UNDERSTANDING PRAGMATIC OUTCOME MEASURES IN ONCOLOGY

Building the roadmap to outcomes-based cancer care

SEPTEMBER 2018

P. Poortmans, I. Banks, J. Levy, K. Meier, R. Price, L. Wiinberg, A. Woolmore, D. Kerr

collaboration for oncology data in europe

ECCO EUROPEAN CANCER ORGANISATION

ABOUT THE AUTHORS

This project was jointly conducted by the European CanCer Organisation (ECCO) and the Collaboration for Oncology Data in Europe (CODE)

European CanCer Organisation (ECCO)

DR. IAN BANKS, Chair, ECCO Patient Advisory Committee (ECCO-PAC); European Men's Health Forum (EMHF)

Ian Banks is the President of the European Mens Health Forum and Past-President the England & Wales Men's Health Forum and Past Vice-President of the International Society of Mens Health.

He is Chair of the ECCO Patient Advisory Committee (ECCO PAC) and Co-Chair of the ECCO 2018 European Cancer Summit.

PROFESSOR KLAUS MEIER, ECCO Board Member; CEO of the Department for Clinical and Hospital Pharmacy, HKK Soltau, Lower Saxony

Klaus Meier is Chief Pharmacist at the Department for Clinical and Hospital Pharmacy at Heidekreis-Klinikum GmbH in Soltau, Germany. He holds a master of theology and pedagogics (1975), is a pharmacist since 1981, obtained his clinical certification in 1989 and the oncology certification in 1995.

In 2009 he became a fellow of the EACS (European Academy for Cancer Sciences) and is acting as Vice-director at IFAHS (Institute for applied healthcare sciences). In 1998–2000 he was President of the International Society of Oncology Pharmacy Practitioners (ISOPP). He has served on the Board of Directors of the European CanCer Organisation (ECCO) for several terms (2008-2011 and 2016-2019), and is currently President of the German Society for Oncology Pharmacy (DGOP) and of the European Society for Oncology Pharmacy (ESOP).

Klaus Meier is Chair of the ECCO Oncopolicy Committee (2018-2019).

PROFESSOR PHILIP POORTMANS, President of ECCO; Head of Department of Radiation Oncology at Institut Curie - Ensemble Hospitalier

After completing his medical studies at the University of Antwerp in 1986, Professor Philip Poortmans was trained as a radiation oncologist at the Middelheim and Vincentius Hospitals in Antwerp. In 2017, he was appointed head of department at the Institute Curie, Paris.

He is the Past-President of European Society for Radiotherapy and Oncology (ESTRO).

In 2016 and 2017, Professor Poortmans served as Chair of the ECCO Oncopolicy Committee and after the elections of the ECCO President 2018-2019, Poortmans took up the role as President of the European CanCer Organisation (ECCO).

Philip Poortmans is Co-Chair of the ECCO 2018 European Cancer Summit.

RICHARD PRICE, ECCO EU Policy Affairs Manager

Richard Price is the EU Affairs Policy Manager at the European CanCer Organisation (ECCO). Prior to this he was Policy and Advocacy Officer at the European Association of Hospital Pharmacists (EAHP) 2012-2017, and Policy Advisor at the Pharmaceutical Society of Northern Ireland 2007-2012.

Collaboration for Oncology Data in Europe (CODE)

PROFESSOR DAVID KERR, Head of Oncology at the University of Oxford and Chair of CODE's Clinical and Analytical Steering Committee

Professor David Kerr, CBE. is a Professor of Cancer Medicine at the University of Oxford, England. He focuses on innovative approaches to cancer treatment, including novel biomarkers and inhibitors of key chemical pathways, and his research has contributed to saving thousands of lives over the past 20 years.

JULIA LEVY, CODE External Engagement Lead

Julia Levy is the External Engagement Lead for CODE across Europe, coordinating with key external stakeholders. She has extensive health strategy and communications experience gained in life sciences including oncology-related products, e-health and the international public sector, as well as European public policy work from time in Brussels and running a health-related think tank.

LINDA WIINBERG, CODE Analyst

Linda Wiinberg is an Analyst for CODE. She holds a Master of Science in Public Health with focus in Health Economics from the London School of Hygiene and Tropical Medicine. She has experience in research within oncology drug delivery and clinical research in endocrinology. Her interest is in improving access to cancer medicines through improved financial sustainability.

DR ASHLEY WOOLMORE, CODE Lead and Senior Vice President, Real World and Analytics Solutions Global Team, Head of European Data and Evidence Networks, IQVIA

Ashley Woolmore is the Initiative Lead for CODE. His driving interest is the development of systematic approaches to realise the potential of real-world data for transforming healthcare delivery and treatment outcomes. He is particularly focussed on cancer and its treatment, real-world data and evidence policy topics and innovative approaches to build and enable collaborative networks. Over the last 15 years, he has led work on the creation and analysis of large datasets to drive insight into oncology and cancer care, survivorship, the impact of multiple morbidities, palliative care, and chronic disease management.

Prior to joining IMS Health (now IQVIA) in 2013, Ashley worked in strategy consulting and was a Partner firstly at Monitor Group, then Deloitte. At the beginning of his career, he trained and practised as a Clinical Psychologist before moving into hospital management and service development within the UK NHS.

For more information about the research, please contact Richard Price, EU Policy Affairs Manager, ECCO, at Richard.Price@ecco-org.eu or Julia Levy, External Engagement Lead, CODE at Julia.Levy@iqvia.com

CONTENTS

FOREWORD

The topic of outcomes measurement is central to ECCO's mission to "improve outcomes for cancer patients through the delivery of higher quality cancer care." The Collaboration for Oncology Data in Europe (CODE) is also highly interested in this topic as part of its commitment to support the establishment of the Oncology Data Network to help inform patient care. Having identified this shared interest, the two organisations embarked on a joint initiative to explore cancer outcomes measurement. The goal was set to examine the novel concept of pragmatic outcomes measurement. The key question being "is there broad agreement across clinicians, patients and patient representatives on the set of real world metrics that provide valuable information for both patients and clinicians, but which can be measured efficiently and consistently at scale with existing clinical systems?".

This research project has explored the value of different outcome metrics, by assessing the relative insight that can be derived, whilst being mindful of the feasibility, complexity and challenges associated with accessing the required information. It also aims to help inform our understanding of the drivers and challenges of information gathering required for outcomes-based health systems and recognises what could be achieved, already today, with existing real-world data from routine clinical practice information systems.

We see this project as the first step in an ongoing collaboration bringing together multiple stakeholders in the cancer community to advance toward the goal of systematic, large-scale and routine use of outcomes measurement to make a real difference to the lives of people with cancer. We welcome feedback and look forward to establishing a broader dialogue and engaging with policy makers to identify ways of bringing outcomes measurement efficiently into daily practice across Europe.

PROFESSOR PHILIP POORTMANS,
President of ECCO and Head of Department of Radiation Oncology at Institut Curie - Ensemble Hospitalier

PROFESSOR DAVID KERR,
Head of Oncology at the University of Oxford and Chair of CODE's Clinical and Analytical Steering Committee

PROFESSOR PHILIP POORTMANS, President of ECCO and Head of Department of Radiation Oncology at Institut Curie - Ensemble Hospitalier	*"Outcomes measurement is seen by many within the oncology community as an exciting opportunity to have a more patient-centric approach to care, and to allow healthcare providers to make informed decisions based on patient current needs and historical research. However, we need to now move the discussion beyond simple expression of aspiration and into the practicalities of how. The results of this research exercise provide excellent advice to decision-makers about the next steps in the journey towards comprehensive outcomes measurement."*
PROFESSOR DAVID KERR, Head of Oncology at the University of Oxford and Chair of CODE's Clinical and Analytical Steering Committee	*"This research provides clarity about immediate opportunities to enable the European cancer community to improve understanding of the value of treatment interventions. Harnessing the insights that are available to us today will enable us to better inform decisions and contribute to the advancement of cancer care. Pragmatic outcome measures are an actionable immediate first step towards widespread collection and use of comprehensive outcomes measurement in the European oncology community. The recommendations in this report also set out a clear roadmap where increased focus and investment in the near term will allow us to gain further insight and work together towards a comprehensive approach over the longer term."*

We would also like to thank all those who have contributed to the report with their time, valuable insight and suggestions. This project would not have been possible without you. In particular we would like to thank:

DR. MATTI AAPRO	Editor-in-Chief of Critical Reviews in Oncology/Haematology (CROH); Member of the Board of Directors of the Genolier Cancer Centre; Executive Board Member of SIOG
DR. BILL ALLUM	Consultant Upper GI Surgeon at the Royal Marsden Hospital NHS Trust, United Kingdom; Chairman of EURECCA Upper GI Cancer; Member of ESSO
PROFESSOR DIRK ARNOLD	Chief Physician for Haematology and Internal Oncology, Asklepios Klinik Altona; Member of the CODE Clinical and Analytical Steering Committee
PROFESSOR RICCARDO AUDISIO	Past President of the European Society of Surgical Oncology (ESSO); Member of the ECCO Oncopolicy Committee
DR. ANNE MARIE BAIRD	Research Fellow based at St. James's Hospital, and holds Visiting Research Fellow status with the University of Dublin, Trinity College and Queensland University of Technology; Member of ECCO Patient Advocacy Committee
PROFESSOR JEAN-YVES BLAY	Director of the European Reference Network on Adult Cancers – ERN EURACAN (Solid Tumours), Director General of the Centre Léon Bérard, the comprehensive cancer centre of Lyon and the Rhône-Alpes region, and an oncologist, researcher and medical oncologist professor at the University Claude Bernard, France; Member of the CODE Clinical and Analytical Steering Committee
PROFESSOR CHRISTIAN BUSKE	Medical Director at the Comprehensive Cancer Centre and the Institute of Experimental Cancer Research at the University of Ulm, and an attending Physician and Professor of Medicine at the University Hospital Ulm, Germany; Member of the CODE Clinical and Analytical Steering Committee
PROFESSOR ALFREDO CARRATO	Director of Medical Oncology and the Institute of Health Research at the Ramon y Cajal University Hospital, and Professor of Medical Oncology at Alcala University, Spain; Member of the CODE Clinical and Analytical Steering Committee
DR. ANDREAS CHARALAMBOUS	Assistant Professor in Oncology and Palliative Nursing Care at the Cyprus University of Technology, Department of Nursing Science and Associate Professor at the University of Turku, Finland, Department of Nursing Science; President-Elect of the European Oncology Nursing Society (EONS) and Co-Chair of its Research Working Group; Member of the ECCO OncoPolicy Committee
MR. JAN GEISSLER	Vice President and Managing Director, Leukaemia Patient Advocates Foundation; Founder and MD of Patvocates; Director, European Patients' Academy on Therapeutic Innovation (EUPATI)/Chair, Leukaemie-Online / LeukaNET e.V; Member of the ECCO Patient Advisory Committee
PROFESSOR WINALD GERRITSEN	Professor of Tumour Immunotherapy at Radboud University Medical Centre Nijmegen. Also serves as an Adjunct Professor at John Hopkins University, and is a member of the Royal Holland Society of Sciences and Humanities; Member of the CODE Clinical and Analytical Steering Committee
MR. GEOFFREY HENNING	Director of Policy of EuropaColon; Member of the ECCO PAC
DR. MARGARET HUTKA	Medical Oncologist and Consultant at St George´s University Hospital; President of the Flims Alumni Club; Member of the ECCO Oncopolicy Committee

