












Fixing the Leaky Pipe: How to Improve the Uptake of Patient-Reported Outcomes–Based Prognostic and Predictive Models in Cancer Clinical Practice

Katie L. Spencer, PhD^{1,2} ; Kate L. Absolom, PhD¹ ; Matthew J. Allsop, PhD¹ ; Samuel D. Relton, PhD³; Jessica Pearce, MBChB^{2,4} ; Kuan Liao, MSc⁵ ; Sairah Naseer, MRes⁶ ; Omolola Salako, MBChB⁷ ; Daniel Howdon, PhD¹ ; Jenny Hewison, PhD¹; Galina Velikova, PhD^{2,4} ; Corinne Faivre-Finn, PhD⁸ ; Hilary L. Bekker, PhD¹ ; and Sabine N. van der Veer, PhD⁵

DOI <https://doi.org/10.1200/CCI.23.00070>

ABSTRACT

Accepted September 29, 2023

Published November 17, 2023

PURPOSE This discussion paper outlines challenges and proposes solutions for successfully implementing prediction models that incorporate patient-reported outcomes (PROs) in cancer practice.

METHODS We organized a full-day multidisciplinary meeting of people with expertise in cancer care delivery, PRO collection, PRO use in prediction modeling, computing, implementation, and decision science. The discussions presented here focused on identifying challenges to the development, implementation and use of prediction models incorporating PROs, and suggesting possible solutions.

RESULTS Specific challenges and solutions were identified across three broad areas. (1) Understanding decision making and implementation: necessitating multidisciplinary collaboration in the early stages and throughout; early stakeholder engagement to define the decision problem and ensure acceptability of PROs in prediction; understanding patient/clinician interpretation of PRO predictions and uncertainty to optimize prediction impact; striving for model integration into existing electronic health records; and early regulatory alignment. (2) Recognizing the limitations to PRO collection and their impact on prediction: incorporating validated, clinically important PROs to maximize model generalizability and clinical engagement; and minimizing missing PRO data (resulting from both structural digital exclusion and time-varying factors) to avoid exacerbating existing inequalities. (3) Statistical and modeling challenges: incorporating statistical methods to address missing data; ensuring predictive modeling recognizes complex causal relationships; and considering temporal and geographic recalibration so that model predictions reflect the relevant population.

CONCLUSION Developing and implementing PRO-based prediction models in cancer care requires extensive multidisciplinary working from the earliest stages, recognition of implementation challenges because of PRO collection and model presentation, and robust statistical methods to manage missing data, causality, and calibration. Prediction models incorporating PROs should be viewed as complex interventions, with their development and impact assessment carried out to reflect this.

JCO Clin Cancer Inform

7:e2300070

© 2023 by American Society of
Clinical Oncology

Licensed under the Creative
Commons Attribution 4.0 License

INTRODUCTION

Cancer care and research have progressed rapidly over recent decades. Restricted patient cohorts in clinical trials of new treatments, however, limit the direct relevance of trial results in routine care settings.¹ Partly in response to this, studies now aim to develop models capable of predicting

outcomes (eg, survival or symptom trajectories) to support clinicians and patients in making shared and personalized decisions in routine cancer care.^{2,3} Given the documented optimism of clinicians delivering cancer care, such predictions may help patients and clinicians make more informed treatment decisions that align with patient preferences, reduce the likelihood of decisions to pursue overly aggressive

cancer care in the final months of life, inform trial participation, when and what to tell family members, and how to prepare for the end of life.⁴⁻¹⁰

Models are developed in curative and adjuvant,^{11,12} as well as advanced incurable cancer settings.¹³⁻¹⁵ The models effectively identify a weighting for observed characteristics to provide predictions of expected outcomes for individuals. These models, however, rarely make it into clinical practice, meaning opportunities to better inform treatment decisions are missed.^{2,16,17}

Models predicting outcomes may be prognostic (indicating expected prognosis or outcomes) or predictive (indicating expected outcomes conditional upon a given treatment approach). Here, we will use the term prediction models to encompass both modeling approaches.

Models in Cancer Care

Typically, prediction models in cancer care include a range of clinical parameters, such as clinical test results, patient or tumor characteristics, biomarkers, and performance status (ie, physician-assessed measurement of function).^{13,18-21} Performance status is a key parameter in many such models but was originally developed to inform patient selection for clinical trials and, although never formally validated beyond this, is now widely used to assess suitability for systemic anticancer treatment.²² Its subjectivity and lack of granularity are increasingly recognized limitations for its ability to assess patients' functioning and suitability for treatment,²²⁻²⁴ leading to a call for incorporating more comprehensive measures of functioning and frailty into treatment decisions, particularly in the context of an aging population.^{22,25} Indeed, patient-reported outcome (PRO) measures are now available to support this.²⁶⁻²⁸ For example, both the Geriatric-8 and Vulnerable Elders Survey-13 offer patient-reported questionnaire-based tools that assess frailty on the basis of multiple domains, including function/mobility, nutrition, and polypharmacy.^{26,29}

PROs in Prediction Models

There is wide consensus that PROs can enhance routine cancer care by streamlining consultations to focus on areas that are important to patients, thus aiding symptom control, empowering patients, reducing health service utilization, and, in some circumstances, improving overall survival and quality of life (QOL).³⁰⁻³⁶ Furthermore, PROs have prognostic value,³⁷⁻⁴⁰ while also providing a patient-reported analog for specialist clinician assessment of symptoms.³⁰ This makes PROs suitable for capturing clinically important information for prediction modeling ahead of or in the absence of specialist review. Finally, when captured repeatedly over time in specialist settings, they may also replace variables such as performance status in prediction models.⁴¹ Together, this suggests that incorporating PROs into prediction models for cancer care should be explored further. A

conceptual framework for the role of such models is presented in [Figure 1](#).

Improving the Uptake of PRO-Based Prediction Models—A Multidisciplinary Workshop

We conducted a multidisciplinary workshop to further explore and reach consensus on the challenges and approaches for research into harnessing PROs for prediction modeling in cancer care. This perspective paper reports on the outcomes of the workshop, considering the whole (often leaky^{42,43}) pipeline from identifying the decision problem through to successful implementation in clinical practice ([Fig 2](#)), with specific focus on how these challenges relate to the use of PROs.

The workshop identified the crucial need, applicable to any prediction model pipeline, to start by carefully defining the decision problem, that is, the clinical decision the model aims to influence ([Fig 1A](#)). Following immediately from this is the need to identify key stakeholders and consider the pathway to implementation.¹⁷ As such, we start our summary with key aspects of model implementation, given the crucial role this has in underpinning all subsequent progress. We then move on to considering how the capture of PROs in routine care will affect model development and highlight some key statistical considerations. In doing this, we aim to suggest next steps by which the leaky pipeline may be fixed. [Table 1](#) displays a summary of the points raised.

METHODS

Two authors (K.L.S. and H.L.B.) developed an outline for a full-day meeting (7 hours) to cover key areas as outlined by the PROGRESS reports (the PROgnosis REsearch Strategy series, which seeks to explain how prognostic modeling research can be used to improve clinical outcomes).¹⁷ Relevant multidisciplinary attendees were identified from the author's existing networks, snowballing from these to ensure program coverage. Attendees were invited by email.

Twenty-three people attended, including those with expertise in routine cancer care delivery (n = 6); the use of PROs in cancer care (n = 4); large-scale PRO data analysis (n = 6) and prediction modeling (n = 5); health informatics (n = 4) and computing (n = 4); implementation (n = 7); and decision science (n = 1). Some attendees had expertise in more than one area. The first author (K.L.S.) facilitated the meeting. Expert presentations included the challenges of PRO implementation in cancer care; PRO-based analyses in cancer care (including prognostic modeling); the challenges of translating model predictions into clinical practice from a clinician perspective and separately from an informatics and implementation science perspective; and how model predictions may inform decision making. Each presentation was followed by an extended opportunity for discussion. Key points were documented during the meeting and subsequently thematically analyzed and synthesized with multiple rounds of review by all coauthors.

