Review

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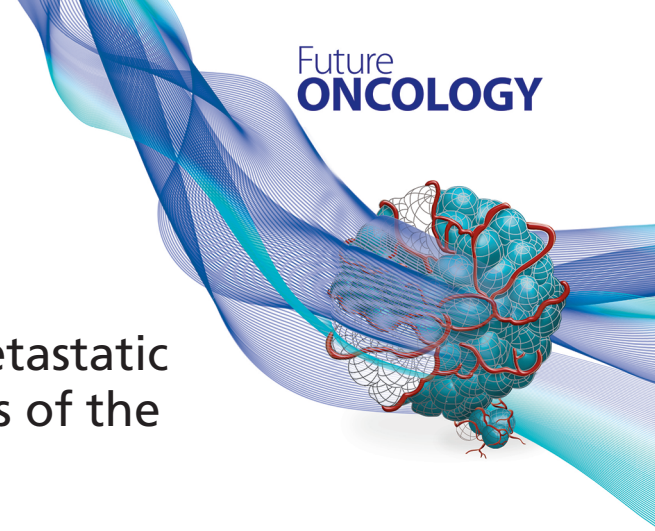

Real-world evidence research in metastatic colorectal cancer: raising awareness of the need for patient contributions

Barbara Moss[1], Edward A Goodall[2], Zorana Maravic[1], Francisca Marti[3], Mark Moss[1], Stephen Rowley[1,4], Cyril Sarrauste[1,5] & Pete Wheatstone*[,6]

[1]Digestive Cancers Europe, Rue de la Loi 235/27, 1040 Brussels, Belgium
[2]Northern Ireland Cancer Research Consumer Forum, Belfast City Hospital, 51 Lisburn Road, Belfast, BT9 7AB, UK
[3]Department of Medical Oncology, The Christie NHS Foundation Trust, Wilmslow Road, Manchester, M20 4BX, UK
[4]Bowel Cancer Support Group UK
[5]Mon Réseau Cancer Colorectal/Patients en Réseau, 15 Rue Gît le Coeur, 75006 Paris, France
[6]DATA-CAN, c/o St. James University Hospital, Beckett Street, Leeds, LS9 7TF, UK
*Author for correspondence: Tel.: +44 7828 59 9557; wheatpd@yahoo.co.uk

Real-world evidence (RWE) research helps determine whether outcomes observed in clinical trials happen in real-life clinical practice. RWE research may help patients receive more appropriate treatment, closer to their needs and wishes. RWE for metastatic colorectal cancer is currently limited. The PROMETCO RWE study is an important example of an ongoing initiative that focuses on patient-reported outcomes in metastatic colorectal cancer. Patients play an active role throughout the RWE research process, including study design, participation and results dissemination. This involvement can encourage greater patient empowerment through active engagement, potentially resulting in various benefits that can lead to improved clinical outcomes. Greater patient engagement can increase involvement in RWE, helping more patients to access the benefits of RWE research.

Plain language summary – Real-world evidence research in metastatic colorectal cancer: raising awareness of the need for patient contributions: Real-world evidence (RWE) research provides information that is essential to improving medical treatment. When it comes to metastatic colorectal cancer – cancer that has spread to other parts of the body – only a few RWE studies have been conducted. RWE studies, such as the ongoing PROMETCO study in patients with metastatic colorectal cancer, differ from clinical trials in that they include a wider range of people with fewer restrictions on type of treatments received. They can also place more attention to the patients' own opinions. By joining RWE studies, patients are likely to become more interested in their disease and take a more active role in their treatment. In the end, this can help to improve their quality of life and possibly improve the outcomes of their treatment. Doctors need to work in partnership with patients to increase participation in RWE studies.

Clinical Trial Registration: NCT03935763 (ClinicalTrials.gov)

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Keywords: education • empowerment • metastatic colorectal cancer • patient-reported outcomes • PROMETCO • quality of life • real-world evidence

This article aims to explore and increase understanding of the value that real-world evidence (RWE) research can bring to patients with metastatic colorectal cancer (mCRC) and the wider medical community. In addition, the authors hope to raise awareness of the need for patient contributions to RWE research, drawing on the example of the ongoing PROMETCO study (a real-world evidence prospective cohort study in the management of metastatic colorectal cancer: a clinical and patient perspective; NCT03935763), which aims to provide insights into the perspectives of patients with mCRC who have had two disease progressions from diagnosis and are receiving subsequent treatment. Recruitment for the study was finalized in October 2022, with 738 patients enrolled in 96 participating sites across 18 countries in Europe and South America [1].

