

Sustainability and time trends in electronic patient-reported outcome assessment in routine cancer care: A systematic scoping review and follow-up survey

Niclas J Hubel, Samuel M Vorbach, Kelly M de Ligt, Ines S Rathgeber, Katharina Beyer, Lisa M Wintner, Barbara Faller, Jasmin Nemec, Bernhard Holzner, Monika Sztankay, Jens Lehmann

Submitted to: Journal of Medical Internet Research
on: November 28, 2024

Disclaimer: © The authors. All rights reserved. This is a privileged document currently under peer-review/community review. Authors have provided JMIR Publications with an exclusive license to publish this preprint on its website for review purposes only. While the final peer-reviewed paper may be licensed under a CC BY license on publication, at this stage authors and publisher expressly prohibit redistribution of this draft paper other than for review purposes.

Table of Contents

Original Manuscript..... 5

Supplementary Files..... 36

..... 36

Multimedia Appendixes 37

 Multimedia Appendix 0..... 37

 Multimedia Appendix 1..... 37

 Multimedia Appendix 2..... 37

Sustainability and time trends in electronic patient-reported outcome assessment in routine cancer care: A systematic scoping review and follow-up survey

Niclas J Hubel¹; Samuel M Vorbach² MD; Kelly M de Ligt³ PhD; Ines S Rathgeber¹; Katharina Beyer⁴ PhD; Lisa M Wintner¹ PhD; Barbara Faller⁵ MSc; Jasmin Nemec⁵ MSc; Bernhard Holzner¹ PhD; Monika Sztankay^{1*} PhD; Jens Lehmann^{1*} PhD

¹ University Hospital of Psychiatry II Medical University of Innsbruck Innsbruck AT

² Department of Radiation Oncology Medical University of Innsbruck Innsbruck AT

³ Department of Psychosocial Research and Epidemiology Netherlands Cancer Institute Amsterdam NL

⁴ Department of Urology Erasmus MC Cancer Institute University Medical Center Rotterdam Rotterdam NL

⁵ Universität Innsbruck Innsbruck AT

*these authors contributed equally

Corresponding Author:

Jens Lehmann PhD

University Hospital of Psychiatry II
Medical University of Innsbruck
Anichstrasse 35
Innsbruck
Innsbruck
AT

Abstract

Background: Routine electronic assessment of patient-reported outcomes (ePRO) can improve cancer care, yet its implementation in routine practice and long-term sustainability remain unclear. Understanding these aspects is critical to advancing the field.

Objective: To review and describe the past and current status, time trends and the long-term sustainability of clinical ePRO applications in routine oncology care.

Methods: We conducted a systematic review of publications on ePRO use in oncology care up to December 31, 2023, extracting data on clinical ePRO applications. A follow-up survey was sent to authors of published ePRO applications to assess their current use. Data were analyzed using descriptive statistics and regression models to evaluate time trends, with year of publication as the predictor.

Results: Of 2,933 references screened, 303 met inclusion criteria. Publications increased significantly over time (2003–2023, $P < .001$). Trends showed a rise in mobile application use ($OR = 1.211$, $P < .001$), remote assessments ($OR = 1.094$, $P = .002$), and feedback provided to patients ($OR = 1.060$, $P = .036$). The survey had a 35.3% response rate (78/221), with 61.1% of ePRO applications still in use, lasting a median of 5 years. The most common reason for discontinuation was a lack of funding and resources (42.9%, 12/28).

Conclusions: The field of ePRO assessment in oncology is growing, and shifting towards remote and app-based assessment, as well as increasingly providing feedback to patients. We present, for the first time, data on sustainability of ePRO use in routine care and show that financial and resource barriers remain a key challenge to sustainable implementations.

(JMIR Preprints 28/11/2024:69398)

DOI: <https://doi.org/10.2196/preprints.69398>

Preprint Settings

1) Would you like to publish your submitted manuscript as preprint?

Please make my preprint PDF available to anyone at any time (recommended).

Please make my preprint PDF available only to logged-in users; I understand that my title and abstract will remain visible to all users.

Only make the preprint title and abstract visible.

✓ **No, I do not wish to publish my submitted manuscript as a preprint.**

2) If accepted for publication in a JMIR journal, would you like the PDF to be visible to the public?

✓ **Yes, please make my accepted manuscript PDF available to anyone at any time (Recommended).**

Yes, but please make my accepted manuscript PDF available only to logged-in users; I understand that the title and abstract will remain visible to all users.

Yes, but only make the title and abstract visible (see Important note, above). I understand that if I later pay to participate in <http://www.jmir.org/>, I will be able to make my manuscript available to all users.

No. Please do not make my accepted manuscript PDF available to anyone.



Original Manuscript

Sustainability and time trends in electronic patient-reported outcome assessment in routine cancer care:

A systematic scoping review and follow-up survey

Authors:

Niclas J Hubel¹, Samuel M Vorbach², Kelly M. de Ligt³, Ines S Rathgeber¹, Katharina Beyer⁴, Lisa M Wintner¹, Barbara Faller⁵, Jasmin Nemec⁵, Bernhard Holzner¹, Monika Sztankay^{1*} & Jens Lehmann^{1*+}

Affiliations:

¹ University Hospital of Psychiatry II, Medical University of Innsbruck, Innsbruck, Austria.

² Department of Radiation Oncology, Medical University of Innsbruck, Innsbruck, Austria.

³ Department of Psychosocial Research and Epidemiology, Netherlands Cancer Institute, Amsterdam, The Netherlands

⁴ Department of Urology, Erasmus MC Cancer Institute, University Medical Center Rotterdam, 3015 Rotterdam, The Netherlands.

⁵ Department of Psychology, University of Innsbruck, Innsbruck, Austria

* contributed equally

⁺ Corresponding author:

Jens Lehmann, jens.lehmann@i-med.ac.at

University Hospital of Psychiatry II, Anichstrasse 35, 6020 Innsbruck, Austria.

Abstract

Background

Routine electronic assessment of patient-reported outcomes (ePRO) can improve cancer care, yet its implementation in routine practice and long-term sustainability remain unclear. Understanding these aspects is critical to advancing the field.

Objectives

To review and describe the past and current status, time trends and the long-term sustainability of clinical ePRO applications in routine oncology care.

Methods

We conducted a systematic review of publications on ePRO use in oncology care up to December 31, 2023, searching Pubmed and Web of Science, and extracting data on clinical ePRO applications. We included peer-reviewed studies including patients with cancer using ePRO assessments in clinical practice, excluding research letters and conference abstracts. Data from the review were analysed using descriptive statistics and univariate regression models to evaluate time trends, with year of publication as the predictor. A follow-up survey was sent to authors of published ePRO applications to assess their current use of the application or reasons for discontinuation. Responses from the follow-up survey were analysed descriptively.

