Adv Ther
https://doi.org/10.1007/s12325-026-03537-z

COMMENTARY

Clinically Meaningful, Patient-Centered Endpoints for Real-World Evidence Generation in Breast Cancer: Perspectives from the Multidisciplinary TRIUMPH Initiative

Sean Khozin · Nancy A. Dreyer · Dominic Galante · Raymond Liu · Peter Neumann · Nathan Nussbaum · Joyce O'Shaughnessy · Mothaffar F. Rimawi · Hope S. Rugo · Sara M. Tolaney · Marisa Weiss · Adam Brufsky

ABSTRACT

Stakeholders have made major advances in generation of real-world evidence (RWE); however, core challenges remain, limiting its value and utility in guiding treatment decision-making. In particular, persisting lack of industry consensus on standardized, clinically meaningful, patient-centered endpoints was considered a critical area of interest for the multidisciplinary Think tank on RWE In the US from Multiple Perspectives in Healthcare (TRIUMPH). Collaborating in a group forum, TRIUMPH assembled and reviewed a first draft of potential endpoints that may be more consistently incorporated into RWE research. Among this list, time to next treatment, adherence/persistence, psychosocial well-being, and frailty were prioritized for subsequent discussion on ways to enable their broader adoption.

Prior Presentation: The contents of this manuscript are not based on work that has been previously published or presented.

S. Khozin (✉)
Massachusetts Institute of Technology, Cambridge, MA, USA
e-mail: sean@phyusionbio.com

S. Khozin
Phyusion Bio LLC, New York, NY, USA

N. A. Dreyer
University of North Carolina, Chapel Hill, NC, USA
e-mail: NDreyer@dreyerstrategies.com

N. A. Dreyer
Dreyer Strategies LLC, Newton, MA, USA

D. Galante
Precision AQ, Gladstone, NJ, USA
e-mail: dominic.galante@precisionaq.com

R. Liu
San Francisco Medical Center, Kaiser Permanente, Northern California, San Francisco, CA, USA
e-mail: raymond.Liu@kp.org

P. Neumann
Center for the Evaluation of Value and Risk in Health, Institute for Clinical Research and Health Policy Studies, Tufts Medical Center, Boston, MA, USA
e-mail: peter.Neumann@tuftsmedicine.org

N. Nussbaum
Target RWE, Durham, NC, USA
e-mail: nnussbaum@targetrwe.com

J. O'Shaughnessy
Baylor University Medical Center, Texas Oncology, US Oncology, Dallas, TX, USA
e-mail: joyce.OShaughnessy@usoncology.com

J. O'Shaughnessy
Sarah Cannon Research Institute, Dallas, TX, USA

M. F. Rimawi

Published online: 17 March 2026

Across the four endpoints, key opportunities for improving adoption included additional education for researchers, standardization of algorithms, and exploration of new approaches for derivation in real-world data. Over the course of discussion, TRIUMPH also identified frailty and area/neighborhood socioeconomic status as key baseline characteristics that may guide stratified analyses of the prioritized endpoints, to increase patient-centric value of the resulting RWE. In the future, other endpoints and characteristics (beyond those in focus for TRIUMPH) will also likely emerge, and should similarly be incorporated into routine care and research, to continue growing the utility of RWE in better informing treatment decision-making.

Keywords: Breast cancer; Patient-centricity; Real-world data; Real-world evidence; Treatment decision-making

Dan L Duncan Comprehensive Cancer Center at Baylor College of Medicine, Houston, TX, USA
e-mail: rimawi@bcm.edu

H. S. Rugo
City of Hope Comprehensive Cancer Center, Duarte, CA, USA
e-mail: hrugo@coh.org

H. S. Rugo
University of California San Francisco Helen Diller Family Comprehensive Cancer Center, San Francisco, CA, USA

S. M. Tolaney
Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA
e-mail: Sara_Tolaney@dfci.harvard.edu

M. Weiss
Breastcancer.Org, Ardmore, PA, USA
e-mail: mweiss@breastcancer.org

A. Brufsky
University of Pittsburgh Medical Center, Hillman Cancer Center, Pittsburgh, PA, USA
e-mail: brufskyam@upmc.edu

Key Summary Points

The multidisciplinary Think tank on Real-world evidence (RWE) In the US from Multiple Perspectives in Healthcare (TRIUMPH) reconvened given current lack of consensus on standardized, patient-centered endpoint frameworks to enhance RWE validity, reproducibility, and value in guiding treatment decision-making.

TRIUMPH considered well-established and potentially novel endpoints to guide assembly of a first draft of clinically meaningful, patient-centered endpoints from the real world, organized across three overarching categories: disease and treatment, function, and environment and patient experience.

From the initial list, four endpoints were selected for more detailed evaluation, based on relevance to overarching categories and breast cancer: time to next treatment (TTNT), adherence/persistence, psychosocial well-being, and frailty.

TRIUMPH also considered frailty and area/neighborhood socioeconomic status (SES) as baseline characteristics suitable for stratified analyses, to strengthen the interpretability and applicability of selected endpoints.

SETTING CONTEXT

Real-world evidence (RWE) plays an important role in supplementing data from randomized controlled trials (RCTs) [1]. While RCTs are traditionally used to establish efficacy of new therapies, RWE can provide additional insight into treatment benefit, especially post-approval when studied in diverse patient populations who may not be represented in RCT due to narrow inclusion and exclusion criteria or systemic barriers to participation [2]. Significant progress has been made in generating RWE, bolstered by access to electronic health records (EHR), registries, claims databases, and evolving regulatory frameworks [3, 4]. However, core methodological issues persist, notably in ensuring real-world data (RWD)

fitness-for-purpose, defining reliable operational endpoints, managing bias and missingness, and verifying endpoint validity. Such uncertainties remain a barrier to RWE integration by guideline bodies, payors, and clinicians [5]. Moreover, inconsistent endpoint definitions—ranging from surrogate markers like time-to-treatment discontinuation to traditional clinical outcomes—diminish comparability and interpretability across studies [6].