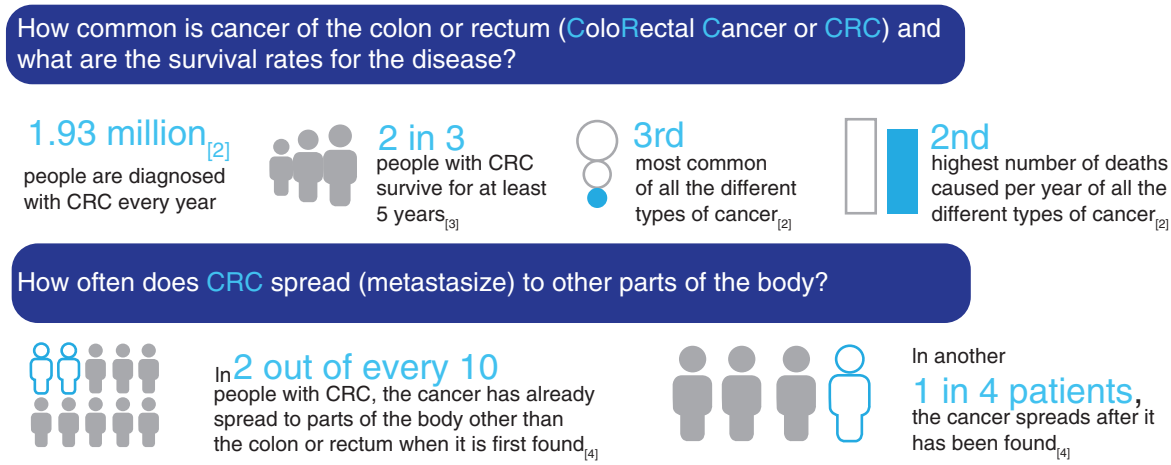

Figure 1. Overview of colorectal cancer.

Colorectal cancer (CRC) is the third most commonly diagnosed cancer worldwide, with 1.93 million cases recorded in 2020 (Figure 1) [2]. The disease is preventable and treatable when diagnosed early. Most CRCs develop from non-cancerous polyps that can be detected in regular screening programs. However, it remains the second leading cause of cancer-related mortality worldwide, with 916,000 deaths in 2020 [2]. A trend of decreasing CRC incidence (except in young adults as screening is not routinely carried out in this population [5,6]) and mortality rates has been observed over recent decades. This is largely due to the introduction of screening programs and the availability of new management options [7].

Among newly diagnosed CRC cases, one-fifth of patients have metastatic disease at presentation and a further quarter who initially present with localized disease will later develop metastases [4]. A recent study found that patients with CRC aged below 55 years were 58% more likely to be diagnosed with advanced disease [8]. Clinical outcomes for patients with mCRC have improved over the last 20 years and reported median overall survival of patients with mCRC who were treated with systemic therapy in clinical and RWE research is now over 30 months, representing a 50% increase over the previous 2 decades [9,10]. These advances have been primarily driven by the development of new treatments, evaluated in the 'gold standard' of clinical research – randomized controlled trials (RCT). Despite advances in treatment options improving clinical outcomes, the personal impact of mCRC on patients diagnosed with this disease remains significant. mCRC substantially impacts health-related quality of life (QoL) for both patients and their carers, particularly when patients progress through several lines of treatment [11].

In RWE research, data relating to patient health or experience, or healthcare delivery, are collected outside the context of RCTs [12]. Common sources of real-world data include patient demographics, medical history, clinical outcomes (including patient-reported outcomes [PRO]), and laboratory measurements [12]. Compared with RCTs, RWE research is conducted under less tightly controlled requirements [12]. The aim is to gather information that reflects more closely with what happens in daily clinical practice [13,14]. It is anticipated that RWE research in oncology will become a valuable source of information for all stakeholders; clinicians, patients and healthcare payers are increasingly looking at this type of research to inform treatment and funding decisions [13,14]. RWE research can help answer questions on the more appropriate treatment that matches the needs and wishes of a patient. It also helps determine whether outcomes observed in clinical trials are reproduced in real-life practice, in the hospital, or in clinics [13,14].

Background & rationale

Overview of RWE research

Key differences between RCTs and RWE are summarized in Figure 2 and Table 1. RCTs have been and still are considered the 'gold standard' of clinical research, and currently provide the evidence base for a product to be approved for use on patients and for the development of treatment guidelines [15]. However, they usually employ strict inclusion and exclusion criteria, often only including patients of a certain age, weight, or stage of cancer, for example, and excluding those with comorbidities or certain types of previous treatment. This means that only a proportion of the entire patient population affected by a specific cancer is represented [14,21].