Results

For the review, we screened 2,933 references and 303 met inclusion criteria. Results showed that Europe was the most common region (n = 141, 46.5%) and study populations consisted mostly of adult patients (n = 276, 91.1%) under chemotherapy treatment (n = 124, 40.9%) assessed in an outpatient setting (n = 261, 86.1%). EORTC (n=77, 25.4%) and PRO-CTCAE questionnaires (n=65,

21.5%) were most frequently integrated into ePRO applications.

In the univariate analysis, we found that publications increased significantly over time (2003–2023, $P < .001$). Trends showed a rise in mobile application use (OR = 1.211, $P < .001$), remote assessments (OR = 1.094, $P = .002$), and feedback provided to patients (OR = 1.060, $P = .036$). Of the 303 studies, 221 unique clinical ePRO applications were identified, merging publications at the application level. The follow-up survey had a 35.3% response rate (78/221), with 61.1% of ePRO applications still in use, lasting a median of 5 years. The most common reason for discontinuation was a lack of funding and resources (42.9%, 12/28).

Conclusion

The field of ePRO assessment in oncology is rapidly evolving, with a shift toward remote, app-based tools and a growing emphasis on providing feedback to patients. We present, for the first time, data on the sustainability of ePRO use in routine care. While our findings offer valuable insights, they should be interpreted in light of potential response bias in the follow-up survey. Several ePRO applications remain in active use, highlighting potential for long-term integration into clinical practice. However, financial constraints, limited reimbursement models, and challenges with workflow integration continue to hinder broader and more sustainable adoption. Addressing these barriers will be essential to support the continued use of ePROs in clinical care.

KEYWORDS:

Patient Reported Outcome Measures; Cancer, Clinical Routine; Health-Related Quality of Life; Quality of Care; Mobile Applications; Digital Technology

Introduction

Adequate symptom monitoring is a cornerstone of clinical care for patients with cancer. During and after treatment, patients frequently experience symptoms that can impact their health-related quality of life (HRQOL), therapy compliance, or even be life-threatening [1–3]. Routine assessment and use of patient-reported outcomes (PROs) in clinical care can improve care for patients with cancer resulting in better HRQOL, reduced hospitalisation rates and even prolonged survival [1,4–9].

Accordingly, the European Society for Medical Oncology (ESMO) advises the routine assessment of PROs in clinical care, emphasizing the importance of electronic PRO (ePRO) assessments [10].

In recent years, electronic approaches to collecting PRO data—commonly referred to as electronic PRO (ePRO) assessments—have gained increasing importance. Real-time digital platforms (hereafter referred to as ePRO software) offer an efficient and scalable solution to systematically collect, store, and report PRO data in clinical settings. Compared to traditional paper-based methods, ePRO software facilitates standardized and timely assessments, can potentially reduce response burden and missing data, and enhance overall usability and patient satisfaction [7,11–14].

Despite all these advantages, there seems to be a challenge to sustainably implement such ePRO interventions into routine workflows [15,16]. The complex nature of routine care, fragmented workflows, limited resources, and reluctance to change within healthcare systems may contribute to the slow progress in implementing ePRO software tools outside of research settings [16–18]. Another common difficulty lies in obtaining reliable data on the use of ePRO software in clinical practice settings [19]. While many studies are published during the initial development and implementation phase [20], there is little information on the long-term use of those *clinical ePRO applications* (referring to the use of ePRO software in a specific clinical context). A considerable portion of developed clinical ePRO applications may be discontinued following the completion of research initiatives, potentially failing to transition into long-term use in clinical care.

The landscape of ePRO assessment in routine oncology is evolving rapidly, with an increasing

number of publications emerging. However, since the review by Warrington et al. in 2019 (which included studies published until 2017) [21], no recent comprehensive reviews have captured this trend across the field of oncology as a whole – a considerable time span for a fast-changing field. Current reviews on clinical ePRO applications often have limitations that prevent a comprehensive overview of the current landscape of clinical ePRO applications used in oncology practice, like focusing on specific patient populations, or applying narrow inclusion criteria (e.g., focusing on palliative care applications only or on ePRO use for specific types of treatment) [20,22].

The objectives of this systematic scoping review and follow-up survey are:

- To review and describe the past and current practice of published ePRO use in oncology clinical care
- To assess potential trends in the clinical use and assessment of ePRO data over time
- To assess the sustainability and long-term use of the reported clinical ePRO applications.

Methods

Review

The review was conducted according to the methodological framework by Arksey and O'Malley and reported according to the PRISMA 2020 Checklist extension for scoping reviews (see eMethods 1 in the supplementary) [23,24].

We searched Pubmed and Web of Science for studies published until 31.12.2023 without restrictions regarding the publication date. A detailed description of the search strategy is provided in eMethods 2 in the supplementary. Reviews and meta-analyses identified in the initial search were used for a backward search (identifying relevant studies based on the cited references).

We included studies that were conducted exclusively with oncology patients, reported on the electronic assessment of PROs, were peer-reviewed primary research, and were available in English

language. We excluded studies that evaluated experimental interventions other than the clinical ePRO application, research letters, editorials and conference abstracts.

The review software DistillerSR [25] was used for the two-level study selection process and the subsequent data extraction. References were independently screened and reviewed by two individual reviewers experienced with ePROs. Disagreements were resolved in discussion. If no agreement was reached, a third (senior) reviewer was consulted. The data extraction followed the same procedure.

For general study characteristics, we extracted details on authors, address of correspondence, year, and country of origin. We categorized the respective studies into the following publication types reflecting different stages of the clinical ePRO application and its use: *system development* (incomplete system, still under technical evaluation), *feasibility study* (finalized system, still under practical evaluation), *study protocol, trial* (evaluating a finalized ePRO System), *implementation study* (integration of finalized system into clinical workflow), and *routine application* (describing use of or PRO data from an implemented system).

We charted the purpose of ePRO use according to the ISOQOL user guide for implementing PROs in clinical practice [26]. *Screening tools* (one-time PRO assessment with feedback to clinicians), *Monitoring tools* (repeated assessment with feedback of results to clinicians), *Patient-centred care* (feedback of PRO results to patients), *ePRO assessment without direct feedback*, *Decision aids* (information about treatment options or similar), *Evaluating quality of care*, and *Facilitating multidisciplinary team communications*. Patient groups were classified into inpatients and outpatients and the time of PRO assessment was determined according to the respective care phase.

Review: Analysis

We report descriptive statistics of the publication characteristics and all extracted variables. All missing data were classified as “not reported” and excluded from all analyses. To investigate time trends in ePRO data capture over time, we calculated a binomial Poisson and logistic regressions with the year of publication as the predictor and the number of publications per year as the outcome. Further, we conducted univariate logistic regressions with the year of publication as the predictor and one of the following selected variables as the criterion: inpatient population, outpatient population, remote assessment, in-hospital assessment, use of website, use of app, provision of PRO feedback to patients, provision of PRO feedback to clinicians, internal PRO software development, external PRO software development. These variables were selected as markers for overall shifts within the field and indicators of technological advancements in the last 20 years. They reflect evolving approaches to data collection and to the integration of digital tools in clinical care.