MS. TEODORA KOLAROVA	Executive Director of the International Neuroendocrine Cancer Alliance; Member of ECCO Patient Advisory Committee
DR. SARAH JAYNE LIPTROTT	Research Nurse/Infermiera di Ricerca, Divisione di Ematoncologia, IEO Istituto Europeo di Oncologia; Member of the ECCO Patient Advisory Committee
DR. LYDIA MAKAROFF	Director of the European Cancer Patient Coalition; Board member of Pancreatic Cancer Europe and an Associate Researcher at the Translational Immunology laboratory at the University of Leuven
PROFESSOR PETER NAREDI	Professor of Surgery and Chairman of the Department of Surgery at the Sahlgrenska Academy, University of Gothenburg; Member of ECCO Board of Directors
DR. JOHN O'DONNELL	Vice President, Worldwide Health Economics and Outcomes Research at Bristol-Myers Squibb; Adjunct Professor of Health Policy and Management at the Gillings School of Global Public Health; Adjunct Professor at the University of North Carolina at Chapel Hill
PROFESSOR MARC PEETERS	Head of the Oncology Department at Antwerp University Hospital and the Multidisciplinary Oncology Centre (MOCA). He is also Digestive Oncology Co-ordinator of the oncology care programme at University Hospital Ghent (UZ Gent), and Chairman of the Belgian Centre for Oncology; Member of the CODE Clinical and Analytical Steering Committee
MS. MARIKA PORREY	President of the Thyroid Cancer Alliance; Member of the ECCO Patient Advisory Committee
PROFESSOR CARLO RICCARDO ROSSI	Full Professor of Surgery, University of Padova; Director, Surgical Oncology Unit, Veneto Institute of Oncology; Chair EURECCA Melanoma
PROFESSOR RICCARDO SOFFIETTI	Professor of Neurology and Neuro-Oncology at the University of Turin/ Founding Member and Member of the Steering Committee of the European Association for Neuro-Oncology; Member of the EANO Executive Board
PROFESSOR HENDRIK VAN POPPEL	Chairman of the Scientific Committee of Europa Uomo/Faculty Member of the European Society of Medical Oncology (ESMO); EAU Adjunct Secretary General in charge of Education; Member of the ECCO Oncopolicy Committee
PROFESSOR GILLES VASSAL	Head of Clinical Research at Institut Gustave Roussy/ITCC chair/Professor of Oncology in University Paris-Sud ; Board Member of SIOPE; Member of the ECCO Oncopolicy Committee

EXECUTIVE SUMMARY

The measurement of outcomes is increasingly important for all oncology stakeholders. Initiatives already exist that signal the need to improve outcomes measurement and their use to improve care delivery, notably the International Consortium for Outcomes Measurement (ICHOM), the Farr Institute, and the Organisation for Economic Co-operation and Development (OECD).

Key cultural and socio-economic factors leading to this increasing interest in outcomes measurement include the increase in overall life expectancy. In addition, cancer patients are living longer with their disease. As cancer increasingly transitions from being a terminal to a chronic disease, the complexity of care will increase. Many new, innovative oncology treatments are in development or being adopted into clinical practice. The cost of these innovative therapies, coupled with the evolving more chronic status of the disease, creates financial sustainability concerns. In addition, variation is known to exist in both cancer treatment and outcomes across countries.

Advances in medical and health information technology capabilities mean healthcare systems are now better positioned to capture information, compute measures and utilise outcomes measurement for quality of care improvement. However, despite the positive momentum behind outcomes measurement, there are clearly challenges to overcome to achieve widespread adoption and to embed systematic outcomes measurement into routine care. These will include a lack of time, resources and expertise needed to implement health information systems. Differences in how health data are recorded e.g. if the data are recorded in a structured or unstructured (free text format), and in the use of health information systems creates variation and limits the comparability of the metrics that are computed. The goal of achieving high quality outcomes measurement may require a step-wise approach, which builds in complexity and sophistication over time in a realistic and planned manner.

ECCO and CODE brought together insights from 26 interviews with stakeholders from organisations across the European cancer community including patient representatives, a radiation oncologist, surgeons, oncology pharmacists, oncology nurses, a neuro-oncologist, a paediatric oncologist, and medical oncologists.

Key findings from the research include:

- There was consensus around the value that systematic outcomes measurement at scale can provide to all involved in cancer care
- Challenges that limit the systematic uptake of outcomes measurement include:
  - A lack of resources and current inability to capture, collate and analyse outcome measures with existing technologies
  - A lack of interoperability between health technology systems was also noted
- Alignment does exist on the relative value to patients and clinicians of real world metrics and these metrics differ substantially in the complexity and sophistication of collection
- Pragmatic outcome measures are defined as 'real world metrics' that provide meaningful insights to clinical teams but importantly they can be collected systematically, efficiently and continuously today

- The identified set of pragmatic outcome measures includes:
  - Treatment related measures and measures as part of clinical evaluation
  - Pragmatic outcome measures were considered as relevant surrogate endpoints for more complex metrics.
- The need to explore certain metrics that are currently perceived as having different value to patients and to clinicians; and to consider distinctly the applications for either direct clinical decision making, or the collation/gathering of data across teams to collectively understand the value of interventions

Based on the level of complexity of the various metrics, a three step approach has been proposed as a roadmap to comprehensive outcomes measurement in cancer care:

Step 1 – Immediately harness the outcome measures which are achievable today i.e. those with a low level of complexity which can be most easily collected today, identified as Pragmatic Outcome Measures.

Step 2 – Focus resources and attention on overcoming barriers to large scale capture of those measures identified as having medium complexity (e.g. through investment in the framework behind outcomes measurement, governance and implementation).

- Patient Reported Data should become standard practice an no longer only standard practice for interventional trials
- 'Date of Death' should also be integrated into relevant infrastructure and databases

Step 3 – Continue to harness the clinical value of those measures associated with the highest level of complexity in informing individual patient care and work towards their large scale use over the longer term. This will require investment in the standardisation of metrics and access/integration/collation of the data. In the diagram, these metrics are those in the upper right hand corner.

- Tools such as Artificial Intelligence and Machine Learning will be powerful enablers to help extract value from the dataset

As a consequence, there is a recognition that a call for collective action is required so that efforts to capture outcome measures are properly resourced and prioritised.

In addition, there is a need to develop and embed outcomes measurement into European-level 'essential requirements'[a].

[a]The ECCO Essential Requirements for Quality Cancer Care (ERQCC) are checklists and explanations of organisation and actions that are necessary to give high-quality care to patients who have a specific type of cancer.

INTRODUCTION

The measurement of outcomes is becoming increasingly important for all stakeholders within the oncology community

MICHAEL E. PORTER, What is Value in Health?, 2010[1]

"Achieving good patient health outcomes is the fundamental purpose of health care. Measuring, reporting, and comparing outcomes is perhaps the most important step toward unlocking rapid outcome improvement and making good choices about reducing costs."

Recently, a number of initiatives focused on improving outcomes measurement have been launched to better understand how the delivery of care can be improved. The International Consortium for Outcomes Measurement (ICHOM) is developing disease specific standardised sets of outcome measures which capture outcomes meaningful to patients.[2] The Farr Institute have also been working on building collaborative frameworks to increase outcomes measurement and the collection of health data to improve health outcomes in a number of different therapeutic areas.[3] One such framework is the Innovative Healthcare Delivery Programme developed in partnership with NHS Scotland to improve cancer care.[3] The Organisation for Economic Co-Operation and Development (OECD), is also collaborating with a number of its member countries to identify metrics that can be used to improve the quality and performance of their health systems and influence health policies.[4] However, despite the growing realisation of the importance of outcomes measurement for value-based health care, systematic implementation of outcomes measurement is yet to occur in routine clinical practice.

There are a number of cultural and socio-economic factors leading to this increasing interest in outcomes measurement within cancer care

Life expectancy has risen by almost a decade over the last 50 years and the World Health Organisation (WHO) predicts that by 2050, 35 percent of Europeans will be over the age of 60, up from only 17 percent in 2000.[5] With the increasing age of the population, the incidence of cancer is rising. Yet cancer is no longer viewed as a terminal illness as innovations in and improved access to healthcare are helping patients to live longer.[6–8] As patients are living longer with cancer, it is now emerging as a chronic disease increasingly found along with a number of associated comorbidities. This creates greater complexity in the care required to treat these patients.[9] The rising sophistication and complexity of care offers multiple options for treatment but also different consequences in terms of impact on survival, quality of life and cost to the healthcare system adding to the challenges of applying evidence based treatment decisions.

Meanwhile, new oncology medicines, including in innovative areas such as biological medicine and immunotherapy, are coming to market at pace. This, coupled with the increased rates of prevalence and longer treatment periods are driving up the costs of cancer care.[10] IQVIA's 2018 Annual Oncology report forecast that in the period from 2018-2022, the EU5's total spend on Oncology will increase by 10-13% to $40-45 billion (€31-35 billion). Already, one in five European National Cancer Control Plans cannot be implemented due to financial barriers.[8]

To help ensure timely access to new innovative medicines in areas of high unmet need, the European Medicines Agency (EMA) and regulatory agencies have allowed accelerated access to many new medicines. Accelerated access is granted through earlier, more flexible, approval of the medicines using less mature evidence, e.g. using preliminary or interim results from randomized controlled trials (RCTs).[11] This places a greater need to determine the value of a therapy using post-approval data to capture use and effectiveness once it is in clinical use.

Furthermore, in their 2016 report, EFPIA and Healthier Future reported a large variation in healthcare systems within and across different regions and countries.[7] There are significant disparities in access to anti-cancer medicines, radiotherapy usage (30% of cancer patients do not have access to radiotherapy when recommended by clinical guidelines), and surgical procedures.[8] The varying provision of, and adherence to cancer treatment, creates significant variation in measures of survival e.g. across OECD countries there is a four-fold variation in 5-year survival for patients with lung cancer.[7]

MICHAEL PORTER, Evidence-Based Medicine and the Changing Nature of Healthcare, 2008.[12]

"If outcomes were universally measured, it would quickly become clear that the value of care is highly variable, even for patients with access"

The vision of addressing unwarranted variation in health outcomes has highlighted a need to measure outcomes efficiently and at scale in order to identify where variation exists, understand the root causes of the variation, and finally put in place remediating actions.

Value-based healthcare (VBHC) is a healthcare delivery model where payment for care to providers is dependent on the achieved health outcomes, as opposed to more traditional models of payment per volume of drugs/treatment provided.[13] VBHC can help to alleviate these pressures by allowing us to better understand the impact (and value) of treatments and thereby where to best focus resources, which ultimately could reduce the variation in the provision of care and in the health outcomes themsleves.[14,15] Furthermore it can help to improve the quality of healthcare provided and reduce inefficiencies.[6,7] Moves toward the development and implementation of value-based healthcare for cancer care would be facilitated if outcomes of treatment could be captured efficiently from information available during routine clinical care, i.e. embedded into practice and not a supplementary burden on clinical teams.

Outcomes measurement is also seen by many within the Oncology community as an opportunity to enable a more patient-centric approach to care and allow healthcare providers to make informed decisions based on patient needs and preferences.[6,7,14,16] In a round table discussion hosted by the

New England Journal of Medicine in 2017 on addressing the challenges of involving patients in the delivery of healthcare, it was agreed that both patients and clinicians want to better understand the impact of care on daily life and further involve patients in treatment decisions.[17] Routine measurement of patient reported data (Patient Reported Outcome Measures (PROMs[b]) and Patient Reported Experience Measures (PREMs[c])) can enable the assessment of the impact of treatment and care on the patient's daily life.[18] In a study exploring the use of a web-based tool to capture patient (self-) evaluated symptoms in a cohort of lung cancer patients, it was found that the tool significantly improved patient survival in comparison to routine imaging by enabling the earlier detection of cancer relapse and on average detected cancer 5 weeks earlier than routine imaging follow-ups.[19] Furthermore, systematic outcomes measurement can make more information available to patients, thereby informing patient choice, which may empower patients to better participate in their treatment decisions.[6,16,20,21] This may also facilitate the optimisation of cancer care to specific patients and patient profile types.[7,22]

Ultimately, the systematic measurement of outcomes enables the health system to better understand the impact of the cancer care being provided, and the efficiency with which this care is being provided. It can be used to answer key questions such as: are we delivering the care that patients want? Which treatment is right for these groups of patients? And, how can we reduce inefficiency to alleviate some of the burden on our clinical teams and health systems? This burden could be reduced by having an agreed set of outcome measures that can be routinely captured or computed about routine care delivery and spares clinical teams from more burdensome data collection.

[b] PROMs measure the patient perception of their health state.
[c] PREMs measure the patient satisfaction and experience of care.

