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The Purpose of Patient-Reported Outcome (PRO) Post Its Digitalization and Integration into Clinical Practice: An Interdisciplinary Redefinition Resembling PROs Theoretical and Practical Evolvement

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Abstract: Patient-reported outcomes (PROs) digitalization and integration into clinical practice has widened its purpose, which makes it relevant to reconceptualize PRO accordingly. Therefore, this study aims to describe and critically discuss the purposes of PRO and to suggest an interdisciplinary definition of PRO aligned with current applications. The findings in this study are based on a formerly conducted scoping review on PRO and patient participation; hence, a sub-study focusing on the purpose of PRO. The purposes of PRO pertain to research and drug testing; quality and economy; patient-centered care; politicization and democratization; and organization and culture. The suggested definition describes PRO as *a validated questionnaire; developed* in collaboration between patients, clinicians, and other pertinent stakeholders; *systematically* applied; *mediated* digitally or paper-based; *completed* directly by the patient, with assistance or by a qualified proxy; composed of generic, disease-specific, condition-specific or preference-based *measures*; consisting of *content* pertaining to the patient's physical and mental health condition, functioning, symptoms, well-being or health-related quality of life (HRQoL); providing objective and/or subjective outcomes, and individual and/or population *data*. An alternative understanding of PRO is meant to enhance the link between purposes and definitions of PRO, facilitating interdisciplinary stakeholder discussions on PRO, potentially improving future PRO interventions.

Keywords: Patient-reported outcome measures (PROM); patient-reported outcome (PRO); quality of life; patient-centered care; definition of PRO; purpose of PRO

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1. Introduction

Since the 1880s, Western healthcare systems have successfully and primarily focused on acute diseases, the reduction of deaths, and the treatment and prevention of such conditions [1]. However, presently healthcare systems in Western countries are facing several challenges due to aging populations; increasing amounts of chronically ill citizens; continuous accumulation of information and data and innovations in clinical practice and technology [2]. Consequently, a paradigm shift in healthcare is slowly evolving, which entails a shift from a heavy focus on deadly diseases and acute conditions, towards a heavier emphasis on chronic illness and patient's health-related quality of life (HRQoL) [3]. On top of this, a new type of patient is emerging, demanding adequate information, and active participation when managing their health [2]. Therefore, new healthcare measures, value-based healthcare, standardization of data, coordination of patient pathways, and more holistic healthcare systems are focal subjects in current healthcare [4–6].

It is within this complex context, Patient-reported outcome (PRO) is anticipated to be an advantageous instrument, on an individual level as part of clinical practice or on a population level as part of research and preventive healthcare [7]. Thus, PROs are spreading horizontally across sectors and disease areas and vertically across organizational levels, widening its functionality [8]. An evolvement especially made possible by PROs digitalization, supported by current health data policies regarding themes such as e.g., "the patient as an active partner", "health by and with people", "knowledge on time", "prevention" and "a health knowledge commons" [9,10].

A common definition of PRO was coined by the American Food and Drug Administrations (FDA) in 2009, as part of their "Guidance for Industry" report, where PRO is considered: "Any report of the status of patient's health condition that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else" [11]. A definition making it clear that PRO concerns patients' health condition, reported directly by the patient; however, the phrase 'any report'; allows flexible interpretations of a PROs actual content as this remains quite unclear. However, a full read of the white paper, reveals that PRO, according to FDA, mainly is an instrument used in clinical trials when testing drugs [11]. Hence, the report "does not address the use of PRO instruments for purposes beyond the evaluation of claims made about a medical product in labeling" [FDA]; meaning that patient-oriented and disease management purposes are not included in this description of PRO. Patient-reported outcome measures (PROMs) are applied when measuring patients' health conditions and belongs under the umbrella term patient-reported data. Other types of data in this category are patient-reported experience measures (PREMs), used to assess the quality of care based on patient's satisfaction and surveys based on patient-reported data [7]. The different scopes of PREM and PROM mean they act as complementary tools when evaluating the quality of healthcare [12]. The term PROM is typically used when PRO is considered a measure or when referred to as a questionnaire. Examples of frequently used PROM questionnaires are the five-item World Health Organization Well-Being Index (WHO-5) and Short Form-36 (SF-36), which measures patients' well-being and HRQoL, respectively [13,14]. The WHO-5 questionnaire is used to calculate patients well-being over the last two weeks on a six-point Likert scale by asking patients to consider the following statements: (a) I have felt cheerful and in good spirit, (b) I have felt calm and relaxed, (c) I have felt active and vigorous, (d) I woke up feeling fresh and rested, (e) My daily life has been filled with things that interest me [13]. The SF-36 measures patients HRQoL on eight different dimensions categorized as, (1) physical functioning, (2) social functioning, (3) role physical, (4) role emotional, (5) bodily pain, (6) mental health, (7) general health, (8) vitality. Scores can be summarized within each domain, in a physical component score (PCS), and as a mental component score (MCS) [14]. Thus, examples of two typical uses of PROM questionnaires to assess the health status of patients. However, some of the more notable strengths of PROs as part of clinical practice concern their ability to provide a more holistic description and produce actionable data [15–17]; subsequently, allowing more individualized healthcare [18], features typically promoted through the application of disease-specific PROM questionnaires.