The selected outcomes were coded as 1 = [true] and 0 = [false]. Model coefficients are expressed as odds ratios (ORs) for the logistic regressions and as risk ratio (RR) for the Poisson regression, each with 95% confidence intervals (CIs) and an alpha level of .05. Calculations were done using R Version 4.3.1 [27].

Follow-up survey

We sent a follow-up questionnaire to the corresponding authors of all clinical ePRO applications that were identified based on the publications in the review (i.e., merging publications on the distinct use of an ePRO software in a specific clinical context). The questionnaire was distributed via email and up to two reminders were sent if needed. We developed the questionnaire among the authors who are experienced with the implementation of ePROs, and pilot-tested it internally before distribution.

Follow-up survey: Measures

The survey aimed to evaluate the status of clinical ePRO application use. Participants were asked whether the application was still in use, with follow-up questions tailored accordingly: reasons for

discontinuation or details about current usage practices were explored in alignment with the ISOQOL user guide[26]. Non-users were invited to share what changes or features would encourage them to consider adopting ePRO assessments or systems in the future.

Additional questions addressed the duration of ePRO application use, the average number of participating patients per month, and satisfaction levels, which were rated on a four-point scale.

Participants also had the opportunity to provide suggestions for improvement through an open-text field. The complete survey is detailed in eMethods 3 in the supplementary.

Follow-up survey: Analysis

We report descriptive statistics of all variables, missing data were classified as “not reported” and excluded from all analyses. To evaluate potential response bias within our data we calculated differences in the distribution of the respondents to our survey using Chi-squared tests and univariate logistic regressions for the following variables: the year of the last publication related to the respective ePRO clinical application, the total number of published articles referring to the clinical ePRO application, the region of the cancer centres, and the publication type of the last article published based on the clinical ePRO application.

Calculations were done using R Version 4.3.1 [27].

Results

Review

The initial literature search yielded 3,346 references. After the removal of 413 duplicates, the remaining 2,933 records underwent title abstract screening for eligibility, of which 409 studies were included in the full-text review. A final 303 studies were included in the review. Figure 1 depicts the PRISMA flowchart. The complete list of references can be found in eReferences. The main reasons for exclusions were that the full text did not include a clinical ePRO application ($n = 58$) and alternative interventions other than ePRO monitoring were examined ($n = 18$). Publication dates

ranged from 2003 until 2023.

Based on the 303 publications included in the review, we identified 221 unique clinical ePRO applications. Most clinical ePRO applications (175, 57.8%) were reported only in a single publication, while 46 clinical ePRO applications were reported in multiple publications (median 2 publications, IQR 1-1, range 2-10).



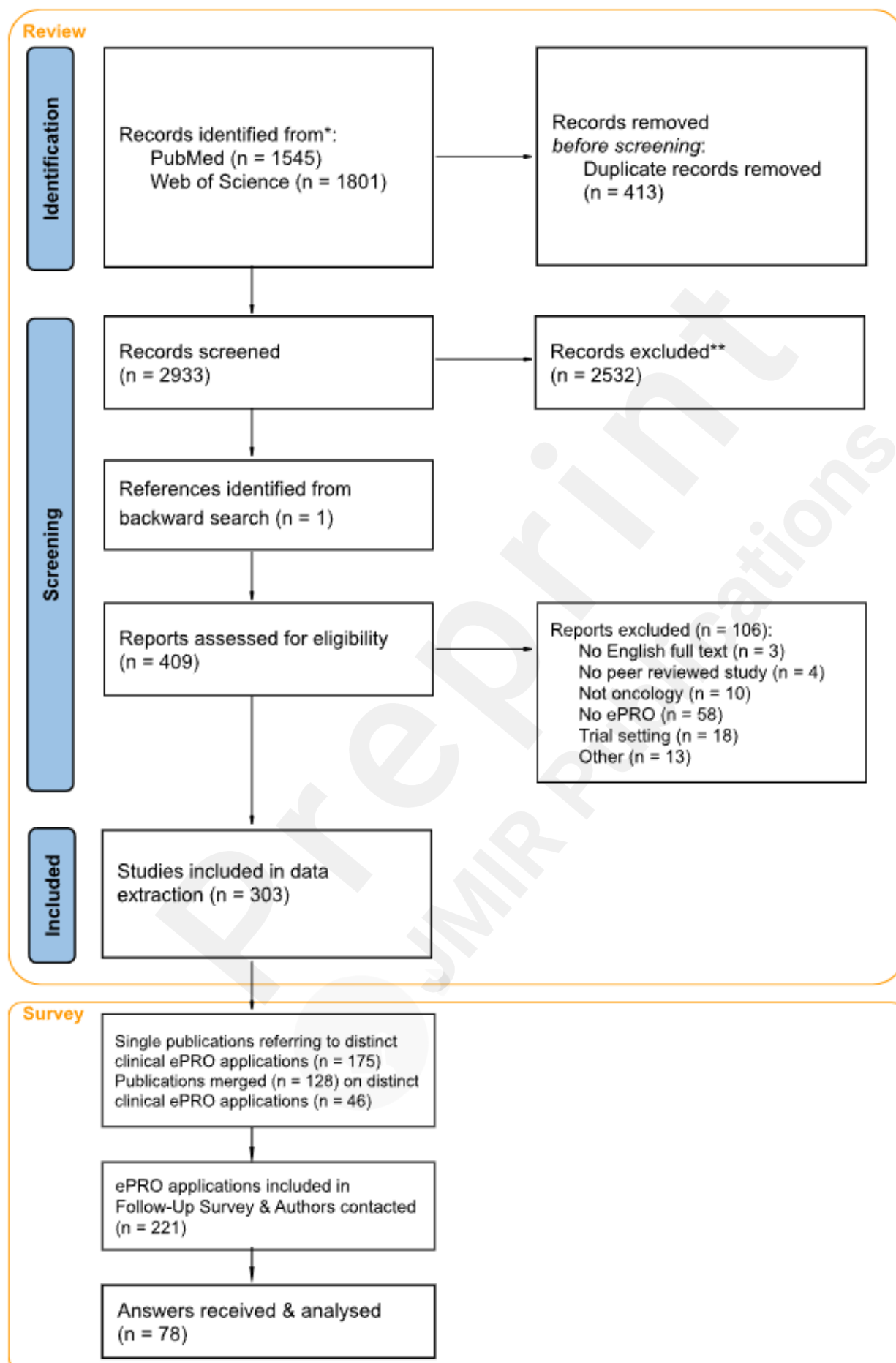


Figure 1: PRISMA Flowchart

Study Characteristics

The majority of included studies were conducted in Europe (46.5%) and North America (39.6%), with the USA being the most common country (34.3%, see Table 1 and eTable 1 in the supplementary). According to our classification, the most used study types were ePRO feasibility studies (33.0%) and studies describing the routine use of clinical ePRO applications in clinical practice (17.8%). The complete study data are shown in the multimedia appendix 1.

