

BMJ Open Shifting, overlapping and expanding use of “precision oncology” terminology: a retrospective literature analysis

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ABSTRACT

Importance The terms “personalized oncology” and “precision oncology” have increased in usage and have generated considerable traction in terms of public attention and research funding. To our knowledge, no prior study has as thoroughly documented the use of the “precision oncology” terminology over the last decade.

Objective To determine how the use of the terms “personalized oncology” and “precision oncology” have changed over time.

Design A retrospective literature analysis using two databases (PubMed and Scopus) over 10 years was performed. Manuscripts using either term “personalized oncology” or “precision oncology” were collected. Manuscripts published in 2011, 2013, 2015, 2017 and through 30 June 2019 were pulled for text analysis. Common reasons for exclusion were if the search term appeared in the institution name only, the search term appeared only in keyword or publication title, or the search term was used to justify the relevance or application of research with no clear definition.

Setting Manuscripts published and catalogued in PubMed or Scopus.

Results In our study, we analysed 399 unique manuscripts published over the last decade. Over time, the terminology has shifted from “personalized oncology” to “precision oncology”. Targeted therapy, molecular biomarker-guided tumour profiling and next generation sequencing (ie, “omics-guided tumor profiling”) are the three most common definitions of the term. While these definitions are somewhat overlapping in concept, over the decade we observed an increase in the number of distinct interpretations of “precision oncology”, ranging from structural biology to clinical practice.

Conclusions and relevance We have observed that the phrase “precision oncology” is shifting, overlapping and expanding in definition. This all-encompassing approach to defining “precision oncology” ironically renders the term imprecise. Our analysis highlights the inherent challenges in defining novel movements in medicine.

INTRODUCTION

Over the last decade, the terms “personalized oncology” and “precision oncology” have generated considerable traction in the media coverage of medicine and research

Strengths and limitations of this study

- To our knowledge, this study is the first to document and quantify the use of “precision oncology” over the past decade.
- Other strengths include a large and systematic assessment of literature and use of figures to succinctly communicate the ambiguity that the term “precision oncology” has adopted in the literature.
- Limitations of the study include the choice of search term selected (eg, “precision oncology” and “personalized oncology”) which may influence the results returned, the omission of even-numbered years in our decade-wide search and the acknowledgement that the interpretation of the use of terms may be susceptible to user bias.

funding. Some commentators have argued the profession has entered a new ‘era’ of oncology care.¹

Formal definitions of “precision” and “personalized” oncology exist but are broad. In the USA, the Precision Medicine Initiative defines it as ‘an emerging approach for disease treatment and prevention that takes into account individual variability in genes, environment, and lifestyle for each person’.² According to the UK Medical Research Council, ‘precision’ and ‘stratified’ approaches are ‘based on identifying patients or subgroups of patients with distinct mechanisms of disease, or particular responses to treatments’.³ Lastly, in Germany, at the well-established German Cancer Research Center, “precision” or “personalized” oncology is described functionally, as it ‘aims to offer individualized treatment to each cancer patient by applying a comprehensive molecular, cellular, and functional analysis of tumors’.⁴ Even with these institution-specific definitions, what precisely precision medicine means within the discipline of oncology has not been previously described in the literature.

Therefore, we sought to ask: how are the terms “precision” or “personalized” oncology used in the biomedical literature? Has the definition changed over time, and if so, how? To our knowledge, there has been no empirical analysis on the use of the terms “precision oncology” and “personalized oncology”. A small prior survey outside the peer-reviewed literature sampled 50 articles over 3 years to determine trends in the use of the term “precision oncology”, but did not use multiple search terms and provided only limited analysis.⁵ Here, we sought to provide a broad, updated analysis of these terms in the biomedical literature. Our work aimed to infer the authors’ interpretation of the term, even if it was not explicitly offered as an official definition. If the term itself is vague, it suggests that the field of “precision oncology” itself may be unstructured, nascent or still coalescing. Our analysis sheds light on the way in which a novel movement in medicine defines itself over time.