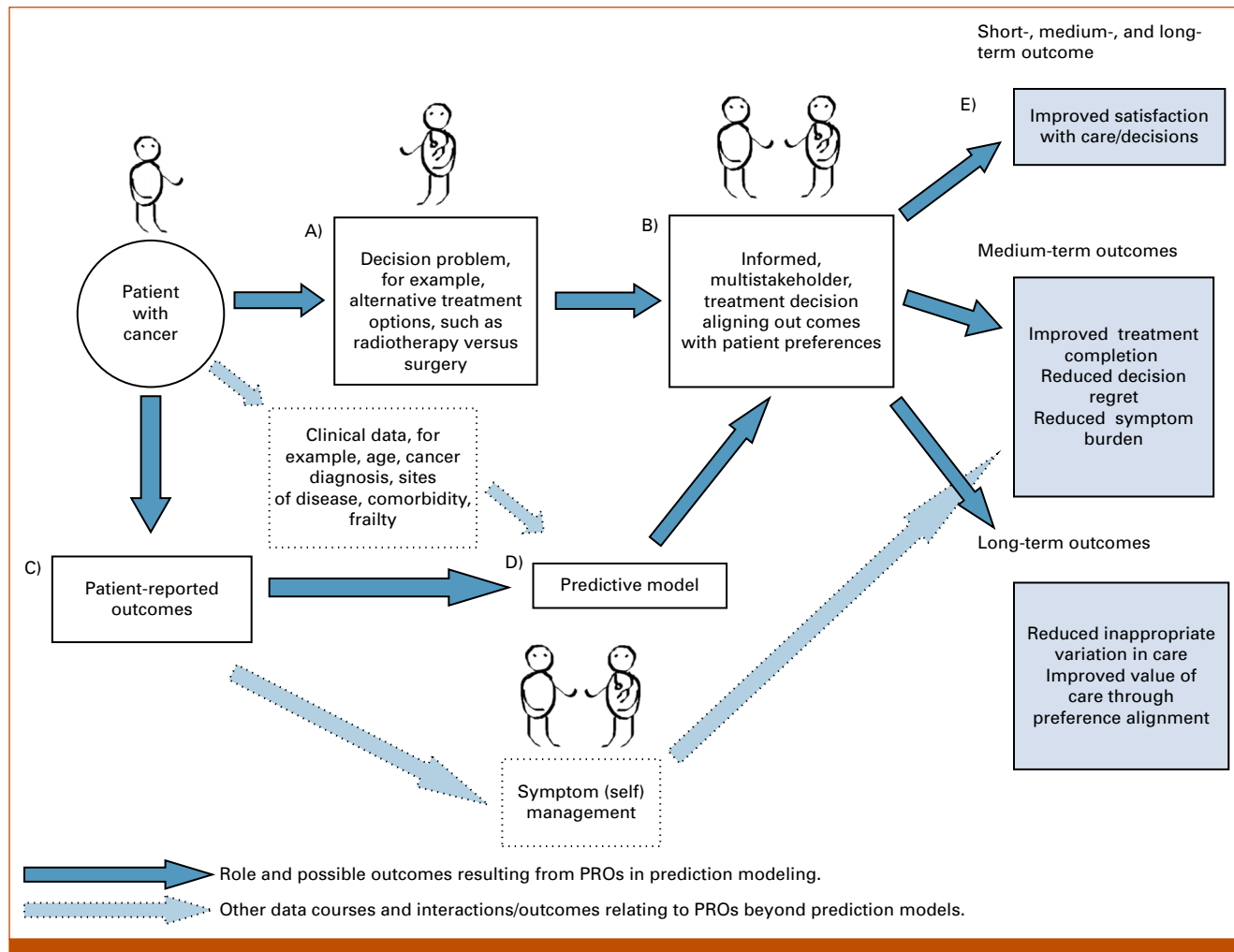


FIG 1. Conceptual framework for the role of PROs in predictive modeling. PROs, patient-reported outcomes.

Discussions focused principally on the high-resource setting, extending to low-resource settings, where possible, if expertise was available within the group.

Starting With the Last Drop—Understanding Implementation and Decision Making Ahead of Modeling

Defining the Decision Problem

An insufficient understanding of the decision problem and the intended role of the prediction model in this will hamper model implementation (Figs 1A, 1D and 2). Decision scientists have provided evidence and theories to understand how people make decisions under (un)certainty and risk.⁴⁴ The theoretical approaches are informed by (1) economic and statistical modeling of the ideal decision,⁴⁵ (2) descriptions of how people make decisions naturalistically,⁴⁶ and (3) evidence to inform active thinking in real-world contexts.⁴⁷ Broadly, these models identify the components on which people draw to make decisions such as the options (eg, available treatments), attributes (eg, treatment practicalities and side

effects), probabilities (eg, expected survival and side-effect probabilities), and values individuals place on these consequences. Decision science has identified the types of factors that affect our attention and help or hinder our decision-making processes. Furthermore, in health care, most decisions are made by multiple stakeholders with different goals (Fig 1B).⁴⁸ Actions arising from multiple stakeholder decision making require a shared understanding of other people’s perspectives to agree and implement a health care choice of benefit and relevance to the patient.⁴⁹ Prediction models could contribute to interventions designed to support clinical reasoning and shared decision making between multiple stakeholders.

When developing a prediction model, working within a multidisciplinary team from the earliest possible stage, there is a need to use decision science theories and all available evidence to pinpoint the specific clinical decision (Fig 1A); determine the aims of providing model predictions (eg, to communicate risk, inform patients/clinicians, or reduce variation; Fig 1E); and identify the individual/s who will interact with these (Fig 1D). On the basis of this information, it is then critical to define

