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ORIGINAL RESEARCH ARTICLE

Maintaining Clinical Freedom Whilst Achieving Value in Biologics Prescribing: An Integrated Cross-Specialty Consensus of UK Dermatologists, Rheumatologists and Gastroenterologists

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Abstract

Background Biologics are now key drugs in the management of immune-mediated inflammatory diseases. However, the increasingly complex biologics environment and growing cost pressures in the UK have led to variability in drug commissioning and inequity of patient access across regions.

Objectives Our objectives were to provide consensus recommendations for enhancing the current situation in biologic prescribing in the UK by balancing clinical freedom with equitable distribution of biologics given the limited availability of resources.

Methods A modified Delphi approach was used to reach integrated, cross-specialty consensus among dermatologists, rheumatologists and gastroenterologists practising within the English National Health Service (NHS).

Results We describe the concepts of clinical freedom and clinical judgement and demonstrate how, together with patient choice, they can be exercised in the context of biologic prescribing in the NHS. We highlight that in England, local variations occur that are at odds with National Institute for Health and Care Excellence (NICE) guidance; these variably limit the degree to which clinicians can exercise clinical freedom and impact on equity of patient access to treatments. We define factors encompassing a drug's value and identify challenges to the measurement and interpretation of this concept, which can raise barriers to the freedom of clinical choice and appropriate prescribing decisions allowing practices of holistic and personalised medicine. Cross-specialty consensus recommendations on ensuring equitable access to biologics in the NHS while protecting appropriate and individualised drug selection for patients are provided. We have also provided strategies for improving physician–commissioner communication to harmonise equity of patient access to biologics across England and improve patient outcomes. Commentary from patient advisory groups indicates that they welcome our exploration that value does not equal cost and agree that there should be an emphasis on shared decision making, which requires the clinician to practice clinical freedom by aligning the patient's needs and preferences with available treatment choices.

Conclusions This consensus highlights the need to strike a balance between clinical freedom and short-term cost restrictions to support equitable resource distribution within the English NHS. Consideration of these recommendations may help to harmonise local, regional and national services and balance equity of patient access to biologic treatments with excellence in the NHS.

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Key Points

Clinical freedom and consideration of patient choice and preference are vital for individualised care. The increasing availability of new biologics and biosimilars adds cost-based complexity to prescribing decisions for patients who may require these drugs. Clinical freedom should be exercised within a value framework that forms the backbone of rigorous, transparent evidence reports to include available evidence and clinical experience.

Although UK National Institute for Health and Care Excellence (NICE) clinical guidance theoretically allows a degree of clinical freedom, local variations in interpretation occur, with a resulting impact on equity of patient access to treatments. The clinical freedom within UK NICE clinical guidelines could therefore be harmonised across local services to ensure equity of patient access to treatments.

Communication and collaboration between clinicians and commissioners can foster optimal pathway development for better value, access and patient outcomes.

1 Introduction

Biologics are a core part of treatment for many patients with moderate-to-severe immune-mediated inflammatory diseases (IMIDs), such as psoriasis, psoriatic arthritis (PsA), rheumatoid arthritis (RA) and inflammatory bowel diseases (IBDs; Crohn's disease and ulcerative colitis) [1–4]. These diseases have a number of commonalities in terms of pathophysiological mechanisms, overlap in patient population and management strategies [5–8]. In addition to potential synergies, this presents a number of shared challenges, of which, the balance between clinical freedom and equitable distribution of biologics is key.

Clinical practice guidelines increasingly acknowledge the benefits that biologics can offer patients [1, 9, 10]. Yet, although biologics demonstrate superior efficacy over conventional therapies, particularly in patients with moderate-to-severe IMIDs, they are notably more expensive. The recent availability of biosimilar agents for tumour necrosis factor inhibitors (TNFi) has relieved some aspects of cost pressures on healthcare systems [11–13]. However, biosimilar availability has coincided with the introduction of a number of biologics with novel modes of action, including inhibitors of interleukin (IL)-12/23, IL-23, IL-17 and anti-integrins, which have different efficacy and safety profiles. In certain therapy areas, some of these novel biologics have demonstrated improved clinical outcomes versus TNFi in direct head-to-head clinical trials (see the Table in the electronic supplementary material [ESM]), meta-analyses and real-world observational studies in terms of short- and long-term efficacy, durability, safety and longevity [9, 10, 14–31].

Clinical freedom, or a physician's right and duty to do what they regard as the best for their individual patient, is a key concept in choosing treatments together with patients through shared decision making [32]. Interlinked with this concept is clinical judgement, or the physician's ability to combine clinical experience and expertise with the best available evidence and resources to choose the appropriate treatment [33]. Both clinical freedom and clinical judgement are becoming increasingly important as the choice of available biologics continues to grow. The UK National Institute for Health and Care Excellence (NICE) guidelines are generally phrased to allow a degree of interpretation [34–37], which enables a physician to exercise some clinical freedom. Yet, within healthcare systems with finite resources, understandable onus is placed on decision makers to opt for the most cost-effective choice [11]. Emerging data show that this is translating into variations in biologic use across England due to local commissioning decisions and mandated clinical pathways [38]. There are likely multiple reasons behind this variability, including local expertise and historical patterns of use, which can leave patients subjected to an inequitable 'postcode lottery' of available treatments [38].