The applications were most frequently designed for patients with breast ($n = 78$, 25.7%), gastrointestinal ($n = 37$, 12.2%), and lung ($n = 37$, 12.2%) cancers. Most studies were conducted with adult patients ($n = 276$, 91.1%), and among outpatients ($n = 261$, 86.1%) treated with chemotherapy ($n = 124$, 40.9%).

Table 1: Study Characteristics (N = 303)

	<i>n</i> of publications	% of publications
Region^a		
Europe	141	46.5
North America	120	39.6
Asia	22	7.3
Australia	12	4.0
South America	4	1.3
International	1	0.3
Not reported	3	1.0
Publication types		
Feasibility Study	100	33.0
Routine application	54	17.8
System Development	42	13.9
Trial	41	13.5
Study Protocol	40	13.2

Implementation Study	26	8.6
Patient group		
Outpatients	261	86.1
Inpatients	10	3.3
Both	18	5.9
Not reported	14	4.6
Patient age groups		
Adults	276	91.1
Children & Adolescents (<18 years)	13	4.3
Not reported	14	4.6
Cancer type		
Not specified/defined	110	36.3
Application used in specific cancer types (multiple could apply):	193	63.7
Breast	78	40.4
Gastrointestinal	37	19.2
Lung	37	19.2
Prostate	34	17.6
Colorectal	31	16.1
Head & Neck	26	13.5
Haematological	25	13.0
Gynaecological	17	8.8
Other ^b	15	7.8
Treatment (multiple could apply)		
Chemotherapy	124	40.9
Radiotherapy	64	21.1
Surgery	56	18.5
Hormonal Therapy	31	10.2
Targeted Therapy	24	7.9

Immunotherapy	23	7.6
No active treatment	21	6.9
Other ^c	6	2.0
Not reported	90	29.7

Notes:

^a see eTable 1 in the supplementary for full list

^b Bladder, Central nervous system, Liver, Neuroendocrine, Renal, Retinoblastoma, Thyroid, Genitourinary

^c Active Surveillance, Cryotherapy, Stem Cell Transplantation

Reported use of ePRO assessment in clinical practice

The most common use cases of ePROs, according to the ISOQOL classification, were as monitoring tools ($n = 219$, 72.3%) and for patient-centred care ($n = 123$, 40.6%) (Table 2). Physicians ($n = 166$, 54.8%) and nurses ($n = 154$, 50.8%) were the main users of ePRO software, while other healthcare professionals were rarely mentioned (less than 3%). The user groups were not specified in 30.7% of the publications.

The ePRO assessment was predominantly conducted remotely ($n = 147$, 48.5%) via a website interface ($n = 122$, 40.3%). The respective ePRO software tools were partly developed in-house at the respective cancer centres ($n = 106$, 35.0%) or by external IT vendors ($n = 109$, 36.0%). A total of 145 unique ePRO software tools were identified, of which 39 were mentioned in more than one publication (median 1 publication, IQR 1-3, range 1-16). 55 (18.2%) publications did not report any distinctive tool (see eTable 2 in the supplementary for more information).

The questionnaires most commonly assessed via ePRO were EORTC measures ($n = 77$, 25.4%), closely followed by PRO-CTCAE ($n = 65$, 21.5%). A full list of the 136 used questionnaires can be found in eTable 3 in the supplementary.

Table 2: Characteristics and use of ePRO assessments (N=303)

	<i>n</i> of publications	% of publications
Assessment setting		
Remote	147	48.5
In clinic	79	26.1
Both in clinic and remote	55	18.2
Not reported	22	7.3
Clinical user group (multiple could apply)		
Physicians	166	54.8
Nurses	154	50.8
Psychologists	8	2.6
Pharmacists	7	2.3
Social workers	6	2.0
Dietitians	3	1.0
Others (Physiotherapists, Case managers, etc.)	10	3.3
Not reported	93	30.7
Technology		
Website interface	122	40.3
App	75	24.8
Both, website interface and app	41	13.5
Not reported	65	21.5
Technical Development of the software		
External IT vendors	109	36.0
In-house	106	35.0
Joint development	5	1.7
Not reported	83	27.4
Time of ePRO assessment (multiple could apply)		
During active treatment	213	70.3

During early follow-up (<2 years after treatment)	125	41.3
During long-term follow-up (≥ 2 years after treatment)	45	14.9
In palliative care	36	11.9
Pre-treatment	12	4.0
Not reported	31	10.2
Purpose of ePRO use (multiple could apply)		
Monitoring tools (data collection over time with feedback of results to clinicians)	219	72.3
Patient-centred care (data collection with feedback of PRO results to patients)	123	40.6
ePRO assessment without feedback	59	19.5
Decision aids (for shared decision-making)	10	3.3
Evaluating quality of care	8	2.6
Screening tools (one-time PRO assessment with feedback to clinicians)	7	2.3
Facilitating multidisciplinary team communications	5	1.7
PROMs assessed within the ePRO software tool (multiple could apply)		
EORTC questionnaires (C30 and/or modules)	77	25.4
PRO-CTCAE	65	21.5
EQ-5D	29	9.6
FACIT questionnaires	27	8.9
Own development	27	8.9
Others ^a	307	93.4
Not Reported	34	11.2

Note: ^a see eTable 3 in the supplementary for full list

Time trends in electronic patient-reported outcome use

The number of publications increased significantly over time (RR = 1.20, 95% CI: 1.17–1.22, $P < .001$), rising from just 2–4 publications per year in the early 2000s to a peak of 42 in 2023. Notable increases occurred from 2014 onward, with particularly sharp growth between 2015 and 2017 and again after 2019. A detailed annual overview is provided in multimedia appendix 2.

The binomial logistic regression model for app use was statistically significant (OR = 1.21, 95%-CI 1.12 - 1.32, $P < .001$), meaning that for each additional year, the likelihood that the ePRO assessment was embedded in an app increased by 21.1%. At the same time, fewer publications per year reported the use of a website interface (OR = 0.85, 95%-CI 0.77 - 0.93, $P < .001$).

Remote assessments were more frequently reported in recent years (OR = 1.09, 95%-CI 1.03 - 1.16, $P = .002$) with an increase of 9.4% per year. The likelihood of articles describing in-clinic assessments decreased by 8.0% per year, (OR = 0.92, 95%-CI 0.87 - 0.97, $P = .004$).