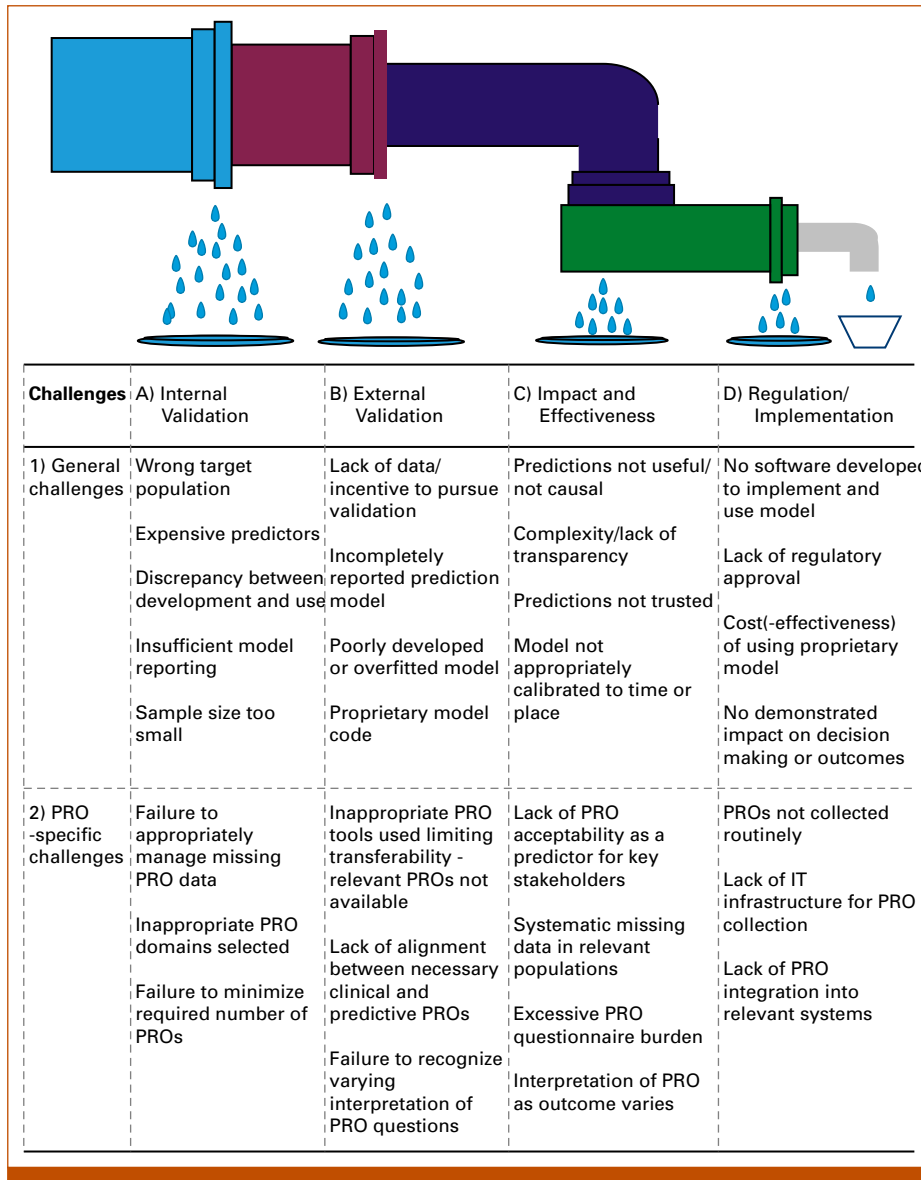


FIG 2. The leaky pipe—why developed prognostic and predictive models do not make it into clinical practice. IT, information technology; PRO, patient-reported outcome. Adapted with permission from Royen et al.⁴³

which outcomes (and time horizons) will be of most value; determining the key outcomes of interest at an early stage can ensure that model outcomes will be actionable (Figs 1D and 2).

Models as Complex Interventions

The greater regulation of prediction models as medical devices and increasing desire to use them in routine care highlight the need to assess model impact ahead of widespread implementation.^{17,50} The complexity of the decisions and environments in which these models are implemented warrants consideration of the updated Medical Research Council guidance on developing and evaluating complex interventions.⁵¹ A program theory should describe assumptions on how the model is expected to deliver the

desired outcomes and how different individuals and features of the context may interact with the final model to influence the success of implementation⁵¹ (eg, on the basis of Fig 1). These assumptions may need revisiting and refinement during exploratory and preparatory phases (considering feasibility) with input from relevant stakeholders (eg, patients, clinicians, and information technology teams) ahead of impact assessment.^{50,51} For example, is it realistic to think that predictions will be acted upon, even if they conflict with hoped-for outcomes or interventions? Do all stakeholders accept the role of PROs as predictors or outcomes (Figs 1C and 2C)? Furthermore, clinicians may be concerned about issues of overdependence on models, loss of clinical autonomy, and lack of confidence in the model predictions (Figs 1B, 1C and 2).⁵² These concerns/considerations should

TABLE 1. Summary of Meeting Findings

Section	Findings
Understanding implementation and decision making ahead of modeling	<p>The acceptability of PROs as predictors should be assessed with stakeholders</p> <p>The proposed PROs for inclusion in prediction models should align with those of clinical value</p> <p>The proposed, context-specific, mechanism for model implementation should be identified early (eg, PRO and model integration into the EHR)</p> <p>Like all potential predictor variables, the benefit of PRO inclusion in a prediction model should be assessed during model development</p> <p>Presentation of PRO outcomes and uncertainty should be discussed with key stakeholders</p> <p>Where model implementation is planned to involve integration in an EHR or other existing system, the regulatory requirements for this should be considered early on</p>
Limitations to PRO collection and their impact upon prediction	<p>The impact of challenges to implementing PRO collection in the relevant routine care setting should be considered during model development</p> <p>Missing data should be minimized as far as possible when capturing PROs, including through consideration of proxy completion</p> <p>The systematic exclusion of populations less likely to complete digital PROs must be assessed and model validity in these populations determined</p> <p>The use of validated PRO questionnaires may support more widespread model implementation by ensuring predictors are consistent between health care providers</p> <p>Overlap between PROs of use in delivering clinical care and those used as model predictors may help increase PRO engagement, minimizing missing data and ultimately increasing the likelihood of successful model implementation</p>
Statistical and modeling challenges	<p>Missing PRO data should be characterized and, where possible, techniques to reduce and manage this used</p> <p>Where proxy PRO collection is used to minimize missingness, the predictive value of proxy completion should be considered in model development</p> <p>Decision curve analysis can be used to determine the incremental benefit of additional PRO predictors and balance this against questionnaire burden and possible increased risk of missing data</p> <p>Causal relationship between treatment options and PRO outcomes appropriately incorporated to minimize bias by confounding</p> <p>Mechanisms to ensure recalibration and to address regional and temporal variation should be considered</p>

Abbreviations: EHR, electronic health record; PRO, patient-reported outcome.

be documented and addressed (eg, through training for clinicians and parallel patient information) to support wider implementation and dissemination.

Enabling Implementation

A range of factors should be considered when planning implementation. Model predictions must be presented in a timely way to influence clinical care (Figs 1C, 1D and 2). With PRO prediction models, wider integration of PROs into electronic health records (EHRs) may enable this (Fig 2D)⁵³⁻⁵⁵ and avoid the presentation of predictions after the decision point. This also minimizes the need for multiple logins or opening a separate webpage to access predictions, both of which are recognized barriers to implementing routine PRO collection and model-based interventions.^{52,56,57} When integrated, the risk of repeated alerts interrupting clinical workflows and leading to alert fatigue may also be a potential barrier to model implementation.^{56,57} Conversely, the presentation of predictions should not introduce attention bias, as the decision-maker allocates greater importance to the model outputs than other relevant domains that inform the decision-making process (Fig 1B).

Finally, prediction models are increasingly used in low-resource cancer care settings^{58,59} because of wider EHR system implementation alongside increasing recognition of the role and value of PROs.^{60,61} PROs can be readily delivered with

the support of mobile devices to facilitate patient-centered care in geographically dispersed populations and inform health service responses, for example, in patients nearing the end of life.^{61,62} Context-specific model implementation strategies are, however, required. For example, they must be congruent with clinical workflows and a limited health workforce,^{63,64} recognize the high frequency of advanced disease in low-resource settings,⁶⁵ account for treatment availability and financial toxicity (Figs 1C and 2), adapt to unreliable internet connections and electricity supply, and support a business case for investment in infrastructure to enable access to timely, reliable, and practical health information, a prerequisite for delivering universal health coverage.⁶⁶

Presenting Model Outcomes

Once the mechanism for presenting model predictions has been defined, the presentation needs tailoring to the decision-makers' needs (Fig 2C). Prediction models that are directive rather than assistive when implemented (ie, not only present an expected outcome but also a decision recommendation) may be more readily incorporated into clinical practice.⁵² This may be challenging, however, where predictions of PRO domains are included, as the relative value placed on domains may differ between patients (whether due to language, culture, or personal preference; Fig 2B). It may also be necessary to provide details of the model inputs (eg, PRO dimensions) and rationale behind the

recommendation (Figs 1C and 2).⁵² Although, patients may value model accuracy more than explainability for health care decision making, and are therefore willing to accept the black-box nature of models,⁶⁷ clinicians may be more willing to use model predictions if clinical utility and validity has been demonstrated (Figs 1D and 2).⁵²

The presentation of statistical uncertainty should also be considered during model development; for example, how should survival and patient-reported QOL, and the uncertainty around it, be presented, especially if communicated to patients? Presentation and visualization is particularly important when considering longitudinal PRO-based models. Although these allow for dynamic predictions reflecting the patient's changing clinical condition, they also raise additional challenges in communicating risk trajectories to both clinical and public audiences (Figs 1C and 2). Early stakeholder engagement should ensure that the presentation of model outcomes and uncertainty supports the clinical decision-making process rather than confusing it (Figs 1B and 1D). Patient, or indeed clinician, education maybe required, particularly to ensure accurate interpretation and communication of the model outcomes (eg, where causal relationships are represented or around prediction uncertainty). There is a danger otherwise that a lack of understanding may hamper successful implementation and thus a positive impact on outcomes (Figs 1D and 2).