In addition to societal and cultural changes, advancing technological capabilities mean healthcare systems are now better positioned to capture and utilise outcome measures

Recent advances in medical and health information technologies enable the healthcare community to improve data capture and support the use of real world data. These advances are making systematic and widespread outcomes measurement more accessible.

There has been a shift from paper-based medical records to Electronic Health Records (EHR), offering the potential for more efficient data collection, which in turn could increase the transparency of health outcomes and data interoperability e.g. collating information from different sources allowing multi-disciplinary care teams to access integrated patient records for treatment decision-making.[6] Improvements in health information technology also provide opportunities to integrate other sources of data such as patient-reported data into the patient's health record by using tools to automate data extraction and integration.[2]

Simultaneously, this accessibility of health outcomes data has created a space for Real World Data (RWD) to be used to better understand the behaviour of anti-cancer medicines and other treatments in the real world, such as radiation oncology and surgery, beyond clinical trials.[23] As such, RWD is increasingly being used to support effectiveness studies, clinical trial design, the monitoring and regulation of drug safety, and the development of clinical practice guidelines.[23,24]

However, despite the positive momentum behind outcomes measurement, there are a number of challenges to overcome in order for it to gain widespread adoption

Time and resources, including expertise, are needed to implement health information systems capable of integrating multiple aspects of care and the manual reporting of outcome measures. As a result, limited resources are creating significant differences in the quantity and quality of data recorded in health systems.[25] There is also a need to build in interoperability and universality in health information systems to enable different systems to communicate. As a result, we have seen 'study based' approaches, instead of system-wide approaches. The cost of implementation and maintenance (including clinician time) of outcomes measurement should also be considered in the adoption of more widespread and systematic outcomes measurement.

For example, in a study which explored the use of aggregated Patient Reported Outcomes to improve healthcare, Greenhalgh et al. found that PROMs and other patient reported data collected through paper surveys or questionnaires often require manual data entry by the healthcare team. This places an administrative burden on healthcare professionals, which can result in a time lag between the completion of the survey and when the results become accessible and used to inform decision making.[26]

This variation in the availability of time and resources to capture health outcomes and the differences in the outcome measures selected, impacts the quality of the data and how the data can be used to inform decision making.[26,21,25]

Furthermore, there are limited standards and guidelines on the target outcomes for measurement which creates variation in the definition of outcomes and in data collection.[7,27] This is exacerbated by the fragmentation seen in healthcare, where care pathways, treatment choices and the use of outcomes in budget systems vary between hospitals and across countries.[7] It is, therefore, important to maintain a consistent definition of health outcome measures, identify a set of outcomes that can be easily collected, and ensure the language surrounding outcome measures is understandable, universally agreed upon and can be used systematically in routine practice.[2,7,27]

The European CanCer Organisation (ECCO) is an umbrella organisation of 24 member organisations representing professionals delivering care to patients across the cancer care continuum. ECCO's vision is "to improve outcomes for all cancer patients in Europe through multidisciplinarity" by providing a platform for European cancer stakeholders to address policy issues to address variation in cancer outcomes, and to promote the delivery of high quality cancer care.

As part of ECCO's strategy for delivering this mission, in 2016 it established the Essential Requirements for Quality Cancer Care (ERQCC) programme. The ERQCC papers are organisational specifications, not clinical guidelines, and are intended to give oncology teams, patients, policymakers and managers an overview of the elements needed in any healthcare system to provide high-quality care throughout the patient journey. References are made to clinical guidelines and other resources where appropriate, and the focus is on care in Europe. As part of these requirements, ECCO recommends oncology teams to collect data pertaining to clinical outcomes, process outcomes, and patient reported outcomes (PROs). Additionally, key outcome measures should be collected systematically across Europe.[28]

In 2017, ECCO published a consensus paper representing the combined views of its members on the topic of Access to Innovation[d]. Amongst the calls within the paper are for decisions on innovation, and accompanying investment of resource therein, to be guided by high-quality real-world data, including outcomes relevant to the patient and actual costs of care.

Most recently, ECCO put forth a principal resolution for the ECCO 2018 European Cancer Summit for Quality Cancer Care (Measurement[e]). This resolution states: "By 2023 an agreed set of core standards and evidence-based indicators (based on processes and patient outcomes) to measure the quality of all cancer services in European countries should be in place."

The Collaboration for Oncology Data in Europe (CODE) aims to expand the knowledge of anti-cancer medicines use, by supporting the development of a dedicated Oncology Data Network (ODN). The data collated will enable the oncology community to derive greater value from anti-cancer medicines for patients. The ODN has been conceived to be able to aggregate data for all forms of cancer, in all patients at Europe's cancer treatment centres, in near real-time, on how anti-cancer medicines are being used in today's clinical practice, in which patient groups and in which combinations and sequences.

The members of CODE believe that, only by understanding how anti-cancer medicines are used will it be possible to create the necessary foundation for new approaches to access of innovative therapies, helping to connect treatment innovation to patient benefit and broaden the opportunity for individual patients to receive the therapies that are appropriate for them.

CODE has been established to achieve two parallel and equally important objectives. The infrastructure of the ODN flexibly provides reliable, up-to-date information on how anti-cancer medicines are used in clinical practice, which can be used to:

- Address today's information gap by providing timely real-world insights on anti-cancer medicine use back to the healthcare system;
- Enable flexible payment agreements, to address the challenges of financial sustainability which may improve access to innovation.

In line with the vision and activities of ECCO, and identified synergy of interest, this collaborative research project set out to identify a set of pragmatic outcomes that have value to clinical teams and patients, but which can be derived from readily available real-world data collected as part of routine care. The ECCO-CODE research project was jointly developed through open conversations and dialogue with oversight by both parties' advisory boards: the ECCO OncoPolicy Committee Executive and the CODE Clinical and Analytical Steering Committee (CASC), whereby areas of mutual research interest were identified, and was supported via grant funding from IQVIA, which is leading the CODE initiative, to ECCO.

[d] https://www.ecco-org.eu/Policy/Policy-Priorities/Access-to-Innovation
[e] https://www.eccosummit.eu/Resolutions/Quality-Cancer-Care

The aim of this research was to provide an initial exploration of pragmatic outcomes measurement in oncology and identify areas for further research

The primary goals of this project were to:

1. Identify a set of outcome measures which can be easily captured and analysed using today's available infrastructure whilst offering clinical value to the oncology community and relevance for patients
2. Provide a set of recommendations to accelerate the uptake of pragmatic outcomes measurement as part of a step on the journey to implementing value-based healthcare in cancer care
3. Better understand the benefits of outcomes measurement in the context of cancer care
4. Identify the challenges with realising broader adoption of outcomes measurement and recommend ways in which these could be overcome.

APPROACH

To explore the topic of pragmatic outcomes measurement, 26 semi-structured interviews were conducted with a range of stakeholders from the European oncology community identified by the European CanCer Organisation (ECCO) and the Clinical and Analytical Steering Committee (CASC) of the Collaboration for Oncology Data in Europe (CODE). These were made up of: 5 patient representatives, 9 medical oncologists, 1 neuro-oncologist, 1 paediatric oncologist, 1 oncology pharmacist, 1 radiation oncologist, 5 surgeons, 1 nurse, 1 nurse/patient representaive and 1 policy maker.

The interviews combined quantitative and qualitative questions. Details of the specific questions are available on request to one of the authors.

Each interview explored the following topics:

- The impact routine outcomes measurement will have on their organisation or profession
- The accelerators and barriers to widespread outcomes measurement within cancer care in Europe
- Specific parameters, value and complexity, of a list of outcomes measurements in cancer care
  - The value of each measure in regards to clinical level of insight and meaningfulness to patients
  - The complexity and cost to capturing these outcome measures
- Recommendations to policy makers to encourage the systematic and widespread measurement of outcomes

The quantitative analysis consisted of a simple analysis to describe the responses from the group of participants and the identification of particularly heterogeneous findings. The analysis of the qualitative components of the interviews were conducted by clustering key comments into themes and the collection of quotes to illustrate particular points interviewees wanted to highlight.

RESULTS

There was agreement across stakeholder groups on the value that efficient and systematic outcomes measurement could provide to all involved in cancer care

All of the surveyed interviewees agreed that the systematic measurement of outcomes will provide significant value to patients and the wider oncology community. Despite interviewees coming from a variety of professional backgrounds, there were no major differences in the types of benefit they predicted outcomes measurement would generate. The most commonly cited benefits included:

Category of benefit	Specific Feedback
Increased ability to understand the effectiveness of current treatment patterns and thereby understand which treatments provide the greatest value to patients	PROF. PHILIP POORTMANS (Radiation Oncologist) *"We need these measures to do our job properly… As healthcare professionals, we cannot decide for our patients what they want to get from treatment, only they can truly know what they want."* DR. LYDIA MAKAROFF (Patient Representative) *"Outcomes measurement is very important… We can't change what we can't measure."* INTERVIEWEE (Paediatric Oncologist) *"For me, the outcomes are very much how to improve by better knowing what is happening and better monitoring the effects of what we are proposing."* PROF. RICCARDO AUDISIO (Surgeon) *"For me [outcomes measurement in a real world setting] is fundamental and crucial."*
Increased ability to understand and address variations in practice (within and across countries)	PROF. PETER NAREDI (Surgeon) *"The less you measure, the larger the variation."* PROF. MARC PEETERS (Medical Oncologist) *"Now there is more focus on centralising/ standardising surgery and the reason is to reduce variations in outcomes."* PROF. ALFREDO CARRATO (Medical Oncologist) *"If you want to measure variation across countries, you have to start measuring among regions and hospitals."*

Category of benefit	Specific Feedback
Providing a data set that will facilitate value-based healthcare and more efficient pricing of anti-cancer medicines	INTERVIEWEE (Paediatric Oncologist) *"These outcome measures, I think are absolutely crucial regarding how society affords the cost of care for each individual patient and, clearly, at the moment, the health authority systems lack the tools to evaluate best how to do this. Also, to evaluate and monitor, and I think the big problem, at the moment, is at some point when there is a new treatment there is no data to really measure in real-life."* DR. LYDIA MAKAROFF (Patient Representative) *"Reducing waste and improving efficiency is absolutely vital to healthcare, and will be underpinned by outcomes measurement… the systematic capture of these measures will enable changes such as outcomes-based pricing."*
Ensuring that patients' views, as well as those of their carers, are well represented thereby allowing for care to target the outcomes that matter most to patients and their loved ones.	INTERVIEWEE (Medical Oncologist) *"In all oncology settings, it is important to take into account not only the so called tumour response, but what does this really mean to the patient."* DR. ANNE MARIE BAIRD (Patient Representative) *'It's no longer just about ensuring patients live for longer, we now want to ensure that patients are able to live with a high quality of life for longer."* DR. MARGARET HUTKA (Medical Oncologist) *"When you are asking what makes a drug valuable, first and foremost we need to know what the clinical benefit is, then we should consider what additional time that patient can continue to be productive, continue to be in employment, and to be a valuable member of their family or community."*
Driving professional pride and motivation to improve performance if reported at an individual or organisational level	DR. ANDREAS CHARALAMBOUS (Oncology Nurse) *"Outcome measures can have a huge impact, for example they can demonstrate the impact that nurses have on patients' lives."*

Accelerators

The majority of interviewees agreed that the seven factors discussed as potential considerations accelerating the move towards widespread outcomes measurement were important drivers to consider. It was agreed that this list was comprehensive and no additional accelerators were suggested. The description of accelerators shared with interviewees and a summary of their feedback can be found in the Appendix Table 1.

The mean ratings (out of maximum of 5, where 5 is strongly agree and 1 is not an accelerator) ranged from 4.2 (±0.9 Information technology advances) to 3.3 (± 1.3; Medical technology advances), indicating that all of the accelerators were deemed as having at least a moderate impact on the uptake of outcomes measurement. Due to the small sample size and use of a 5-point Likert scale, the standard deviations were relatively large and there was no significant difference between the mean rankings.