Considering the paradigmatic and structural changes of Western healthcare systems and the digitalization of PRO, it is interesting to clarify how the purposes and interpretations of PRO have evolved. Hence, the aim of this study is to identify and critically discuss the purposes of PRO, while describing different interpretations of PRO; enabling, the construction of an interdisciplinary definition of PRO that bridges the conceptualization and purpose of PRO. Thus, this article offers a critical and interdisciplinary understanding of PRO, supplementing descriptive and functional presentations of PRO. An alternative definition potentially having a beneficial impact on clinical practice, as stronger coherence between theory and practice should improve stakeholders' understanding and use of PRO. Thus, the clarification of different purposes from a critical perspective is meant, not only as a conceptual contribution but also as an attempt to improve future initiatives and interventions based on PRO. At the very least, the critical and interdisciplinary angle on PRO presented in this article has the potential to instigate relevant discussions among stakeholders, which is a starting point when aiming to optimize the application of PROs as part of clinical practice.

In Section 2, "Materials and Methods," the applied method and analytical approach are explained. Section 3, "Results," contains examples of different definitions and various descriptions of PRO's purposes. In Section 4, "Discussion," the identified purposes are scrutinized critically to elucidate challenges when operationalizing the purposes, leading to the suggestion of an interdisciplinary reconceptualization of PRO.

2. Materials and Methods

The identified purposes of PRO presented in this article emanates from empirical material stemming from a formerly conducted scoping review regarding the link between PRO and patient participation [19]. Thus, the analysis of the empirical data with a focus on the identification of PRO's purposes, presented in this article, functions as a sub-study of the original scoping review. A second sub-study on PRO's functionalities is presented in a different article, where 25 different functionalities are identified; with a particular focus on PROs functionality post its digitalization [20]. The literature included in this paper derives from the following databases: PubMed, Embase, CINAHL, and Scopus. During the search, the term "patient-reported outcome" was combined with search strings containing words and concepts deemed to cover aspects of "patient recognition," "patient participation," or "patient empowerment." Studies of primary care RCT studies where PRO functions as a secondary endpoint and children's studies were excluded, while articles explaining what PRO is and literature on PRO's functionality, purpose, and application in clinical practice were included. An approach, initially leading to 6,895 articles, diminishing to 4,343 articles after duplicates were removed, which therefore equals the number of abstracts screened for eligibility; resulting in the full read of 256 articles. Detailed explanations and visualizations of the original search process are accessible in the original review manuscript concerning the association between PRO and patient participation [19].

The articles were analyzed systematically and thematically, in accordance with theoretical guidelines [19,21]. The magnitude of the scoping review allowed different analytical approaches to the data material. Thus, inspired by Braun and Clarke's (2006) conceptualization and approach to thematic analyses, the scoping review is considered the data corpus (the research project's entire data), whereas the empirical data incorporated in this article should be considered a data set (data used for a particular analysis) [22]. Hence, findings presented in this article are based on a thematic analysis with a narrow focus on PRO's purposes and conceptualization. Arguably, the analysis did to some extent begin during the analytical work with the scoping review, since this process inductively revealed "purposes of PRO" as a relevant theme to explore further. Hence, the reason why the data corpus subsequently was scrutinized with a "theoretical" focus on the purposes of PRO. The first step was to identify empirical material that provided an understanding of PRO's purposes, which was then sorted into one single document. The next step was to categorize the various purposes of PRO into categories based on repeated patterns identified in the empirical data; resulting, in the identification of five overall purposes. In the description of PRO's purposes in this article, additional inputs from books and grey literature have subsequently been added when deemed relevant.