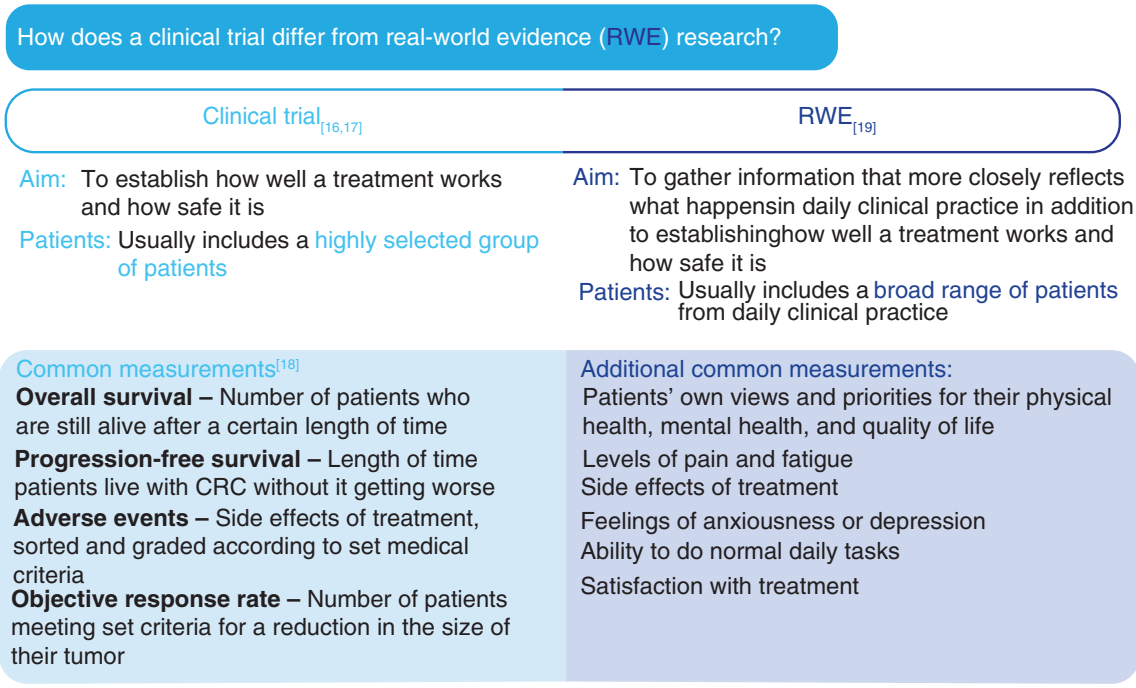

Figure 2. Differences between a clinical trial and real-world evidence research.
CRC: Colorectal cancer.

Table 1. Overview of RWE versus RCTs.

	RCT	RWE research	
Type of study	Experimental/interventional	Observational/non-interventional	Interventional/pragmatic
Design	Prospective	Retrospective/prospective	Prospective
Primary focus	• Efficacy • Safety • Quality • Cost-effectiveness	• Efficacy • Safety • Quality • Cost–effectiveness • Natural history • Compliance and adherence • Service models • Patient preferences • Comparative	
Patient population	Narrow, restricted, motivated	Diverse, large, unrestricted	
Monitoring	Intense (ICH-GCP compliant)	Not required	Reflects SoC
Comparators	Gold standard/placebo	None/SoC/multiple iterations	Placebo/SoC/multiple iterations
Outcomes	Clear sequence	Wide range	
Data collection	Standardized, controlled	Routine; potential for recruitment bias or recall/interviewer bias	
Randomization	Yes	No	Yes
Blinding	Yes	No	Sometimes (participants or outcome assessment)
Follow-up	Generally short	Reflects SoC plus patient input	Reflects SoC plus patient input; long time period

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Blinding: study participant/person providing treatment/data collector/data analyst are kept unaware of the treatment group assignment to limit the risk of bias.
Interventional: a drug, device, or procedure is administered to research participants as part of the research protocol.
Monitoring: periodic tracking of progress by systematic gathering and analysis of data and information.
Pragmatic: focuses on correlating treatment and outcomes in real-world clinical practice.
Prospective: research participants are observed and followed over a period of time.
Retrospective: research questions are raised about participants who have already participated in research in the past.
ICH-GCP: International Conference on Harmonisation of Good Clinical Practice; RCT: Randomized controlled trial; RWE: Real-world evidence; SoC: Standard of care.