Regulatory Approval

After assessing the impact of a model, regulatory approval can be sought. Regulators across health care jurisdictions increasingly recognize that software tools with an expert function for the diagnosis, prevention, monitoring, or treatment of individual patients, including risk prediction, require regulation similar to more traditional medical devices (Figs 1D and 2).⁶⁸⁻⁷⁰ This has consequences for the implementation of prediction models that aim to inform patient care. Robustly determining the model's impact in clinical practice is crucial in this context (Figs 1D and 2). This should consider not only model accuracy in routine care, but also the experience of those using the model, and its effect on delivered care, outcomes, and cost-effectiveness (ideally in the context of a clinical trial),^{17,71} all of which support regulatory approvals.

As stated earlier, models are more likely to be implemented successfully if integrated in existing systems and EHRs (Figs 1D and 2D). Consideration of regulatory approval will, however, be needed at an early stage to determine if the model will be approved as part of an existing medical device/software (potentially aligning with PRO collection) or as a standalone tool.⁶⁸ These regulations have only recently been defined or are undergoing development currently.^{70,72} Indeed, a recent scoping review of guidelines informing the development of artificial intelligence-based prediction models highlighted a dearth of relevant guidance

addressing the later phases of development: software development, impact assessment, and implementation.⁷³ Vigilance is required to identify ongoing regulatory requirements at all stages of model development.

Limitations to PRO Collection and Their Impact Upon Prediction

Challenges to Capturing Routine PROs in Cancer Care

Despite extensive evidence of their benefits, PRO implementation within routine clinical care has been patchy and not without challenges. These have been widely considered in qualitative and implementation research.⁷⁴ Many will have consequences for the use of PROs in prediction models, while other more general issues (such as the cost and perceived workload associated with routine PRO collection) may limit implementation entirely (Figs 2A-2C), despite examples of successful implementations with evidence of improved symptom awareness and streamlining of consultations.^{36,75}

Reasons for Absent/Missing Data and How to Address Them

An issue particularly relevant for prediction modeling is that of absent or missing data, and crucially, its potential causes (Figs 2A and 2C). Where paper questionnaire completion comes with inherent physical limitations with delayed/missing responses and risk of human error in subsequent input to electronic systems,⁷⁶ patient participation in electronic PRO collection depends upon digital engagement. For example, although mechanisms to reduce barriers to digital engagement have been identified,^{77,78} people who are older or who have cognitive impairment, language or literacy barriers, or limited digital access and skills, among others, are less likely to engage with electronic PROs in their routine cancer care (Fig 2C).^{74,79,80} Recent improvements notwithstanding,⁸¹ it is paradoxical that irrespective of the desire to inform decisions for those not routinely included in clinical trials, this structural digital exclusion may systematically exclude the same patient groups, further exacerbating existing inequalities as a result of absent data.⁸² Consequently, a review is now underway in the United Kingdom to determine the extent and impact of this on inequalities in health care.⁸³

Beyond these patient-level characteristics, there are also time-varying characteristics that may diminish PRO use; crucially, in this context, qualitative studies have found that patients report feeling unable to complete PROs when feeling too unwell (Fig 2C).^{74,84} Deterioration in QOL with proximity to death is well documented,⁸⁵ thus risking systematic exclusion of individuals with poorer prognosis and introducing bias in prediction models through missing data. Conversely, patients are unlikely to continue engaging with PROs if they do not feel that this enhances their clinical care⁷⁴; using PROs for prediction may therefore provide an additional way to make it worthwhile for patients to complete PROs.

Mechanisms to address both person-level and time-varying challenges for PRO collection are required.^{78,86,87} These can include alternative mechanisms to collect PROs; support for patients to complete PROs inside and outside the clinic; minimizing literacy and language barriers (resulting from, eg, sensory and cognitive impairment, or reduced health literacy) through PRO development and selection; cross-cultural validation of PROs to ensure understanding and accessibility for ethnically diverse patient groups; support for clinician engagement with PROs to—in turn—encourage ongoing patient engagement; allowing proxy PRO completion if appropriate, for example, by family or carers⁸⁸⁻⁹⁰; identifying tools that maximize patient engagement, particularly near the end of life; minimizing data sets for model development, with clear justification for adding items; and the use of statistical approaches to address missing data (see below; Figs 2A-2C).⁹¹

PRO Selection

An extensive array of PRO measures have been developed and validated for many cancer types and populations (eg, Reinhardt et al,⁹² Engstrom et al,⁹³ and Salas et al⁹⁴). When selecting which PROs to use for routine collection, meeting the needs of clinicians and patients is of primary importance (Fig 2B). Recommendations detailing possible PRO sets have been developed by the International Consortium for Health Outcome Measurement covering some, but not all, cancer diagnoses.⁹⁵ Avoiding the use of unvalidated PRO measures to capture the same outcome (eg, nausea/sickness, overall QOL) can help subsequent transferability of model outcomes (Fig 2B).⁹⁶

An additional criterion for selecting PROs may be their predictive value (Fig 2A). Some PROs may be strongly predictive for outcomes in the final months of life but less so where prognosis is over a year,⁴¹ and there will inevitably be variation between different PRO dimensions.³⁷ As with all predictors, the role of PROs within a final model should be justified based on the benefit they offer in the model (further discussed below). However, selecting those of greatest relevance to routine care may facilitate wider use of routinely collected PROs, enable integration of the model into EHR systems, reduce variation of PRO collection between health care providers, and support external validation of developed models (Figs 2A-2C). Finally, despite cognitive interviews undertaken in the development of PROs, interpretation of PRO questions may differ between patients (Fig 2B) depending on their cultural background, language skills, or other individual differences.^{97,98} This may lead to increased variation in the reported outcome between patient groups, which affects model development and validity.

Statistical and Modeling Challenges

Existing guidelines for the development, reporting, and assessment of bias in prediction models should inform the development of any prediction model, including those

incorporating PROs^{17,99,100} (Figs 1B and 2). Updates to these, recognizing aspects specific to the use of artificial intelligence in modeling—such as additional model complexity, the increased risk of overfitting to data, and subsequent lack of transparency—are in progress.¹⁰¹ There are, however, a number of specific challenges in the development of models incorporating PROs.

Handling Missing Data

Many of the statistical challenges of developing and implementing prediction models relate to those outlined above in the implementation of PROs, particularly resulting in missing data (Figs 2A and 2C), whether due to the absence of patient subgroups or time-varying missingness. Both of these can, to a degree, be addressed using statistical methods to complement strategies for improving data completeness. The systematic absence of PRO data from specific subgroups can be partially addressed through the use of inverse probability weighting, giving greater weight to data relating to individuals who are less likely to complete PROs (Fig 2C).^{102,103} This can enhance representativeness of models for the relevant population and aligns with an increasing recognition among regulators of the risk that models pose in introducing bias in decision making as a result of missing data and limited applicability.^{99,104} In terms of managing missingness because of, for example, deteriorating clinical condition, multiple imputation can be considered where missingness occurs at random (ie, conditional upon observed covariables, eg, when a concurrent decline in PROs and blood parameters is observed¹⁰⁵⁻¹⁰⁷; Fig 2A). The plausibility of underpinning assumptions and alternative methods should be assessed, as imputation where data are missing not at random will reinforce bias. Finally, when considering proxy PRO reporting (eg, by family or carers in the context of increasing frailty), understanding of the impact of this on the predictive value of PROs is required.