Across the three specialty areas, local, regional and national harmonisation of commissioning and prescribing services is required to permit synergies in NICE guideline interpretation and ensure equity of patient access to biologics through shared decision making. The Delphi process, which is a structured, egalitarian method for incorporating multiple expert views, can help to establish and document recommendations in instances such as this in which evidence is lacking and issues are difficult to define [39–42]. In this report, we aimed to use a modified Delphi process to generate an integrated consensus on clinical freedom and equitable use of biologics in England. We also offer practical strategies to optimise patient access to biologics and to enhance existing guidance and excellence in clinical outcomes for patients with IMIDs by balancing treatment choice with value for the English National Health Service (NHS).

2 Methodology

The panel consisted of invited representatives of specialties from across England, representing dermatology ($n=3$), rheumatology ($n=2$) and gastroenterology ($n=3$).

A modified Delphi process was used to reach consensus, consisting of an e-survey and a group meeting in January 2020. A literature review of 144 unique references was conducted to inform the e-survey content, using PubMed Central and the European, UK national and NICE clinical guidelines. Details of the search strategy and the full list of articles identified are presented in the ESM.

Consensus statements were voted on in the e-survey and using an anonymous mobile application during the meeting. E-surveys and meeting voting were programmed, administered and collated by OPEN Health Medical Communications to maintain blinded voting. Consensus statements assessed the level of agreement using the terms 'strongly disagree', 'disagree', 'agree' or 'strongly agree'. Consensus was defined as achievement of at least 75% 'agree' or 'strongly agree'. Results are reported as n/N voting 'agree' or 'strongly agree' (e.g. 7/8 indicates seven of eight panellists voting 'agree' or 'strongly agree'). Additional comments and discussions were recorded to supplement specific statements.

Following analysis of results and development of the manuscript, representatives from three UK patient advisory groups (National Rheumatoid Arthritis Society, Crohn's & Colitis UK and the Psoriasis Association) were asked to comment on this manuscript and the relevance of its recommendations for patients with IMIDs in England.

3 Results

3.1 Defining the Principle of Clinical Freedom and its Role in Clinical Choice

3.1.1 Expert Consensus

(i) Clinical freedom enables a physician to select the best treatment option in partnership with each individual patient (8/8 [100%]).
(ii) Clinical freedom should be exercised within a value framework, utilising all available evidence (8/8 [100%]).

Table 1 Factors that should be considered when deviating from a population pathway and that impact the choice of biologic prescription and influencing switching decisions, by consensus

Factors	To consider when deviating from a population pathway	Impacting choice of biologic prescription and influencing switching decisions
Disease factors		
Disease severity	7/8 (87.5)	–
Disease phenotype and/or pattern of area affected	6/8 (75)	8/8 (100)
Patient factors		
Disease impact on the individual patient	8/8 (100)	8/8 (100)
Response to previous treatments	7/8 (87.5)	8/8 (100)
Previous AEs or family history thereof	6/8 (75)	8/8 (100)
Comorbidities	8/8 (100)	8/8 (100)
Patient's age	6/8 (75)	6/8 (75)
Patient's race	6/8 (75)	–
Patient's preferences and beliefs	8/8 (100)	8/8 (100)
Patient's adherence	7/8 (87.5)	8/8 (100)
Clinical biomarkers or appropriate predictors of clinical response	–	6/8 (75)
Treatment factors		
Efficacy	6/8 (75)	7/8 (87.5)
Safety and tolerability profile	7/8 (87.5)	7/8 (87.5)
Treatment convenience/acceptability	7/8 (87.5)	8/8 (100)
Cost effectiveness of treatment	–	7/8 (87.5)
Value of treatment	–	7/8 (87.5)

Data are presented as *n*/*N* (%) unless otherwise indicated

AE adverse event

(iii) In the UK, factors affecting the degree to which clinicians can exercise clinical freedom include geographical location and disease specialty (8/8 [100%]).

(iv) Clinical judgement involves the interpretation of all available sources of information to formulate a recommended management plan for a patient (8/8 [100%]).

(v) Clinical guidelines provide a useful framework for how treatment options may be used at a population level. However, when determining an individualised treatment plan, the exercise of clinical judgement remains vital (8/8 [100%]).

- The panel reached consensus on factors that should be considered when deviating from a population pathway, which are summarised in Table 1.

(vi) In order to optimise care for both individual patients and the larger population, it is important for clinical guidelines and commissioning groups to strike a balance between clinical freedom and restrictions that support equitable resource distribution (8/8 [100%]).