In real-world practice, prescribing patterns may differ from those in trial settings. Treatment decisions in the clinic are influenced by various factors, such as the previous experiences of the patient or clinician, the patient's wishes and preferences, treatment accessibility and availability, and reimbursement constraints [1,22]. Real-world data relate to the patient's health status and/or the delivery of healthcare routinely collected from a variety of sources other than RCTs, such as prospective observational studies, product and disease registries, patient cohorts, prescription and administrative claims databases and electronic health records [23–25]. Data can be recorded by patients or their carers using various approaches, including smart wearable devices or social media platforms [26]. Personal data collected in RWE research are stored securely in the same way as data collected in an RCT, with country-specific legislation and/or guidelines in place to protect patient confidentiality and ensure that any personal data collected cannot be used to identify individual patients.

RWE research can play a key role in providing information to help patients to evaluate their treatment choices, to learn about the experiences of other patients, and potentially improve their own outcomes. However, for clinicians to understand the needs and priorities of individual patients, they must communicate effectively with patients and their carers and families [27]. RWE research should be designed in partnership with patients and carers, and the results should be communicated clearly and without bias to help inform decision-making [23]. This goal is, of course, dependent on accurate and comprehensive data collection during the study. Similar to the approach taken in RCTs, the type of statistical analyses undertaken on data collected in RWE research will depend on the study objectives in question. In the PROMETCO study, for example, descriptive statistics will be employed to address the study objectives, with continuous variables summarized using mean, standard deviation, median and range and categorical variables reported as number and percentage of patients [1]. Progression-free survival and overall survival will be summarized using Kaplan–Meier survival analysis, and a Cox regression model will be used to analyze the relationship between survival end points and different independent baseline variables [1]. CIs will be reported to provide the reader with an opportunity to draw conclusions about the importance of the size or strength of the results.

Information relating to the benefits and risks of a treatment is obtained by addressing specific research questions through the analysis of real-world data, rather than data from conventional RCTs [24]. The value of RWE research for guiding the clinical management of patients is increasingly recognized [26,28,29]. This type of research has the potential to increase the understanding of treatment efficacy and safety (particularly rare adverse events) in large, diverse populations. It can also provide valuable insights into the disease burden, treatment patterns and patient behaviors in everyday clinical practice [20,28,29] and help determine the place of a particular intervention within the overall treatment landscape. In the surgical field, RWE research is increasingly being utilized to identify prognostic factors for successful surgical outcomes and guide decision-making [30,31].

Standardized questionnaires are currently used in both RCT and RWE research to assess PROs. Such outcomes are defined as '*any report of the status of a patient's health condition that comes directly from the patient without interpretation of the patient's response by a clinician or anyone else*' [32]. PRO questionnaires often focus on clinically-defined aspects such as QoL measures, levels of fatigue, and specific symptoms such as pain and constipation [33]. This information can be valuable in differentiating between interventions with similar clinical outcomes and in describing patients' experiences of the disease and treatment that might not otherwise be recorded [26,34]. It is important to have this information as, even in real-world data generation, the focus has traditionally been on clinical end points, which are objective tools used to assess the safety and efficacy of a given therapy or medical intervention [35]. Examples of clinical end points used in oncology research include overall survival, progression-free survival and time to progression. By using a 'one-size-fits-all' approach, clinical end points fail to reflect the needs of individual patients, such as their personal priorities for improved QoL.

The plethora of potential combinations and sequences of treatments for mCRC make it challenging for clinicians and patients to determine the optimal approach for an individual patient or patient subgroup [36]. PRO measures (PROM) can include intangible factors that have now been shown to influence outcomes. These can include such non-medical aspects as the financial impact of cancer and its treatment and any side effects, which may result in an inability to work, especially pertinent in the current economic climate. These factors may also impact on other non-medical priorities such as leisure interests and holidays. These factors can reinforce and complement clinician-reported outcome measures, so it is important that PROM data are included in the decision-making process and are part of a shared dialog [37]. However, there are limited real-world data on overall survival, treatment patterns, and the effectiveness, safety and impact on QoL related to treatments for patients with mCRC, especially those who have progressed twice [1].