Assessing the Benefit of Alternative/Additional PRO Questions in Prediction Models

Once mechanisms to reduce and mitigate missing data have been identified, analysts should carefully consider the value offered by incorporating and thus asking additional PRO questions; excessive questions may reduce engagement,¹⁰⁸ particularly near the end of life (Fig 2C).¹⁰⁹ Equally, differing question structures may offer varying predictive value, for example, the three-level versus five-level EQ-5D questionnaire (with the latter providing greater detail, which may be valuable for model development; Fig 2A). Decision curve analysis can assess the comparative utility of adding further questions or the yield from additional detail.¹¹⁰ The results can then be presented to the multidisciplinary team to identify the extent to which the benefit delivered by these variables is clinically meaningful and worth pursuing through modifications to data collection methods. Conversely, if free-text answers are sought from patients, the use of qualitative analysis and natural language processing can be considered to

inform model development and incorporate these responses in prognostic or predictive models.

Ensuring Calibration Here and Now

Models will, inevitably, reflect the populations in which they are developed and the treatments available at the time. In a rapidly changing area, such as cancer care, model predictions should be monitored for temporal drift (eg, using statistical process control methods) and recalibrated when necessary (Figs 1C and 2).^{111,112} This is increasingly recognized by regulators, and mechanisms to enable recalibration in implemented models must be planned into their design, for example, through dynamic prediction systems.¹¹³ Indeed, such approaches can enable calibration to institution specific outcomes, thus ensuring predictions reflect local care and outcomes.¹¹⁴⁻¹¹⁶ This can be delivered within an EHR (offering a potential benefit for the implementation of PRO-based models) and will not only improve predictive performance but may also deliver greater clinical acceptance if it is understood that the model is appropriately calibrated to reflect the local population. Caution is required, however, to avoid embedding inequalities in care and outcomes through the use of such local calibration.¹¹⁷

Beyond these changes with time and place, there is a need to capture alternative treatment approaches within developed models; the question of “but what if I have this treatment?” is highly relevant to clinicians and patients alike. As such, predictions may need to incorporate causal assumptions and counterfactual predictions, requiring careful consideration of which parameters would deliver robust predictions with minimal risk of unobserved confounding.^{104,118,119} Fully addressing confounding variables (eg, because of comorbidities) is challenging; the extent to which this can be achieved must be recognized and documented to prevent model predictions being applied to individuals for whom they are not appropriate to inform clinical decisions. This can be undertaken in parallel with wider documentation of model limitations that helps to ensure model use aligns with the

population, parameters, and limitations of model development (Fig 2C). For example, where prediction is the focus, comorbidities may remain important, as they can result in reduced model performance for specific populations (eg, as a result of reduced precancer mobility).

Strengths and Limitations

This summary and the meeting it represents include the perspectives of a broad multidisciplinary group ensuring inclusion of all disciplines relevant to developing and implementing PRO-based prediction models with a potential to improve outcomes for patients with cancer. The structured meeting ensured all key areas were discussed, while the limited group size provided opportunities for all to contribute. A larger, international group including patient and public representatives might, however, have enabled incorporation of further aspects not captured here. The meeting was funded by the EuroQoL group; however, EuroQoL had no influence over the content or outcomes of the meeting.

In conclusion, this workshop and the findings generated from it, alongside the existing literature, have shown that although PROs are increasingly used in cancer care to provide a more complete picture of a patient’s symptoms and QoL, they can also be useful for enriching prediction models. Although cancer care formed the primary clinical context for the workshop discussions, we anticipate this discussion paper to also be relevant for other clinical areas. In all settings, multidisciplinary working, from the earliest stages of such model development, can help to define the decision problem, deliver broad stakeholder engagement, identify and mitigate the causes of missing PRO data, and ensure the proposed model implementation strategy aligns with the clinical pathway to be addressed and the wider health care context. Although outside of the sphere of expertise for many researchers involved in early model development and validation, this work is crucial to ensuring that the predictions produced can ultimately be used to deliver benefit to patients with cancer.

AFFILIATIONS

¹Leeds Institute of Health Sciences, University of Leeds, Leeds, United Kingdom

²Leeds Cancer Centre, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom

³Leeds Institute of Data Analytics, University of Leeds, Leeds, United Kingdom

⁴Leeds Institute of Medical Research, University of Leeds, Leeds, United Kingdom

⁵Division of Informatics, Imaging and Data Sciences, Faculty of Biology, Medicine and Health, Centre for Health Informatics, Manchester Academic Health Science Centre, The University of Manchester, Manchester, United Kingdom

⁶School of Medicine, University of Leeds, Leeds, United Kingdom

⁷College of Medicine, University of Lagos, Lagos, Nigeria

⁸Institute of Cancer Sciences, University of Manchester, Manchester, United Kingdom

CORRESPONDING AUTHOR

Katie L. Spencer, PhD, Academic Unit of Health Economics, Leeds Institute of Health Sciences, University of Leeds, Level 10, Worsley Bldg, Clarendon Way, Leeds LS2 9LU, United Kingdom; e-mail: k.spencer@leeds.ac.uk.

SUPPORT

Supported by project funding from the EuroQoL group. The group had no input into the design of the workshop or development of the resulting manuscript. Prof Corinne Faivre-Finn was supported by the NIHR Manchester Biomedical Research Centre (NIHR203308).

AUTHOR CONTRIBUTIONS

Conception and design: Katie L. Spencer, Kate L. Absolom, Samuel D. Relton, Daniel Howdon, Galina Velikova, Corinne Faivre-Finn, Hilary L. Bekker, Sabine N. van der Veer

Financial support: Katie L. Spencer

Provision of study materials or patients: Katie L. Spencer, Kate L. Absolom, Samuel D. Relton, Daniel Howdon, Galina Velikova, Corinne Faivre-Finn, Hilary L. Bekker, Sabine N. van der veer

Collection and assembly of data: All authors

Data analysis and interpretation: All authors

Manuscript writing: All authors

Final approval of manuscript: All authors

Accountable for all aspects of the work: All authors

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated unless otherwise noted. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO's conflict of interest policy, please refer to www.asco.org/rwc or ascopubs.org/cci/author-center.

Open Payments is a public database containing information reported by companies about payments made to US-licensed physicians (Open Payments).

Katie L. Spencer

Research Funding: EuroQoL Foundation (less than \$10,000 USD in a single calendar year)

Omolola Salako

Employment: Pearl Oncology

Consulting or Advisory Role: Stack Diagnostics (\$10,000 USD or above in a single calendar year)

Speakers' Bureau: Janssen and Janssen (less than \$10,000 USD in a single calendar year)

Research Funding: Pfizer Global

Patents, Royalties, Other Intellectual Property: I have intellectual property rights to Oncopadi Digital Cancer Clinic (\$10,000 USD or above in a single calendar year)

Travel, Accommodations, Expenses: Global Health Catalyst

Galina Velikova

Honoraria: Eisai (less than \$10,000 USD in a single calendar year), Pfizer (less than \$10,000 USD in a single calendar year), Novartis (less than \$10,000 USD in a single calendar year)

Consulting or Advisory Role: Roche UK (less than \$10,000 USD in a single calendar year), Eisai (less than \$10,000 USD in a single calendar year), Novartis (less than \$10,000 USD in a single calendar year), Sanofi (less than \$10,000 USD in a single calendar year), Pfizer (less than \$10,000 USD in a single calendar year), AstraZeneca, Seagen (less than \$10,000 USD in a single calendar year)

Speakers' Bureau: Novartis

Research Funding: Pfizer (\$10,000 USD or above in a single calendar year), IQVIA (\$10,000 USD or above in a single calendar year)

Travel, Accommodations, Expenses: Roche UK, Novartis, Eisai

Other Relationship: University of Leeds

Corinne Faivre-Finn

Consulting or Advisory Role: AstraZeneca (Inst)

Research Funding: AstraZeneca/MedImmune (Inst) (\$10,000 USD or above in a single calendar year), Merck Sharp & Dohme (Inst) (\$10,000 USD or above in a single calendar year), Elekta (Inst) (less than \$10,000 USD in a single calendar year)

Travel, Accommodations, Expenses: AstraZeneca/MedImmune (less than \$10,000 USD in a single calendar year), Elekta (less than \$10,000 USD in a single calendar year)

No other potential conflicts of interest were reported.