3.1.2 Additional Comments

Debate on the exercising of clinical freedom and healthcare system resourcing practices is ongoing. Clinical judgement and clinical freedom are interlinked with patient choice and preference, and all play a role in appropriate prescribing for individual patients in a given value framework. Value frameworks, such as that devised by the Institute for Clinical and Economic Review, aim to provide sustainable access to high-value care for all patients. They offer a conceptual framework to assess an intervention's long-term value for money through its incremental cost effectiveness—including additional benefits, disbenefits and potential cost offsets for new treatments over a patient's lifetime—to inform decisions both at the patient/physician level and at the population level [43–45]. Clinical practice decisions are based on available evidence and experience; individual patients require tailored treatment according to the physician's judgement, and decisions should only be made after discussion with the patient [32]. Indeed, many clinicians argue that primary focus on the individual patient is the basis of clinical freedom [46], meaning that clinical freedom is a significant facilitator to the practice of personalised care. Table 1, which shows factors to consider when deviating from a population pathway, could be construed as suggesting that cost is not a consideration. Rather, it is intended that cost should not be the sole consideration, unless all other factors listed are equal.

In the specific case of the English healthcare system, a balance between clinical freedom and equitable resource distribution would continue to ensure fair implementation of NICE guidance.

Table 2 Factors encompassed in the concept of a drug's value, by consensus

Factors encompassed in the concept of a drug's value
Quality (6/8 [75])
Efficacy (8/8 [100])
Safety profile (8/8 [100])
Patient-centredness (6/8 [75])
Convenience (6/8 [75])
Unit cost (6/8 [75])
Potential to offset other healthcare costs (8/8 [100])

Data are presented as *n*/*N* [%] unless otherwise indicated

3.2 The Value of Biologics

3.2.1 Expert Consensus

(i) Interpretation of drug value is hampered by a lack of available evidence relating to long-term impact across a range of outcome measures of importance to patients, the healthcare system and society (8/8 [100%]).

- The panel reached consensus on factors that are encompassed by a drug's value, which are shown in Table 2.

(ii) Lack of transparency on drug pricing, regional variations, cost fluctuations and complex contracting arrangements present additional challenges to physicians' abilities to assess value (8/8 [100%]).

3.2.2 Additional Comments

The term 'drug value' can often be misunderstood or improperly used. This may present a challenge to the freedom of clinical choice and appropriate prescribing decisions that allow the practice of holistic and personalised medicine.

Efficacy was agreed to be a factor encompassed by a drug's value and that should impact choice of biologic prescription or the decision to switch between agents. However, efficacy is a composite of several aspects, including short- and long-term clinical scores (e.g. Psoriasis Area and Severity Index response, American College of Rheumatology response, Crohn's Disease Activity Index), speed of response, durability and patient-reported outcome measures. Clinical trial data suggest that novel biologics appear to offer additional value for particular patients over older agents or conventional non-biologics. The evidence base for drug impact across a range of clinical outcomes is limited but growing. For example, there is now evidence showing reductions in the incidence of cardiovascular disease in patients receiving adalimumab for RA [47], whilst there is increasing evidence and guidance to state that some TNFi

(adalimumab, certolizumab pegol, golimumab, infliximab) may be possible treatment options during pregnancy in certain patients for whom the benefit of staying on treatment outweighs any potential risk to the foetus [9, 10, 48–53]. Yet, most registration study data are short term in nature, typically demonstrating outcomes of no longer than 1 year and with primary focus on clinical scores [35, 54–71]. This highlights the continued lack of published evidence to demonstrate a drug's value.

It has been argued that clinical freedom may be limited by proscriptive treatment and resourcing mandates or reimbursement practices [72]. However, the authors argue that a lack of evidence to demonstrate value can also be a limiting factor. In the absence of unlimited resources, medical care must be restricted to interventions of proven value. Therefore, some suggest that, without evidence of efficacy and safety, resources should not be allocated to a particular treatment [73–75]. Although biologics have revolutionised the management of many IMIDs, there remains interpatient variability in clinical and safety responses to therapies [76], and some published literature from randomised controlled trials (RCTs) is not always applicable to a certain patient's situation. Therefore, the clinician's experience should be included among available evidence to be used within the value framework, enabling them to choose from multiple agents or classes of agents, and to optimise outcomes for each patient.

3.3 Equitable Use of Biologics in the English Healthcare System

3.3.1 Expert Consensus

(i) Clinical freedom to prescribe across all available treatment modalities is important to offer personalised care to patients (8/8 [100%]).

- Consensus was reached on a number of factors that can impact choice of biologic prescription and influence the decision to switch from one biologic class to another (Table 1).

(ii) Local pathways can help commissioners and clinicians reach a shared understanding of how national guidelines may impact upon their patient populations. However, variable interpretations and setting of additional barriers and targets create inequity of patient access (8/8 [100%]).

(iii) Effective development, implementation and updating of current pathways requires close cooperation between clinicians and local commissioners. It is vital that these two groups maintain ongoing, open and transparent dialogue (8/8 [100%]).

3.3.2 Additional Comments

The availability of newer biologic options has expanded therapeutic options for patients with IMIDs; however, it should be noted that their availability in IBD has so far been slower than in psoriasis and PsA, which is mirrored by a slower rate of change in NICE guidelines and treatment choice availability for biologic-eligible patients in clinical practice.