To advance RWE utility, it is essential to develop standardized, patient-centered endpoint frameworks, which may involve refining established measures or generating new clinically-meaningful constructs. Multiple organizations, initiatives, and expert groups have recognized the importance of such efforts in supporting RWE utility, and have proposed potential frameworks over the past several years, demonstrating a shared interest in real-world endpoint development. For example, in addition to exploring evaluation of real-world endpoints (RWE Pilot 1.0), Friends of Cancer Research also developed a framework specifically focused on harmonizing patient-reported outcomes (PROs) collected in the real-world setting [7–9]. The Duke–Margolis Institute for Health Policy similarly published a white paper outlining a roadmap for study endpoints in real-world settings, from selecting a concept of interest through validation [10]. Furthermore, the National Health Council, as part of reporting on an evidence-based consensus process, also reinforced the importance of understanding "how patient input, gathered through meaningful patient engagement, can be identified and incorporated into the design, conduct, and translation of real-world research that reflects patients' lived experience" [11].

TRIUMPH Objectives

The Think Tank on RWE in the United States (US) from Multiple Perspectives in Healthcare (TRIUMPH) initiative was established in 2023 to convene multi-disciplinary experts—including oncologists, patient advocates, Food and Drug Administration (FDA) policy experts, payor advisors, health economists, and real-world methodologists—to further advance acceptance and use of RWE when it comes to treatment decision-making (by clinicians, patients, guideline bodies, payors, etc.), for breast cancer. While breast cancer was selected as a specific example to guide thinking, concepts discussed may have relevance to oncology more broadly.

The first TRIUMPH meeting took place in November 2023 and focused on: identifying perceptions of RWE acceptance and barriers to use in treatment decision-making, and developing "calls-to-action" to drive implementation of highest-priority solutions. As detailed in Khozin et al. [12], findings and "calls-to-action" were published to present TRIUMPH's position and directly engage fellow healthcare stakeholders.

Subsequently, additional TRIUMPH meetings were held in September and October 2024, to reconvene for follow-up on the primary "call-to-action," to "develop clinically-relevant (and patient-informed) endpoints for the real-world" [12]. Given current lack of consensus within the industry, this follow-up entailed the following ingoing objectives:

1. Assembling a preliminary, broad list of clinically meaningful, patient-centered endpoints
2. Reviewing the list in a group forum and applying a framework designed around three categories (disease and treatment, function, environment and patient experience) and relevance to breast cancer
3. Prioritizing a select set of endpoints from the broad list for more detailed discussion

Over the course of discussion, a fourth objective organically emerged, around considering baseline characteristics suitable for stratified analyses, to further strengthen interpretability and applicability of selected endpoints.

Taking into account members' multidisciplinary perspectives, TRIUMPH discussed strengths, limitations, and opportunities for the select set of clinically meaningful, patient-centered endpoints. Recognizing research questions and objectives will vary across studies, TRIUMPH focused on high-level endpoint potential, in terms of (1) consistent adoption in RWE generation and (2) benefit in clinical treatment decision-making.

Defining Clinically Meaningful, Patient-Centered Endpoints from the Real-World

To guide identification of clinically meaningful, patient-centered endpoints from the real-world, TRIUMPH considered both well-established and potentially novel endpoints, alongside three prerequisite criteria (Fig. 1). First, endpoints were termed "clinically meaningful" if they indicate a treatment effect, measuring how a therapy impacts patient survival, functioning, or experience [13]. Second, endpoints were termed "patient-centered" if they are understandable and meaningful from a patient perspective, such as avoiding complex or vague terms (e.g., "time to worsening") and focusing on clear, relatable measures like health-related quality of life (HRQoL) or physical function [14]. Finally, endpoints were termed "from the real world" if they can be credibly and reliably measured in real-world settings (e.g., hospital EHR, medical claims database, etc.), for evaluation in representative populations [10].

Based on these criteria, TRIUMPH assembled a first draft of endpoints to consider (Table 1), informed by a targeted search of literature on real-world endpoints in oncology. Endpoints were organized across three overarching categories: disease and treatment (e.g., treatment response, cancer progression, survival), function (e.g., physiological, HRQoL), and environment and patient experience (e.g., contextual factors, healthcare access, external systems). From a patient's perspective, these categories may correspond to questions such as "How controlled is my cancer?", "How well can I carry out routine activities?", and "How am I feeling within my personal context and surrounding environment?". Collectively, these categories cover clinical response to treatment, assess HRQoL, and articulate the influence of external