Evaluation of PROs across the mCRC continuum of care is central to the objectives of the PROMETCO study, with the combined use of three questionnaires: the 5-level EuroQol 5D questionnaire (EQ-5D-5L) [38]; the Brief Fatigue Inventory (BFI) [39] and a modified version of the Acceptance by the Patients of their Treatment (ACCEPT©) questionnaire [40]. These questionnaires explore complementary aspects as follows:

- EQ-5D-5L assesses five aspects of patient health – mobility, self-care, usual activities, pain/discomfort and anxiety/depression – using a 5-level scale (no problems, slight problems, moderate problems, severe problems and extreme problems) [38].
- The nine-item BFI measures fatigue in terms of severity and interference with daily life, on 10-point scales [39].
- The ACCEPT© questionnaire assesses the acceptability of long-term medication [40].

By including PROs alongside established (objective) measures of efficacy and safety (e.g., overall survival, rate of adverse events), the intention of PROMETCO is to capture information of key interest to both patients and clinicians. However, more studies with this approach are needed to ensure that patients with mCRC routinely have the opportunity to participate in these types of initiatives and have access to the data they generate.

Patient involvement in RWE research design & delivery

A summary of potential roles, benefits, and barriers to patient contributions to RWE research is shown in Figure 3 and Box 1. Issues that are important to the patient can be addressed by including them in the design of RWE research. This ensures that research processes and outcomes engage the patient, and that reported changes in patient outcomes are meaningful [41,42]. Patients can play an active role at all stages of the research process as collaborators, partners, or co-researchers [43]. Patient perspectives on treatment can also be provided through direct engagement or participation in surveys, interviews, or focus groups [44]. Engaging patients early in the research development process can improve the design of a research study, reducing the potential for unexpected issues once the study has begun [45]. This can also lead to enhanced recruitment and continued participation.

Various opportunities facilitate patients becoming engaged in RWE research [46], for example:

- Identifying research priorities, contributing to study design (e.g., providing input on PRO questionnaires), reviewing study protocols that set out how the study should be run, and what is going to be measured;
- Disseminating research findings, and informing participants and other patients about the study results;
- Acting as a patient expert, providing information about the study to other patients to encourage participation, and reviewing and supporting the development of patient information sheets and other related materials [47,48].

Initiation of patient engagement at the early stages of study design has been identified as best practice. By ensuring that PROs are relevant to the patient, the likelihood of questionnaires being completed throughout a study will be increased. In the PROMETCO study, for example, the patient advocacy organization Digestive Cancers Europe (DiCE) participated in the discussion about which PRO questionnaires should be included [1].

Patient participation in RWE studies

RWE research has gained importance as a valuable tool to help inform shared decision-making between clinicians and patients, while also providing evidence to payers as to the real value of differing treatment options [14,26,28,29,49]. Therefore, the recruitment of patients into this type of study is also becoming increasingly important, as summarised in Box 2. Patients participating in RWE research are usually required to complete questionnaires that evaluate symptom burden, functional status, and psychological and emotional wellbeing. These subjective experiences are best reported by patients themselves [50]. Some authors have advocated standardization of questionnaires and interview approaches to reduce the risk of healthcare providers under-detecting symptoms or underestimating their importance [51–53]. However, this approach has the potential to limit the scope for capturing individual patients' personal perspectives and thus reduces patient motivation for completing such questionnaires; reduced standardization is one of the potential advantages of RWE research versus RCTs. There has been a general move toward electronic methods for PRO reporting, enabling data to be collected either during clinic visits or while patients are at home between visits [33,34]. For example, in the PROMETCO study, participants have the option to complete electronic PRO questionnaires either remotely or during scheduled clinic visits.

A 2014 systematic review of controlled trials in patients undergoing active cancer treatment investigated whether the inclusion of PROMs in routine clinical practice would improve patient outcomes [54]. Although the studies were