In psoriasis and PsA, novel biologics may be considered over TNFi, especially for patients with specific disease characteristics such as those with a more aggressive disease course, involvement of vulnerable areas (e.g. genitals), a worse phenotype, or other comorbidities, all of which may increase impact on quality of life [1, 9]. In addition to potential improvements in efficacy, access to drugs with better safety profiles is particularly important for certain patient subgroups [9, 10, 20, 23, 77]. Clinicians may have a choice of biologic classes and will therefore need to consider variations in a patient's disease presentation, disease severity and comorbidities when deciding which drug to use. For example, in patients presenting with multiple IMIDs, it may be logical to select an agent that is effective across disease areas and that would not otherwise be first choice. TNFi biosimilars have an important role in clinical practice by reducing direct drug costs. However, as with any biologic, biosimilar use must be exercised within a framework that considers clinical value as far as evidence is available. This includes the growing literature base assessing factors beyond direct costs such as tolerability issues (e.g. injection site reactions with citrate-containing agents), efficacy (e.g. the nocebo effect) and indirect costs (e.g. the administrative costs or increased healthcare utilisation associated with non-medical switching) [78–85]. Of note, although these recommendations were made with a specific focus on biologics, the concept can be extrapolated to other drugs with a high unit cost, e.g. targeted systemic small molecule inhibitors such as Janus kinase (JAK) and phosphodiesterase E4 (PDE4) inhibitors.

3.4 Practical Strategies to Optimise Patient Access

3.4.1 Improving Dialogue

Enhanced communication between clinician and commissioner is critical to improve equity of access that aligns with the principles of NICE guidelines and permits clinical freedom. Commissioners should understand the commonalities and differences between IMIDs. Although recommendations for one may not necessarily transfer to others, there are significant overlaps in the specialties. Similarly, understanding the pricing factors involved in commissioning decisions would aid physicians in assessing a drug's value,

which cannot be complete without knowledge of cost. Some clinical commissioning groups (CCGs) or clinician pathway groups use tables that group biologics by cost bands to aid decision making. These may be beneficial if implemented more widely across England.

Clinicians are best placed to shift the focus from resources and costs to health outcomes, quality of life and patient satisfaction. Hence, medical participation in management, as well as perhaps commissioning decisions around it, is imperative [74]. Understanding decision making by clinicians helps clinical leaders and policy makers to determine resource allocation, which then allows clinicians to make appropriate treatment selections [86].

A good relationship between commissioners and clinicians is key to good communication; conversely, the lack of such a relationship can present challenges to current practices. Strategies for improving communication could help resolve the majority of disagreements around commissioning decisions (see Box 1). In rare circumstances, it may be necessary to consider formal proceedings such as a letter to the medical director outlining the grounds of concern and invoking the formal complaint process. In this instance, we regard it as good practice to copy the patient into correspondence so they can be fully aware of ongoing discussions regarding their care.

Box 1 Methods for improving physician–commissioner communication

Regular informal meetings, emails or phone calls between commissioners and clinicians to facilitate open, ongoing communication and reduce the overall burden at official commissioning meetings.
Physician attendance at relevant commissioning meetings, particularly with presentation of case studies, highlighting patient impact to illustrate why pathways need to be adapted or developed.
Patient focus groups to help practitioners and commissioners understand patient perspective.
Patient organisations can help with focus groups by recruiting patients with different characteristics.
Agreements to share cost savings (note that this will rely on transparent drug costings).
Investment by commissioners in clinical services or projects that improve efficiency or allow savings (e.g. funding posts that facilitate switching to biosimilars).
Consideration of management strategies beyond biologics.

3.4.2 Aligning Clinical Judgment and Commissioning Decisions

Ideally, collaboration between physicians and commissioning groups should foster the development of suitable pathways and protocols that reflect the clinical freedom permitted by NICE guidelines, which not only respect the physician's ability to select management strategies for individual patients but also eliminate geographical variations in care. Improved dialogue between specialties would additionally benefit pathway development due to differences in clinical outcomes: the effectiveness of a specific biologic in one disease may be suboptimal in another, knowledge of which can be improved through interactive working and cross-specialty dialogue.

In some cases, it may be necessary to challenge a commissioning decision, such as where the clinician believes a particular CCG pathway mandates limits and targets for certain agents to the detriment of a patient. Improved communication and informal discussion between clinicians and commissioners should be the first port of call to reach a solution or compromise. Figure 1 depicts a process and resource bank that aims to support physicians and patients to resolve a misalignment between clinical judgement, as per NICE guidelines and a CCG pathway.