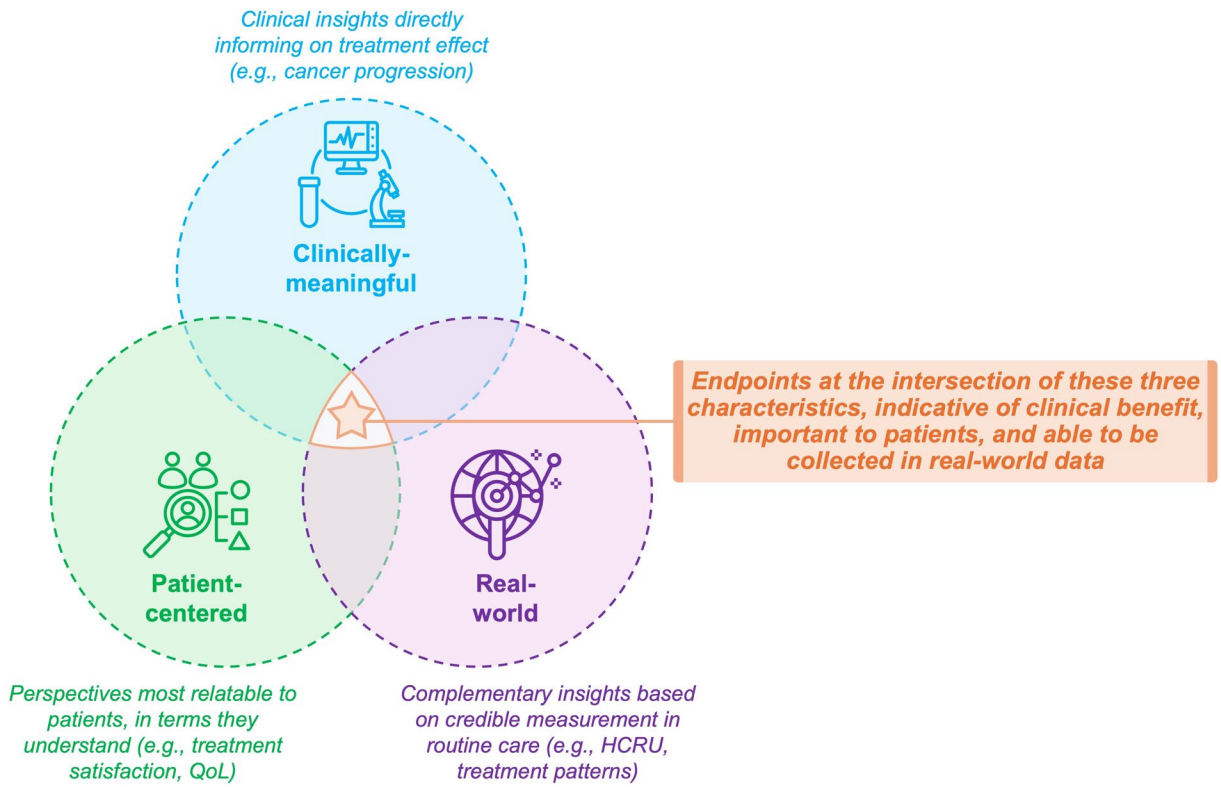

Fig. 1 Intersection of clinically meaningful, patient-centered, and real world, to guide identification of endpoints that could benefit from wider adoption in RWE research. *HCRU* healthcare resource utilization, *ORR* objective response rate, *PFS* progression-free survival, *QoL* quality of life

Table 1 Broad list of endpoints identified by TRIUMPH for consideration

Category	Endpoint
Disease and treatment	Time to next treatment: Time from treatment initiation to discontinuation (for reasons including lack of effectiveness, toxicity, progression)
	Long-term survivorship and late effects: Long-term consequences of disease (e.g., cardiovascular issues, secondary cancers)
	Tumor marker velocity: Change in tumor marker levels over time, assessing likelihood of disease recurrence or progression
	Clinical progression: Worsening of disease as observed by providers based on signs or symptoms
	Time to distant metastasis: Time to diagnosis of first spread to a distant metastatic site
	Symptom burden and management: Symptoms experienced (e.g., pain, fatigue, nausea) with disease/while on treatment
	Treatment tolerability: Patient ability to remain on treatment without dose modification or discontinuation
Function	Frailty: Measure of older patients or those with comorbidities at higher risk of adverse outcomes (falls, disability, hospital admission, long-term care)
	Time to functional decline; Functional consequences of disease: Impact on functioning (e.g., renal, anemia)
	Ability to fulfill/continue roles; Time to return to normal activities: Capacity to restart work, family, and/or social roles
	Mobility and independence: Changes in patient ability to autonomously perform daily physical activities
	Work productivity: Measure of economic/business implication of health-related suboptimal or lost work performance
	Composite measure (benefit and HRQoL): Combined measure of treatment effectiveness and HRQoL
	Standalone HRQoL measure: Simple/brief assessment of patient HRQoL
Environment and patient experience	Psychosocial well-being: Psychological and social effects of cancer (e.g., anxiety, depression, isolation)
	Days at home: Time a patient spends outside of hospitals and healthcare institutions
	Impact on caregiver burden: Impact of patient disease and treatment on caregiver (emotional, physical, financial strain)
	Patient satisfaction with treatment: Patient experience with treatment received
	Patient empowerment and self-management: Patient sense of empowerment related to care, such as involvement in decision-making, ability to communicate opinion, and support received
	Adherence and persistence: Patient consistency in following treatment regimen over time

Table 1 continued

Category	Endpoint
	Measure linked to SDOH: Measurement associated with impact of SDOH factors on health outcomes
	Healthcare resource utilization; Financial toxicity: Economic burden, including use of healthcare systems (e.g., hospitalization, emergency visits) and other financial consequences

HRQoL health-related quality of life, *SDOH* social determinants of health

factors; all of which are crucial for holistic decision-making in real-world settings.

Notably, this first draft resulted in limited overlap with endpoints often observed in oncology RCTs, such as progression-free survival (PFS) or objective response rate (ORR) for efficacy, or frequency of high-grade adverse events (AEs) for safety. While undoubtedly clinically meaningful, such outcomes may be less intuitive for patients (failing the "patient-centered" criteria; e.g., ORR) and/or not credibly and reliably measured in RWD (failing the "from the real-world" criteria; e.g., PFS). This disconnect, between endpoints identified by TRIUMPH and those commonly used in RCTs, reaffirmed the role of RWE in supplementing data from trials, especially in the absence of endpoints consistently defined and used across both research settings. The finding was also consistent with existing literature such as LoCasale et al., which similarly articulated an "RCT/RWE endpoint misalignment," due to instances where RCT endpoints have low availability and/or relevance in routine clinical practice [15].