METHODS

Literature search and use-of-term analysis

We sought to assemble a systematic collection of articles that used the terms “personalized oncology” and “precision oncology”. To do so, the terms “personalized oncology” and “precision oncology” and British spellings were searched on PubMed and Scopus literature databases between 1 January 2011 through 30 June 2019. We then attempted to characterise the definition of precision oncology over time. We prespecified that we would perform this analysis in odd years only, which we felt would be sufficient to document time trends and remain tractable. Manuscripts from 2011, 2013, 2015, 2017 and 2019 were obtained and stored on EndNote. We set a cut-off date of 30 June 2019 for article inclusion. Redundant entries were removed. All articles not originally published in English were translated with Google Translate. Articles that could not be obtained through the library were excluded from analysis. Publications that were errata, replies to letters, full-length books and book reviews were excluded from analysis.

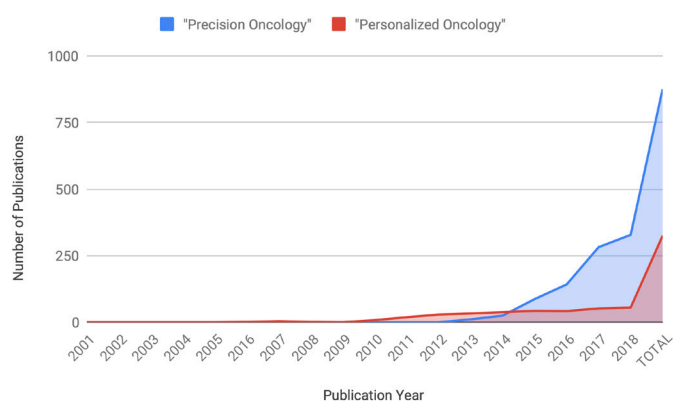


Figure 1 Total number of publications identified with the search term “precision oncology” (blue) and “personalized oncology” (red) on PubMed and Scopus, 2000–2018.

A number of centres or institutes use the terms “precision” or “personalized” in their title. Search engines produce these articles in the search results, even if the term may not be used in the manuscript text. As such, we excluded articles where the search term appeared only in the manuscript title without further definition, only in the name of the associated research institution (eg, DKFZ-Heidelberg Center for Personalized Oncology), only in introductions or discussion paragraphs without further definition, or when the search term appeared in the manuscript without any attempt at definition.

Manuscripts were assessed for their opinion towards the field of precision oncology and relevant quotes surrounding the search term “precision oncology” or “personalized oncology” that supported our assessments of either enthusiasm or scepticism were collected.

Data organisation, statistical methods and RStudio analysis scripts

Data analyses were conducted using Microsoft Excel and R/RStudio, package Tidyverse. The analysis was conducted between 24 June 2019 and 31 August 2019.

Patient and public involvement

The development of the research question stemmed from a patient-centred approach to care. Specifically, as multiple new “precision oncology” drugs become available through the pipeline, and as media coverage increases its communication about the “precision oncology” concept, we felt it was worth exploring how the field defined “precision oncology” treatments to quantify and assess the consistency of the term. This study was not submitted for institutional review board approval as it involved not personally identifiable data, and all data are publicly available. No patients were involved in the design, analysis or interpretation of this study.

RESULTS

From 1 January 2011 to 30 June 2019, there were a total of 1547 publications using either term “precision oncology” or “personalized oncology” (PubMed (n=823) and Scopus (n=724)). Over this decade, the “precision oncology” phrase was more commonly used, and the number of publications that used either term has steadily increased, with “precision oncology” rising with a steeper slope than “personalized oncology”. These trends are shown in [figure 1](#).

We analysed content in prespecified years (2011, 2013, 2015, 2017 and 2019). In these years, there were a total of 717 publications from PubMed (n=410) and Scopus (n=307). Removing duplicate publications, there were 565 unique entries retrieved between the two literature databases in our selected years.