Most interviewees rated information technology advances (4.2), and increased use of real world data (RWD; 4.1) as clear accelerators (highest ranked) and the two factors were seen by interviewees to be closely interlinked. On some of the other accelerators there was a large range of views showing that there was not a consensus in terms of the level of impact they are having on the uptake of outcomes measurement. Many felt that advances in medical technology are important to consider but not the most important driver. There was particular debate around 'pressures on the healthcare system'. Most interviewees agreed that this was an accelerator but two of the Clinicians we interviewed and a Patient Representative felt that, on the contrary, these pressures are slowing the uptake of outcome measures as hospitals lack the finances and skilled resources to initiate the capture and analysis of an additional data set.

MR. JAN GEISSLER (Patient Representative)	*"Real-world data will be important in regards to where the data comes from, as data we currently get from clinical studies are highly optimised data to measure the therapeutic effects of two treatments, while we know that minimising risk for the participants the population that we recruit is largely optimised. If you look at, especially, the average incidence of the disease is 65 or something and the average age on these studies is 45, just because we exclude all the people with comorbidities, which means that real-world applicability is very different. I think that is why real-world data will be extremely important and it will also have an impact on the outcomes."*
DR. SARAH JAYNE LIPTROTT (Nurse and Patient Representative)	*"Advances in health information technology will enable outcomes measurement. I have so much experience of programs that don't speak to each other, people having to enter the same data twice and double check it. It is an enormous waste of time and resources."*

PROF. RICCARDO AUDISIO (Surgeon)	*"The overall community appreciates that advances in [medical] technology are not leading to benefits as the costs are enormous. Patient rights need to be protected, and the gains of these advances are fake, the medical technology is an important driver but adversely because of the misinformation to patients."*
PROF. PHILIP POORTMANS (Radiation Oncologist)	*"Pressures on healthcare systems should help, they should accelerate (the uptake of outcomes measurement), but the reality in a lot of countries in Europe is that we are pressured to do more in less time which isn't possible with our limited resources."*

Barriers

As with the accelerators, there was broad agreement that the 8 barriers to outcomes measurement identified from the secondary research were comprehensive. The description of barriers shared with the interviewees and a summary of their feedback can be found in the Appendix Table 2.

All of the barriers included in the survey averaged a mean score of >3 out of a 5 point scale indicating that they are all important to consider when identifying strategies to overcome obstacles and drive adoption of outcomes measurement at scale.

The challenge of capturing data in a structured and standardised manner was the most important barrier identified by the interviewees (mean score of 4.4 out of 5). They highlighted that this barrier has two primary dimensions: A lack of user-friendly technology to capture the relevant information alongside a lack of resources and time to do so.

The top three rated barriers were all related to the ability to capture outcome measures and effectively record them within electronic health records (Data Access, Data Quality and Data Recording). A lack of suitable guidelines was also frequently cited as a key barrier and many interviewees recognised that there is a difficulty in identifying whether to focus on improving guidelines or data capture as a first step.

When asked if any barriers had been missed, two of the interviewees highlighted an additional barrier being healthcare professionals' (HCPs) potential resistance to having their own performance measured and available. A clinician also commented that HCPs may be concerned about capturing additional data points with the recent introduction of the General Data Protection Regulation 2016/679 (GDPR).

Specific Measures Feedback

The below list of outcome measures was shared with the interviewees. Interviewees broadly agreed that the list captured the major outcome measures related to cancer treatment.

Group	Outcome description	Example measures
Patient Reported Data	Outcome measures made through direct patient observations captured in questionnaires	Standardised measures of quality of life [repeated measure]
		Standardised measures of patient experience
		Activities of daily living [e.g. return to work]
		Reporting of disease-related symptoms [permits symptom free survival]
Measures of Survival	Outcome measures based on duration of survival (with or without aspects of survival e.g. place of death or quality of death)	Overall survival
		1 year mortality [1 year survival]
		5 year mortality [5 year survival]
Clinical Evaluation Scales	Outcomes measurement using simple grading scales that capture information about the patient's status or their response to a therapy	Physician evaluation of treatment response [at end of therapy]
		Physician confirmation of absence/ suspension of response [during therapy]
		[Change in] patient performance status
		Presence or absence of grade 3 (or above) adverse event
		Physician decision to move to palliative care/ Best supportive care/Cease active treatment
Direct Measure of Disease	Outcome measures related to disease characteristics collected through imaging or pathology	Measurement of tumour volume/mass and its evolution
		Disease progression
		Time-based measure of disease evolution, e.g. progression-free survival
		Radiographically confirmed recurrence

Group	Outcome description	Example measures
Measures Derived from Treatment Delivery	Outcome measures derived from treatment delivery and reported by Physician or Pharmacist and/or from transactional data	Completion of intended treatment plan, e.g. all cycles/administrations completed as planned
		Adjustments to intended treatment plan (Premature cessation of therapy, pause or suspension of therapy, or reduction of dose, strength, or regimen component)
		Treatment interval: time from completion of Treatment X before starting Treatment Y
Measures Derived from Healthcare Encounters	Outcome measures based on events/encounters in the end-to-end care of a cancer patient (proxy for outcomes impacted by health system)	A&E/ER: during active treatment, or subsequent to treatment
		Most recent healthcare encounter (to derive a proxy measure of survival)

A few participants suggested additional measures to consider. Suggestions included: 10 year survival (due to the increased probability of long term survival in certain types of cancer thanks to innovations in treatment), additional 'safety' measures (e.g. toxicity), tumour-specific measures, and population-level measures (i.e. those that take into account the entire population rather than just those in active treatment). Note: We decided to focus on metrics that applied to all tumour types and not include tumour-specific and population-based metrics at the outset of the project to ensure that we had a manageable list of measures to work with during the interviews.

It was also highlighted that evaluative measures, e.g. stage of disease at presentation, are also needed before drawing any conclusions based on the outcome measures provided.

One of the Patient Representatives interviewed suggested that it is not only Grade 3 (severe) adverse events that should trigger a review and adjustment to treatment. If someone is suffering from a chronic Grade 1 or 2 adverse event (e.g. long-term diarrhoea), this will also have a serious impact on their quality of life and may be at least as important to the patient, as a one-off Grade 3 event. This further supports the importance of capturing a variety of outcome measures to develop a holistic view of the patient and their condition. Many participants highlighted this need for outcome measures to be considered together.

PROF. KLAUS MEIER (Oncology Pharmacist)

"The most important aspect of these measures is the interpretation; you need to use many of these measures together because when you have only one you will not be able to pull meaningful conclusions."

There was also one suggestion to capture the support systems that patients have as it will have a direct impact on the outcomes.

DR. IAN BANKS (Patient Representative)

"You have to take [carers] into consideration because the carer influences the outcomes enormously and especially the patient reported outcomes because it will depend on what kind of support that patient has. If they have nobody looking after them they are going to have a completely different view of the value of the medicine, of the outcomes according to the treatment regime than somebody closer to them looking after them."

Many interviewees also highlighted that the value of the measures would differ between different stakeholders and the level of complexity may vary between settings. Additionally, a few participants discussed how geographic differences may impact the list of measures.

PROF. KLAUS MEIER (Oncology Pharmacist)

"I think it is quite difficult to have objective outcomes measurements for many different people."

PROF. MARC PEETERS (Medical Oncologist)

"This list will vary between countries, for example, progression free survival - this measure may be very cheap to measure in a certain country, and be very pricey in another due to the cost of monitoring."

Value of the Measures

All interviewees were asked firstly to consider the clinical value of the set of measures; secondly how meaningful the [set of] measures would be to patients. Many clinicians felt they were not in a position to answer from a patient perspective.

On average, interviewees found change in tumour volume, disease progression and time-based measure of disease evolution (e.g. progression-free survival) to have the highest level of clinical value. These measures were closely followed by overall survival and adverse events. Treatment related metrics had similar levels of clinical value as the radiographically confirmed recurrence. The measures with a higher level of variation include: physician evaluation of treatment response, physician confirmation of absence/suspension of response, treatment interval, and activities of daily living.

Interestingly, patients rated the clinical value (value to clinicians) of patient reported data lower than the clinicians. In particular, patients assessed patient experience and daily living as only somewhat valuable clinically, whereas clinicians felt they had higher clinical value.

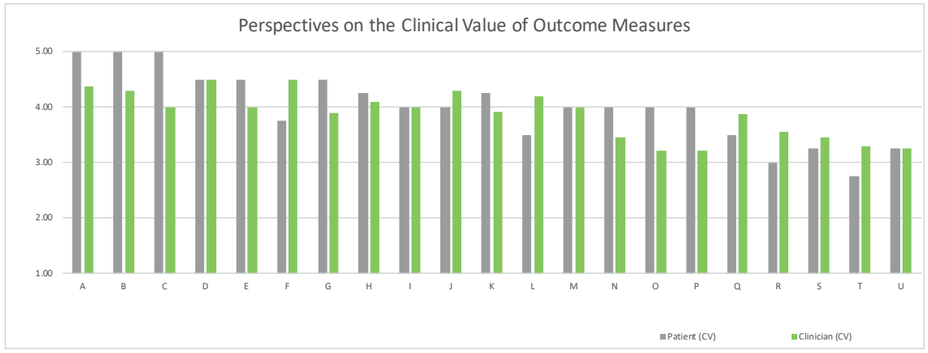

Figure 1: All interviewees were asked to rate the clinical value of the outcome measures show, where 1 is no to little value and 5 is high value. Results in this table separate the average ratings of patients compared to clinicians.

LEGEND:

A. Time-based measure of disease evolution, e.g. progression-free survival (PFS)
B. Disease progression
C. Overall survival (OS)
D. Measurement of tumour volume/mass and its evolution
E. Reporting of disease-related symptoms [permits symptom free survival]
F. Presence or absence of grade 3 (or above) adverse event
G. Completion of intended treatment plan, e.g. all cycles/administrations completed as planned
H. Adjustments to intended treatment plan (Premature cessation of therapy, pause or suspension of therapy, or reduction of dose, strength, or regiment component)
I. Radiographically confirmed recurrence
J. 5-year mortality (5-year survival)
K. (Change in) patient performance status
L. Standardised measures of quality of life (repeated measure)
M. 1-year mortality (1-year survival)
N. A&E/ER: during active treatment, or subsequent to treatment
O. Physician evaluation of treatment response (at the end of therapy)
P. Physician confirmation of absence/suspension of response (during therapy)
Q. Physician decision to move to palliative care Best Supportive Care/Cease active treatment
R. Activities of daily living (e.g. return to work)
S. Treatment interval: time from completion of Treatment X before starting Treatment Y
T. Standardised measures of patient experience
U. Most recent healthcare encounter (to derive a proxy measure of survival)

The meaningfulness to patients from a patient perspective was compared to the clinicians' perspectives on clinical value, see table below. On average, there was very little difference between the patient and clinical value. Patient reported data were seen as more valuable to patients than clinicians, specifically, activities of daily living and standardised measures of patient experience. There was also a large value gap in change in performance status and physician confirmation of absence/suspension of response [during therapy], where they were seen as more valuable to patients than to clinicians. On the contrary, measurement of tumour volume/mass and its evolution, adjustments to intended treatment plan (Premature cessation of therapy, pause or suspension of therapy, or reduction of dose, strength, or regimen component, treatment interval: time from completion of Treatment X before starting Treatment Y, and most recent healthcare encounter (to derive a proxy measure of survival)) were seen as much more valuable to clinicians than to patients. Interestingly, overall survival had higher value to patients than to clinicians.