Publications over time increasingly described providing patients PRO feedback (increase of 6.0% per year, OR = 1.060, 95%-CI 1.00 - 1.12, $P = .04$). There was no significant change over time in providing PRO feedback to physicians ($P = .22$), but this number was consistently high throughout the years (data not shown). Similarly, no time trend was observed regarding the reported patient population for either inpatient ($P = .97$) or outpatient settings ($P = .87$). The odds of using software tools developed by an external IT vendor increased significantly over time (OR = 1.08, 95%-CI 1.01 - 1.15, $P = .02$), whereas the trend for in-house development was not significant ($P = .06$).

Follow-up survey

The follow-up survey was sent out to all corresponding authors and received a response rate of 35.3% (78/221).

There was no link between whether someone responded and the year their last clinical ePRO

publication appeared ($P = .15$) or the type of publication ($P = .13$). However, response rates varied significantly between regions ($\chi^2(6) = 17.00$, $P = .009$). Specifically, response rates were lower in Asia (3/20, 15.0%) and North America (24/90, 26.7%), while they were higher in Australia (5/6, 83.3%), Europe (43/97, 44.3%), and South America (2/4, 50.0%). Finally, authors who had published more articles on their clinical ePRO application were also more likely to respond (OR = 1.44, 95% CI 1.08–2.06, $P = .02$).

Of the 78 responses received, 50 (64.1%) indicated that the respective application was still in use and had been operational for a median of five years (IQR 3-10, see Table 3).

The most prevalent use cases, according to the ISOQOL classification, were using the clinical ePRO application as a monitoring tool (34/50, 68.0%), for patient-centred care (32/50, 64.0%), and research purposes (36/50, 72.0%), with respondents able to select multiple options. Further, respondents reported 1-50 (40.0%) or 51-200 (30.0%) average patient users per month.

Among the authors who reported that their ePRO application was no longer in use (28/78, 35.9%), a lack of funding was the most common reason for discontinuation (12/28, 42.9%). About the same number of respondents reported that they would resume the ePRO application in case the required funding or resources (e.g., administrative support, dedicated personnel or IT support) were available (13/28, 46.4%). Eight (28.6%) authors reported that they were no longer using the ePRO application they had been contacted for but that they had switched to a different ePRO software.

Table 3: Follow-up survey ($N = 78$)

		<i>n</i> of publications	% of publications
Clinical ePRO application still in use		50	64.1
	Patients participating per month		

	1 - 50	20	40.0
	51 - 200	15	30.0
	201 - 500	4	8.0
	> 500	10	20.0
	Not reported	1	2.0
	Satisfaction with clinical ePRO application		
	Not at all	0	0.0
	A little bit	7	14.0
	Quite a bit	23	46.0
	Very much	20	40.0
	Purpose of ePRO use (multiple could apply)		
	Research	36	72.0
	Monitoring Tools (data collection over time with feedback of results to clinicians)	34	68.0
	Patient-centred care (data collection with feedback of PRO results to patients)	32	64.0
	Screening Tools (One-time PRO assessment with feedback to clinician)	17	34.0
	Facilitating multidisciplinary team communications	17	34.0
	Decision aids (for shared decision-making)	15	30.0
	Evaluating quality of care	15	30.0
	Areas for improvement^a (multiple could apply)		
	Functionality (e.g., reports, graphs, reminders)	13	26.0
	Integration with electronic medical records	9	18.0
	Patient & clinician engagement	8	16.0

	User-friendliness and accessibility	7	14.0
	None reported	14	28.0
Clinical ePRO application not used anymore		28	35.9
	Reasons why (multiple could apply):		
	Lack of funding	12	42.9
	Logistical or organisational challenges	9	32.1
	Technical problems	8	28.6
	Change to different software for ePRO assessment	8	28.6
	Underutilization	3	10.7
	Lack of user-friendliness	2	7.1
	Change in clinical needs	1	3.6
	Requirements for reconsidering ePRO use^a (multiple could apply):		
	Funding or resources	13	46.4
	Integration with existing clinical systems	5	17.9
	Improved usability	4	14.3
	Patient & clinician engagement	2	7.1
	None reported	9	32.1

Note: ^a These questions were a free text field the answers to which we categorised

Discussion

In this study, we systematically reviewed studies reporting on ePRO assessment in clinical practice and present the results of a follow-up survey investigating the long-term use of the identified clinical ePRO applications. The results show a significant increase in publications on clinical ePRO applications over time including time trends towards app-based ePRO software, patient-centred care

(data collection with feedback of PRO results to patients), and remote assessments. Information on the current use of identified ePRO applications could be gathered for about a third, of which 64% were reportedly still in use, primarily for monitoring, feedback of PRO results to patients, and research. Lack of funding was the main reason for discontinuation of ePRO application use, with more resources being the key requirement for reconsidering reuptake.

ePRO use in clinical practice and time trends

The review highlights the growing role of clinical ePRO applications in routine care, especially for monitoring symptoms and HRQOL during treatment and early aftercare. Unlike research-focused data collection, PRO monitoring and subsequent management by healthcare providers can offer direct patient benefits [8,9]. Increased ePRO publications over the last decade, [28,29] were likely spurred by two landmark trials in 2017 showing survival benefits from remote ePRO monitoring [30,31]. Basch et al. demonstrated overall survival benefits in patients with solid tumours who were monitored via an ePRO application, where nurses received alerts when patients reported severe symptoms [30]. Similarly, Denis et al. reported an improved overall survival of the ePRO arm when compared to standard of care [31]. These results highlighted the potential of ePROs to improve outcomes, possibly driving their broader adoption. Clinical ePROs are increasingly used to provide patients with feedback on their scores, enabling them to actively manage their health and make informed care decisions [7,32].

Our follow-up survey found discrepancies between published reports of ePRO use and their actual use in clinical practice. This may be due to varied interpretations of survey categories, unreported use cases, or the evolving role of ePROs over time. For instance, quality of care evaluation was cited more in the survey (30%) than in studies (3%). Overall, our findings suggest that clinical ePRO use is broader and more diverse than reflected in current literature.

Our findings also show that website interfaces remain dominant, however, mobile apps are becoming

increasingly more prevalent in the field of oncology, as Lu et al. showed in their review of 41 symptom-tracking apps [33]. Apps can offer more accessible, user-friendly interfaces for patients and have shown notable growth in utilisation. For example, a study by Pho et al. demonstrated a significant increase in mobile app log-ins over time, particularly in younger patient populations, leading to a higher overall frequency of ePRO use compared to users of the website interface [34]. Looking ahead, one might expect patient apps to become even more prevalent and ePROs to become more often integrated into electronic health record (EHR) systems to facilitate access for healthcare professionals.