REFERENCES

1. Rothwell PM: External validity of randomised controlled trials: "To whom do the results of this trial apply?" *Lancet* 365:82-93, 2005
2. Yang C, Kors JA, Ioannou S, et al: Trends in the conduct and reporting of clinical prediction model development and validation: A systematic review. *J Am Med Inform Assoc* 29:983-989, 2022
3. Harding R, Simms V, Calanzani N, et al: If you had less than a year to live, would you want to know? A seven-country European population survey of public preferences for disclosure of poor prognosis. *Psychooncology* 22:2298-2305, 2013
4. Weeks JC, Cook EF, O'Day SJ, et al: Relationship between cancer patients' predictions of prognosis and their treatment preferences. *JAMA* 279:1709-1714, 1998
5. Temel JS, Greer JA, Admane S, et al: Longitudinal perceptions of prognosis and goals of therapy in patients with metastatic non-small-cell lung cancer: Results of a randomized study of early palliative care. *J Clin Oncol* 29:2319-2326, 2011
6. Earle CC, Park ER, Lai B, et al: Identifying potential indicators of the quality of end-of-life cancer care from administrative data. *J Clin Oncol* 21:1133-1138, 2003
7. Wallington M, Saxon EB, Bomb M, et al: 30-day mortality after systemic anticancer treatment for breast and lung cancer in England: A population-based, observational study. *Lancet Oncol* 17:1203-1216, 2016
8. Gwilliam B, Keeley V, Todd C, et al: Prognosticating in patients with advanced cancer—Observational study comparing the accuracy of clinicians' and patients' estimates of survival. *Ann Oncol* 24:482-488, 2013
9. White N, Reid F, Harris A, et al: A systematic review of predictions of survival in palliative care: How accurate are clinicians and who are the experts? *PLoS One* 11:e0161407, 2016
10. Innes S, Payne S: Advanced cancer patients' prognostic information preferences: A review. *Palliat Med* 23:29-39, 2009
11. Predict breast. <https://breast.predict.nhs.uk/>
12. Predict prostate. <https://prostate.predict.nhs.uk/>
13. Simmons CPL, McMillan DC, McWilliams K, et al: Prognostic tools in patients with advanced cancer: A systematic review. *J Pain Symptom Manage* 53:962-970.e10, 2017
14. Stone PC, Lund S: Predicting prognosis in patients with advanced cancer. *Ann Oncol* 18:971-976, 2007
15. Pobar I, Job M, Holt T, et al: Prognostic tools for survival prediction in advanced cancer patients: A systematic review. *J Med Imaging Radiat Oncol* 65:806-816, 2021
16. Craddock M, Crockett C, McWilliam A, et al: Evaluation of prognostic and predictive models in the oncology clinic. *Clin Oncol* 34:102-113, 2022
17. Steyerberg EW, Moons KGM, van der Windt DA, et al: Prognosis research strategy (PROGRESS) 3: Prognostic model research. *PLoS Med* 10:e1001381, 2013
18. Mascarella MA, Mannard E, Silva SD, et al: Neutrophil-to-lymphocyte ratio in head and neck cancer prognosis: A systematic review and meta-analysis. *Head Neck* 40:1091-1100, 2018
19. Boakye D, Rillmann B, Walter V, et al: Impact of comorbidity and frailty on prognosis in colorectal cancer patients: A systematic review and meta-analysis. *Cancer Treat Rev* 64:30-39, 2018
20. Budach V, Tinhofer I: Novel prognostic clinical factors and biomarkers for outcome prediction in head and neck cancer: A systematic review. *Lancet Oncol* 20:e313-e326, 2019
21. Bollen L, Jacobs WCH, Van der Linden YM, et al: A systematic review of prognostic factors predicting survival in patients with spinal bone metastases. *Eur Spine J* 27:799-805, 2018
22. Simcock R, Wright J: Beyond performance status. *Clin Oncol* 32:553-561, 2020
23. Hurria A, Togawa K, Mohile SG, et al: Predicting chemotherapy toxicity in older adults with cancer: A prospective multicenter study. *J Clin Oncol* 29:3457-3465, 2011
24. Hurria A, Mohile S, Gajra A, et al: Validation of a prediction tool for chemotherapy toxicity in older adults with cancer. *J Clin Oncol* 34:2366-2371, 2016
25. Mohile SG, Dale W, Somerfield MR, et al: Practical assessment and management of vulnerabilities in older patients receiving chemotherapy: ASCO guideline for geriatric oncology. *J Clin Oncol* 36:2326-2347, 2018
26. Saliba D, Elliott M, Rubenstein LZ, et al: The Vulnerable Elders Survey: A tool for identifying vulnerable older people in the community. *J Am Geriatr Soc* 49:1691-1699, 2001
27. Bellera CA, Rainfray M, Mathoulin-Pélissier S, et al: Screening older cancer patients: First evaluation of the G-8 geriatric screening tool. *Ann Oncol* 23:2166-2172, 2012