3. Results

In this section, the identified purposes of PRO are presented. The five overall purposes of PRO concerns: research and drug testing, quality and economy, patient-centred care, politics and democracy, and organization and culture. The reason why some themes are grouped is that the concepts in the literature and practice are difficult to separate from one another; hence, the choice of making coupled categories.

3.1. PRO as a Research and Drug Testing Tool

Historically, PRO is a product of different healthcare developments. Thus, the collection of patient data is traced all the way back to the Crimean War (1854), where Florence Nightingale initiated a systematic collection of data regarding soldiers' cause of death [23,24]. Furthermore, PRO is connected to certain disease-specific and generic health measures, developed since the 1940s [25,26]. Measures initially perceived as indicators of "outcomes" and "health status"; however, as the collection and development of health status assessment measures evolved during the 1970's the concept of "quality-of-life" (QoL) gained ground; subsequently, paving the way for "health-related quality-of-life" (HRQoL) measures [26–28]. The same period, where theoretical frameworks such as e.g., Avedis Donabedian's structure-process-outcome model (1966) [29] and the biopsychosocial model (1977) emerged [30]. Furthermore, the 1970s was the decade where the collection of aggregated PROs was initiated in Sweden, establishing the beginning of systematic integration of PROs into national clinical databases [31,32]. Later on, Arthur Kleinmann's (1988) ideas regarding the separation of health status and psychosocial outcomes in chronic disease care were introduced, marking a shift regarding the relevance of patient participation and patient empowerment, essentially, accentuating a less paternalistic healthcare approach [33]. During the last part of the 20th century, the evidence-based medicine approach gained support, emphasizing systematization, measurability and standardization of healthcare interventions [23,34], paradigmatic aspects, aligned with focal methodological requirements concerning PRO instruments [11].

Originally, PRO was used for group-level research and medical research [26,35], as secondary endpoints in clinical trials [36,37], e.g., when testing new drugs [38,39] or evaluating the comparative effectiveness of healthcare interventions [40,41]. Hence, the collection of PRO data established a systematic approach eliciting patients' perspectives on how healthcare interventions affected their health status [35]; whether they, for example, experienced adverse effects [27,28], side-effects [38], comorbidity or an increased burden of illness due to a specific treatment [26]. PRO data is also useful in cases where treatments or drugs have almost similar clinical efficacy [42] since it might help explain non-compliance with the drug regime based on patients' experiences [32], potentially enhancing appraisals of drugs effect [11,30]. Consequently, the FDA made the use of PROs to support claims in approved medical product labelling mandatory in 2009 [11].

Thus, considering PROs genealogy and original application the International Society for Quality of Life Research (ISOQOL) definition of PRO as: "... a measurement of any aspect of a patient's health that comes directly from the patient, without interpretation of the patient's response by a physician or anyone else" [43], is quite fitting. An interpretation having commonalities with the FDA version elaborated upon in the introduction; however, ISOQOL explicitly refers to PRO as a measurement tool.

3.2. PRO as a Quality and Economy Instrument

PRO as a measurement tool paved its way into healthcare as it offers supplementary indicators on quality and economy. The conceptualization of quality in healthcare is linked to a striving towards an economically effective system, based on the premise that more care does not necessarily lead to better outcomes [44]. In other words, the increased focus on economic effectiveness aspires from a perception that an increase in quality of healthcare and a decrease in expenses not only are attainable but also more sustainable [45]. An approach immanent in the so-called '*Triple Aim*', where improvements in the quality of healthcare and the health of the population are assessed in comparison to economic efficiency [46,47]. Aims aligned with PRO's functionality, making it a reasonably useful tool concerning the measurement and assurance of the quality of healthcare [44,48]. Furthermore, PRO-based quality assessments incorporate patients' perspectives regarding health outcomes most important to them [25,48]; enabling qualitative healthcare improvements in concordance with a patient-centred approach [49], while ensuring more useful parameters when evaluating patients' health and well-being improvements [46]. A configuration of quality and patient value based on economic terms, meaning that the quality of healthcare supposedly mirrors patients' needs, as it adapts to consumers' wishes [50].

Especially the digitalization of PROs has enabled its integration into value-based healthcare (VBHC) systems, where quality is captured through the comparison of patient outcomes weighted against treatment costs [45,48]. In practice, VBHC systems integrate aggregated PRO data providing a more structured measurement of patient value. Consequently, the VBHC approach may to some extent replace, or the least complement the traditional volume-based reimbursement system; in other words, quality gains (values) are to a greater extent merged with quantity measures (volume) when assessing the quality of healthcare [32,47,48,51]. As a result, providers are benchmarked and paid according to their performances; hence, a tool complementing market-oriented healthcare systems [46,50,52]. A system that might lead to more transparency by improving the accountability of providers [53,54], and an approach facilitating knowledge sharing by accentuating best practices, potentially improving for instance patient safety [46].