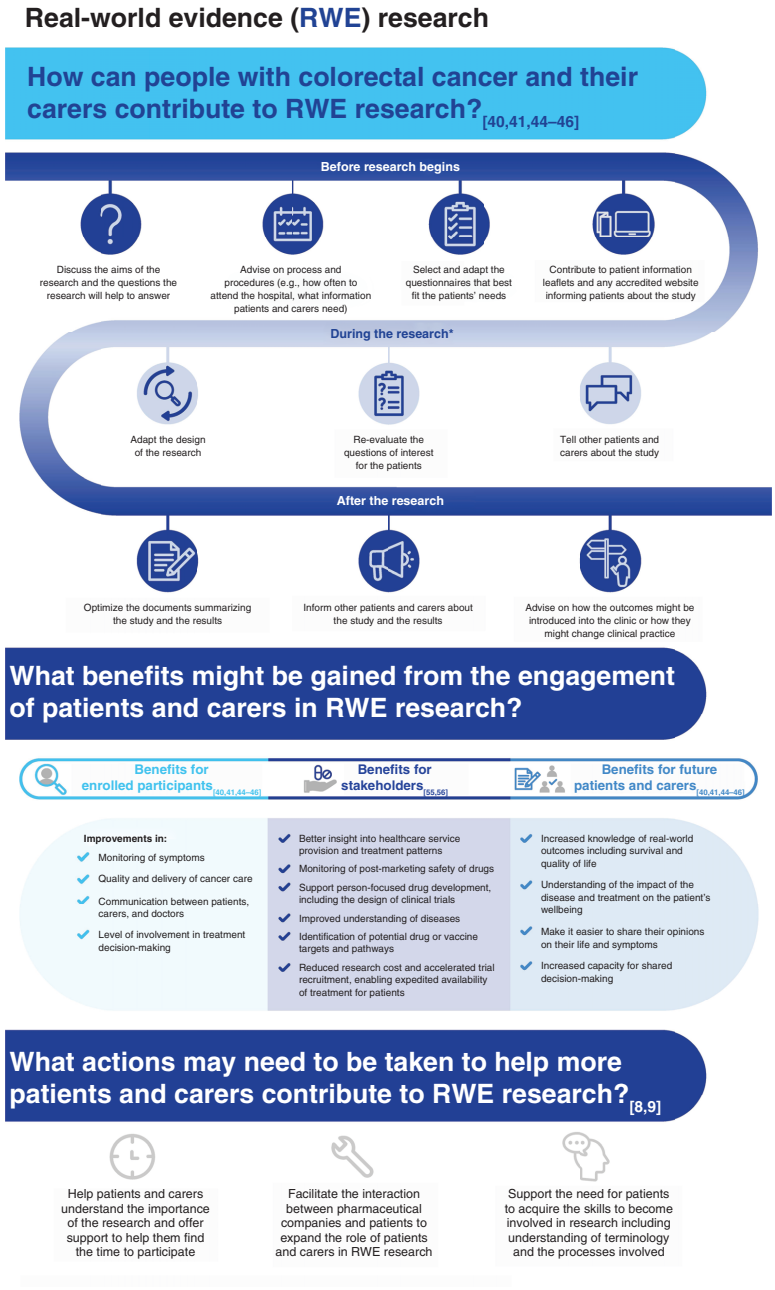

Figure 3. Real-world evidence research overview.
* Personal communication: Pete Wheatstone and Barbara Moss 6 April 2022. Written permission provided.

Box 1. What are the benefits of patient involvement in research design and delivery?

- Helping to identify the outcomes that need to be assessed and which are relevant to patients and carers - patient engagement has a critical role in achieving true translational research.
- Improving patient recruitment and continued participation in both RCTs and RWE research (participants contributing to research design and delivery may be more motivated and through discussions they may motivate other patients within their network).
- Improving relevance of PROM tools helps to ensure that patients are more likely to complete the PROM because they are being asked about aspects that are important to them. They are therefore also more likely to continue to do so throughout the research period, thus improving data quality and leading to more meaningful results.

Box 2. What are the implications of patient participation in RWE research, from the perspective of the patient and the wider medical community?

- Producing evidence that may be more relevant to patients' needs than data from clinical trials.
- Informing best practices, guidelines, policies and resource allocation.
- Patients can refer to RWE from study participants with a similar profile to them to understand how a treatment might benefit them personally.
- Helping with symptom monitoring and therefore optimizing treatment adherence, and quality and delivery of care, particularly in the management of treatment side effects.
- Facilitating communication between clinicians, patients and carers.

heterogeneous in terms of settings and methods, the review reported that PROMs could help improve symptom control, increase supportive care measures and improve patient satisfaction.

Research has shown that using electronic patient-reported symptom monitoring, versus usual care, improves overall survival in patients with metastatic cancer. In a study by Basch *et al.*, one group of patients was encouraged to discuss symptoms during clinic visits and by telephone between visits [57]. Overall survival was 31.2 months (95% CI: 24.5–39.6) in the group reporting their symptoms versus 26.0 months (95% CI: 22.1–30.9) in the usual care control group (difference of 5 months; p = 0.03). A statistically significant difference was maintained when a multivariable model was applied, with a hazard ratio of 0.83 (95% CI: 0.70–0.99). The study findings could be explained by clinicians receiving early warning of adverse events, allowing treatment to be adjusted and adherence to be maintained [34,57]. Patients in the intervention group continued their chemotherapy for longer than patients in the usual care group (mean: 8.2 months vs 6.3 months, respectively [95% CI: 0.7–3.0; p = 0.002]) [57]. In a more recent RCT by Basch *et al.*, patients with metastatic cancer completed weekly PRO surveys (European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire) by telephone or online for up to 1 year [58]. Compared with a control group not undertaking PRO surveys, statistically significant improvements in physical function, symptom control and health-related QoL were observed [58].