Exploring Select Endpoints, and Opportunities to Further Improve Use in Research

From the initial list, four endpoints were selected for more detailed evaluation, based on their relevance across disease and treatment, function, and environment and patient experience categories, and to breast cancer (irrespective of stage): time to next treatment (TTNT), adherence/persistence, psychosocial well-being, and frailty. Subsequently, a targeted literature review (TLR) was conducted to further understand current use of the selected endpoints in RWE generation, including extent of use, approaches for sourcing in the real world, and potential limitations. Findings from the TLR confirmed importance of the selected endpoints and provided insights to guide TRIUMPH discussion around their relevance and utility. Using PubMed and Google Scholar, with focus on oncology RWE research published in the past ~ 5 years (January 1, 2019–October 1, 2024), 9 articles were identified and reviewed (Table 2) [16–24].

TTNT measures treatment effectiveness, as well as toxicity/tolerability, by showing how long patients remain on a therapy before switching to a subsequent treatment. TTNT may also be considered patient-focused, providing ease of understanding and an ability to address key patient questions such as "What treatment am I on and for how long?" and "What treatment comes next?". Data elements to derive TTNT in the real world are typically captured in EHR or medical claims, such as prescription dates for initial and subsequent treatments [25]. However, derivation of TTNT—which requires structuring lines of therapy and defining explicit criteria for when a treatment is considered switched or discontinued—can exhibit substantial variability across studies, influencing endpoint comparability and reproducibility. Observations from ongoing research also find that TTNT, while often used as an alternative, may underestimate or overestimate PFS (i.e., TTNT being meaningfully shorter or longer compared to PFS), or not always account for patient death (due to inconsistency in capture of mortality data in real-world datasets) [26–28]. Therefore, while TTNT

may not be considered equivalent to PFS, it still offers clinical utility and is potentially more appropriate for a real-world setting. To support broader adoption of TTNT in RWE, researchers would benefit from educational materials that distinguish it from PFS, while articulating its strength as a feasible effectiveness measurement to derive from RWD. Additionally, a consensus-driven proposal for a standardized algorithm can enable more consistent measurement in the real world across studies. Lastly, EHR- or claims-derived TTNT can be complemented with further context from other data sources, such as patient surveys, to fully understand the value of this endpoint.

Adherence/persistence, while not necessarily novel, measures how consistently patients follow prescribed treatment regimens over time, and can reflect patient experience, including factors that may impact compliance [20, 29]. Recognizing that patients in RCTs are more likely to adhere to treatment due to strict protocol requirements, real-world adherence/persistence can provide insights that may not be available from trial data [20, 30] (e.g., reasons for discontinuation, particularly among patients in the community setting who are not well represented in RCTs [31, 32]). As observed in studies such as Bhimani et al.'s of characteristics associated with delayed chemotherapy among patients with early-stage breast cancer, patient behaviors surrounding treatment initiation—and modification or continuation—will differ in real-world scenarios from those typically seen in RCTs [33]. Adherence/persistence can be studied in the real world via a range of RWD sources, such as prescription records, claims, or EHRs, but such data may be a crude indicator [34, 35]. Alternatives such as patient-reported data should also be explored, while acknowledging the risk of self-report bias [36]. However, irrespective of potential challenges with data collection, opportunities remain for further advancing adherence/persistence as an endpoint in RWE research, especially in terms of critical use cases. For example, adherence/persistence measurement may be combined with investigation into access to therapy, as a way to holistically understand barriers preventing patients from remaining on necessary treatment.

Psychosocial well-being encompasses emotional, mental, and social domains of HRQoL, reflecting dimensions that are both highly salient to patients and increasingly prioritized in contemporary breast cancer research. Its relevance is underscored by recent investigations into psychological distress, depression, and social isolation among individuals diagnosed with cancer and/or undergoing treatment, with growing interest in integrating these factors into both observational studies and care pathways. Recent studies by Fleege et al. and Arana et al. discussed disparities and gaps in mental health screening among patients with cancer, despite the negative association of depressive symptoms with prognosis and survival [37, 38]. Additionally, a review by Kim et al. focused on implementation of solutions; specifically, web-based interventions which may help reduce anxiety and depression in patients with breast cancer [39]. Measurement of psychosocial well-being in clinical practice is subjective, using regularly-completed patient surveys. However, routine collection is typically resource-intensive, requiring significant effort by sites of care. Completion can be similarly time-consuming and burdensome for patients due to confusing or seemingly repetitive questions, potentially leading to inconsistent capture. The data may also not be systematically collected if the information is exchanged verbally, during dialogue between providers and patients. Despite many challenges with measurement, advances have been made in artificial intelligence (AI) (e.g., reliable measure of Patient Health Questionnaire 9-item [40]), and other validations are likely in development. Psychosocial well-being also undoubtedly remains a highly patient-centric endpoint. Mitigations and/or potentially innovative approaches should be considered in further developing this endpoint for broader, easier adoption. For example, compliance policies around screening, such as for distress or depression, could be implemented to support better data capture via existing patient self-report tools [41].

Frailty is indicative of physiological vulnerability, particularly with respect to aging or comorbidities, and is especially relevant for patients with breast cancer who are often treated

Table 2 Description of endpoints selected for evaluation by TRIUMPH, based on TLR

	Time to next treatment	Adherence/persistence	Psychosocial well-being	Frailty
Conceptual definition	Time from start of treatment to start of subsequent treatment	Patient compliance with prescribed interval and dosing schedule	Psychological health, including anxiety and depression	Physiological vulnerability, especially with respect to aging
Operational definition	Duration via proxy (dates of events, e.g., treatment initiation, discontinuation or initiation of subsequent treatment(s))	Medication possession ratio: proportion of days covered	Psychological scales (e.g., GAD-7, PHQ-9)	Comprehensive geriatric assessment; patient-reported frailty phenotype
RWD sourcing	EHR; claims	EHR; claims (algorithm); prescription records	EHR (potentially); PROs survey; claims; prescription records	EHR; PROs survey; claims (algorithm); prescription records
Clinical relevance	Demonstrates effectiveness, as PFS proxy (may underestimate)	Impacts treatment effectiveness and outcomes	Impacts treatment outcomes and social functioning	Informs on optimal treatment selection, tolerability, and mortality
Potential limitations	Discontinuation not based on formal criteria like RECIST in trial, and all reasons may not be captured (e.g., patient preference)	Potential for self-report bias or data missingness in prescription records (e.g., infusion records)	Assessments not always part of clinical care and may be subjective	Assessments may be or missing; claims algorithms may not be validated
Interpretation	Shorter TTNT indicative of faster progression, ineffective treatment, and/or reason not captured in chart (e.g., preference)	Poor adherence potentially indicative of lower tolerability	Poor well-being potentially associated with worse outcomes	Higher frailty associated with toxicity or mortality
Novelty	Established, with use in real-world research continuing to grow	Well established	Established, but underreported in oncology research	Increasingly recognized in oncology