28. van Walree IC, Scheepers E, van Huis-Tanja L, et al: A systematic review on the association of the G8 with geriatric assessment, prognosis and course of treatment in older patients with cancer. *J Geriatr Oncol* 10:847-858, 2019
29. van Walree IC, Vondeling AM, Vink GR, et al: Development of a self-reported version of the G8 screening tool. *J Geriatr Oncol* 10:926-930, 2019
30. Basch E, Iasonos A, McDonough T, et al: Patient versus clinician symptom reporting using the National Cancer Institute Common Terminology Criteria for Adverse Events: Results of a questionnaire-based study. *Lancet Oncol* 7:903-909, 2006
31. Basch E, Deal AM, Kris MG, et al: Symptom monitoring with patient-reported outcomes during routine cancer treatment: A randomized controlled trial. *J Clin Oncol* 34:557-565, 2016
32. Denis F, Basch E, Septans AL, et al: Two-year survival comparing web-based symptom monitoring vs routine surveillance following treatment for lung cancer. *JAMA* 321:306-307, 2019
33. Di Maio M, Basch E, Denis F, et al: The role of patient-reported outcome measures in the continuum of cancer clinical care: ESMO Clinical Practice Guideline. *Ann Oncol* 33:878-892, 2022
34. Velikova G, Absolom K, Hewison J, et al: Electronic self-reporting of adverse events for patients undergoing cancer treatment: The eRAPID research programme including two RCTs. Programme Grants for Applied Research. Southampton, United Kingdom, NIHR Journals Library, 2022. <http://www.ncbi.nlm.nih.gov/books/NBK577715/>
35. Absolom K, Warrington L, Hudson E, et al: Phase III randomized controlled trial of eRAPID: eHealth intervention during chemotherapy. *J Clin Oncol* 39:734-747, 2021
36. Yang LY, Manhas DS, Howard AF, et al: Patient-reported outcome use in oncology: A systematic review of the impact on patient-clinician communication. *Support Care Cancer* 26:41-60, 2018
37. Trajkovic-Vidakovic M, de Graeff A, Voest EE, et al: Symptoms tell it all: A systematic review of the value of symptom assessment to predict survival in advanced cancer patients. *Crit Rev Oncol Hematol* 84:130-148, 2012
38. Quinten C, Coens C, Mauer M, et al: Baseline quality of life as a prognostic indicator of survival: A meta-analysis of individual patient data from EORTC clinical trials. *Lancet Oncol* 10:865-871, 2009
39. Liao K, Wang T, Coomber-Moore J, et al: Prognostic value of patient-reported outcome measures (PROMs) in adults with non-small cell lung cancer: A scoping review. *BMC Cancer* 22:1076, 2022
40. Mierzynska J, Piccinin C, Pe M, et al: Prognostic value of patient-reported outcomes from international randomised clinical trials on cancer: A systematic review. *Lancet Oncol* 20:e685-e698, 2019
41. Howdon D, van den Hout W, van der Linden Y, et al: Replacing performance status with a simple patient-reported outcome in palliative radiotherapy prognostic modelling. *Clin Transl Radiat Oncol* 37:137-144, 2022
42. van Smeden M: Five questions about artificial intelligence. <https://www.slideshare.net/MaartenvanSmeden/five-questions-about-artificial-intelligence>
43. van Royen FS, Moons KGM, Geersing GJ, et al: Developing, validating, updating and judging the impact of prognostic models for respiratory diseases. *Eur Respir J* 60:2200250, 2022
44. Bekker H: Using decision making theory to inform clinical practice, in Edwards SA, Elwyn G (eds): *Shared Decision Making Evidence Based Patient Choice in Healthcare*. Oxford, UK, Oxford University Press, 2009, pp 45-52
45. Von Neumann J, Morgenstern O: *Theory of Games and Economic Behavior* (ed 2 rev). Princeton, NJ, Princeton University Press, 1947, p xviii, 641
46. Klein GA: *Decision Making in Action: Models and Methods*. Norwood, NJ, Ablex Pub, 1993, p 480
47. Ritov I, Baron J: Reluctance to vaccinate: Omission bias and ambiguity. *J Behav Decis Making* 3:263-277, 1990
48. Von Winterfeldt D, Edwards W: *Decision Analysis and Behavioral Research*. Cambridge, MA, Cambridge University Press, 1993
49. Toft BS, Rodkjaer L, Andersen AB, et al: Measures used to assess interventions for increasing patient involvement in Danish healthcare setting: A rapid review. *BMJ Open* 12:e064067, 2022
50. Wallace E, Smith SM, Perera-Salazar R, et al: Framework for the impact analysis and implementation of Clinical Prediction Rules (CPRs). *BMC Med Inform Decis Making* 11:62, 2011
51. Skivington K, Matthews L, Simpson SA, et al: A new framework for developing and evaluating complex interventions: Update of Medical Research Council guidance. *BMJ* 374:n2061, 2021
52. Kappen TH, van Klei WA, van Wolfswinkel L, et al: Evaluating the impact of prediction models: Lessons learned, challenges, and recommendations. *Diagn Progn Res* 2:11, 2018
53. Hassett MJ, Cronin C, Tsou TC, et al: eSYM: An electronic health record-integrated patient-reported outcomes-based cancer symptom management program used by six diverse health systems. *JCO Clin Cancer Inform* 6:e2100137, 2022
54. Zhang R, Burgess ER, Reddy MC, et al: Provider perspectives on the integration of patient-reported outcomes in an electronic health record. *JAMIA Open* 2:73-80, 2019
55. Holch P, Warrington L, Bamforth LCA, et al: Development of an integrated electronic platform for patient self-report and management of adverse events during cancer treatment. *Ann Oncol* 28:2305-2311, 2017
56. Lee TC, Shah NU, Haack A, et al: Clinical implementation of predictive models embedded within electronic health record systems: A systematic review. *Informatics* 7:25, 2020
57. Hayward J, Thomson F, Milne H, et al: 'Too much, too late': Mixed methods multi-channel video recording study of computerized decision support systems and GP prescribing. *J Am Med Inform Assoc* 20:e76-e84, 2013
58. Were MC, Savai S, Mokaya B, et al: mUzima mobile electronic health record (EHR) system: Development and implementation at scale. *J Med Internet Res* 23:e26381, 2021
59. Kabukye JK, Casaceli AM, Ball E, et al: Towards an open-source oncology electronic medical records system for low-resource settings: Development of chemotherapy management in OpenMRS. *Stud Health Technol Inform* 264:634-638, 2019
60. Cheung YT, Chan A, Charalambous A, et al: The use of patient-reported outcomes in routine cancer care: Preliminary insights from a multinational scoping survey of oncology practitioners. *Support Care Cancer* 30:1427-1439, 2022
61. Harding R, Selman L, Agupio G, et al: Validation of a core outcome measure for palliative care in Africa: The APCA African Palliative Outcome Scale. *Health Qual Life Outcomes* 8:10, 2010
62. Karera MGD, Omar MA, Nabirye E, et al: Mobile technologies for palliative cancer care in Uganda: Qualitative secondary analysis of health professional perspectives. *Health Policy Technol* 11:100608, 2022
63. Trapani D, Murthy SS, Boniol M, et al: Distribution of the workforce involved in cancer care: A systematic review of the literature. *ESMO Open* 6:100292, 2021
64. Kabukye JK, Kakungulu E, de Keizer N, et al: Digital health in oncology in Africa: A scoping review and cross-sectional survey. *Int J Med Inform* 158:104659, 2022
65. Brand NR, Qu LG, Chao A, et al: Delays and barriers to cancer care in low- and middle-income countries: A systematic review. *Oncologist* 24:e1371-e1380, 2019
66. Royston G, Pakenham-Walsh N, Zielinski C: Universal access to essential health information: Accelerating progress towards universal health coverage and other SDG health targets. *BMJ Glob Health* 5:e002475, 2020
67. van der Veer SN, Riste L, Cheraghi-Sohi S, et al: Trading off accuracy and explainability in AI decision-making: Findings from 2 citizens' juries. *J Am Med Inform Assoc* 28:2128-2138, 2021
68. European Commission: Guidelines on the qualification and classification of stand alone software used in healthcare within the regulatory framework of medical devices, 2016. <https://ec.europa.eu/docsroom/documents/17921/attachments/1/translations/en/renditions/native>
69. Health C for D and R; US Food and Drug Administration: Assessing the credibility of computational modeling and simulation in medical device submissions. FDA, 2022. <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/assessing-credibility-computational-modeling-and-simulation-medical-device-submissions>
70. UK Government: Software and AI as a medical device change programme—Roadmap. <https://www.gov.uk/government/publications/software-and-ai-as-a-medical-device-change-programme/software-and-ai-as-a-medical-device-change-programme-roadmap>
71. Stone P, Kalpakidou A, Todd C, et al: Prognostic models of survival in patients with advanced incurable cancer: The PIPS2 observational study. *Health Technol Assess* 25:1-118, 2021
72. Health C for D and R: Artificial intelligence and machine learning in software as a medical device. FDA, 2022. <https://www.fda.gov/medical-devices/software-medical-device-samd/artificial-intelligence-and-machine-learning-software-medical-device>
73. de Hond AAH, Leeuwenberg AM, Hooft L, et al: Guidelines and quality criteria for artificial intelligence-based prediction models in healthcare: A scoping review. *npj Digit Med* 5:2-13, 2022
74. Nguyen H, Butow P, Dhillon H, et al: A review of the barriers to using patient-reported outcomes (PROs) and patient-reported outcome measures (PROMs) in routine cancer care. *J Med Radiat Sci* 68:186-195, 2021
75. Chen J, Ou L, Hollis SJ: A systematic review of the impact of routine collection of patient reported outcome measures on patients, providers and health organisations in an oncologic setting. *BMC Health Serv Res* 13:211, 2013
76. Horevoorts NJ, Vissers PA, Mols F, et al: Response rates for patient-reported outcomes using web-based versus paper questionnaires: Comparison of two invitational methods in older colorectal cancer patients. *J Med Internet Res* 17:e1111, 2015
77. Flannery MA, Mohile S, Culakova E, et al: Completion of patient-reported outcome questionnaires among older adults with advanced cancer. *J Pain Symptom Manage* 63:301-310, 2022
78. Fox R, Saeed Z, Khan S, et al: Lessons learnt for digital inclusion in underserved communities from implementing a covid virtual ward. *PLoS Digit Health* 1:e0000146, 2022
79. Basch E, Artz D, Dulko D, et al: Patient online self-reporting of toxicity symptoms during chemotherapy. *J Clin Oncol* 23:3552-3561, 2005
80. Sisodia RC, Rodriguez JA, Sequist TD: Digital disparities: Lessons learned from a patient reported outcomes program during the COVID-19 pandemic. *J Am Med Inform Assoc JAMIA* 28:2265-2268, 2021
81. Subbiah IM, Peek A, Daftary U, et al: Is the digital divide between older adults and other age groups closing? Impact of telemedicine and adherence with remote symptom monitoring in older adults compared to middle age and AYA patients with cancer. *J Clin Oncol* 41, 2023 (suppl 16; abstr e13689)
82. Weiss D, Rydland HT, Øversveen E, et al: Innovative technologies and social inequalities in health: A scoping review of the literature. *PLoS One* 13:e0195447, 2018
83. UK Government: Equity in medical devices independent review: Terms of reference. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1070096/equity-in-medical-devices-independent-review-terms-of-reference.pdf
84. Judson TJ, Bennett AV, Rogak LJ, et al: Feasibility of long-term patient self-reporting of toxicities from home via the internet during routine chemotherapy. *J Clin Oncol* 31:2580-2585, 2013