“Precision oncology” and “personalized oncology” were used in 306 unique journals. The journal with the most publications containing either search term was *Onco-target*, with 22 entries within our search. Other journals

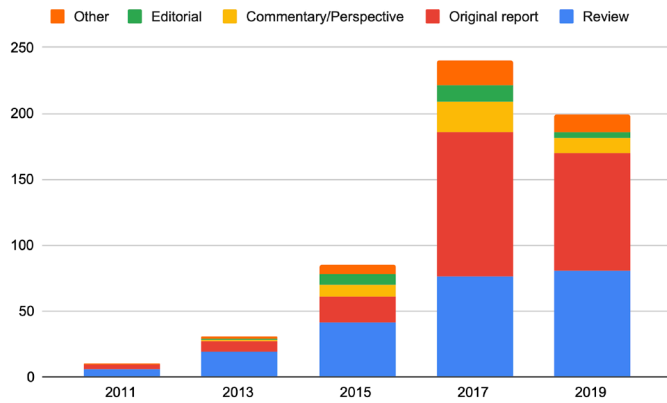


Figure 2 Flow chart of study design.

that frequently included articles using our search terms included *Cancer Research* (n=13), *Clinical Cancer Research* (n=13), *NPJ Precision Oncology* (n=10) and *Annals of Oncology* (n=8).

Characteristics of the search results, by year, are summarised in [figure 2](#). Review articles were the most common form of article retrieved in 2011 (60% or 6 articles of 10), while original reports constituted 30% (3 of 10). By 2019, original reports were most prevalent, comprising 45% of articles, and reviews represented 41% of articles.

Of the 565 unique entries, we identified 399 eligible articles eligible for the use-of-term analysis: 2011 (n=8 of

10, 80%), 2013 (n=25 of 31, 80.6%), 2015 (n=74 of 85, 87.1%), 2017 (n=169 of 240, 70.4%), and 2019 (n=123 of 199, 61.8%), respectively, as shown in [figure 3](#). [Figure 3](#) also shows reasons for exclusion. The total number of articles excluded due to using the search term without offering a definition is 25.4% (n=144 of 565). The other common reasons for exclusion were due to the search term appearing only in the name of the institution without appearing in the manuscript text (n=89, 15.8%), the search term appearing in the manuscript text without an explicit attempt at definition, explanation or context (n=20, 3.5%), and the search term appearing only in the keywords without appearing in the manuscript text (n=12, 2.1%).

Across all years of interest, “precision oncology” is most commonly defined as using next generation sequencing and ‘omics’ data to identify an actionable mutation (n=6 (75%) in 2011; n=13 (52%) in 2013%; n=46 (62%) in 2015; n=115 (68%) in 2017; n=76 (62%) in 2019). However, many publications define the term with more than one definition; in addition to omics-guided tumour profiling, manuscripts also referenced other interpretations of “precision oncology”. These definitions included but were not limited to: (A) targeted therapy drugs; (B) use of a molecular biomarker to delineate subgroups, laboratory platforms for basic research (eg, high-throughput drug screens), (C) omics (genomics,