EHR electronic health record, *PFS* progression-free survival, *PRO* patient-reported outcome, *RECIST* response evaluation criteria in solid tumors, *TTNT* time to next treatment

with multiple regimens in the curative or metastatic setting [42]. Ongoing research efforts aim to shift clinical practice towards incorporating standard geriatric assessment tools that can better inform management of age-associated vulnerabilities [43–45]. While frailty indices and screening tools exist, completion in clinical practice may be suboptimal [44, 46], leading to inconsistent data capture. As a result, identification of frailty markers for retrospective analysis is challenging [47]. Development of a computable frailty phenotype—defining frailty based on widely-accepted physical criteria [48]—may support better capture in RWD and enable greater use in RWE research. Supporting educational materials for researchers can also explain how to derive this phenotype from RWD sources like EHRs, such as outlining what specific data elements are required or describing potential AI tools. Given current limitations of existing datasets, such collection will likely need to begin prospectively, to enable subsequent retrospective analyses after data accrues.

Considering Baseline Characteristics for Patient-Centric Subgroup Analysis

Over the course of discussion, a secondary objective emerged, with TRIUMPH also considering baseline characteristics suitable for stratified analyses—particularly those associated with clinical heterogeneity and differential treatment outcomes—to strengthen the interpretability and applicability of patient-centered real-world endpoints. A major strength of RWE is its ability to include broader patient populations, such as those typically underrepresented in RCTs (e.g., heavily pre-treated, older, sociodemographic groups with limited access to participate [49, 50]). Analyzing endpoints in such subgroups can result in evidence tailored to specific populations in the real world. Through de novo ideation on potential baseline characteristics to define subgroups of interest, TRIUMPH identified and reached consensus around focusing on frailty and area/neighborhood socioeconomic status (SES). As baseline characteristics, both frailty and area/neighborhood SES have demonstrated their relevance and patient-centric value in breast cancer RWE research. Frailty was observed to be associated with increases in both all-cause mortality and breast cancer-specific mortality, as well as decreases in adherence to hormonal therapy [51, 52]. Similarly, lower area SES has been shown to be associated with reduced rates of screening and higher mortality among US patients [53].

By combining selected clinically meaningful, patient-centered, real-world endpoints with these key baseline characteristics (Fig. 2), research may be made more pragmatic and impactful in informing treatment decisions in clinical practice. For example, TTNT may be compared in populations with lower and higher area/neighborhood SES, to better understand potential disparities in outcomes and to quantify the impact of social determinants of health on treatment effectiveness in these specific groups. Or, adherence/persistence may be studied in frail and not frail subgroups, as there may be a meaningful difference between the two and help inform optimal treatment selection.

Using baseline characteristics for subgroup analysis of selected endpoints may not necessarily be novel, but has yet to be done purposefully and on a broad scale using RWD. To date, such studies in breast cancer have only been conducted ad hoc, like recent studies assessing the effect of SES and race on survival and treatment outcomes among older, including frail, patients [54, 55]. With greater adoption of these practices—namely, analysis of endpoints, relevant and understandable to patients, in real-world populations that are like them—TRIUMPH sees potential to shift RWE generation towards more impactful evidence that can be truly practice-informing and tailored to specific patient populations in the real world. Adoption may be stepwise; in the near-term, stakeholders can explore ways to further standardize these endpoints in RWD, and educate others on how to derive them. Subsequently, studies can then investigate how these endpoints compare across subgroups, as determined by key baseline characteristics.

CLINICALLY MEANINGFUL, PATIENT-CENTERED ENDPOINTS FOR THE REAL-WORLD	KEY BASELINE CHARACTERISTICS FOR SUBGROUP ANALYSIS			
	Frailty		Area / Neighborhood SES	
	Frail	Not Frail	Low SES	High SES
Time to Next Treatment	*Quantify how long frail vs. non-frail patients can remain on treatment*		*Evaluate impact of SES on effectiveness and / or tolerability*	
Adherence / Persistence	*Determine extent of adherence among frail vs. non-frail patients*		*Understand how resource mobilization / access enables or limits compliance*	
Psychosocial Well-being	*Identify differences in well-being depending on frailty status*		*Assess how SES may improve or worsen treatment impact on well-being*	
Frailty	*Explore potential changes in frailty status over time*		*Consider variations in frailty status or risk depending on SES*	

Fig. 2 Example RWE research objectives, based on baseline characteristics for subgroup analysis of selected endpoints, to inform treatment decision-making. *AE* adverse events, *SES* socioeconomic status

CONCLUSION

Complementing what is already known from RCT data, RWE generation is valuable in expanding the totality of evidence available on treatments. Given the diversity of healthcare stakeholders using RWE to inform treatment decision-making, RWE research should be based on endpoints that are clinically meaningful and patient-centered, reflecting the priorities of these users. During TRIUMPH discussion, four endpoints were prioritized—TTNT, adherence/persistence, psychosocial well-being, and frailty—as indicators that have potential for broader adoption and have demonstrated relevance in breast cancer. To support widespread adoption of the selected endpoints, several opportunities remain, such as broader education for researchers, standardization of algorithms, and exploration of new approaches for derivation in RWD (including AI). Alongside adoption of the endpoints, key baseline characteristics of frailty and area/neighborhood SES may also guide subgroup analyses, to further increase the patient-centric value of RWE that is generated. Looking ahead, additional endpoints and characteristics will likely emerge and reaffirm the value and necessity of balancing clinical meaningfulness, patient-centricity, and real-world feasibility. These future ideas may similarly be relevant to breast cancer (across all or only specific stages), or expand to other disease areas in oncology. As the potential of the endpoints and baseline characteristics becomes actualized and more broadly adopted in routine care and research, we envision that the clinical utility of RWE will continue to expand, with patients, clinicians, and other healthcare stakeholders benefitting from better informed treatment decision-making.