85. Westhoff PG, Verdam MGE, Oort FJ, et al: Course of quality of life after radiation therapy for painful bone metastases: A detailed analysis from the Dutch Bone Metastasis Study. *Int J Radiat Oncol Biol Phys* 95:1391-1398, 2016
86. Mercieca-Bebber R, Palmer MJ, Brundage M, et al: Design, implementation and reporting strategies to reduce the instance and impact of missing patient-reported outcome (PRO) data: A systematic review. *BMJ Open* 6:e010938, 2016
87. Aiyegbusi OL, Roydhouse J, Rivera SC, et al: Key considerations to reduce or address respondent burden in patient-reported outcome (PRO) data collection. *Nat Commun* 13:6026, 2022
88. Tang ST, McCorkle R: Use of family proxies in quality of life research for cancer patients at the end of life: A literature review. *Cancer Invest* 20:1086-1104, 2002
89. Snyder CF, Aaronson NK, Choucair AK, et al: Implementing patient-reported outcomes assessment in clinical practice: A review of the options and considerations. *Qual Life Res* 21:1305-1314, 2012
90. Kroenke K, Stump TE, Monahan PD: Agreement between older adult patient and caregiver proxy symptom reports. *J Patient Rep Outcomes* 6:50, 2022
91. Gomes M, Gutacker N, Bojke C, et al: Addressing missing data in patient-reported outcome measures (PROMS): Implications for the use of PROMS for comparing provider performance. *Health Econ* 25:515-528, 2016
92. Reinhardt ME, Sun T, Pan CX, et al: A systematic review of patient-reported outcome measures for advanced skin cancer patients. *Arch Dermatol Res* 315:1473-1480, 2023
93. Engstrom T, Tanner S, Lee WR, et al: Patient reported outcome measure domains and tools used among adolescents and young adults with cancer: A scoping review. *Crit Rev Oncol Hematol* 181:103867, 2023
94. Salas M, Mordin M, Castro C, et al: Health-related quality of life in women with breast cancer: A review of measures. *BMC Cancer* 22:66, 2022
95. International Consortium for Health Outcomes Measurement: Patient-centered outcome measures. ICHOM. <https://www.ichom.org/patient-centered-outcome-measures/>
96. Howell D, Molloy S, Wilkinson K, et al: Patient-reported outcomes in routine cancer clinical practice: A scoping review of use, impact on health outcomes, and implementation factors. *Ann Oncol* 26:1846-1858, 2015
97. Acquadro C, Conway K, Hareendran A, et al: Literature review of methods to translate health-related quality of life questionnaires for use in multinational clinical trials. *Value Health* 11:509-521, 2008
98. Krogsgaard MR, Brodersen J, Christensen KB, et al: How to translate and locally adapt a PROM. Assessment of cross-cultural differential item functioning. *Scand J Med Sci Sports* 31:999-1008, 2021
99. Wolff RF, Moons KGM, Riley RD, et al: PROBAST: A tool to assess the risk of bias and applicability of prediction model studies. *Ann Intern Med* 170:51-58, 2019
100. Collins GS, Reitsma JB, Altman DG, et al: Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): The TRIPOD Statement. *Eur Urol* 67:1142-1151, 2015
101. Collins GS, Dhiman P, Andaur Navarro CL, et al: Protocol for development of a reporting guideline (TRIPOD-AI) and risk of bias tool (PROBAST-AI) for diagnostic and prognostic prediction model studies based on artificial intelligence. *BMJ Open* 11:e048008, 2021
102. Seaman SR, White IR: Review of inverse probability weighting for dealing with missing data. *Stat Methods Med Res* 22:278-295, 2013
103. Seaman SR, White IR, Copas AJ, et al: Combining multiple imputation and inverse-probability weighting. *Biometrics* 68:129-137, 2012
104. van Geloven N, Swanson SA, Ramspek CL, et al: Prediction meets causal inference: The role of treatment in clinical prediction models. *Eur J Epidemiol* 35:619-630, 2020
105. Sterne JAC, White IR, Carlin JB, et al: Multiple imputation for missing data in epidemiological and clinical research: Potential and pitfalls. *BMJ* 338:b2393, 2009
106. McLernon DJ, Giardiello D, Van Calster B, et al: Assessing performance and clinical usefulness in prediction models with survival outcomes: Practical guidance for cox proportional hazards models. *Ann Intern Med* 176:105-114, 2023
107. Rombach I, Gray AM, Jenkinson C, et al: Multiple imputation for patient reported outcome measures in randomised controlled trials: Advantages and disadvantages of imputing at the item, subscale or composite score level. *BMC Med Res Methodol* 18:87, 2018
108. Rolstad S, Adler J, Rydén A: Response burden and questionnaire length: Is shorter better? A review and meta-analysis. *Value Health* 14:1101-1108, 2011
109. Groenvold M, Petersen MA, Aaronson NK, et al: The development of the EORTC QLQ-C15-PAL: A shortened questionnaire for cancer patients in palliative care. *Eur J Cancer* 42:55-64, 2006
110. Van Calster B, Wynants L, Verbeek JFM, et al: Reporting and interpreting decision curve analysis: A guide for investigators. *Eur Urol* 74:796-804, 2018
111. Davis SE, Lasko TA, Chen G, et al: Calibration drift among regression and machine learning models for hospital mortality. *AMIA Annu Symp Proc* 2017:625-634, 2017
112. Alwan LC, Roberts HV: Time-series modeling for statistical process control. *J Bus Econ Stat* 6:87-95, 1988
113. Jenkins DA, Martin GP, Sperrin M, et al: Continual updating and monitoring of clinical prediction models: Time for dynamic prediction systems? *Diagn Progn Res* 5:1, 2021
114. Riley RD, Ensor J, Snell KIE, et al: External validation of clinical prediction models using big datasets from e-health records or IPD meta-analysis: Opportunities and challenges. *BMJ* 353:i3140, 2016
115. van den Boogaard M, Schoonhoven L, Maseda E, et al: Recalibration of the delirium prediction model for ICU patients (PRE-DELIRIC): A multinational observational study. *Intensive Care Med* 40:361-369, 2014
116. Futoma J, Simons M, Panch T, et al: The myth of generalisability in clinical research and machine learning in health care. *Lancet Digit Health* 2:e489-e492, 2020
117. Martin AR, Kanai M, Kamatani Y, et al: Clinical use of current polygenic risk scores may exacerbate health disparities. *Nat Genet* 51:584-591, 2019
118. Hernán MA, Brumback B, Robins JM: Marginal structural models to estimate the joint causal effect of nonrandomized treatments. *J Am Stat Assoc* 96:440-448, 2001
119. Groenwold RHH, Moons KGM, Pajouheshnia R, et al: Explicit inclusion of treatment in prognostic modeling was recommended in observational and randomized settings. *J Clin Epidemiol* 78:90-100, 2016