessary care. However, there is not enough evidence on the extent to which GEP has been successful in reducing unnecessary care because it is a genomics test – and thus whether this example might translate to other precision medicine interventions. We assert that the example of GEP suggests missed opportunities to understand the potential impact of precision medicine and how to harness its benefits, which are relevant not only to this specific example but also more broadly.

Importantly, we did not find any studies directly examining whether the use of precision medicine *per se* is facilitating a greater willingness to forgo treatment and its contribution relative to other factors. We cannot determine from existing studies whether GEP had an influence simply because it met a diagnostic gap or because GEP is based on genomic information and such tests are viewed as more accurate and useful. Studies could shed light on this question through longitudinal, time-series studies that directly examine preferences and beliefs about precision medicine and relationship to actual behaviors. This would enable analysis of changes over time and whether specific evidence such as adoption of a new precision medicine test contributed to changes in forgoing treatment.

Few studies have directly asked patients and clinicians about their preferences regarding forgoing treatment and the impact of precision medicine on their preferences. Such studies could examine the hypothesis that the increasing use of precision medicine could change individual and societal norms by increasing confidence in test results (either because results are more targeted and accurate or because patients and clinicians simply believe that they are). In addition, it is important to explore whether patients and clinicians perceive forgoing treatment as a potential loss (because they are choosing to forgo therapy that, although unlikely to benefit them, could provide benefits). There is extensive literature from the field of behavioral economics that losses are perceived to be much greater than the equivalent gains [4,5]. Studies that examine when and how patients and clinicians perceive forgoing treatment as a loss or a gain would provide useful insights not only for precision medicine but also for other initiatives to reduce unnecessary care. This information could be used to better understand and – as relevant – shape decision-making through appropriate decision aids that enable patients and clinicians to understand the potential benefits of forgoing treatment.

The intersection of patient and clinician beliefs about forgoing treatment based on precision medicine and its impact on behaviors needs further exploration. Although there is evidence that clinicians consider their patients’ preferences in their decisions to use GEP, there is limited evidence on how patient and clinician decision-making interact in practice to either facilitate or hinder the appropriate use of GEP testing and the implications for reducing unnecessary care [8]. Are there characteristics of precision medicine tests that could explain discrepancies in decision-making (e.g., when physicians order GEP even when the patient is not willing to change treatment based on test results) or be used to ameliorate these discrepancies?

There are other examples of clinical areas where precision medicine potentially could facilitate a willingness to forgo treatment. One example is the use of rapid exome sequencing in neonatal intensive care units to diagnose seriously ill newborns. Emerging evidence suggests that such testing enables parents, in the case of terminally ill children, to make the difficult choice for palliative care [12]. A diagnosis thus enables the forgoing of futile care that will not benefit the patient and can cause increased parental distress and unnecessary burdens on the health care system.

In conclusion, precision medicine could potentially facilitate an increased willingness of patients and clinicians to forgo treatment. Although it might be assumed that precision medicine will, by definition, achieve this objective, there needs to be more evidence on whether, why, how and when this effect might occur. It would also be useful to examine where precision medicine could facilitate forgoing unnecessary care but has failed to do so and the reasons, as well as to examine future opportunities for precision medicine to contribute to reduction of unnecessary care.

The need to have patients and clinicians forgo unnecessary and potentially harmful care is great. Precision medicine is not a ‘silver bullet’ that can solve this challenge but it may offer opportunities to achieve this objective. This potential benefit needs further exploration and analysis.

Acknowledgments

The authors gratefully acknowledge input on conceptualization from E Elkin, PhD (Memorial Sloan Kettering Cancer Center) and input and research assistance from M Douglas, MS (University of California, San Francisco). E Elkin was not compensated for this contribution. M Douglas was compensated as part of his employment. Written permission from each person acknowledged has been obtained.

Financial & competing interests disclosure

This study was funded by grants from the National Human Genome Research Institute (R01 HG007063; U01 HG009599) and from the National Cancer Institutes (R01 CA221870). KA Phillips receives consulting income and received support for attending a conference where this work was discussed from Illumina, Inc. A W Kurian has received research funding from Myriad Genetics. Disclosures have been reviewed by the University of California San Francisco. Dr Marshall received travel support for attending a conference where this work was discussed from Illumina Inc. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

No writing assistance was utilized in the production of this manuscript.

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