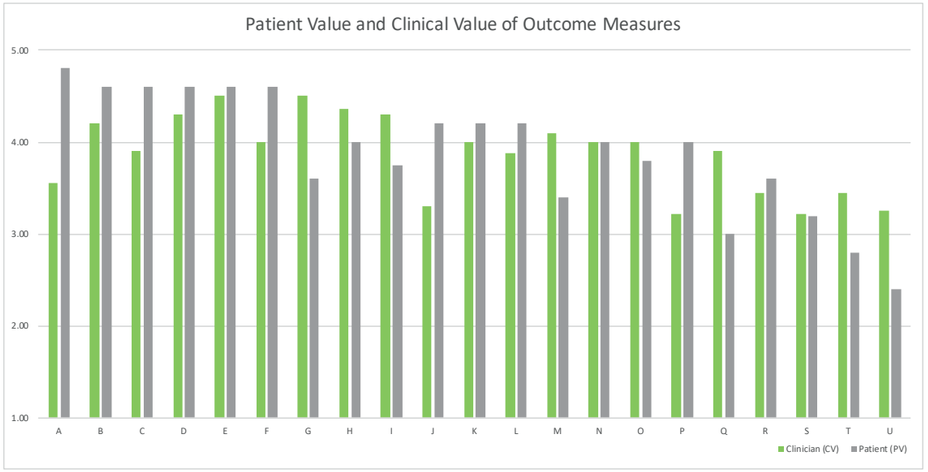

Figure 2: All interviewees were asked to rate the level of meaningfulness to patients (patient value) and the clinical value of the outcome measures show, where 1 is no to little value and 5 is high value. This table shows the patient value as rated by patients compared to the clinical value as rated by clinicians.

LEGEND:

A. Activities of daily living (e.g. return to work)
B. Standardised measures of quality of life (repeated measure)
C. (change in) patient performance status
D. Disease progression
E. Presence or absence of grade 3 (or above) adverse event
F. Overall survival (OS)
G. Measurement of tumour volume/mass and its evolution
H. Time-based measure of disease evolution, e.g. progression-free survival (PFS)
I. 5-year mortality (5-year survival)
J. Standardised measures of patient experience
K. Reporting of disease-related symptoms (permits symptom-free survival)
L. Physician decision to move to palliative care / Best Supportive Care / Cease active treatment
M. Adjustments to intended treatment plan (Premature cessation of therapy, pause or suspension of therapy, or reduction of dose, strength, or regiment component)
N. Radiographically confirmed recurrence
O. 1-year mortality (1-year survival)
P. Physician confirmation of absence/suspension of response (during therapy)
Q. Completion of intended treatment plan, e.g. all cycles/administrations completed as planned
R. A&E/ER: during active treatment, or subsequent to treatment
S. Physician evaluation of treatment response (at end of therapy)
T. Treatment interval: time from completion of Treatment X before starting Treatment Y
U. Most recent healthcare encounter (to derive a proxy measure of survival)

Complexity of the measures [Cost of measurement]

The complexity of capturing and analysing the groups of measures was also discussed. A ranking framework, shown in the figure below, was used as a stimulus for debate and discussion. This ranking of the groups are based on IQVIA's extensive experience working with health data, complemented by secondary research on the topic. The relative complexity and cost of measurement of the outcome metrics was based on four elements which are incorporated into the framework:

1) Structured format: Are these data typically captured in a structured format, or do they typically need to be derived from unstructured format?
2) Does the collection of these data require specific (non-invasive or invasive) procedures and expert evaluation or interpretation from different members of the multidisciplinary team"? [Column: Expert Skillset]
3) Are these data typically collected as part of routine patient care? [Column: Routine Care]
4) Does the collection or collation of these data extend beyond the 'reach' of the patient's cancer treatment team? [Column: Collected Beyond the Cancer Treatment Team]

	Group	Structured Format	Expert Skillset	Routine Care	Collected Beyond the Cancer Treatment Team	Overall Level of Complexity	
						Complexity	Rank
1	**Patient Reported Data**	Yes	No	No	No	Middle	4
2	**Measures of Survival**	Yes	No	No	Yes	Middle	5
3	**Clinical Evaluation Scales**	Yes	No	Yes	No	Low	3
4	**Direct Measure of Disease**	No	Yes	Yes	No	High	6
5	**Measures derived from treatment delivery**	Yes	No	Yes	No	Low	1
6	**Measures derived from treatment delivery**	Yes	No	Yes	No	Low	1

In discussions around the complexity of the measures, just over half of the interviewees agreed with all of the proposed rankings whilst the remaining interviewees generally cited only one or two points of difference. These challenges arose around three of the groupings:

- Measures derived from healthcare encounters and patient reported data were deemed more complex to capture/analyse
- Measures of survival were deemed simpler to capture/analyse

Pragmatic Outcome Measures

A definition of pragmatic outcomes measurement was developed based on feedback from interviewees. The resulting definition was:

> *"Measures of the outcomes of cancer care which can be efficiently generated, recorded and accessed at-scale in a real world setting and provide meaning to patients, providers and the wider healthcare community."*

This definition encompasses both the value and the complexity of outcome measures. Therefore, to identify a set of pragmatic outcome measures, the average scores of clinical value were compared with the proposed ratings of complexity/cost of collection. Figure 3 (below) shows where the outcome measures lie in terms of value and complexity. Outcome measures in the upper left hand corner are considered 'pragmatic', i.e. those of high value and relatively low complexity to capture and analyse.

As all the outcome measures were considered to be of clinical value (average scores higher than 3 out of a 5 point scale) by interviewees, all outcome measures fall above the x-axis in the figure. As a result, the level of complexity was the key driver in determining the feasibility and pragmatism of the outcome measures.

From this exercise, a set of 8 pragmatic outcome measures were identified. These are shown in the smaller rectangle in the diagram below. They consist of:

- Completion of treatment
- Adverse events
- Treatment response (end of therapy)
- Change in performance status
- Treatment interval
- A&E/ER visits
- Cease active treatment
- Absence/suspension of response

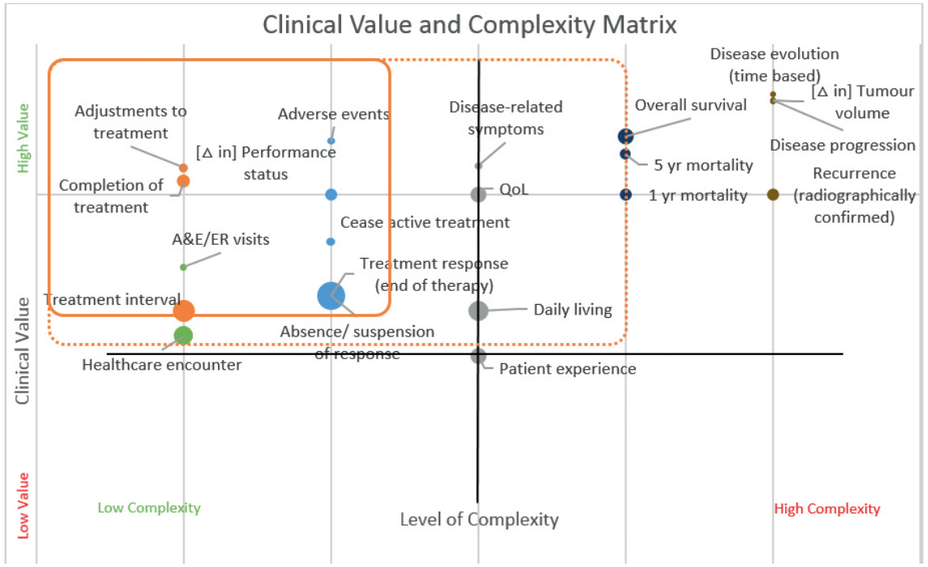

Figure 3: This figure compares the average scores of clinical value with the scores in the complexity framework. The identified pragmatic outcomes are contained within the smaller rectangle. These are outcome measures which have a high clinical value and a relatively low level of complexity/cost to measure. The larger rectangle is an expanded pragmatic outcomes data set which includes outcome measures that could be more easily captured and seen as pragmatic if implementation/ capture was optimised.

The size of the data points indicate the variance in the response of the clinical value of the measures. The smaller the point, the more consistent the response, i.e. 'Absence/ suspension of response' had the largest variance in responses.

Group and Outcome Measures

- Patient Reported Data
- Measure of Survival
- Clinical Evalution Scales
- Direct Measures of Disease
- Measures Derived from Treatment Delivery
- Measures Derived from Healthcare Encounters

DISCUSSION

Factors accelerating the shift towards an outcomes-based approach to cancer care

Interviewees highlighted that, within Europe, the factors accelerating the uptake of outcomes measurement will differ significantly depending on the country and associated health system maturity. Based on where a country sits on this spectrum, they will have different accelerators. For example, in less advanced countries, the current focus is on implementing the required technology and shifting mindsets to understand the value of capturing outcome measures. In more advanced countries, where the technology is already available, resources may be less of an issue and many stakeholders understand the significance of capturing outcome measures, the increasing focus on patient centricity and value-based healthcare models are now the most important accelerators.

The top two ranked accelerators (information technology advances and increased use of RWD) were seen by the interviewees to be closely interlinked. The improved technology available to healthcare systems has enabled better capture of health-related data. This is forming a virtuous circle as the increased volume and quality of RWD encourages policy makers and payers to utilise them more for quality of care improvement and reimbursement decisions aligned with value-based healthcare. This in turn stimulates further utilisation of emerging RWD technology by industry and healthcare providers. However, it was suggested that new technologies such as wearables and better connected health records still need to prove their reliability before true value-based frameworks will be embedded across Europe.

Interviewees were aware of, and advocated for, the move towards value-based care but felt that it is yet to gain widespread adoption in most countries.

PROF. KLAUS MEIER (Oncology Pharmacist) — *"Some countries are seeing the impact of new payment models… but others are working from different IT systems. We must find a way to actually implement the new payment models in these countries as well."*

Many agreed that value-based healthcare was important to ensure the long-term sustainability of healthcare systems but were unclear on the practicalities of how this will work. Specifically, they reported a lack of clarity around:

1. What outcome measures should be captured as a first step towards value-based care
2. How these measures could be captured at-scale, across sites/countries
3. How these measures could be standardised across sites and countries to allow benchmarking

Identifying these areas of ambiguity was an important finding from this research and highlights the

value of identifying and agreeing a set of 'pragmatic outcome measures' to be used as a first step towards value-based healthcare. By definition, these measures can be computed from existing EHR data with relative ease across most European countries and, used in combination as a set, are able to create a good picture of a patient's response to their treatment, which in turn will provide information and insight into the value of the treatment.

Pragmatic Outcome Measures

As identified in the results, a set of 8 pragmatic outcome measures were identified through the interviews. Patients and clinicians agreed that these measures have a high clinical value whilst being relatively simple to capture/analyse with existing infrastructure if they are embedded into routine care. These pragmatic outcome measures have the potential to be captured today in a real world setting and can be used in a standalone manner to provide insight into the impact of cancer treatments as a first step towards comprehensive value-based healthcare. An expanded set of outcome measures were also identified, where the additional measures could be captured systematically and routinely if the implementation of outcomes measurement was optimised. These measures can be seen as the next step on the journey towards comprehensive outcomes measurement in cancer care.

Furthermore, there is a growing body of evidence that a subset of these pragmatic outcome measures can be used as surrogate indicators for more difficult-to-capture measures such as Overall Survival (OS).[29] In clinical trials, OS is seen as the 'gold standard' of outcomes, as it is used as a metric for evaluation and comparative evaluation of a therapy's efficacy. However, in real world settings, most patients die outside the clinic, making OS measures difficult to obtain for the majority of patients.[30]

PROF. ALFREDO CARRATO (Medical Oncologist)

"There is a registry (that captures mortality data) but it is a separate system, which is not easy to incorporate into general EHRs. The challenge to capturing this data in the clinic is that 20% of patients are dying at hospital, 80% are dying at home or in other places so the clinical records are missing information. Collaboration with population-based registries is a must."

To overcome this issue, the option of using other measures as surrogates to calculate/estimate survival-related measures has been explored in recent years. Measures related to 'treatment delivery' are becoming increasingly popular for this surrogate endpoint approach. This is supported by a number of recent studies which have identified correlations between treatment-related real world outcome measures and real world OS measures.[21,24] A pilot project by Friends of Cancer Research explored whether routine captured EHR data correlated or not with key real-world outcomes. The project found that several data endpoints could be used as surrogates for OS, including real world time to next treatment (rwTTNT), RW Progression Free Survival (rwPFS), and RW Time to Treatment Discontinuation (rwTTD).[24] Similarly, Ricketts et al. also found that routinely captured RWD (in the UK), such as data on admissions, chemotherapy and radiotherapy, can be used to estimate OS and PFS in head and neck cancer using a computer algorithm with promising levels of accuracy. After calibration by comparing with data manually collected and extracted from hospital records, the algorithm was optimised.[21] It was noted that further work is needed to develop similar algorithms for other tumour types. In Kemp & Prasad's study, a correlation between real world 'time to next treatment' and real world OS was found

for NSCLC patients with correlation coefficients ranging from 0.36 to 0.7 (n=1,779). This study also found a correlation between real world OS and rwTTD, with correlation coefficients ranging from 0.62 to 0.88 (n=6,709). Whilst the authors are careful to state that this finding requires further investigation, it does highlight the potential of using non-traditional endpoints as surrogates for metrics such as OS which are more complex to capture. These surrogate endpoints, in other words pragmatic outcomes, can be especially useful for this if a large data network or 'surveillance system' of very low cost-to-measure outcomes is used and coupled with the ability to take findings from this research and over time move towards a more sophisticated data set.