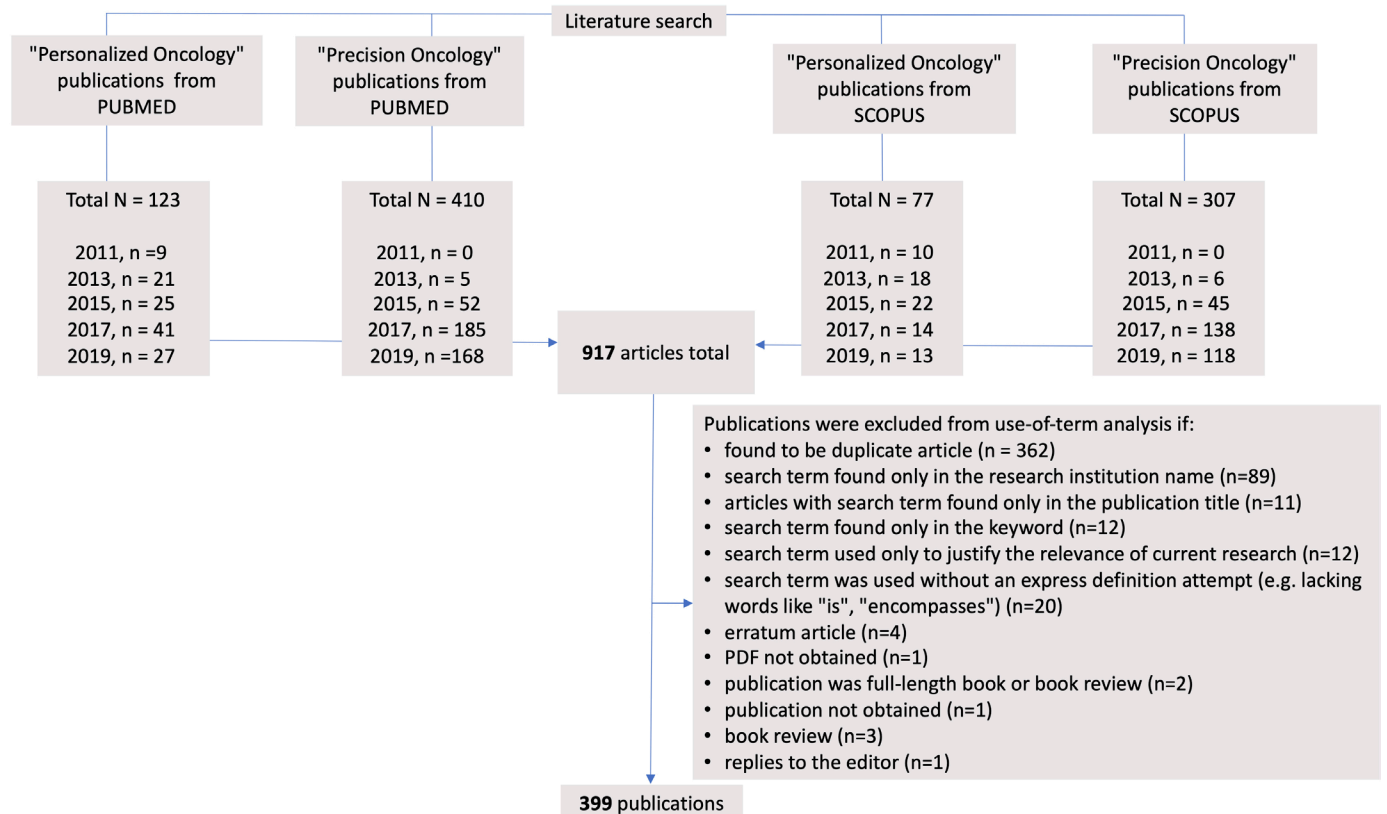


Figure 3 Baseline characteristics of the study. Analysis of 565 unique entries identified from the literature search in prespecified years (2011, 2013, 2015, 2017 and 2019) across two literature databases (PubMed and Scopus). Manuscripts were classified by publication type (Review, Original Report, Editorial, Commentary/Perspective and Other).