Independent/individual funding requests (IFRs) may also be a route to funding of a drug that is not supported in a CCG pathway or by the English NHS. They are submitted when the clinician believes that an individual patient has an 'exceptional health need' and are considered by a panel of clinicians, health experts and laypeople on the basis of evidence for clinical and cost effectiveness, as well as equity for the whole population [87, 88]. IFRs are not appropriate where a drug is NICE approved and when proposed use is within the relevant NICE technology appraisal guidance. The authors express variable sentiments towards IFRs, which is likely reflective of local CCG variations. Some feel that they are not a pragmatic way to reach a solution, due to the demand for specific, robust outcome and economic evidence, despite the fact that the patient's case is exceptional and is therefore unlikely to align with evidence published in RCTs. Others have successfully argued that a lack of evidence does not mean a lack of efficacy and have used published case reports or phase II studies to support an application.

Clinicians and commissioners should be aware that the NHS has a duty to fund and resource medicines and treatments recommended by NICE's technology appraisals. Patients have the right to drugs and treatments that have been recommended by NICE for use in the NHS if their doctor believes they are clinically appropriate [89]. Although this may not currently be the case in certain CCGs, the authors emphasise that ongoing communication can optimise development of sufficiently flexible pathways that can account for a variety of patient situations and minimise the need for a physician to challenge them.

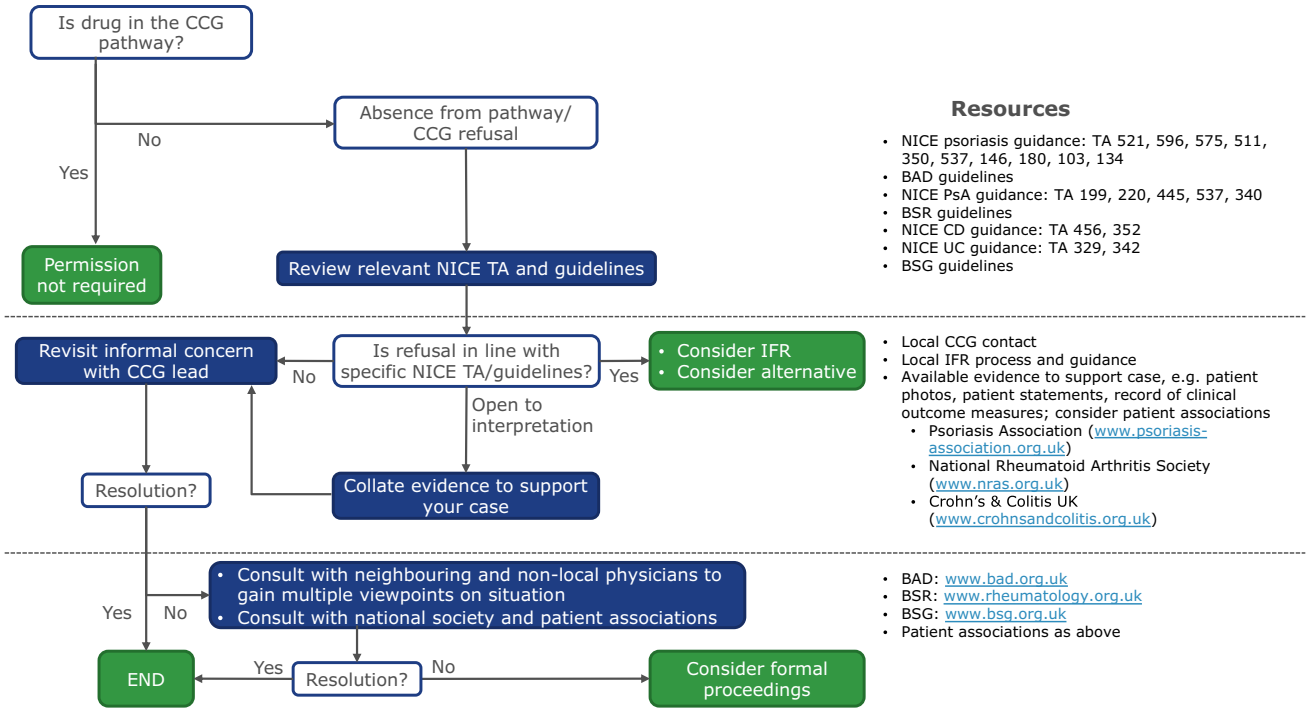

Fig. 1 Process and resources for reaching a solution in the event of misalignment between clinical judgement as per NICE guidelines and a CCG pathway. *BAD* British Association of Dermatologists, *BSG* British Society of Gastroenterologists, *BSR* British Society for Rheumatology, *CCG* Clinical Commissioning Group, *CD* Crohn's disease, *IFR* individual/independent funding request, *NICE* National Institute for Health and Care Excellence, *TA* treatment appraisal, *UC* ulcerative colitis

4 Discussion

The panel has discussed clinical freedom and clinical judgement, which are two related concepts in the context of biologics prescribing in England. Although both play a part in treatment decisions, clinical judgement is broader and goes beyond just treatment selection, considering situational factors such as those imposed by the healthcare system. The consensus reached shows that it is vital for physicians to be able to make clinical choices to best serve the variety of patients that they treat.