SURVIVAL METRICS

The fact that OS, 1 year and 5 year survival were all deemed as highly clinically valuable is in-line with expectations as traditionally, the primary aim of cancer treatment was to extend the life of a patient. Historically these measures have also been the primary endpoints within most oncology-focused clinical trials. Their focus in clinical trials reinforces a perception that survival metrics are the most important measures of outcomes. But interestingly, these metrics were valued marginally less than more immediate patient progression measures.

Overall, there appears to be a gradual shift in the acceptability of RWD-computed metrics as a complement to traditional survival-related measures. Specifically, there is a change in focus towards measures that highlight the impact of cancer treatments on the day-to-day lives of patients. A Patient Representative discussed how the value of survival measures (such as OS) will become less important over time as cancer survivorship increases due to personalised medication and other improvements to cancer treatment. Instead, measures such as quality of life, toxicity, and the real-world performance of therapies will come to the fore. However, it is important to note that today, toxicity has a high level of complexity, specifically in regards to measuring toxicity and the legal and regulatory aspects associated with mandated declaration of adverse events. The varying levels of complications (toxicity or adverse event) following the administration of a cancer drug can be difficult to capture in a consistent manner which may impact the quality of toxicity data.

DR. MARGARET HUTKA (Medical Oncologist)

"Beyond Overall Survival, Progression Free Survival and the other survival metrics, I think with all the new drugs that are coming in we have to think about toxicities and what is the worth of this additional life in terms of the quality of life. This is what we are thinking about now when we discuss new therapy drugs and combinations of chemotherapy drugs."

In support of this, another point raised by several interviewees was that in some tumour types, 'one year mortality' is no longer viewed as particularly relevant. This is because, in all but the most aggressive of cancers, prognosis has improved significantly over the past 10-20 years. These improvements were attributed to: earlier diagnosis, advancing anti-cancer medicines, and better utilisation and coordination of the MDT. In cancers where this is the case, interviewees stated that an extended mortality timeframe of 10-15 years was now more appropriate.

In terms of the complexity of capturing these measures, there was a perception that because the mortality status of an individual is commonly captured in available registries in a structured format, it should be relatively simple to embed within the patient's electronic record. A number of interviewees also highlighted the possible option of conducting 'campaigns' to gather this information from other systems such as health insurance companies or national mortality registries.

TREATMENT RELATED MEASURES

Interestingly, both patients and clinicians felt that the measure Time to Next Treatment (or Treatment Interval) was less valuable in a real-world setting, relative to most other measures, when used as a single measure without the context of typical 'reference intervals' with which to compare. This was somewhat surprising as measures of Time to Next Treatment (or Treatment Interval) have been shown to be good indicators of prognosis and of treatment efficacy. For example, if there is a delay to start first treatment, then the prognosis of the patient may be poorer.[31] A shorter pause between treatments, indicates that the treatment is not working and there is urgency in the patient's prognosis (i.e. the patients prognosis is becoming increasingly severe).[32] Lastly, studies have shown that the time to next treatment modality, e.g. beginning adjuvant therapy after surgery or surgery after chemotherapy, could impact the efficacy of the treatment. A retrospective study of 12,473 patients with Non-Small Cell Lung Cancer (NSCLC) Salazar, Rosen, Wang et al. found adjuvant chemotherapy to be most effective (lowest mortality rate) when administered 7-8 weeks after tumour resection surgery.[33]

DR. ANDREAS CHARALAMBOUS (Oncology Nurse)

"Most of the times the treatment intervals are taken for granted, unless treatment is interrupted by unforeseen reasons. It doesn't have a value in terms of clinical decision making, as these are pre-specified intervals. On a routine basis where everything goes by the book it doesn't offer anything, but where it differs from routine, then it is very valuable. It is the variance of intervals that is the key to where it can offer insight."

There was close agreement amongst interviewees on the clinical value rating for 'HCP decision to cease treatment/move to palliative care'. Interviewees confirmed that this measure provides a good indication of the treatment's impact as healthcare professionals are likely to cease treatment if there is no response or patients experience adverse events. Whilst these are negative indicators of the treatment's effectiveness, it was felt that they do provide clear clinical value in terms of understanding how the patient has responded to the current treatment. Furthermore, if a large number of observations about a treatment using this measure are aggregated, then the value of the treatment becomes clear.

The change in performance status (PS) was also highlighted as a clinically important measure. On average, patients found PS more meaningful than clinicians. Patients also thought PS was more clinically valuable than clinicians. Whilst variables such as age and tumour stage are seen to impact prognosis, multiple interviewees felt that PS was one of the most important variables. This is because patients with a poor PS are less likely to tolerate rigorous treatment regimens. These patients will also typically have less favourable survival and QoL scores than fitter patients with better PS scores, irrespective of the treatment given. Therefore, PS is said to be a good indicator of premature cessation of therapy given its strong association with toxicity related discontinuation of therapy.[34]

Two of the interviewees who provided lower scores for the clinical value of PS attributed this to the fact that a decline in PS can be ascribed to the cumulative adverse effects of treatment rather than a worsening of the disease itself. It should also be noted that this score is defined by the clinician treating the patient so there may be variation in perceptions of what score a given patient should receive. Two scales were mentioned as useful to measure PS: the Zurbod and Karnofsky scales. The former is a simple scale that rates PS from 1-5 whilst the Kanofsky scale rates PS on a scale from 0-100 in intervals of 10. There wasn't a consensus on which provided the most value to clinicians, but there was agreement on the need to align the scales used across healthcare systems to enable effective cross site/country comparison.

'Adjustments to intended treatment plan (Premature cessation of therapy, pause or suspension of therapy, or reduction of dose, strength, or regiment component)' was found to be the most pragmatic of outcome measures, as it had the lowest level of complexity and a very high level of clinical value.

'Treatment response at end of therapy' and 'absence of response' both had the largest degree of variability in terms of the clinical value interviewees felt they offered. Patients and clinicians were aligned on the value treatment response provided. Interestingly, patients rated the clinical value higher than clinicians. However, one of the issues raised was that these measures are subjective so different clinicians may rate the same patient differently, thereby decreasing the perceived value they offer.

Treatment related measures were also found to have a similar level of clinical value (marginally higher) to the measure of radiographically confirmed recurrence, which was found to be very complex to measure. This finding is consistent with the Friends of Cancer Research that these measures are valuable in being surrogate endpoints for OS.[24]

There were a number of other measures deemed to be valuable but more complex to capture/analyse that fall into the extended set of pragmatic outcome measures

PATIENT REPORTED DATA

All of the patient reported data (QoL, Disease-related symptoms, patient experience and impact on daily living) were deemed to provide significant clinical value but would be more challenging to capture/analyse than the pragmatic outcomes. These are included in an extended set of pragmatic outcomes, where if the challenges of complexity could be addressed they would be systematically and routinely collected. The common reasons for this perception of increased complexity included:

- PRD are commonly collected through long, paper-based questionnaires which have a high burden in terms of time to complete and resources needed to assist the patient.

DR. ANNE MARIE BAIRD (Patient Representative)

"In terms of admin, there is not always the time to sit with the patients and given the varying levels of patient literacy, you will need time to explain the questionnaires with them. There could also be patients who need more time to fill out and need more help. You could end up missing the patients missed due to technology and literacy."

- A lack of clarity over the correct measures to use and variability in the tools used to capture making cross site comparison difficult.

INTERVIEWEE (Medical Oncologist)

"The reason [patient reported outcomes have not yet been incorporated in to day to day clinical practice], is mainly related to the fact that we don't have easily recognised instruments to capture them. It takes a certain amount of organisation to capture these data and to have them analysed and that is where the present shift towards IT is going to help."

- Lack of available systems to capture PRD in a structured format.

DR. ANDREAS CHARALAMBOUS (Oncology Nurse)	*"You don't see the capture of patient reported outcomes being done routinely and when captured it in a real world setting it is often not in a structured form."*

The interviewees' perception of PRD being complex to measure is in line with IQVIA's experience, which has shown that it technically possible to capture PRD within EHRs now given the advances in health information technology. The advent of mobile apps and connected devices means patients are now empowered to provide PRD with minimal effort and from outside the clinical setting. This reduces the resource pressure within the hospital and allows a continuous longitudinal flow of data. Many applications can now be linked directly with patients' EHRs in a structured format providing near real-time updates on their experiences and outcomes.

INTERVIEWEE (Medical Oncologist)	*"We started a long time ago to incorporate some quality of life determinants in our protocols but it was very difficult… They are now much easier to implement and people have to fill-in less questions."*

MEASURES DERIVED FROM HEALTHCARE ENCOUNTERS

The use of health care visits to derive a proxy of survival were generally seen to be of lower clinical value, despite being easy to capture. Most interviewees felt that these were not as clinically valuable as the other measures as they are not direct measures themselves, rather they are being used as proxy measures to indicate actual outcomes. It was also highlighted that these measures can be complex to measure as in a number of hospitals, the systems that capture emergency room visits are completely separate to the system used by oncology patient's multidisciplinary team so wouldn't currently be easy to link-up. This is potentially less of a hurdle than clinicians perceive it to be. Clinicians are still recording emergency visit information in a systematic manner so there is clear potential for a technical fix to ensure that the systems are able to 'talk' to one another thereby, allowing potentially valuable healthcare encounter information to be held within patients' EHRs.

DR. ANDREAS CHARALAMBOUS (Oncology Nurse)	*"Treatment delivery and health care encounter are very important metrics, especially when you are thinking about patients moving from care to palliative care - they don't know how to do it, there are currently no golden standards on when or how to determine the best way of doing this."*

Measures of survival were found to have a higher level of complexity/cost to measure than the measures in the extended rectangle of pragmatic outcomes.

MR. JAN GEISSLER (Patient Representative)	*"Unless someone dies while under active treatment, or if they are in a large study centre, quite often that kind of information is not recorded in the medical record or is inaccessible."*

Yet, the complexity of these measures was lower than the direct disease measures ('measurement of tumour volume/mass and its evolution', 'disease progression', and 'time-based measure of disease evolution e.g. progression-free survival'). Therefore, survival measures can be seen as included in the next level of maturity for outcomes measurement in cancer care.

Direct measures of disease (e.g. measurement of tumour volume and evolution) were found to be valuable in clinical decision making for a specific individual but are more complex to measure and difficult to collate, particularly in near real time and at scale. These metrics would be those captured in the final step towards comprehensive outcome measures after barriers to their capture have been overcome.

The gap between what is valuable to patients and what is valuable to clinicians is closing, yet patients perceive the gap to be larger

The measures within the PRD group were reported as more meaningful to patients than to clinical teams. 'Activities of daily living' and 'patient experience' had a particularly large gap between patient and clinical value. This gap can be explained by the fact that, to the patient, having a good individual experience and being able to live a 'normal' life are commonly cited as the most important outcomes to them. This can even come at the cost of factors such as length of survival which have historically been regarded as most important clinically.

Quality of life (QoL) was also deemed to be more important to patients than clinicians but the gap here wasn't as large. Some interviewees highlighted that this was because recently there has been "a lot of discussion about the importance of quality of life measures" (medical oncologist). Additionally, the fact that QoL measures are now commonly included within clinical trials and used by payers to identify whether a product provides additional value beyond standard survival measures has led to increased recognition of their value in the eyes of hospital professionals.