Sustainability of clinical ePRO applications

Participants in the follow-up survey reported that about two-thirds of the ePRO applications were still in use, with some applications being active for over 20 years. However, it is important to note that this represents only 23% of the total number of applications reviewed. Authors with ePRO applications still in active use may have been more likely to respond to our survey, potentially leading to an overestimation of sustainable use. Hence, the true rate of sustainable use likely falls between the 64% of applications still in use according to our survey (50/78) and the more conservative estimate of 23% according to all applications initially identified (50/221). Additionally, other research shows that mobile applications in oncology are often no longer available once their respective research project is concluded [35].

Interestingly, some centres that discontinued their original ePRO applications reported to have transitioned to different software solutions for continued ePRO assessment. For example, in Denmark and Ontario, Canada ePRO assessment was implemented on a national (regional) level showing the possibility of evolving and adapting ePRO applications [36,37].

Despite these encouraging examples, the sustainability of clinical ePRO applications remains a

significant challenge, particularly due to financial constraints. The high initial costs of implementing clinical ePRO applications can often come without a clear direct return on investment, making it difficult to maintain these tools over the long term. Additionally, switching to another software or vendor can double these expenses, further straining budgets. The lack of follow-up financing was cited as the primary reason for discontinuing many applications. Some countries, such as France, are exploring reimbursement models for remote patient monitoring to offset these financial challenges that can also apply to ePRO applications in clinical care [38]. Notably, reimbursement has recently been granted for a clinical ePRO application in 33 cancer centres with an additional 18 about to follow, demonstrating the policy's potential impact on broader adoption [39].

In addition to financial barriers, integrating ePRO assessment into EHRs and clinical workflows, the need for appropriate user support, and the demand for features like enhanced data visualisation and real-time feedback to improve sustainability are frequently mentioned challenges [18,40].

Correspondingly, a review of fifteen ePRO systems in nephrology identified sustained patient involvement, clinician champions and expanding existing electronic platforms to integrate ePROs as important factors for a sustainable ePRO implementation [41].

To address these challenges and promote long-term success, we recommend using established methodologies designed to support successful clinical implementation, where sustainability is a key outcome criterion (see for example [42–44]).

Strength & Limitations

Our paper offers valuable insights into the long-term use and sustainability of clinical ePRO applications, backed by both a comprehensive literature review and follow-up survey data. Another key strength lies in the novel exploration of time trends over the past 20 years that illustrate the use of clinical ePRO applications in oncology. The key limitation of the follow-up survey and the sustainability analysis is potential response bias: Potentially, authors whose ePRO application is still

in use might be more prone to reply to the survey, thereby biasing the analysis. We also identified an increased likelihood of a response from clinical ePRO application with a higher total number of published articles which can be seen as an indicator for a bias towards more active research groups. Hence, we have interpreted our sustainability analysis based on all the applications initially identified and provide a more conservative estimate based on the total number of identified applications. Furthermore, we found that specific regions were overrepresented among respondents therefore biasing our results geographically.

Inconsistent reporting of ePRO systems in the literature poses another challenge in comprehensively reporting on the current practices of ePRO applications in clinical care. The lack of a specific reporting framework (or limited compliance with more general guidelines like [45]) makes it difficult to compare studies and draw conclusions about best practices for ePRO implementation. However, ongoing efforts to develop specific guidelines for reporting patient-reported outcome measures (PROMs) in routine care offer hope for addressing this issue (Patient-Reported Outcome Measures – Guideline for Reporting In clinical Practice (PROM-GRIP)[46]).

Conclusion

Our study presents data on the sustainability and growing use of clinical ePRO applications in routine cancer care, with the potential to improve symptom monitoring and patient-centred care. While many applications remain in use, financial challenges and integration barriers might limit widespread adoption. Addressing these obstacles through reimbursement models, improved workflow integration, and enhanced support features will be essential for the sustained success of clinical ePRO applications in oncology.

Declarations

Acknowledgements

No generative artificial intelligence tools were used to create the original content for publication.

However, the authors declare that they have used generative artificial intelligence (ChatGPT-4o, OpenAI, 2025) to improve the readability and language of the work. All input was thoroughly checked for accuracy by the authors to ensure the integrity of the content.

We acknowledge Open Access Funding provided by the Medical University of Innsbruck.

Author contributions

Niclas J Hubel: Conceptualization, Methodology, Project administration, Investigation, Data Curation, Formal analysis, Writing - Original Draft, Writing - Review & Editing

Samuel M Vorbach: Investigation, Writing - Review & Editing

Kelly M. de Lig: Investigation, Writing - Review & Editing

Ines Rathgeber: Investigation, Writing - Review & Editing

Katharina Beyer: Investigation, Writing - Review & Editing

Lisa M Wintner: Investigation, Writing - Review & Editing

Jasmin Nemec: Data Curation, Writing - Review & Editing

Barbara Faller: Data Curation, Writing - Review & Editing

Bernhard Holzner: Supervision, Writing - Review & Editing

Monika Sztankay: Conceptualization, Methodology, Investigation, Supervision, Resources, Writing - Review & Editing

Jens Lehmann: Conceptualization, Methodology, Investigation, Data Curation, Supervision, Writing - Original Draft, Writing - Review & Editing

Competing interests

BH reports intellectual property rights to the Computer-based Health Evaluation Software, outside of

the submitted work. JL reports consultancy for Evaluation Software Development and a research grant from Takeda, both outside of the submitted work. NH, JN, and BF report consultancy for Evaluation Software Development outside the submitted work. The other authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Availability of data and materials

All data from the review are available as supplementary materials. Data from the follow-up survey are available in anonymized form upon reasonable request from the authors.

Funding

None.