Another application of PROs having economic implications is as part of an algorithmic triage system. In this context, patients are automatically sorted into predetermined color categories (green, yellow, red), based on their health status; thus, some patients are allowed to skip consultations at the hospital. A system, potentially ensuring reallocation of resources as it allows providers to move resources from green to red patients; hence, a tool providing room and time for those patients most in need [55]. Essentially, an increase in productivity since the patients staying at home and those showing up at the hospital site are handled simultaneously by the digitalized healthcare system.

3.3. PRO as Patient-Centred Care

In 2001, the Institute of Medicine (Washington D.C., US) accentuated the importance of patient-centered care [56] and defined it as: " … care that respects and responds to the individual patient's preferences, needs and values and ensures that clinical decision incorporates patients' values" [57]. Thus, there is a conceptual connection between patient-centred care and PRO-based VBHC, since values, needs and preferences are focal in both cases.

Patient-centered care is a holistic approach focusing on the well-being of patients, preferably reflected in every action taken by healthcare professionals [58], what PRO then enables are the patients to get involved and take a central position in their healthcare [25,49]. Consequently, patient-centered care might result in more independent and active patients with improved management of their health, which is a paradigmatic shift compared to the traditional provider paternalism, where patients were placed as passive, non-responsible receivers of healthcare [33,59]. Therefore, as part of a patient-centered approach, the collaboration between physicians and patients is supposed to transform into a sort of partnership, which however rests on active and genuine engagement by the actors involved [57,60,61].

This demonstrates that there are common grounds between PRO and patient-centered care. Thus, as part of clinical practice, PRO might facilitate a more holistic care approach and an environment promoting patient engagement [49,62,63]. Moreover, PRO is known to promote patient-centered care by capturing and explicating issues that matter to the majority of patients [16,25], since it integrates the patient voice and facilitates patient involvement in health care [64,65]; thus, evidence supports that PRO enhances physician-patient communication [66,67] and that PRO encourage and affects the degree of shared decision-making (SDM) in clinical practice [32,46,50,68]. Furthermore, PRO's facilitation of patient participation might have an empowering effect on patients [3,69,70] and ensure that patients are recognized and treated as individuals, and not merely as diagnoses [18].

In this context, the definition of PRO presented by a Danish expert group, hosted by the Danish Knowledge Center for User Involvement in Health Care (ViBIS) in 2016, is of relevance, since they interpret PRO as: "Data concerning the patient's health condition such as physical and mental health, symptoms, health-related quality of life and functional ability reported directly by the patients themselves" [7]. Once more, a definition essentially complying with the FDA version; however, a more detailed version of what constitutes a PRO. Furthermore, PROs interpretative evolvement is interesting as it, based on the presented definitions in this article, chronologically shifts from being "any report," "measurement," to "data." Therefore, it is deliberate that VIBiS definition is placed in this section since the emphasis on PRO as data arguably is linked to a more patient-oriented focus; hence, it is the use of PRO data that might promote patient's engagement, empowerment, and self-management.

3.4. PRO as a Political and Democratic Tool

Another theme regards PROs' political and potential democratic attributes. The current politicization of the healthcare sector stems, among other things, from two coinciding developments. Firstly, as health care costs increase in many western countries, the sustainability of the sector is being questioned, turning it into a hot political topic [58,71]. Secondly, patients' increased accessibility and accumulation of knowledge through digital platforms; subsequently, mobilizing and empowering them, might affect their expectations and their political engagement pertaining to the quality of healthcare [58].

A development embedded in recent healthcare policies where patient involvement exists as a sort of axiomatic strategy [72]. Therefore, the present political agenda is underpinned by PROs functionality, since it is plausible to perceive PRO as an instrument giving voice to individual patients and patient groups; hence, the reason why it might be categorized as a political and democratic tool [36,71]. The inclusion of the patient perspective as a valuable source of information is on the one hand, based on an acknowledgement that patients are experts on their health situation and on the other hand, a result of increasing consensus that patient involvement is the ethically right path to take [36,58]. A normativity, which presently becomes apparent during funding processes, where patient involvement more often is part of the requirements when designing research projects. Therefore, patients' voice mediated by PRO, might directly or indirectly, influence the forming of clinical practice and the shaping of healthcare policies [36].