One of the interviewees noted that "many of us (clinicians) are increasingly motivated to work with patient reported outcomes", a sentiment echoed by several of the interviewees. This is an important change in thinking which could have a major impact on how care is provided to patients. It was discussed that in the future, treatments may increasingly focus on the outcomes patients' desire over and above those that are solely focused on extending life.

Patients perceived the clinical value of PRD to be lower than clinicians. This provides further support for the supposition that clinicians are increasingly seeing value in focusing on the outcomes that matter to patients and that these measures can be factored into clinical decision making. However, the clinical value of patient reported data should be communicated back to the patients, which should drive patients' engagement with their treatment and willingness to complete PRD more frequently.

Unlike the PRD measures, direct disease measures were generally reported as of less value to patients than clinicians. This was especially true for change in tumour size. Many attributed this difference to patients' desire to maintain a 'normal' quality of life. It was highlighted that patients are less interested in the mechanisms by which their condition is improving/declining, then by the outward symptoms and results that these clinical changes will have on their day-to-day life.

DR. ANNE MARIE BAIRD (Patient Representative)	*"When talking with patients, if they're responding well to a drug and the tumour is shrinking, but because of side effects their ability to go about their daily tasks has changed, sometimes it's this that's more important to them."*
DR. MARGARET HUTKA (Medical Oncologist)	*"The possibility of continuing their life as normal is what patients consider to be most important in the whole treatment."*

Interestingly, interviewees rated the progression metrics (i.e. disease progression and disease evolution over time) above the measures of survival. As shown in the table "Perspectives on the Clinical Value of Outcome Measures", patients rated measures of survival as having more clinical value than how clinicians' rated them. However, when comparing how patients rated the meaningfulness to the patients (patient value) and clinicians rated the clinical value of these measures, they were actually closely aligned.

Barriers to a pragmatic approach to outcomes measurement

Barriers to outcomes measurement within cancer care were discussed during the interviews in order to identify the most feasible path to comprehensive measurement and propose recommendations.

Many interviewees highlighted that the inability to capture information efficiently within EHRs was a major barrier for clinicians already stretched for time. They often had to record outcomes in separate systems which was time consuming and put them off capturing non-mandated metrics. It was highlighted that there is a need for oncology services in Europe to be more standardised on the data that is captured and the feasibility of the capture and processing of data. The ability to capture the required information easily in a structured manner differed across, and even within, countries. In those countries that had dedicated nursing staff, it was said that the lack of resources was less of a barrier as they commonly had dedicated admin or nursing staff on-hand to support with recording information such as patient reported outcomes. On the other hand, other countries who reported having fewer clinical staff had less focus on recording data within EHR so would find the capture of data more challenging.

From the interviews, it was clear the lack of resource and time to capture outcomes data typically results in poor data quality due to incomplete data fields for these particular fields within EHRs. One suggestion to overcome this was to follow in the footsteps of some NHS trusts and mandate the relevant data entry within the EHR interface before next steps, such as prescriptions can be made. However, this could also lead to poor data quality as those recording data may rush data entry and provide incorrect entries.

It was also highlighted that access to state of the art health information technology is a challenge that creates a barrier to innovation. Five of the interviewees added that even when the technology and processes are currently in place to capture outcomes, the systems fail to provide useable information/analyses back to HCPs in a timely manner. These individuals commented that the outcome-related data they record is seemingly never used (especially by frontline staff) so they quickly lose motivation to complete these fields accurately as they don't receive any value from doing so.

PROF. PHILIP POORTMANS (Radiation Oncologist)	*"Most HCPs see outcome capture as a burden... Even when outcomes are recorded, they often don't then get shared with healthcare professionals in a useful manner so they don't see its value and stop recording them as frequently or with the required accuracy."*
DR. IAN BANKS (Patient Representative)	*"There are tons of data out there but most of it is not structured and most of it is not analysed, it is just out there as raw data… I think the biggest barrier is how you fund and resource the structuring of that data and analysis, not just the collecting of it."*

Beyond the processes and technology used to capture outcomes, a lack of standard guidelines for the use of outcome measures was another commonly cited barrier. There were a variety of issues interviewees mentioned in relation to this topic, including:

1. A lack of Country or European-level guidelines and standard operating procedures (SOPs) to guide hospitals on the best outcome measures to use. This is both at a disease and tumour-level. Some of the interviewees recognised that ICHOM have made good progress in this area but many were unaware of these guidelines or stated that their specific tumour specialisms were not covered.

PROF. MARC PEETERS (Medical Oncologist)	*"Lack of guidelines is an issue… for certain tumour types there is a complete lack of guidelines."*

2. A lack of guidance on how to effectively use outcome measures, if they are being captured.

PROF. PHILIP POORTMANS (Radiation Oncologist)	*"There is a big debate on how to best develop guidelines for outcomes measurements at national and international level; we are in its early days, we are only at the beginning of defining guidelines for outcomes measurement."*

3. A need to ensure that when guidelines have been created, they get disseminated to the entire oncology community in an effective manner.

MS. TEODORA KOLAROVA (Patient Representative)	*"A key issue is not only the lack of guidelines but the inability to ensure that these guidelines are clear and pushed to the relevant decision makers in a way that will ensure they are adopted."*

4. Although most interviewees felt there was a lack of relevant guidelines, one respondent commented that there were too many competing/conflicting opinions on how to best utilise outcomes measurement.

Recommendations to drive adoption of outcomes measurement by overcoming perceived barriers

Based on the level of complexity of the various metrics, a three-step approach has been proposed as a roadmap to comprehensive outcomes measurement in cancer care:

Step 1 – Immediately harness the outcome measures which are achievable today i.e. those with a low level of complexity which can be most easily collected today, identified, as Pragmatic Outcome Measures.

Step 2 – Focus resources and attention on overcoming barriers to large scale capture of those measures identified as having medium complexity (e.g. through investment in the framework behind outcomes measurement, governance and implementation).

- Patient Reported Data should become standard practice and no longer only standard practice for interventional trials
- 'Date of Death' should also be integrated into relevant infrastructure and databases

Step 3 – Continue to harness the clinical value of those measures associated with the highest level of complexity in informing individual patient care and work towards their large scale use over the longer term. This will require investment in the standardisation of metrics and access/integration/collation of the data. In the diagram, these metrics are those in the upper right hand corner.

- Tools such as Artificial Intelligence and Machine Learning will be powerful enablers to help extract value from the dataset

Interviewees provided more than fifty recommendations to address the barriers that were identified during this research to drive the adoption of outcomes measurement at scale. These have been aligned with the 3-step approach and have been summarised below.

	1. HARNESS POMS	2. OVERCOME NEAR-TERM BARRIERS	3. WORK TOWARDS COMPREHENSIVE OM
	Today	Mid-term: Collective Action	Longer Term
RECOMMENDATIONS	Increase knowledge of, and buy-in to, the value of outcome measures across oncology stakeholder types Develop and embed European-level 'essential requirements' and/or guidelines for outcomes measurement to make data capture 'business as usual' and move away from a need to do 'studies'	Identify a systematic approach to incorporating PRD into routine clinical practice Investigate ways of combining use of date of death with treatment data to calculate survival and draw conclusions on treatment efficacy Better utilise existing systems to capture outcome measures	Provide additional resources (or reallocate existing ones) to support outcomes measurement Increase uptake of innovative technologies to support the capture and analysis of outcome measures
EXAMPLE ACTIVITIES	Facilitate best practice sharing and dissemination of successful pilot studies Continue fostering education through conferences and round table sessions Establish the standard outcomes measurement tools/scales to be used Implement an audit function to assess treatment centres compliance with the essential requirements/guidelines	Standardise PRD instrument or specific questions within these instruments which can be routinely captured Develop guidelines on how PRDs can be fed into existing health information technology systems Develop guidelines on how date of death can be used with treatment data Mandate the capture of the 8 pragmatic outcome measures within existing EHRs (e.g. some UK hospitals won't let HCPs prescribe without completing predefined field)	Embed someone with a focus on outcomes measurement within the multidisciplinary team to drive their adoption and utilisation Provide real-time feedback of outcome measures to HCPs to encourage high data quality Trial usage of patient apps and other innovative technology to capture PROs
BARRIERS ACTIVITY WILL OVERCOME	Skills and tech to analyse and lack of resources to record data Skills and expertise to analyse Lack of standardisation/guidelines for outcomes measurement	Lack of standardisation/guidelines for outcomes measurement Data access Cost to measure	Skills and expertise to analyse and lack of resources to record data Lack of data quality Data recording and data access

Limitations of the research to date

This research offers a starting point to understanding pragmatic outcomes measurement in cancer care and perceptions of the various stakeholders in the European cancer community. In this exploratory research, only 26 individuals were interviewed. A larger sample size is needed to truly understand differences in perceptions between stakeholder groups particularly between patient representatives and health care professionals. Future research should also include a broader range of stakeholders to encompass the viewpoints of additional stakeholder groups such as policy makers, economists and industry (including pharmaceutical and device industries, e.g. molecular diagnostic companies). The inclusion of these groups will be key in determining how these outcomes will be used to address the challenges faced by European health systems (e.g. financial pressures) and the investment to overcoming barriers to systematic capture of outcome measures at scale.

CONCLUSION

Based on the findings from this research and the high level of engagement amongst the interviewees, the topic of "pragmatic outcome measures" is a promising and fruitful area of research.

All the outcome measures presented to interviewees were perceived as important and providing a high level of clinical insight and meaningfulness to patients. However, by adding the dimension of "complexity to capture" to our analysis, we were able to identify a set of "pragmatic outcome measures" which offer real potential to make a difference to clinical care in the near term as they can be routinely collected at scale across Europe today.

In addition, the 3-step roadmap identified in the Recommendations sets out a path towards the longer-term ambition of achieving comprehensive outcomes measurement at scale. This roadmap will enhance the ability of the European oncology community to provide quality cancer care through informed decisions and better incorporating the needs and perspectives of patients.

In order to embrace the concept of pragmatic measurement it will be necessary to explore the difference between two ways of considering outcomes measures:

- Those that clinical teams require to understand and define the optimal treatment for an **individual cancer patient**
- And, the set of metrics that, if collected, aggregated and analysed across multiple European centres, provide insight into the real-world clinical value of a particular intervention **across a patient population**

Whilst this report highlights areas where further investment is required, one of the key messages it contains is that the journey towards outcomes measurement at scale can start today by harnessing outcome measurements which are, in many cases, already being captured. With the right infrastructure, these measures can be aggregated and made available to the clinical community.

Another key theme of the research was the identification of differences in perspectives, between patients and clinicians, around the relative importance to them of key outcomes measurements. In parallel, there was an acknowledgement amongst clinicians of the opportunity for them to explore further how to integrate patient reported data and patients' priorities into their clinical decision making. Together, these highlight the value of bringing patients and clinical stakeholders together to explore how to build alignment around the priority that different measures should play in informing clinical decision making. Equally, its draws attention to the need for mechanisms to ensure that this information is readily available to the multidisciplinary team to support them in decision making.

The widespread adoption of outcomes measurement in cancer care will need to be encouraged and supported with the necessary resources by policy makers. The recommendations from the interviewees serve as a call to action which will be further explored in the Roundtable meeting taking place in November 2018. At this meeting, policy makers and key stakeholders will have the opportunity to explore the recommendations from this report together, including the need to ensure that efforts to capture outcome measures are properly resourced and prioritised. The potential to embed an increased focus on the practical implementation of outcomes measurement into ECCO's "Essential Requirements'" series will be further considered.

The authors welcome feedback and contributions to build on this research and the follow-up currently being planned.