REFERENCES

1. Barbera L, Sutradhar R, Seow H, Earle CC, Howell D, Mittmann N, Li Q, Thiruchelvam D. Impact of Standardized Edmonton Symptom Assessment System Use on Emergency Department Visits and Hospitalization: Results of a Population-Based Retrospective Matched Cohort Analysis. *JCO Oncol Pract* 2020 Sep;16(9):e958–e965. PMID:32463762
2. Lizán L, Pérez-Carbonell L, Comellas M. Additional Value of Patient-Reported Symptom Monitoring in Cancer Care: A Systematic Review of the Literature. *Cancers* 2021 Jan;13(18):4615. PMID:34572842
3. Reilly CM, Bruner DW, Mitchell SA, Minasian LM, Basch E, Dueck AC, Cella D, Reeve BB. A literature synthesis of symptom prevalence and severity in persons receiving active cancer treatment. *Support Care Cancer* 2013 Jun 1;21(6):1525–1550. PMID:23314601
4. Barbera L, Sutradhar R, Seow H, Mittmann N, Howell D, Earle CC, Li Q, Thiruchelvam D. The impact of routine Edmonton Symptom Assessment System (ESAS) use on overall survival in cancer patients: Results of a population-based retrospective matched cohort analysis. *Cancer Med* 2020;9(19):7107–7115. PMID:32794634
5. Velikova G, Booth L, Smith AB, Brown PM, Lynch P, Brown JM, Selby PJ. Measuring quality of life in routine oncology practice improves communication and patient well-being: a randomized controlled trial. *J Clin Oncol* 2004;22(4):714–724. PMID:14966096
6. Kotronoulas G, Kearney N, Maguire R, Harrow A, Di Domenico D, Croy S, MacGillivray S. What is the value of the routine use of patient-reported outcome measures toward improvement of patient outcomes, processes of care, and health service outcomes in cancer care? A systematic review of controlled trials. *J Clin Oncol* 2014 May 10;32(14):1480–1510. PMID:24711559
7. Lu S-C, Porter I, Valderas JM, Harrison CJ, Sidey-Gibbons C. Effectiveness of routine provision of feedback from patient-reported outcome measurements for cancer care improvement: a systematic review and meta-analysis. *J Patient-Rep Outcomes* 2023 Jun 5;7(1):54. PMID:37277575
8. Balitsky AK, Rayner D, Britto J, Lionel AC, Ginsberg L, Cho W, Wilfred AM, Sardar H, Cantor N, Mian H, Levine MN, Guyatt GH. Patient-Reported Outcome Measures in Cancer Care: An Updated Systematic Review and Meta-Analysis. *JAMA Netw Open* 2024 Aug 1;7(8):e2424793. PMID:39136947
9. Perry MB, Taylor S, Khatoon B, Vercell A, Faivre-Finn C, Velikova G, Marsden A, Heal C, Yorke J. Examining the Effectiveness of Electronic Patient-Reported Outcomes in People With Cancer: Systematic Review and Meta-Analysis. *J Med Internet Res* 2024 Jul 31;26:e49089. PMID:39083791
10. Di Maio M, Basch E, Denis F, Fallowfield LJ, Ganz PA, Howell D, Kowalski C, Perrone F, Stover AM, Sundaresan P, Warrington L, Zhang L, Apostolidis K, Freeman-Daily J, Ripamonti CI, Santini D, ESMO Guidelines Committee. Electronic address: clinicalguidelines@esmo.org. The role of patient-reported outcome measures in the continuum of cancer clinical care: ESMO Clinical Practice Guideline. *Ann Oncol Off J Eur Soc Med Oncol* 2022 Sep;33(9):878–892. PMID:35462007

11. Allenby A, Matthews J, Beresford J, McLachlan SA. The application of computer touch-screen technology in screening for psychosocial distress in an ambulatory oncology setting. *Eur J Cancer Care (Engl)* 2002;11(4):245–253. PMID:12492461
12. Bliven BD, Kaufman SE, Spertus JA. Electronic collection of health-related quality of life data: validity, time benefits, and patient preference. *Qual Life Res* 2001;10(1):15–21. PMID:11508472
13. 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* 2013 Jun 11;13(1):211. PMID:23758898
14. Kongsved SM, Basnov M, Holm-Christensen K, Hjollund NH. Response rate and completeness of questionnaires: a randomized study of Internet versus paper-and-pencil versions. *J Med Internet Res* 2007;9(3):e611. PMID:17942387
15. Basch E, Barbera L, Kerrigan CL, Velikova G. Implementation of Patient-Reported Outcomes in Routine Medical Care. *Am Soc Clin Oncol Educ Book Am Soc Clin Oncol Annu Meet* 2018 May 23;38:122–134. PMID:30231381
16. Morris ZS, Wooding S, Grant J. The answer is 17 years, what is the question: understanding time lags in translational research. *J R Soc Med* 2011;104(12):510–520. PMID:22179294
17. LeBlanc TW, Abernethy AP. Patient-reported outcomes in cancer care—hearing the patient voice at greater volume. *Nat Rev Clin Oncol* 2017;14(12):763–772. PMID:28975931
18. Laitio A-M, Giunti G, Halonen R. Perceived Barriers and Facilitators in Using Patient-Reported Outcome Systems for Cancer Care: Systematic Mapping Study. *JMIR Cancer* 2023;9:e40875. PMID:37379076
19. Anatchkova M, Donelson SM, Skalicky AM, McHorney CA, Jagun D, Whiteley J. Exploring the implementation of patient-reported outcome measures in cancer care: need for more real-world evidence results in the peer reviewed literature. *J Patient-Rep Outcomes* 2018 Dec 27;2(1):64. PMID:30588562
20. Consolo L, Castellini G, Cilluffo S, Basile I, Lusignani M. Electronic patient-reported outcomes (e-PROMs) in palliative cancer care: a scoping review. *J Patient-Rep Outcomes* 2022 Sep 23;6(1):102. PMID:36138279
21. Warrington L, Absolom K, Conner M, Kellar I, Clayton B, Ayres M, Velikova G. Electronic Systems for Patients to Report and Manage Side Effects of Cancer Treatment: Systematic Review. *J Med Internet Res* 2019;21(1). PMID:30679145
22. Lai-Kwon J, Cohen JE, Lisy K, Rutherford C, Girgis A, Basch E, Jefford M. The Feasibility, Acceptability, and Effectiveness of Electronic Patient-Reported Outcome Symptom Monitoring for Immune Checkpoint Inhibitor Toxicities: A Systematic Review. *JCO Clin Cancer Inform* 2023 Sep;(7):e2200185. PMID:37220322
23. Arksey H, O'malley L. Scoping studies: towards a methodological framework. *Int J Soc Res Methodol Taylor & Francis*; 2005;8(1):19–32. doi: 10.1080/1364557032000119616
24. Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, Moher D, Peters MDJ,