3.5. PRO as an Organizational and Cultural Shift

Based on the former sections PROs purpose concerns, among other things, research, clinical practice, and healthcare policies, which means that PRO also affects organizational structures and cultures. For example, the application of PRO on a routine basis might impact clinical workflow, work practice, organizational structures, infrastructures as well as stakeholders' attitudes and values, [69,73–76]. Hence, the reason why PRO in this section is claimed to be a tool, which actively or passively can be used to commence changes and cultural shifts in healthcare organizations.

PRO is supposed to function as a system composed of outcomes that matters to patients, which is relevant as prior systems and data at times acted as alternative representations of reality deviating from patients' values and needs [42]. Hence, PROs' evocation of patients' values allows managers to construct a more patient-centered healthcare system [64]; a cultural shift and system change promoted by political institutions as they encourage providers and stakeholders to focus more on outcome measures and less on processual indicators [41,57].

As part of clinical practice, the application of PROs faces several organizational and cultural barriers; especially, insufficient time seems to be one of the more pronounced barriers [77,78]. On the one hand, some physicians perceive PRO as being too time-consuming as it makes decision-making more complex and less effective [34]. On top of this, doctors' inability to interpret data due to no clear guidelines and lack of education is another aspect affecting the amount of time spent on PRO as part of clinical practice [41,79,80]. On the other hand, different studies have shown that PROs do not increase the length of clinical encounters [81–83]. Thus, PRO does to some extent affect the time dimension as part of patient-clinician consultation; however, to what extent is being contested. Another organizational aspect pertains to whether PROs fit into clinical workflow and practice [26,67]; however, numerous studies have verified that PROs are feasible in such a context [83,84]. Secondly, the increased work burden of the health care professionals should be kept to a minimum to avoid it turning into an implementation barrier [62,85]. Thirdly, proper and timely PRO data availability during a consultation is decisive for its use in clinical practice [50,86]. Therefore, even though PROs have a huge potential, its functionality rests on attitudinal cultures supporting patient engagement and genuine partnerships between patients and physicians supported by appropriate organizational setups [57,62]. Put differently, to ensure that PRO's purpose is fulfilled organizational and cultural changes are mandatory; vice versa, it is reasonable to perceive PRO as a tool potentially instigating such transformations, since PROs "automatically" affects time, workflow, and use of data in clinical practice. Therefore, it is not surprising that attitudes towards PRO among healthcare professionals are differing; nonetheless, a central point since a cultural shift relies heavily on healthcare professionals' and leaders' engagement [30,49]. Moreover, PRO data might be utilized as a communication tool within multidisciplinary teams [35,67] or serve as a coordination tool by sharing data across different healthcare actors [30], potentially enhancing coordination of for example patient pathways across organizations and sectors [8].

4. Discussion

As described in Section 3, results are visualized in Figure 1, PRO's purpose is multifaceted as it might act as a: research and drug testing tool; quality and economy instrument; a way to enhance and enable patient-centred care; means to politicize and democratize healthcare and an artefact facilitating organizational and cultural transitions.

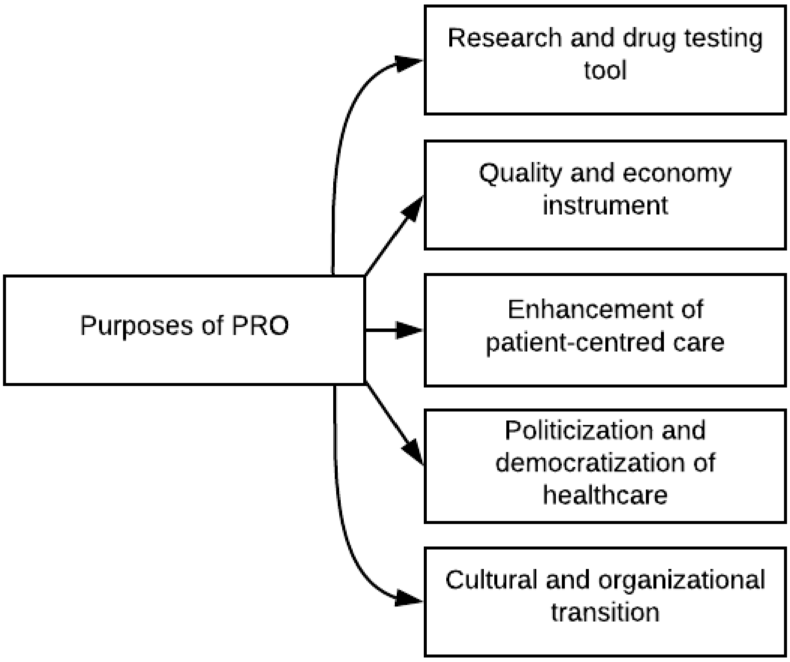

Figure 1. Identified purposes of Patient-Reported Outcome (PRO).