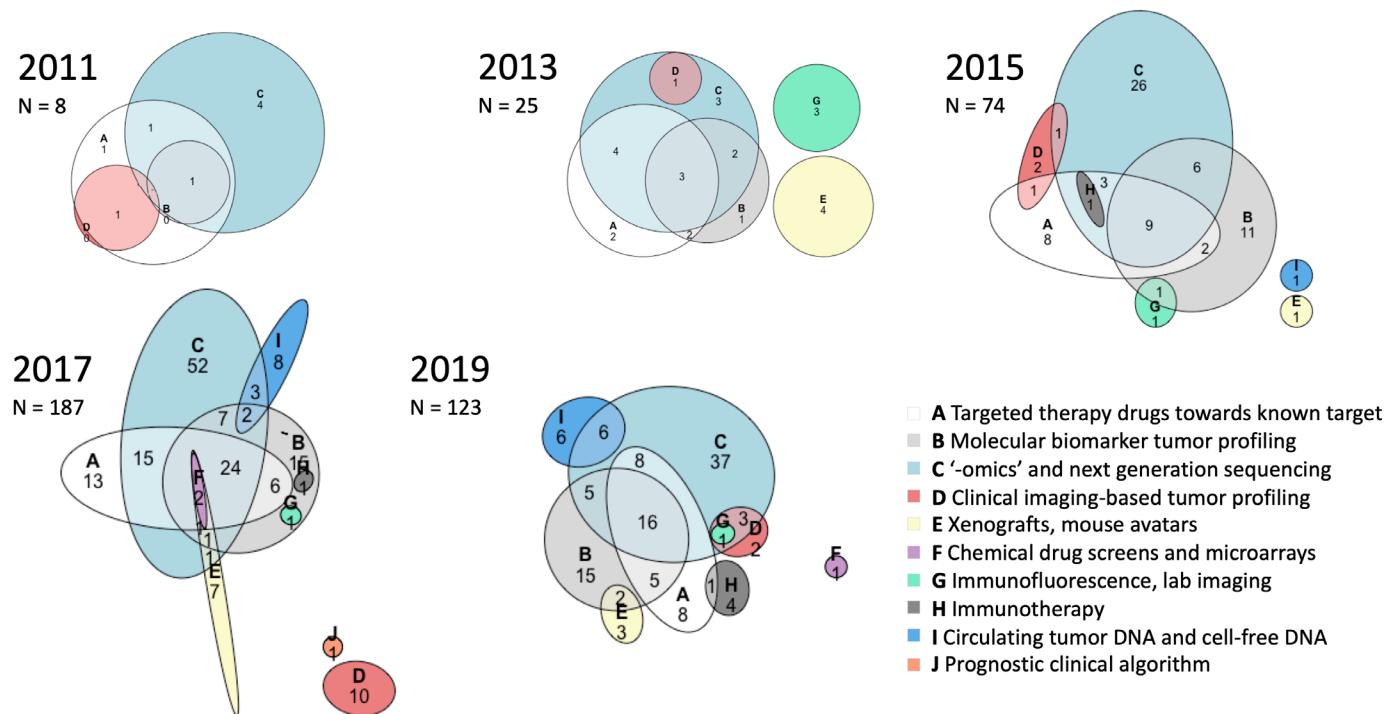


Figure 4 Euler diagram of various definitions of “precision oncology” and “personalized oncology” over 2011, 2013, 2015, 2017 and 2019. (A) Molecularly targeted therapy, typically drugs inhibiting cell signalling pathways. (B) Molecular biomarker for subclassification of cancer type. (C) ‘Omics’ (eg, genomics, transcriptomics, proteomics, epigenomics, etc) and bioinformatics to profile tumours, identify actionable mutations and guide therapy. (D) Radiomics, radiogenomics, radiology-guide and imaging-guide tumour profiling. (E) Using patient-derived xenografts, genetically engineered mouse models, three-dimensional organoids. (F) High-throughput chemical drug screen for laboratory research. (G) Immunohistochemistry, immunofluorescence for clinical applications. (H) Immunotherapy. (I) Circulating tumour DNA, liquid biopsy. (J) Patient-specific prognostic clinical algorithm.

transcriptomics, epigenomics, etc) to guide therapy or genome sequencing to identify actionable targets; (D) radiology and clinical imaging-based tumour profiling, (E) patient-derived xenografts and genetic engineering of mouse models, mouse or fly avatars to test drugs; (F) chemical drug screens and lab microarrays, (G) laboratory imaging and immunofluorescence; (H) immunotherapy and checkpoint inhibitors; (I) using circulating tumour DNA in the bloodstream to identify cancer recurrence and (J) prognostic clinical algorithms. As such, we mapped the overlapping and distinct uses of the terms, which is shown in [figure 4](#).

Since 2011, there has been an increase in the number of distinct interpretations of “precision oncology”, represented by circles (from 4 in 2011 to 9 in 2019). The number of overlaps, representing a single article that uses multiple concepts to define “precision oncology”, has also increased from one overlap (eg, between targeted therapy and omics-guided tumour profiling) in 2011, to three overlaps in 2013, to five overlaps in 2017. The most common triple overlap is between targeted therapy, molecular biomarkers to delineate subgroups and identify actionable mutations, and omics-guided tumour profiling (n=1 in 2011, 12.5%; n=3 in 2013, 12%; n=9 in 2015, 12%; n=24 in 2017, 14%; and n=16 in 2019, 13%) was consistently seen throughout all years.

Manuscripts were also assessed for their opinion towards the field of precision oncology. Of the articles that took a stand about current or future prospects (n=280), 80.3% (n=225) were enthusiastic without any reservation, and 19.6% espoused some scepticism or reservation (n=55). Selected quotes from enthusiastic and critical publications have been collated to demonstrate the language surrounding precision oncology, as seen in [table 1](#) (full collection of quotes available in online supplementary table 1). Whether enthusiastic or critical, publications commonly use phrases such as the “promise”, “potential”, “paradigm” and “era” of precision oncology.