ACKNOWLEDGEMENTS

The authors would like to thank Chirag Ghai and Cameron Wong from Blue Matter Consulting for their contributions to the TRIUMPH initiative, as well as editorial support on this manuscript; and all participants of the initiative.

Medical Writing/Editorial Assistance. Writing and editorial support in preparation of this article was provided by Chirag Ghai and Cameron Wong of Blue Matter Consulting. This support was funded by Pfizer (New York, NY, USA).

Author Contributions. All authors (Sean Khozin, Nancy Dreyer, Dominic Galante, Raymond Liu, Peter Neumann, Nathan Nussbaum, Joyce O'Shaughnessy, Mothaffar Rimawi, Hope Rugo, Sara Tolaney, Marisa Weiss, Adam Brufsky) equally contributed to the conception, drafting, critical review, and substantial revision of this article, have read and approved the final version, and agree to responsibility for the contents.

Funding. TRIUMPH establishment, the meetings in November 2023, September 2024, and October 2024, and the journal's Rapid Service and Open Access Fees were supported by funding from Pfizer (New York, NY, USA).

Data Availability. Data sharing is not applicable to this article as no datasets were generated and analyzed during the current study.

Declarations

Conflict of interest. Sean Khozin is cofounder and Principal at Phyusion, LLC, providing advisory services to life sciences companies. Nancy Dreyer has received honoraria for consulting from Pfizer. Raymond Liu has received research funding (to institute) from AstraZeneca, Biotheranostics, Beigene, Exact Sciences, and Genentech. Peter Neumann has received honoraria for consulting from Pfizer. Nathan Nussbaum has equity ownership in Verily Life Sciences. Joyce O'Shaughnessy has received honoraria for consulting and/or advisory boards from AbbVie Inc., Agendia, Amgen, Aptitude Health, AstraZeneca, BioNTech, Byondis, Carrick Therapeutics, Daiichi Sankyo, DAVA Oncology, Eisai, Fishawack Health, G1 Therapeutics, Genzyme, GlaxoSmithKline, Genentech, Gilead Sciences, LillyLoxo Oncology, Merck, Novartis, Ontada, Pfizer, Pierre Fabre Pharmaceuticals, Puma Biotechnology, Roche, Samsung Bioepis, Sanofi, Seagen, Stemline Therapeutics, Taiho Oncology, and Veru. Mothaffar Rimawi has received honoraria for consulting from Novartis, Pfizer, AstraZeneca, Gilead, Sermonix, Stemline Therapeutics, and Tempus AI. Hope Rugo has received honoraria for consulting and/or advisory from Napo, Bristol Myers Squibb, Helsinn, and BioNTech; and institutional research support to her former institution, UCSF, from AstraZeneca, Gilead Sciences, Inc., Lilly, Merck & Co., Daiichi Sankyo, Inc., Novartis Pharmaceuticals, Pfizer, F. Hoffman-La Roche/AG/Genentech, Stemline Therapeutics, Ambryx. Sara Tolaney has received honoraria for consulting and/or advisory role from Novartis, Pfizer/SeaGen, Merck, Eli Lilly, AstraZeneca, Genentech/Roche, Eisai, Sanofi, Bristol Myers Squibb, CytomX Therapeutics, Daiichi Sankyo, Gilead, Zymeworks, Zentalis, Blueprint Medicines, Reveal Genomics, Sumitovant Biopharma, Umoja Biopharma, Artios Pharma, Menarini/Stemline, Aadi Bio, Bayer, Incyte Corp, Jazz Pharmaceuticals, Natera, Tango Therapeutics, Systimmune, eFFECTOR, Hengrui USA, Cullinan Oncology, Circle Pharma, Arvinas, BioNTech; research funding (all to institute) from Genentech/Roche, Merck, Exelixis, Pfizer, Lilly, Novartis, Bristol Myers Squibb, Eisai, AstraZeneca, NanoString Technologies, Gilead, Seattle Genetics, OncoPep, Daiichi Sankyo, Menarini/Stemline; and travel support from Eli Lilly, Sanofi, Gilead, Jazz, and BioNTech. Adam Brufsky has received honoraria for consulting from AstraZeneca, Novartis, Lilly, Genetech/Roche, Daiichi Sankyo, Merck, Agendia, Sanofi, Pfizer, Puma, Myriad, Gilead, and Bria Cell; and research support from Agendia and AstraZeneca. Dominic Galante and Marisa Weiss have nothing to disclose. The authors have no other competing interests or relevant affiliations with any organization or entity with the subject matter or materials discussed in the manuscript apart from those disclosed.

Ethical Approval. This article does not contain any new studies with human participants or animals performed by any of the authors. All members of TRIUMPH were fully informed and consented to their thoughts being formulated into a manuscript, invited to contribute as authors on this article, and present as authors.

REFERENCES

1. Eichler HG, Pignatti F, Schwarzer-Daum B, et al. Randomized controlled trials versus real world evidence: neither magic nor myth. Clin Pharmacol Ther. 2021;109(5):1212–8.