In the following section focal issues related to the identified purposes are scrutinized critically to create awareness on challenges when materializing the purposes. Moreover, as elucidated above, various interpretations of PRO co-exist, as PRO is labeled as "any report," "measurement," or "data." Empirical findings indicating that PRO has evolved, not just in purpose, but also conceptually. The issue is that the three definitions of PRO, created by FDA, ISOQOL, and ViBIS, do not fully mirror the complexity of PRO's different purposes. A discrepancy, which might be problematic as a gap between the conceptualization of PRO and its purposes potentially confuses stakeholders; subsequently, impacting the utility of PROs as part of clinical practice. Therefore, the last part of the discussion contains an interdisciplinary interpretation of PRO aiming to provide clarity and strengthen the link between the purposes and the definition of PRO.

4.1. Realization of PRO's Patient-Oriented and Economic Purposes?

As elucidated, PRO traditionally is part of the outcome data branch, which has shaped its use formerly. Hence, PRO was traditionally used as secondary endpoint data when measuring patients' outcomes following a healthcare intervention [37]. However, PRO is currently also used as a primary endpoint, underscoring that the use of PRO has undergone a noticeable change [86]; arguably, reflecting how PRO's purpose has changed as HRQoL aspects have become a crucial part of today's healthcare.

Thus, when PRO is applied as an independent variable, the purposes of PRO alter in a patient-oriented direction, since such interventions are meant to affect patient behavior; hence, the current focus on PRO's effects on SDM, patient participation, empowerment, and self-management. Therefore, PRO no longer merely measure health outcomes but also instigates actions related to patient-centered healthcare by activating patients. An essential shift in PRO's intended purpose, which is decisive to grasp, to fully comprehend the transformative impact PROs plausibly have on clinical practice and healthcare henceforth.

Regarding PRO's economic features these rests on certain assumptions and have important implications. This is because PRO systems where data describes the quality of treatment and outcomes according to the patients require patients that are willing to frequently complete questionnaires and to actively engage in the management of their health condition [43,53]. An important point, making it relevant to continuously evaluate patient participation and response rates, ensuring the feasibility of the system in the long run. In other words, the possibilities the digitalization of PRO offers need to be balanced with patients' needs and preferences. Furthermore, PRO's economic effectiveness as part of a triage system based on algorithms relies on two essential conditions to function properly. Firstly, reallocation of resources requires that resources de facto are moved from "green-patients" and are allotted to those most in need. Alternatively, it might turn into a money-saving exercise, economically enhancing the healthcare system but not necessarily benefiting the most vulnerable patients. Secondly, an increase in productivity rests on the condition that the time formerly spent in each patient-clinician consultation equals or is shorter than the current time spend even if the state of the examined patients' health condition differentiates. In other words, even though a triage system logically results in a clinical practice with fewer "easy patients," since only the most vulnerable individuals and complex patient cases are invited for consultation, healthcare professionals are still expected to spend the same amount or even less time on each patient compared to previous procedures. Therefore, even if PRO makes patient-clinician consultations more time effective by revealing relevant patient issues beforehand, changes in the type of patients showing up for consultation and additional subjects being discussed, which in the past might have been neglected, needs to be kept in mind when considering whether PRO is a time-saving tool.

Moreover, even though the normative ideals VBHC rests on seems attractive and might positively complement the volume-based reimbursement system, results from the UK shows that there are substantial annual variations in hospitals performances; thus, the authors state: "the hard statistical conclusion seems to be that even though there are some identifiably good and bad hospitals, most achieve pretty much the same levels of health gain for patients undergoing surgery" [87]. Therefore, it is questionable whether performance-based financing (PBF) and benchmarking systems are the right paths to take; however, if such tools are widely implemented, their infancy warrants that adequate indicators are developed, which is no simple task considering the multiple purposes of PRO and the complexity of current healthcare systems.

4.2. PRO—Information or Outcome Data?

Since PRO's purpose has broadened, it is ambiguous to determine whether PRO is best thought of as information, outcome data or maybe a combination of both? Thus, it is noticeable that a single PRO questionnaire logically is unable to produce outcome data on its own. If a PRO is to provide outcome data, it requires comparison with a baseline measurement, either being individual health status progression or aggregated population data.