BIBLIOGRAPHY

1. Porter ME. Measuring Health Outcomes : The Outcome Hierarchy. N Engl J Med. 2010;363:2477-2481. doi:10.1056/NEJMp1011024.This
2. Cooter RD, Delaney GP, Duhoux FP. A Standard Set of Value-Based Patient-Centered Outcomes for Breast CancerThe International Consortium for Health Outcomes Measurement (ICHOM) Initiative. 2017;3(5). doi:10.1001/jamaoncol.2016.4851
3. The Farr Institute of Health Informatics Research. Innovative Healthcare Delivery Programme, Scotland. http://www.farrinstitute.org/partnerships/ihdp. Published 2017. Accessed June 6, 2018.
4. Klazinga N. Health Care Quality and Outcomes. OECD: health care quality and outcomes. http://www.oecd.org/health/health-systems/health-care-quality-and-outcomes.htm. Published 2018. Accessed April 30, 2018.
5. United Nations (UN). Population.; 2017.
6. Prats Monné X. Enhancing Value in European Health Systems. 2016.
7. EFPIA, Healthier Future. Healthier future: The case for outcomes-based sustainable healthcare. 2016. https://efpia.eu/media/25156/healthier-future-the-case-for-outcomes-based-sustainable-healthcare.pdf.
8. Wait S, Han D, Muthu V, et al. Towards sustainable cancer care: Reducing inefficiencies, improving outcomes—A policy report from the All.Can initiative. J Cancer Policy. 2017;13:47-64. doi:10.1016/j.jcpo.2017.05.004
9. Prince MJ, Wu F, Guo Y, et al. The burden of disease in older people and implications for health policy and practice. Lancet. 2015;385(9967):549-562. doi:10.1016/S0140-6736(14)61347-7
10. Christen B, Defabis N, Dev-vartak P, et al. Global Oncology Trends 2018 Innovation, Expansion and Disruption. 2018;(May). https://www.iqvia.com/-/media/iqvia/pdfs/institute-reports/global-oncology-trends-2018.pdf?_=1527763175537.
11. Martinalbo J, Bowen D, Camarero J, et al. Early market access of cancer drugs in the EU. Ann Oncol. 2016;27(1):96-105. http://dx.doi.org/10.1093/annonc/mdv506.
12. Porter ME. Defining and introducing value in health care. In: Evidence-Based Medicine and the Changing Nature of Healthcare (McClellan, Mark McGinnis, J. Michael Nabel, Elizabeth G. Olsen, LeighAnne M.). Vol 53. ; 2008:161-172. doi:10.1017/CBO9781107415324.004
13. What is Value-Based Healthcare? NEJM Catal. 2017. https://catalyst.nejm.org/what-is-value-based-healthcare/.
14. Löfberg E. Patient First. 2017;(September). https://www.psshp.fi/documents/7796350/7865759/Karolinska.pdf/040ea021-c4ae-4dc6-86ce-8f6c9d48ca9a.
15. Porter M. Value in Health Care. N Engl J Med. 2010;363(Supplementary Appendix I):1-15. doi:10.1056/NEJMp1011024.This
16. Dias AG, Roberts CJ, Lippa J, et al. Benchmarking Outcomes That Matter Most To Patients : the Globe Programme. 2017;(June):42-49.
17. Heisler M, Niehaus K, Peden CJ, Wagle NW, Seth Mohta N, Prewitt E. Measuring What Matters and Capturing the Patient Voice. 2017;(October).
18. Kingsley C, Patel S. Patient-reported outcome measures and patient-reported experience measures. BJA Educ. 2017;17(4):137-144. doi:10.1093/bjaed/mkw060
19. Denis F, Yossi S, Septans A-L, et al. Improving Survival in Patients Treated for a Lung Cancer Using Self-Evaluated Symptoms Reported Through a Web Application. Am J Clin Oncol Cancer Clin Trials. 2017;40(5). doi:10.1097/COC.0000000000000189
20. Spinks T. Establishing National Metrics for Oncology. In: The University of Texas MD Anderson Cancer Center; 2016. https://www.mdanderson.org/content/dam/mdanderson/documents/Research-Centers-%26-Institutes/Institute-for-Cancer-Care-Innovation/Establishing National Metrics - Spinks.pdf.
21. Ricketts K, Williams M, Liu ZW, Gibson A. Automated estimation of disease recurrence in head and neck cancer using routine healthcare data. Comput Methods Programs Biomed. 2014;117(3):412-424. doi:10.1016/j.cmpb.2014.08.008
22. Tinker A. The top 7 outcome measures and 3 measurement essentials. Heal Catal. 2017:1-10. https://www.healthcatalyst.com/The-Top-7-Outcome-Measures-and-3-Measurement-Essentials.
23. Zuidgeest MGP, Goetz I, Groenwold RHH, Irving E, van Thiel GJMW, Grobbee DE. Series: Pragmatic trials and real world evidence: Paper 1. Introduction. J Clin Epidemiol. 2017;88:7-13. doi:10.1016/j.jclinepi.2016.12.023
24. Friends of Cancer Research. Establishing a Framework to Evaluate Real-World Endpoints. 2018. https://www.focr.org/sites/default/files/pdf/RWE_FINAL 7.6.18.p.
25. Wong S-L, Ricketts K, Royle G, Williams M, Mendes R. A methodology to extract outcomes from routine healthcare data for patients with locally advanced non-small cell lung cancer. BMC Health Serv Res. 2018;18(1). doi:10.1186/s12913-018-3029-6
26. Greenhalgh J, Dalkin S, Gibbons E, et al. How do aggregated patient-reported outcome measures data stimulate health care improvement? A realist synthesis. J Health Serv Res Policy. 2018;23(1):57-65. doi:10.1177/1355819617740925
27. Porter ME. Outcome Measurement. In: Cambridge, Massachusetts USA: Harvard Business School; 2014. https://www.hbs.edu/faculty/Publication Files/Website_Outcomes Measurement_737ae94d-f1b3-48ed-a789-025766d63670.pdf.
28. Beets G, Sebag-Montefiore D, Andritsch E, et al. ECCO Essential Requirements for Quality Cancer Care: Colorectal Cancer. A critical review. Crit Rev Oncol Hematol. 2017;110:81-93. doi:10.1016/j.critrevonc.2016.12.001
29. Kemp R, Prasad V. Surrogate endpoints in oncology: When are they acceptable for regulatory and clinical decisions, and are they currently overused? BMC Med. 2017;15(1). doi:10.1186/s12916-017-0902-9
30. Driscoll JJ, Rixe O. Overall survival: Still the gold standard: Why overall survival remains the definitive end point in cancer clinical trials. Cancer J. 2009;15(5):401-405. doi:10.1097/PPO.0b013e3181bdc2e0
31. Abrao FC, I.R.L.B. A, Rocha RO, Munhoz FD, Rodrigues JHG, Younes RN. Impact of the delay to start treatment in patients with lung cancer treated in a densely populated area of Brazil. Clinics (Sao Paulo). 2017;72(11):675-680. http://europepmc.org/search?query=(DOI:%2210.6061/clinics/2017(11)05%22)%0Ahttp://www.ncbi.nlm.nih.gov/pmc/articles/PMC5706061/.
32. Diaconescu R, Lafond C, Whittom R. Treatment delays in non-small cell lung cancer and their prognostic implications. J Thorac Oncol. 2011;6(7):1254-1259. doi:10.1097/JTO.0b013e318217b623
33. MC S, JE R, Wang Z, al et. Association of delayed adjuvant chemotherapy with survival after lung cancer surgery. JAMA Oncol. 2017;3(5):610-619. http://dx.doi.org/10.1001/jamaoncol.2016.5829.
34. Eichler M, Singer S, Janni W, et al. Pretreatment quality of life, performance status and their relation to treatment discontinuation and treatment changes in high-risk breast cancer patients receiving chemotherapy: results from the prospective randomized ADEBAR trial. Breast Cancer. 2017;24(2):319-325. doi:10.1007/s12282-016-0706-3

APPENDIX

Table 1: Factors accelerating the move towards widespread outcomes measurement. These were discussed and rated by all interview participants. The mean and median scores are shown in the table. The rating scale provided was 1-5 whereby 1 indicated the factor not being an accelerating factor and 5 being an important accelerator.

Accelerator	Description	Mean/Median	High/Low
Information Technology Advances	Advances in the ability to collate data e.g. Improved interoperability between health tech (e.g. devices) and EMRs	4.2 / 4	High
Real World Data (RWD)	Increased use of RWD to inform decision making and contribute to observational studies or pragmatic trials	4.1 / 4	-
Increased patient involvement	Increased focus on ensuring the patient's role in decisions about their own care	4.1 /4	-
Increased Complexity of Care	Need for a multi-disciplinary approach, increased importance of data to inform care and to reduce variability in care	4 / 4	-
Pressures on Healthcare System	E.g. Limited resources and challenges of financial sustainability	3.8 / 4	-
Value Based Healthcare Movement	A movement that aims to change payment models (financial incentives) to pay for the value of the intervention (value is defined as the ratio of health outcome to cost)	3.8 / 4	-
Medical Technology Advances	Advances in the ability to measure novel clinical parameters e.g. tools to detect cancers earlier through precise biomarkers	3.4 / 3.5	Lowest

Table 2: Potential barriers to widespread uptake of outcomes measurement in cancer care across Europe.

Barrier	Description
Data Access / Collection	The feasibility of collecting that information, e.g. PRO survey tools, biomarker test information availability
Data Recording	The need for time and resources to record the data into an appropriate clinical system; information is not always captured in an electronic source; not always captured in a structured and standardised form.
Data Quality	Variations in the details of each data field recorded, and the frequency of capture – not all fields may be consistently filled out by all clinicians
Patient Reported Outcomes/Data	The need for agreement over which points to standardise and measure or which instrument to use of capture (e.g. EuroQoL-5D or FACT-G) and how to incorporate the capture of this in daily routines.
Guidelines	Lack of standard guidelines for consistent capture? of outcome measures
Skills and Technology to Analyse	The need for time, resources and skillset to analyse the outcomes data collected
Cost to Measure	The cost of the instruments and the activity (resources, peoples' time) used to capture/measure the outcome or process/compute the outcome metric.
Patient's Health Literacy	Degree to which patients can obtain, process, and understand health information needed to make appropriate health decisions

ABOUT THE ORGANISATIONS

1. The European CanCer Organisation (ECCO) is a not-for-profit federation that exists to uphold the right of all European cancer patients to the best possible treatment and care, promoting interaction between all organisations involved in cancer at European level. Through its 24 Member Societies - representing over 150 000 professionals - ECCO is the only multidisciplinary organisation that connects and responds to all stakeholders in oncology Europe-wide. It does this by creating awareness of patients' needs and wishes, encouraging progressive thinking in cancer policy, training and education and promoting European cancer research, prevention, diagnosis, treatment and quality care through the organisation of international multidisciplinary meetings. Further information here: www.ecco-org.eu

2. The ECCO-CODE research project was jointly developed through open conversations and dialogue with oversight by both parties' advisory boards: the ECCO OncoPolicy Committee Executive and the CODE Clinical and Analytical Steering Committee (CASC), whereby areas of mutual research interest were identified, and was supported via grant funding from IQVIA World Publications Limited to ECCO.

3. The Collaboration for Oncology Data in Europe (CODE) is an initiative supporting the creation of the Oncology Data Network (ODN) that will provide reliable, up-to-date information on how anti-cancer medicines are actually itself used in clinical practice and enable flexible payment models. The ODN is a collaborative data sharing network open to any cancer treatment centres across Europe that wishes to join, to share non-identified information on how treatment centre-administered anti-cancer medicines are used in clinical practice.

4. CODE is led by IQVIA and has been established with support from leading biopharmaceutical companies as the Biopharmaceutical Members, who joined CODE as part of their commitment to providing patients with access to innovative medicines, in a way that is financially sustainable for the payers, biopharmaceutical research and development and oncology community. The Biopharmaceutical Members are Bristol-Myers Squibb, Eli Lilly and Company, Merck, Pfizer, AstraZeneca and Amgen. To learn more, visit: http://www.code-cancer.com/

EUROPEAN
CANCER
ORGANISATION

ECCO - the European
CanCer Organisation
Avenue E. Mounier 83,
B-1200 Brussels
Belgium

www.ecco-org.eu

Richard Price,
EU Policy Affairs Manager, ECCO
Richard.Price@ecco-org.eu

CODE – the Collaboration
for Oncology Data in Europe
210 Pentonville Road
London, N1 9JY
England

www.code-cancer.com

Julia Levy,
External Engagement Lead, CODE
Julia.Levy@iqvia.com