NHS working groups have already set out the importance of a collaborative approach in the commissioning of biologics, including biosimilars, and offered some guidance as to how this could be achieved in the current climate of cost pressures and evidence gaps [11, 90]. We endeavour to enhance these processes by defining important concepts of clinical freedom, clinical judgement and drug value in the context of biologic prescribing.

In a variety of therapy areas, clinical guidance or decision-making tools have been shown to correlate with expert clinical judgement and to improve patient outcomes [39, 91–94]. It has been demonstrated that improvements in available clinical tools and better knowledge thereof can alter clinical judgement [88]. Guidelines must therefore help to define treatment standards while accurately reflecting areas of uncertainty to avoid limiting innovative practices in clinical care [72]. Treatment guidelines increasingly advocate that patient preference should factor into treatment decisions, thus permitting practice of personalised medicine to optimise patient adherence and treatment outcomes [1, 9, 10, 34, 36, 37, 95, 96]. Furthermore, there will always be patients who fall outside of the available evidence and require expert interpretation for their treatment. For this reason, our proposals are intended to help re-align clinical judgement and commissioning decisions and to include the patient, who is directly impacted, in these discussions.

The debate on how best to balance competing demands when prescribing within a finite budget is ongoing. The quality-adjusted life-year (QALY) measure accounts for life length and quality and was designed to standardise healthcare funding decisions across diseases based on the degree of a treatment's health benefit [45, 97–99]. The QALY is a cornerstone of NICE health technology appraisals and is seen as an important tool for ensuring maximum benefits when healthcare budgets are limited [97]. However, the QALY also remains problematic for applying a uni-dimensional measure to the multi-dimensional nature of health effects without recognising non-health benefits [45, 97–99].

There are limitations to assessing a treatment based on the QALY, including false limitation of clinical freedom and potential hindrance of patient outcomes. Such limitations are likely to be exacerbated by personalised medicine [99]. Particularly pertinent to our recommendations are the ethical issues, wherein the QALY is unable to discriminate between individual patients or situational factors that may have a considerable impact on the patient [97, 99]. In the UK, QALYs are usually based on general quality-of-life instruments that are not sufficiently sensitive to account for small but meaningful health status changes in specific patient subgroups or the disease-specific experience [97, 99]. Examples include the individual with RA unable to type because of hand pain and stiffness, someone whose mobility and hand function are limited by palmoplantar psoriasis, or the person living with Crohn's disease who misses appointments because of the need to remain close to a toilet, thus escaping incorporation into health technology assessments.

Our consensus recommendations align with the views of other groups: there can be advantages to incorporating additional attributes of benefit into analytical frameworks to support explicit and transparent decision making [45]. Yet, whilst there is a need for empirical assessment to support funding decisions and establish appropriate overall expenditure [45], the evidence is usually based on efficacy from strict RCT populations. For the majority of patients, access to medicines falls within QALY remits and calculations; it is for those who sit outside the norm, and who might typically be the subject of an IFR, that readjustment and harmonisation of services across England can be improved. Here, value frameworks could assist with value judgements and support transparency around prescribing decisions. An expanded-value framework has been proposed, incorporating a wider range of elements beyond the core of health gain and offset of cost savings, including productivity, reduction in uncertainty of response to treatment and value of hope [98]. In line with our own recommendations and commentary from patient groups, the importance of including patients in discussions around value has also been highlighted [100]. This would be further enhanced by additional data for both health- and non-health benefits, spanning more complex, real-world cohorts as well as stringent RCT populations. Such elements may not be the most important in definition of value, or the easiest to incorporate, and the relevant data may not yet exist [98, 99]. Yet, without consideration of these elements, patients may be subjected to inappropriate access decisions and the potential exists for suboptimal spending on healthcare [98, 99].

By way of enhancing the current situation, we have supplemented the consensus on clinical freedom and biologics prescribing in England by suggesting practical ways to improve communication between clinicians and commissioners. We have attempted to enhance the existing decision-making processes by offering recommendations for collaboration, communication and resource sharing to facilitate solutions for patients with IMIDs, while considering the economic sustainability of the healthcare system. Finally, input from three relevant expert patient organisations indicates the applicability of these recommendations to the patients who are ultimately affected by any decisions (Box 2). As a future step, it would be valuable to gain perspective from commissioners from multiple CCGs and specialties to further understand the processes and relative differences in commissioning decisions across England.

Box 2 Real-life applicability of these recommendations for patients—statement from the National Rheumatoid Arthritis Society, Crohn's & Colitis UK, and the Psoriasis Association

We welcome the exploration that value does not equal cost and echo the view that drug efficacy is important when considering drug value. Concordance is linked with efficacy, and the poorest-value drug is the one that is prescribed but not used.

We appreciate that clinical guidelines increasingly acknowledge the additional value of novel biologics with different modes of action. However, the guidelines are not being filtered down into practice. When decisions reach a local level, it too often comes back to cost. Better understanding of biologics and therefore personalised medicine has come a long way; however, this is being greatly stifled by the need for prescribing the cheapest biologic and not always following NICE guidance but instead CCG pathways. We would therefore agree with the authors that there is an inequitable postcode lottery in terms of biologic availability to patients.