Discussion

There are potential barriers to patient participation in RWE research. These include time commitment, lack of understanding of the process and/or the focus of the research, lack of awareness of available opportunities in research, previous negative experiences (personal or anecdotal), and the clinician not having the time or being able to participate [59,60]. There is also the issue of trust, in that patients need to be certain that their healthcare data is being used in an appropriate manner. Patients with certain conditions, such as metastatic cancer, may feel that the time required would be better spent with loved ones or carrying out charitable or life ambitions, particularly if the potential benefits of the research are not adequately explained. Specifying the likely amount of time needed to participate in RWE research would be helpful for patients and their carers as well as perhaps being more flexible in scheduling clinical appointments and tests.

Increasing a patient's awareness and understanding of the benefits of RWE research may help increase their willingness to participate. Educational initiatives could include electronic channels such as social media and websites, as well as printed materials given to a patient at the clinic. Publications in the lay press or scientific journals could also help increase a patient's awareness and knowledge. Patient engagement in the design and conduct of RWE research can help to ensure that issues relevant to the patient are addressed, thereby encouraging participation.

The requirement for the patient's clinician to participate in research can be a major barrier to participation, which applies to both RCTs and RWE research [46]. Clinicians may be unwilling to participate for a variety of reasons, including limited familiarity with research methods and procedures or concerns about the amount of time required. There is also the fear of possible disruption to their daily clinical practice. Other factors include a lack of awareness of ongoing trials, lack of interest in the research topic, and a shortage of adequate resources [60,61]. Clinician participation in RWE research may be encouraged by providing adequate training and ensuring research questions are aligned with their interests in improving patient care [61].

There is a growing focus on improving clinician–patient relationships and shared decision-making, which, together with increased disease awareness and knowledge among patients, is described as 'patient empowerment'.

This term has been defined by the World Health Organization as "*a process through which people gain greater control over decisions and actions affecting their health*" [62].

Empowerment generates a desire to learn, and many patients who are involved in RWE research question other factors that influence their cancer treatment [63]. Information about the disease and treatment is available online, but diligence is required to ensure that sources are accurate, and the format of some information may not help patients increase their knowledge. Social media sources demand particular caution due to the risks of misinformation, but it can provide valuable insights while also enabling patients to create content themselves. Alongside (or instead of) conventional medical interventions, patients may choose to explore complementary, integrative, and alternative therapies. The patient may not recognize the need for robust scientific evidence to support an intervention or the potential for adverse events, but it is important that clinicians work with, rather than disregard, the patient's view. Addressing recognized lifestyle factors such as exercise, diet and smoking can trigger a range of improvements (e.g., in mental health, fatigue, sleep and overall QoL), potentially leading to improved cancer-related outcomes [64,65]. Evidence supporting the benefits of exercise is particularly strong [66–68], and recommendations for physical activity in cancer patients are well established [64,69]. The patient may be able to control their lifestyle factors irrespective of any medical services being offered. Such factors can be incorporated into RWE research, potentially helping to engage and motivate the population of patients.

Empowered patients typically also have a better understanding of how to navigate the healthcare system and they tend to be more engaged with their treatment plan. Patient empowerment has been associated with a range of benefits, including improved clinical outcomes, increased patient satisfaction with care, and improved adherence to self-management of treatment [70]. Accurate understanding of the safety and effectiveness of the available treatment options is also needed to ensure that treatment decisions are aligned with the patient's preferences [71]. The role that an empowered and motivated patient can play in improving their own outcomes should not be underestimated, and this can include participation in clinical trials and RWE research. Clinicians can help in the empowerment process by directing patients toward the right educational materials and by including them when making treatment decisions [72]. Resources such as the 'MyDialogue' brochures have been written by patients and clinicians with the aim of improving communication between patients and healthcare professionals. The patient's carer(s) plays a significant role in treatment decisions, necessitating a three-way dialog between clinicians, patients and their carers; mutual respect for each person's knowledge is required throughout.