DISCUSSION

Both precision and personalised oncology have gained popularity over the last decade, with the term precision oncology more frequently used. This is perhaps in part attributable to Dr. Harold Varmus’ preference for the latter term, exemplified by his statement indicating that his father received personalised care before the era of genomics.^{6 7} Care, in his mind, has long been personalised, unique to the patient in front of the physician; thus, a new term—precision oncology—is a better description of a novel effort.

Table 1 Abridged collection of selected quotes from manuscripts extracted from our “precision oncology” and “personalized oncology” search, demonstrating the mixture of enthusiasm and scepticism about the state and future of precision/personalised oncology

Year	Quote	Overall tone towards the field of precision oncology
2011	Maitland and Schilsky ¹² : <i>Medicine has always been personalized. The design and conduct of clinical trials has not yet adjusted to a new era of personalized oncology and so we are more in transition to that era than in it. Advances in both biology and information technology have brought ‘personalization’ forward as a new buzzword in healthcare.</i>	Sceptical
2015	Block ¹³ : <i>Targeted therapies and the consequent adoption of “personalized” oncology have achieved notable successes in some cancers; however, significant problems remain with this approach. Many targeted therapies are highly toxic, costs are extremely high, and most patients experience relapse after a few disease-free months.</i>	Sceptical
2017	Brock and Huang ¹⁴ : <i>Precision Oncology seeks to identify and target the mutation that drives a tumor. Despite its straightforward rationale, concerns about its effectiveness are mounting. What is the biological explanation for the “imprecision?” First, Precision Oncology relies on indiscriminate sequencing of genomes in biopsies that barely represent the heterogeneous mix of tumor cells...Most troublesome is the observation that cancer cells that survive treatment still have suffered cytotoxic stress and thereby enter a stem cell-like state, the seeds for recurrence. The benefit of “precision targeting” of mutations is inherently limited by this counterproductive effect. Cancer is not a disease of DNA or the cell but of the tissue.</i>	Sceptical
2017	Portioli ¹⁵ : <i>However, in these past two years, the term precision medicine has expanded quickly worldwide and has been used by the medical scientific community in a wider and often inappropriate way. Many studies, in every field of Medicine and in clinical practices such as translational research, often refer to or are preceded by the term precision medicine, in order to add scientific credibility or validity to their publication...Thus this term of strong intrinsic value runs the risk of being reduced to a fashionable concept and as a consequence of being kidnapped...In crossing over from a scientific and medical meaning to a political interpretation and back again to a newly altered scientific and medical one, the term precision medicine may migrate from its true meaning. Doctors and scholars must be alert not to fall into the trap of using trendy concepts whose generic appeal may be strong but completely miss the true significance. Our duty as physicians is to convey clarity and truth when dealing with our patients.</i>	Sceptical
2017	Biankin ¹⁶ : <i>The ultimate goal of precision medicine is to use population-based molecular, clinical and other data to make individually tailored clinical decisions for patients, although the path to achieving this goal is not entirely clear...As a consequence, developing therapies that target specific molecular processes for these diseases is becoming more and more challenging, as ever-increasing subgroups of diminishing size are replacing what was previously a single disease entity. This perhaps explains why many potential therapies have failed, particularly in cancer, and why many current therapies are only effective in subgroups that cannot be predicted before treatment.</i>	Sceptical
2011	Madhavan et al ¹⁷ : <i>With the sequencing of the human genome and availability of high-power computational methods and a variety of high-throughput “omics” technologies (eg, genomics, transcriptomics, and metabolomics), cancer research and care are poised to undergo a revolutionary change.</i>	Enthusiastic
2013	Sarivalasis et al ¹⁸ : <i>The potential implications of any cancer-related treatment decisions mean that doctors seek to find the best indicators to limit uncertainties and especially to target the disease with more and more specific treatments. These indicators are called tumor markers... With advances in knowledge of carcinogenesis and new techniques, new markers have emerged. They target cellular or genetic abnormalities. They move away from the established classifications of cancers, can be pro-clinical (testifying to the fate of a tumor in particular) or are predictive of the response to so-called targeted treatments. This is the beginning of the personalization of oncology.</i>	Enthusiastic
2015	Kalia ¹⁹ : <i>Clinical molecular diagnostics and biomarker discoveries in oncology are advancing rapidly as we begin to understand the complex mechanisms that transform a normal cell into an abnormal one. These discoveries have fueled the development of novel drug targets and new treatment strategies. The standard of care for patients with advanced-stage cancers has shifted away from an empirical treatment strategy based on the clinical-pathological profile to one where a biomarker driven treatment algorithm based on the molecular profile of the tumor is used.</i>	Enthusiastic
2017	Subbiah and Kurzrock ¹⁰ : <i>Oncology is at the forefront of implementing personalized/precision medicine, at least in part because cancer is a genomic disease. With unprecedented advances in the understanding of aberrant molecular activation pathways implicated in tumorigenesis coupled with the ever-increasing availability of cognate agents, we have a growing capability to inflict an assault on malignancies. Innovations in personalized medicine including genomic and immunologically targeted therapies have bestowed the gift of time to numerous patients...Many of the major advances in oncology over the past two decades are attributable to precision medicine, defined as biomarker-driven treatment.</i>	Enthusiastic
2019	Keam et al ²⁰ : <i>Recent remarkable progress in the fields of cancer genomics, computational analysis and drug discovery have changed the whole paradigm in cancer research. So called precision oncology, defined as molecular profiling of tumors to identify druggable alterations, is rapidly developing and waiting for entering the mainstream of cancer research as well as practice. In the era of precision oncology, traditional classification based on organ or pathology do not have clinical meaning anymore. Molecular subtype based on next-generation sequencing (NGS) will lead us to appropriate molecular targeted agents.</i>	Enthusiastic