As the patient is directly impacted, it is vital to include them in discussions at all stages of the care pathway. There should be an emphasis on shared decision making throughout, which requires the clinician to practice clinical freedom by aligning the patient's needs and preferences with the available treatment choices. Yet, although shared decision making is listed in many principles of care, it often ends up as just rhetoric. It should involve a meaningful discussion between physician and patient, reflective of the patient's educational level, preferences and their home and work situation, about the risks and benefits of treatment. This enables the physician and patient to reach a joint decision that will suit the patient as an individual in terms of their disease and their personal situation.

In discussions around commissioning and care pathways, the patient's perspective is also of value. This could include picture and video evidence from patients and their carers or families in debates with commissioners, or inclusion of expert patient organisations on decision boards. Patient organisations can help to provide context for commissioning decisions by recruiting patients with different characteristics for focus groups, highlighting the importance of health outcomes and patient satisfaction as clear goals in clinical pathways.

4.1 Strengths and Limitations of These Recommendations

A Delphi process is affected by the number and representativeness of its participants, which will affect the range of discussion and quantity of data [41]. The project's main

limitation is the small number of participants in the Delphi process. No guideline on the standard number of participants or the criteria against which an appropriate number of participants could be judged yet exist [101, 102]. Although Delphi panels most frequently consist of 10–100 participants [101, 102], it has been suggested that confidence in the results could still be maintained with a smaller Delphi panel if participants had similar training, knowledge and understanding of the field [101]. Our panellists were all from academic centres; the drugs discussed here are typically prescribed in secondary care, so physicians in academic centres are likely to have the greatest experience and understanding of their use, benefits and drawbacks in patients with complex needs. As a future step, there could be value in expanding the consensus statements defined and voted upon here to a wider group of physicians, to understand the applicability to the general population of biologic-eligible patients.

A key strength of this project is its cross-specialty focus. Inclusion of both specialist physicians and feedback from multiple patient groups highlight the broad scope of the issues discussed. Each panellist represented a different CCG; although some may be geographically close, such as those in London, there are discrepancies even within neighbouring boroughs of the capital, which further highlight the issue under discussion. The commentary from patients in particular indicates the relevance of these issues to those ultimately affected. Given the interlinked nature of many IMIDs, in both their manifestation and their management, these practical recommendations have the potential to benefit a greater number of patients than if they were to address just one disease.

5 Conclusions

This consensus highlights that clinicians must be able to exercise clinical freedom in order to best serve patients; however, this is necessarily limited by the funding restrictions of a healthcare system. Striking a balance between clinical freedom and short-term cost restrictions is vital to support equitable resource distribution. Consideration of these recommendations may help to harmonise local, regional and national services through a multi-stakeholder approach involving policy and patient groups as well as physicians and commissioners, improve data generation to support value-based prescribing decisions, and ultimately ensure equity of patient access to biologic treatments.