2. Purpura CA, Garry EM, Honig N, Case A, Rassen JA. The role of real-world evidence in FDA-approved new drug and biologics license applications. Clin Pharmacol Ther. 2022;111(1):135–44.

3. Castelo-Branco L, Pellat A, Martins-Branco D, et al. ESMO guidance for reporting oncology real-world evidence (GROW). Ann Oncol. 2023;34(12):1097–112.

4. Rahman M, Dal Pan G, Stein P, et al. When can real-world data generate real-world evidence? Pharmacoepidemiol Drug Saf. 2024;33:e5715.

5. Liu F, Panagiotakos D. Real-world data: a brief review of the methods, applications, challenges and opportunities. BMC Med Res Methodol. 2022;22(1):287.

6. McKelvey BA, Garrett-Mayer E, Rivera DR, et al. Evaluation of real-world tumor response derived from electronic health record data sources: a feasibility analysis in patients with metastatic non-small cell lung cancer treated with chemotherapy. JCO Clin Cancer Inform. 2024;8:e2400091.

7. Friends of Cancer Research. RWE Pilot Projects. [online]. https://friendsofcancerresearch.org/rwe-pilots/. Accessed 3 Feb 2026.

8. Friends of Cancer Research. Establishing a Framework to Evaluate Real-World Endpoints. Published July 10, 2018. Accessed 3 Feb 2026.

9. McKelvey BA, Berk A, Chin L, et al. A study design to harmonize patient-reported outcomes across data sets. JCO Clin Cancer Inform. 2023;7:e2200161.

10. Duke-Margolis Institute for Health Policy. A Roadmap for Developing Study Endpoints in Real-World Settings. Published 28 Aug 2020. Accessed 3 Feb 2026.

11. Oehrlein EM, Perfetto EM, Schoch S, et al. Patient-Centered Real-World Evidence: Methods Recommendations from an Evidence-Based Consensus Process. Published May 2021. Accessed 3 Feb 2026.

12. Khozin S, Dreyer NA, Galante D, et al. Real-world evidence acceptability and use in breast cancer treatment decision-making in the united states: call-to-action from a multidisciplinary think tank. Adv Ther. 2025;42(7):2973–87.

13. Delgado A, Guddati AK. Clinical endpoints in oncology—a primer. Am J Cancer Res. 2021;11(4):1121–31.

14. Araujo DV, Soler JA, de Coriro Lima VC. Patient-centered trials in oncology: time for a change. Med. 2022;3(7):445–9.

15. LoCasale RJ, Pashos CL, Gutierrez B, et al. Bridging the gap between RCTs and RWE through endpoint selection. Ther Innov Regul Sci. 2021;55(1):90–6.

16. Kaufman PA, Neuberger E, Schwartz NRM, et al. Real-world patient characteristics, treatment patterns, and clinical outcomes associated with tucatinib therapy in HER2-positive metastatic breast cancer. Front Oncol. 2023;13:1264861.

17. Dudani S, Graham J, Wells JC, et al. First-line immuno-oncology combination therapies in metastatic renal-cell carcinoma: results from the International Metastatic Renal-cell Carcinoma Database Consortium. Eur Urol. 2019;76(6):861–7.

18. Shinno Y, Goto Y, Watanabe S, et al. Evaluation of time to failure of strategy as an alternative surrogate endpoint in patients with lung cancer with EGFR mutations. ESMO Open. 2018;3(7):e000399.

19. Blumenthal GM, Gong Y, Kehl K, et al. Analysis of time-to-treatment discontinuation of targeted therapy, immunotherapy, and chemotherapy in clinical trials of patients with non-small-cell lung cancer. Ann Oncol. 2019;30(5):830–8.

20. Inotai A, Ágh T, Maris R, et al. Systematic review of real-world studies evaluating the impact of medication non-adherence to endocrine therapies on hard clinical endpoints in patients with

non-metastatic breast cancer. Cancer Treat Rev. 2021;100:102264.

21. Claessens AKM, Ramaekers BLT, Lobbezoo DJA, et al. Quality of life in a real-world cohort of advanced breast cancer patients: a study of the SONABRE Registry. Qual Life Res. 2020;29(12):3363–74.

22. Chau YF, Zhou H, Chen B, et al. Screening for depression and anxiety in lung cancer patients: a real-world study using GAD-7 and HADS. Thorac Cancer. 2024;15(13):1041–9.

23. Sanchez DN, Derks MGM, Verstijnen JA, et al. Frequency of use and characterization of frailty assessments in observational studies on older women with breast cancer: a systematic review. BMC Geriatr. 2024;24(1):563.

24. Murugappan MN, King-Kallimanis BL, Bhatnagar V, et al. Measuring frailty using patient-reported outcomes (PRO) data: a feasibility study in patients with multiple myeloma. Qual Life Res. 2023;32(8):2281–92.

25. Walker B, Boyd M, Aguilar K, et al. Comparisons of real-world time-to-event end points in oncology research. JCO Clin Cancer Inform. 2021;5:45–6.

26. Labaki C, Bakouny Z, Sanglier T, et al. Real-world progression-free survival (rwPFS) and time to next line of therapy (TTNT) as intermediate endpoints for survival in metastatic breast cancer A real-world experience. Ann Oncol. 2022. https://doi.org/10.1200/JCO.2022.40.16_suppl.6520.

27. Walker MS, Herms L, Miller PJE. Performance of time to discontinuation and time to next treatment as proxy measures of progression-free survival, overall and by treatment group. J Clin Oncol. 2020. https://doi.org/10.1200/JCO.2020.38.15_suppl.e19135.

28. Stewart M, Norden AD, Dreyer N, et al. An exploratory analysis of real-world end points for assessing outcomes among immunotherapy-treated patients with advanced non-small-cell lung cancer. JCO Clin Cancer Inform. 2019;3:1–15.

29. Cramer JA, Roy A, Burrell A, et al. Medication compliance and persistence: terminology and definitions. Value Health. 2008;11(1):44–7.