Our analysis suggests that while the term “precision oncology” is currently most commonly understood to mean genomics-based tumour profiling, over the last decade its definition has shifted, overlapped and expanded to connote a variety of research fields that span basic research, clinical research and clinical practice.

Shifting definitions of precision oncology may reflect the natural scientific process where ideas evolve and change while concepts are emerging and undergoing clarification. At the same time, the shift may result in uncertainty among practitioners and the public as to what exactly precision oncology means. Moreover, claims about the ability of precision oncology to result in future advances in therapy are contingent about what precisely constitutes precision oncology. Standardisation and specification as to what precisely constitutes precision oncology may provide assistance in the ongoing debates about the potential of the field.^{8–11}

Interestingly, we find in 2011, when precision oncology was more nascent, there was a high ratio of reviews over original reports (60% and 30%, respectively). This is interesting because the conventional wisdom is that reviews serve as the culmination and summary of decades of work, but perhaps reviews occurring earlier in scientific movements allow researchers to debate, ponder and shape the ideas yet to come. Future research may study this for other fields and topics.

Strengths and limitations

Our study has three strengths worth mentioning. First, this study is the first formal publication to document the in-depth use of “precision oncology” terminology and to quantify its use and definition over the past decade. Second, our approach is a large and systematic assessment of the literature. Third, our figures aim to succinctly communicate the complex ambiguity that the term “precision oncology” has adopted in the literature.

In terms of limitations, we also note at least three. First, the concept of precision oncology is recognised to have interchangeable terminology; “precision oncology” can also be described as personalized oncology, personalised oncology, personalized cancer medicine, precision oncology, precision cancer medicine, precision medicine in cancer or precision therapy. With our limited search parameters, and choice of search terms selected, we acknowledge that there are many papers we may have overlooked due to the limitations of our choice of search terms. Second, we omitted even-numbered years, for the sake of time, though we think their inclusion is unlikely to change the general time trends observed here. Lastly, interpretation of terms may be susceptible to user bias, and other readers may interpret these articles differently. We encourage others to examine these papers.

Even with these limitations, it is clear that the terminology we use to describe progress of “precision oncology” work has expanded, overlapped and shifted—in other words, precision oncology has at times been used imprecisely. And yet, the field of “precision oncology”

is a consequential field and has gained momentum and considerable interest, judging by the growing number of articles in the biomedical literature on this topic (figure 1). If the term itself is vague, it suggests that the field of “precision oncology” itself may be unstructured, nascent or still coalescing.

CONCLUSION

Precision and personalised oncology are important concepts gaining increasing recognition and discussion in the peer review literature. The definitions used to describe these terms have been numerous, have overlapping concepts and have shifted over time. Our analysis sheds light on the way in which a novel movement in medicine defines itself over time.

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Data availability statement All data relevant to the study are included in the article, publicly available or uploaded as supplementary information.

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