Patients are likely to appreciate support from their oncologist in gaining knowledge of their disease, although it is also important for clinicians to recognize that a significant minority of patients prefer not to seek increased knowledge. In practice, patient–clinician communication can be less than optimal and healthcare professionals are not always perceived to consider the patient's voice as a high priority [63,73]. This is driven partly by time pressure and also by historical tendency for clinicians to take a paternalistic approach to cancer care that focuses on the treatment options and clinical end points rather than the patient's perspective [74]. The importance of providing information in straightforward, easy-to-understand language has also been highlighted [75]. Recently, a shift toward patient engagement has seen patients play an increasingly active role in their treatment plan [60]. Clinician–patient relationships are evolving, with many having a greater focus on shared decision-making [46,76]. Patients have the right to knowledge, to be responsible for their own care where they wish to be, and to play a part in the decision-making process [46,60,70]. They should also be encouraged to participate in clinical trials or RWE research whenever the opportunity arises. Increased knowledge can enable patients to feel empowered to help improve their own care, and the overall future treatment of their disease.

It is important to acknowledge that some patients may prefer not to participate actively in the decisions regarding their treatment. In one study, 29% of cancer patients expressed a preference for their clinician to have control over treatment decisions, and this perspective was more common among older individuals or those with high distress levels [77]. A systematic review including 31 studies reported that 27% of cancer patients prefer to be passive in the decisions regarding their treatment [78]. The complexity of cancer treatment and perception of the clinician as the expert were suggested as possible reasons for preferring to be passive. The choice to be passive in the decision-making process should be respected on equal terms with the decision to pursue empowerment. At the same time, clinicians should explain the benefits of shared decision-making and help ensure patients receive support for reducing potential barriers to participation (e.g., reducing the level of distress through counseling and ensuring access to educational resources).

Conclusion

By providing evidence and insights into patient experiences without bias, RWE research is a valuable resource that complements RCT data. The success of RWE research depends upon the active engagement of patients and their carers. Alongside education regarding the disease and its treatment, participation in RWE research may help empower patients with mCRC and other cancers to influence decisions concerning their own treatment. There is potential for increased patient engagement to help improve overall management of the disease. To increase the numbers of patients and carers participating in RWE studies, improved understanding and awareness of RWE research is needed, and clinicians are well placed to encourage this process. Engaging patients and carers throughout disease management is key to unlocking the potential for RWE to improve outcomes in mCRC. We have seen patients already beginning to respond and become empowered through their focus on RWE research. It is now imperative that policy makers consider the value of this in their assessment and inclusion of treatments.

Future perspective

Over the next 5–10 years, our aim should be to normalize patient participation in RWE research. Combined with the implementation of patient-reported experience measures, which evaluate the patients' perceptions of their experience while receiving care, this may help to optimize treatment decisions from the patient's perspective, potentially improving clinical outcomes. Coordinated efforts across healthcare systems are needed to implement practical steps to achieve this aim. Overall survival figures remain poor among patients with mCRC – RWE research could be a means of improving them.

Executive summary

Background & rationale

- Randomized controlled trials have been considered the 'gold standard' of clinical research, but usually include only a limited range of patients based on such factors as age, stage and type of cancer, and geographical location, with restricted treatment options.
- Real-world evidence (RWE) research is less restrictive and provides valuable insights into the disease burden, treatment patterns and patient perspectives in everyday clinical practice.
- Few RWE studies have been performed in patients with metastatic colorectal cancer. PROMETCO (a real-world evidence prospective cohort study in the management of metastatic colorectal cancer: a clinical and patient perspective) is an important example of an ongoing study focusing on PROs.

Patient involvement in RWE research design & delivery

- Patients and their carers can be encouraged to play an active role throughout the research process, ensuring that studies are well designed and successfully executed.

Patient participation in RWE studies

- By participating in studies, patients may become more knowledgeable and interested in their disease, increasing the likelihood that they will receive the best treatment.

Role of the clinician

- Ideally, clinicians should help patients and their carers to learn about their disease and encourage them to participate in RWE research.

Future perspective

- Increased participation in RWE research may help improve quality of life and treatment outcomes in patients with metastatic colorectal cancer.

Author contributions

All authors contributed to the conception, design, drafting, and revising of the paper, and agree to be accountable for all aspects of the work.

Financial & competing interests disclosure

B Moss, EA Goodall, Z Maravic, M Moss, S Rowley, C Sarrauste and P Wheatstone have no conflicts of interest. FM Marti reports being a speaker and receiving advisory honoraria from Servier. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

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Papers of special note have been highlighted as: • of interest; •• of considerable interest

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•• **Outlines the design and aims of the international, real-world PROMETCO study, in which clinical data and patient-reported outcomes (PRO) are collected from patients with metastatic colorectal cancer who have progressed twice with available therapies and are initiating subsequent therapy.**

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