30. Hohneker J, Shah-Mehta S, Brandt PS. Perspectives on adherence and persistence with oral medications for cancer treatment. J Oncol Pract. 2011;7(1):65–7.

31. Acuña-Villaorduña A, Baranda JC, Boehmer J, Fashoyin-Aje L, Gore SD. Equitable access to clinical trials: how do we achieve it? Am Soc Clin Oncol Educ Book. 2023;43:e389838.

32. Tan YY, Papez V, Chang WH, Mueller SH, Denaxas S, Lai AG. Comparing clinical trial population representativeness to real-world populations: an external validity analysis encompassing 43 895 trials and 5 685 738 individuals across 989 unique drugs and 286 conditions in England. Lancet Healthy Longev. 2022;3(10):e674–89.

33. Bhimani J, O'Connell K, Persaud S, et al. Patient characteristics associated with delayed time to adjuvant chemotherapy among women treated for stage I-IIIA breast cancer. Int J Cancer. 2024;155(9):1577–92.

34. Peterson AM, Nau DP, Cramer JA, Benner J, Gwadry-Sridhar F, Nichol M. A checklist for medication compliance and persistence studies using retrospective databases. Value Health. 2007;10(1):3–12.

35. Ho YF, Hu FC, Lee PI. The advantages and challenges of using real-world data for patient care. Clin Transl Sci. 2020;13(1):4–7.

36. Stirratt MJ, Dunbar-Jacob J, Crane HM, et al. Self-report measures of medication adherence behavior: recommendations on optimal use. Transl Behav Med. 2015;5(4):470–82.

37. Fleege NMG, Bunt S, Mecham B, et al. Disparities in mental health screening for veteran women with a new diagnosis of breast cancer. Presented at: 2024 ASCO Quality Care Symposium; September 30, 2024; Chicago, Illinois.

38. Arana I, Liu R, Kushi L, Hahn E, Ragavan M. Screening for comprehensive social needs in patients with cancer: a narrative review. JNCI Cancer Spectr. 2025;9(2):pkaf012.

39. Kim M, Kang KJ, Ryu S. Effects of web-based interventions on anxiety and depression in patients with breast cancer: a systematic review and meta-analysis of randomized controlled trials. Psychooncology. 2025;34(5):e70167.

40. Alves P, Marci CD, Cohen-Stavi CJ, Whelan KM, Boussios C. A machine learning model using clinical notes to estimate PHQ-9 symptom severity scores in depressed patients. J Affect Disord. 2025;376:216–24.

41. Ehlers SL, Davis K, Bluethmann SM, et al. Screening for psychosocial distress among patients with cancer: implications for clinical practice, healthcare policy, and dissemination to enhance cancer survivorship. Transl Behav Med. 2019;9(2):282–91.

42. Tsai HH, Yu JC, Hsu HM, et al. The impact of frailty on breast cancer outcomes: evidence from analysis of the Nationwide Inpatient Sample, 2005–2018. Am J Cancer Res. 2022;12(12):5589–98.

43. Dale W, Klepin HD, Williams GR, et al. Practical assessment and management of vulnerabilities in older patients receiving systemic cancer therapy: ASCO guideline update. J Clin Oncol. 2023;41(26):4293–312.

44. Shaia JL, Liu R, Sun H, et al. Nurse navigator–initiated geriatric assessments in hematology/oncology clinics. J Clin Oncol. 2022. https://doi.org/10.1200/JCO.2022.40.16_suppl.12051.

45. Arora A, Sun H, Shaia JL, et al. Using G8 and carg toxicity score to predict emergency room (ER) visits, hospitalizations, and mortality in older patients with newly diagnosed cancer. J Clin Oncol. 2022. https://doi.org/10.1200/JCO.2022.40.16_suppl.12055.

46. George EL, Arya S. The importance of incorporating frailty screening into surgical clinical workflow. JAMA Netw Open. 2019;2(5):e193538.

47. Soong JTY. Frailty measurement in routinely collected data: challenges and benefits. Lancet Healthy Longev. 2021;2(3):e117–8.

48. Op het Veld LP, van Rossum E, Kempen GI, de Vet HC, Hajema K, Beurskens AJ. Fried phenotype of frailty: cross-sectional comparison of three frailty stages on various health domains. BMC Geriatr. 2015;15:77.

49. Murthy VH, Krumholz HM, Gross CP. Participation in cancer clinical trials: race-, sex-, and age-based disparities. JAMA. 2004;291(22):2720–6.

50. Gomez SL, Shariff-Marco S, Von Behren J, et al. Representativeness of breast cancer cases in an integrated health care delivery system. BMC Cancer. 2015;15:688.

51. Yan CH, Coleman C, Nabulsi NA, et al. Associations between frailty and cancer-specific mortality among older women with breast cancer. Breast Cancer Res Treat. 2021;189(3):769–79.

52. Mandelblatt JS, Cai L, Luta G, et al. Frailty and long-term mortality of older breast cancer patients: CALGB 369901 (Alliance). Breast Cancer Res Treat. 2017;164(1):107–17.

53. Mehta A, Jeon WJ, Nagaraj G. Association of US county-level social vulnerability index with breast, colorectal, and lung cancer screening, incidence, and mortality rates across US counties. Front Oncol. 2024;14:1422475.

54. Puthanmadhom Narayanan S, Ren D, Oesterreich S, Lee AV, Rosenzweig MQ, Brufsky AM. Effects of socioeconomic status and race on survival and treatment in metastatic breast cancer. NPJ Breast Cancer. 2023;9(1):90.

55. Fedele P, Landriscina M, Moraca L, et al. Evaluating CDK4/6 inhibitor therapy in elderly patients with metastatic hormone receptor-positive, HER2-negative breast cancer: a retrospective real-world multicenter study. Cancers (Basel). 2024;16(20):3442.