Moreover, even though there might be a correlation between a healthcare intervention and the subsequent outcome, their causality is quite uncertain as PROs are measuring possible effects in an uncontrolled environment consisting of a multitude of potential confounders. Arguably, it is not due to their enhancement of the internal validity concerning healthcare interventions and subsequent outcomes that PROs are attractive tools, but due to their ability to strengthen the ecological validity, thus, PROs provide a more authentic impression of patients' disease situations as part of everyday settings.

Furthermore, in cases where PRO is considered an independent variable for example when used as an empowerment tool to increase patient participation, their actual potential is still relatively unclear; hence, further studies elucidating PROs capacity in this respect are demanded. Besides eliciting patient outcomes, PRO is also perceivable as an information tool, since it provides healthcare professionals with useful knowledge through the eyes of patients; subsequently, enabling improved patient management. Therefore, PRO may also be labeled as information regarding patients' health status and HRQoL, which through comparison with baseline measures (formerly collected PRO data), and thorough interpretation elicits patients' outcomes and current health situation [31]. Thus, it is no coincidence that researchers are dedicated to determining how to interpret PRO data, which is an imperative endeavor since inconsistent and inaccurate interpretations of the information PRO data provides might have counterproductive effects. In other words, turning the PRO data into clear and useful information, both on a general level but also as part of clinical practice is an important task to handle henceforth.

4.3. Directly from the Patient?

As emphasized in the above definitions, PROs are directly reported by patients; however, even though this might be the case, the initial patient perspective might still be different compared to the version entering the patient-clinician consultation. One issue, related to this topic is patients' potential response shifts, which is an acknowledged challenge in clinical practice, made possible by the timeframe between the completion of a PRO questionnaire and the actual use of the PRO data. However, the point in this section is that the patient perspective change, but not necessarily due to changes within the patient. The idea that PRO answers are "directly reported" by patients are most often accurate; however, it leads to a connotation of PRO data as being completely unaffected before entering clinical practice, which is a focal feature, since it distinguishes PRO-based healthcare from traditional healthcare, based on traditional clinical data and healthcare professionals individual assessment [78]. Nonetheless, the version of 'the unaffected PRO' is modifiable, since interpretation and outcomes of PRO data are shaped by several factors.

Firstly, when developing a PRO questionnaire, the health-related areas within a specific subject field are identified and selected; therefore, at this initial development stage particular interpretations and perceptions of a condition or illness are promoted by those stakeholders constructing the instrument. Therefore, PRO is also perceivable as a socially constructed artifact, promoting specific understandings concerning a healthcare condition, which potentially constrains the individual patient perspective.

Secondly, the mediation of PRO questionnaires is essential, since it affects patients' accessibility and ability to complete PRO questionnaires; therefore, inclusive and appropriate infrastructures and socio-technical setups are decisive if PROs are to provide patient perspectives across all patient groups.

Thirdly, both patients and healthcare professionals require intuitive and informative graphical presentations, if PRO data is to be intelligible and useful [47,88]. Similarly, considerate construction of algorithms is pivotal since their properties determine how patients are sorted into various health status categories, shaping possible interpretations of the PRO data; thus, transparent and judiciously configuration and validation of algorithms are imperative.

Fourthly, when applied in clinical practice PRO data is interpreted by healthcare professionals and applied with a specific purpose, e.g., screening, communication, or monitoring, which ought to improve the usefulness of PROs. Nonetheless, several studies show that healthcare professionals are unsure how to interpret PRO data [88–90] which means that they might refrain from using PRO data, neglect the importance of PRO answers, or use it in an unintended manner [88].

Fifthly, another attention point, taken into account in the PRO definition below, is that to obtain PRO answers patients might require assistance or an actual proxy. This is due to various reasons, such as low health literacy, language barriers, critical state of illness, etc., which prevents patients from completing the PRO questionnaires themselves [76,91]. Hence, in such scenarios assistance or a proxy might be necessary to ensure the completion of a PRO questionnaire, which likely affects the validity of the retrieved PRO data; conversely, it might increase response rates and ensure the inclusion of a wider array of patients.

These examples illustrate that even if patients are unaffected while completing the questionnaires, rigorously speaking it is debatable whether the same goes for the PRO data entering the patient-clinician consultation. This is because the PRO mediated patient perspective integrated into clinical practice is shaped and modified by human and technological actors along its way.