- Horsley T, Weeks L, Hempel S, Akl EA, Chang C, McGowan J, Stewart L, Hartling L, Aldcroft A, Wilson MG, Garritty C, Lewin S, Godfrey CM, Macdonald MT, Langlois EV, Soares-Weiser K, Moriarty J, Clifford T, Tunçalp Ö, Straus SE. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. *Ann Intern Med* 2018 Oct 2;169(7):467–473. PMID:30178033
25. Systematic Review and Literature Review Software by DistillerSR. Available from: <https://www.distillersr.com/> [accessed Jan 10, 2025]
26. Aaronson N, Choucair A, Elliott T, Greenhalgh J, Halyard M, Hess R, Miller D, Reeve B, Santana M, Snyder C. User's guide to implementing patient-reported outcomes assessment in clinical practice. *Int Soc Qual Life Res* 2015;2:1–47.
27. R Core Team. R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing, Vienna, Austria; 2023. Available from: <https://www.R-project.org/>
28. Bennett AV, Jensen RE, Basch E. Electronic patient-reported outcome systems in oncology clinical practice. *CA Cancer J Clin* 2012;62(5):336–347. PMID:22811342
29. Jensen RE, Snyder CF, Abernethy AP, Basch E, Potosky AL, Roberts AC, Loeffler DR, Reeve BB. Review of electronic patient-reported outcomes systems used in cancer clinical care. *J Oncol Pract* 2014;10(4):e215–e222. PMID:24301843
30. Basch E, Deal AM, Dueck AC, Scher HI, Kris MG, Hudis C, Schrag D. Overall Survival Results of a Trial Assessing Patient-Reported Outcomes for Symptom Monitoring During Routine Cancer Treatment. *JAMA* 2017 Jul 11;318(2):197–198. PMID:28586821
31. Denis F, Lethrosne C, Pourel N, Molinier O, Pointreau Y, Domont J, Bourgeois H, Senellart H, Trémolières P, Lizée T, Bennouna J, Urban T, El Khouri C, Charron A, Septans A-L, Balavoine M, Landry S, Solal-Céligny P, Letellier C. Randomized Trial Comparing a Web-Mediated Follow-up With Routine Surveillance in Lung Cancer Patients. *JNCI J Natl Cancer Inst* 2017;109(9):dix029. PMID:28423407
32. Kim SH, Sung JH, Yoo S-H, Kim S, Lee K, Oh EG, Lee J. Effects of digital self-management symptom interventions on symptom outcomes in adult cancer patients: A systematic review and meta-analysis. *Eur J Oncol Nurs* 2023 Oct 1;66:102404. PMID:37517339
33. Lu DJ, Girgis M, David JM, Chung EM, Atkins KM, Kamrava M. Evaluation of Mobile Health Applications to Track Patient-Reported Outcomes for Oncology Patients: A Systematic Review. *Adv Radiat Oncol* 2021 Jan 1;6(1):100576. PMID:33073061
34. Pho KK, Lu R, Gates S, Cai J, Xie D, Xie Y, Lee SJC, Gerber DE. Mobile Device Applications for Electronic Patient Portals in Oncology. *JCO Clin Cancer Inform* 2019 Dec;(3):1–8. PMID:30802142
35. Ana F-A, Loreto M-S, José L-MM, Pablo SM, María Pilar MJ, Myriam S-LA. Mobile applications in oncology: A systematic review of health science databases. *Int J Med Inf* 2020 Jan;133:104001. PMID:31706229
36. Barbera L, Moody L. A Decade in Review: Cancer Care Ontario's Approach to Symptom Assessment and Management. *Med Care* 2019 May;57:S80. PMID:30985600

37. Egholm CL, Jensen S, Wandel A, Hørder M. The implementation of the 2017 national policy on patient-reported outcomes in Denmark: An overview of developments after six years. *Health Policy Amst Neth* 2023 Apr;130:104755. PMID:36878175
38. Vanier A, Fernandez J, Kelley S, Alter L, Semenzato P, Alberti C, Chevret S, Costagliola D, Cucherat M, Falissard B, Gueyffier F, Lambert J, Lengliné E, Locher C, Naudet F, Porcher R, Thiébaud R, Vray M, Zohar S, Cochat P, Guludec DL. Rapid access to innovative medicinal products while ensuring relevant health technology assessment. Position of the French National Authority for Health. *BMJ Evid-Based Med Royal Society of Medicine*; 2024 Feb 1;29(1):1–5. PMID:36788020
39. Franzoi MA, Ferreira AR, Lemaire A, Rodriguez J, Grosjean J, Ribeiro JM, Polastro L, Grellety T, Artignan X, Le Du K, Pagliuca M, Nouhaud É, Autheman M, André F, Basch E, Metzger O, Ferté C, Di Palma M, Scotté F, Vaz-Luis I. Implementation of a remote symptom monitoring pathway in oncology care: analysis of real-world experience across 33 cancer centres in France and Belgium. *Lancet Reg Health - Eur* 2024 Sep 1;44:101005. PMID:39444707
40. Basch E, Rocque G, Mody G, Mullangi S, Patt D. Tenets for Implementing Electronic Patient-Reported Outcomes for Remote Symptom Monitoring During Cancer Treatment. *JCO Clin Cancer Inform* 2023 Dec;(7):e2200187. PMID:36857630
41. Anderson NE, Kyte D, McMullan C, Cockwell P, Aiyegbusi OL, Verdi R, Calvert M. Global use of electronic patient-reported outcome systems in nephrology: a mixed methods study. *BMJ Open* 2023 Jul 12;13(7):e070927. PMID:37438075
42. Powell BJ, McMillen JC, Proctor EK, Carpenter CR, Griffey RT, Bunger AC, Glass JE, York JL. A Compilation of Strategies for Implementing Clinical Innovations in Health and Mental Health. *Med Care Res Rev* 2011;69(2):123–157. PMID:22203646
43. Stover AM, Haverman L, van Oers HA, Greenhalgh J, Potter CM, Ahmed S, Greenhalgh J, Gibbons E, Haverman L, Manalili K, Potter C, Roberts N, Santana M, Stover AM, van Oers H, On behalf of the ISOQOL PROMs/PREMs in Clinical Practice Implementation Science Work Group. Using an implementation science approach to implement and evaluate patient-reported outcome measures (PROM) initiatives in routine care settings. *Qual Life Res* 2021 Nov 1;30(11):3015–3033. PMID:32651805
44. Snyder CF, Aaronson NK, Choucrair AK, Elliott TE, Greenhalgh J, Halyard MY, Hess R, Miller DM, Reeve BB, Santana M. Implementing patient-reported outcomes assessment in clinical practice: a review of the options and considerations. *Qual Life Res* 2012;21(8):1305–1314. PMID:22048932
45. Hoffmann TC, Glasziou PP, Boutron I, Milne R, Perera R, Moher D, Altman DG, Barbour V, Macdonald H, Johnston M, Lamb SE, Dixon-Woods M, McCulloch P, Wyatt JC, Chan A-W, Michie S. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. *BMJ* 2014 Mar 7;348:g1687. PMID:24609605
46. Reporting guidelines under development for other study designs | EQUATOR Network. Available from: <https://www.equator-network.org/library/reporting-guidelines-under-development/reporting-guidelines-under-development-for-other-study-designs/#PROM> [accessed Sep 24, 2024]



Supplementary Files

Untitled.

URL: <http://asset.jmir.pub/assets/cd68c09cef7b21fdd17791acebe2c4d2.docx>

Multimedia Appendixes

Supplementary Materials.

URL: <http://asset.jmir.pub/assets/b679fe7054bff7c95f3c988cfdba0685.pdf>

Overview of the data extraction results (N=303).

URL: <http://asset.jmir.pub/assets/01cac4b0f0efe655652a33d18ccdff80.xlsx>

Number of publications over time.

URL: <http://asset.jmir.pub/assets/f416da7dfddeb72017b8c5f3a297a668.png>