4.4. PRO as a Democratic or Political Tool?

As already mentioned, there are a number of reasons how PRO might be used as a political instrument considering the amount of information it provides. However, whether PRO is a democratic tool seems for a number of reasons doubtful.

Firstly, the way PRO instruments are developed and especially how it was done formerly, where merely healthcare professionals were involved in the process, means that PROs not necessarily are representative instruments. Secondly, since not every patient is able to answer the questionnaires, certain individuals and groups might not have any 'voice' via PROs; hence, another aspect negatively affecting the representativeness. Thirdly, not all patients are keen on completing PRO questionnaires; hence, PROs might act as a sort of chore and increase the patient burden, a third excluding factor.

Therefore, even though PRO as a democratic tool is an interesting ambition, optimizations regarding the development process of PRO questionnaires, the inclusion of broader patient segments, and the insurance that non-participating patients are giving "voice" through other channels is highly recommended.

4.5. An Interdisciplinary Redefinition of PRO

Considering the three definitions by FDA, ISOQOL, and ViBIS, the identified purposes of PRO, and the complexity of the challenges scrutinized in the discussion, it seems appropriate to introduce an alternative definition of PRO. The definition incorporates former aspects of PROs pertaining to research and drug testing while adding more recent clinical practice enabling facets, such as the digitalization of PROs and an alteration regarding who might act as a respondent. Thus, a PRO is defined as a: *validated questionnaire; developed* in collaboration between patients, clinicians, and other pertinent stakeholders; *systematically* applied; *mediated* digitally or paper-based; *completed* directly by the patient, with assistance or by a qualified proxy; composed of generic, disease-specific, condition-specific or preference-based *measures*; consisting of *content* pertaining to the patient's physical and mental health condition, functioning, symptoms, well-being or health-related Quality of life (HRQoL); providing objective and/or subjective outcomes, and individual and/or population *data*.

Essentially, this definition portrays PRO as a multidimensional and interdisciplinary concept; hence, in this version, PRO is a holistic term consisting of several elements regarding specific types of questionnaires, applications, mediations, measures, content, data, and outcomes. Thus, the above interpretation of PRO consists of psychometric measures and/or economic measures and social constructs based on stakeholder perspectives, mediated by a specific technological setup. Therefore, the particular weight on the different aspects shaping a PRO determines its utility and functionality as part of clinical practice.

The broadness of the definition is required to ensure the bridging between purposes of PRO and the conceptualization of PRO. As a result, this version of PRO underscores its interdisciplinary character, which in combination with the presented purposes above, offers stakeholders on various levels a more nuanced understanding and approach to PRO; potentially, enhancing future healthcare policies and management initiatives based on PRO.

Regarding limitations, PRO is described in a general manner, meaning that nuances and contextual differences across disease areas and organizational levels are absent. Furthermore, the empirical materials the article is based on does not cover all literature on PRO; hence, some purposes might be missing. Lastly, since the article has a broad scope it limits how profound every theme can be analyszd and elaborated upon; therefore, we encourage future studies to examine issues concerning PRO's different purposes, with a particular focus on the issues emphasized in the discussion section.

5. Conclusions

The article presents five different purposes of PRO concerning research and drug testing; quality and economy; patient-centered care; politicization and democratization; organization and culture. Hence, the purpose of PRO is currently multifaceted, partly due to PRO's digitalization and integration into clinical practice. An increase in purposes, making it relevant to consider how to: interpret PRO data and turn it into useful information; ensure that PRO as an economic tool functions properly; instigate and maintain patient-centered care; facilitate patient participation via PROs, ensure that genuine patient perspectives enter consultations and development processes; and retain adequate response rates. Despite these challenges, the application and development of PRO tools persist and seem to increase; hence, the necessity to promote a contemporary interdisciplinary definition of PRO. Thus, the presentation of various purposes and the redefinition of PRO aims to create a stronger link between theory and practice; potentially, enhancing the realization of PRO's purposes through enhanced application of PRO initiatives within clinical practice. As a starting point, the description and critical take on PRO's purposes together with the interdisciplinary interpretation of PRO might instigate fruitful stakeholder discussions; subsequently, optimizing how clinical practice and in particular, the patients, benefits from the digitalization of PRO.

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Abbreviations

HRQoL	Health-Related Quality of Life
ISOQOL	International Society for Quality of Life Research
PBF	Performance-Based Financing
PRO	Patient-reported outcome
PROM	Patient-reported outcome measures
QoL	Quality of Life
VBHC	Value-Based Healthcare
ViBIS	The Danish Knowledge Center for User Involvement in Health Care

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