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References

1. Coates LC, Kavanaugh A, Mease PJ, Soriano ER, Laura Acosta-Felquer M, Armstrong AW, et al. Group for research and assessment of psoriasis and psoriatic arthritis 2015 treatment recommendations for psoriatic arthritis. Arthritis Rheumatol. 2016;68:1060–71.
2. Coates LC, Gossec L, Ramiro S, Mease P, Van Der Heijde D, Smolen JS, et al. New GRAPPA and EULAR recommendations for the management of psoriatic arthritis. Rheumatol. 2017;56:1251–3.
3. Gomollón F, Dignass A, Annese V, Tilg H, Assche GV, Lindsay JO, et al. 3rd European evidence-based consensus on the diagnosis and management of Crohn's disease 2016: part 1: diagnosis and medical management on behalf of ECCO. J Crohns Colitis. 2017;11:3–25.
4. Harbord M, Eliakim R, Bettenworth D, Karmiris K, Katsanos K, Kopylov U, et al. J Crohns Colitis. 2017;769–784.
5. Gooderham MJ, Papp KA, Lynde CW. Shifting the focus—the primary role of IL-23 in psoriasis and other inflammatory disorders. J Eur Acad Dermatol Venereol. 2018;32:1111–9.
6. Boutet MA, Nerviani A, Gallo Afflitto G, Pitzalis C. Role of the IL-23/IL-17 axis in psoriasis and psoriatic arthritis: the clinical importance of its divergence in skin and joints. Int J Mol Sci. 2018;19:530.
7. Eppinga H, Poortinga S, Thio HB, Nijsten TEC, Nuij VJAA, Van Der Woude CJ, et al. Prevalence and phenotype of concurrent psoriasis and inflammatory bowel disease. Inflamm Bowel Dis. 2017;23:1783–9.
8. Whitlock SM, Enos CW, Armstrong AW, Gottlieb A, Langley RG, Lebwohl M, et al. Management of psoriasis in patients with inflammatory bowel disease: from the Medical Board of the National Psoriasis Foundation. J Am Acad Dermatol. 2018;78:383–94.
9. Smith CH, Yiu ZZN, Bale T, Burden AD, Coates LC, Edwards W, et al. British Association of Dermatologists guidelines for biologic therapy for psoriasis 2020: a rapid update. Br J Dermatol. 2020;183:628–37.
10. Lamb CA, Kennedy NA, Raine T, Hendy PA, Smith PJ, Limdi JK, et al. British Society of Gastroenterology consensus guidelines on the management of inflammatory bowel disease in adults. Gut. 2019;68:s1–106.
11. NHS England. Commissioning framework for biological medicines (including biosimilar medicines). https://www.england.nhs.uk/wp-content/uploads/2017/09/biosimilar-medicines-commissioning-framework.pdf. Accessed 31 July 2020.
12. Gecse KB, Khanna R, Van Den Brink GR, Ponsioen CY, Löwenberg M, Jairath V, et al. Biosimilars in IBD: hope or expectation? Gut. 2013;62:803–7.
13. Feagan B. Benefits, concerns, and future directions of biosimilars in inflammatory bowel disease. Gastroenterol Hepatol. 2017;13:745–7.
14. Strober BE, Bissonnette R, Fiorentino D, Kimball AB, Naldi L, Shear NH, et al. Comparative effectiveness of biologic agents for the treatment of psoriasis in a real-world setting: results from a large, prospective, observational study (Psoriasis Longitudinal Assessment and Registry [PSOLAR]). J Am Acad Dermatol. 2016;74:851–61.
15. Langley RG, Elewski BE, Lebwohl M, Reich K, Griffiths CEM, Papp K, et al. Secukinumab in plaque psoriasis—results of two phase 3 trials. N Engl J Med. 2014;371:326–38.
16. Gottlieb AB, Langley RG, Philipp S, Sigurgeirsson B, Blauvelt A, Martin R, et al. Secukinumab improves physical function in subjects with plaque psoriasis and psoriatic arthritis: results from two randomized, phase 3 trials. J Drugs Dermatol. 2015;14:821–33.
17. Mease PJ, Van Der Heijde D, Ritchlin CT, Okada M, Cuchacovich RS, Shuler CL, et al. Ixekizumab, an interleukin-17A specific monoclonal antibody, for the treatment of biologic-naive patients with active psoriatic arthritis: results from the 24-week randomised, double-blind, placebocontrolled and active (adalimumab)-controlled period of the phase III trial SPIRIT-P1. Ann Rheum Dis. 2017;76:79–87.
18. Sands BE, Peyrin-Biroulet L, Loftus EV, Danese S, Colombel J-F, Törüner M, et al. Vedolizumab versus adalimumab for moderate-to-severe ulcerative colitis. N Engl J Med. 2019;381:1215–26.
19. Bonovas S, Lytras T, Nikolopoulos G, Peyrin-Biroulet L, Danese S. Systematic review with network meta-analysis: comparative assessment of tofacitinib and biological therapies for moderate-to-severe ulcerative colitis. Aliment Pharmacol. 2018;47:454–65.
20. Wong U, Cross RK. Expert opinion on interleukin-12/23 and interleukin-23 antagonists as potential therapeutic options for the treatment of inflammatory bowel disease. Expert Opin Investig Drugs. 2019;28:473–9.
21. Dávila-Seijo P, Dauden E, Carretero G, Ferrandiz C, Vanaclocha F, Gómez-García F-J, et al. Survival of classic and biological systemic drugs in psoriasis: results of the BIOBADADERM registry and critical analysis. J Eur Acad Dermatol Venereol. 2016;30:1942–50.
22. Egeberg A, Ottosen MB, Gniadecki R, Broesby-Olsen S, Dam TN, Bryld LE, et al. Safety, efficacy and drug survival of biologics and biosimilars for moderate-to-severe plaque psoriasis. Br J Dermatol. 2018;178:509–19.
23. Hendrix N, Ollendorf DA, Chapman RH, Loos A, Liu S, Kumar V, et al. Cost-effectiveness of targeted pharmacotherapy for moderate to severe plaque psoriasis. J Manag Care Spec Pharm. 2018;24:1210–7.
24. Sawyer LM, Malottki K, Sabry-Grant C, Yasmeen N, Wright E, Sohrt A, et al. Assessing the relative efficacy of interleukin-17 and interleukin-23 targeted treatments for moderate-to-severe plaque psoriasis: a systematic review and network meta-analysis of PASI response. PLoS One. 2019;14:e0220868.
25. Blauvelt A, Papp KA, Griffiths CEM, Randazzo B, Wasfi Y, Shen YK, et al. Efficacy and safety of guselkumab, an anti-interleukin-23 monoclonal antibody, compared with adalimumab for the continuous treatment of patients with moderate to severe psoriasis: results from the phase III, double-blinded, placebo- and active comparator–controlled VOYAGE 1 trial. J Am Acad Dermatol. 2017;76:405–17.
26. Gordon KB, Blauvelt A, Foley P, Song M, Wasfi Y, Randazzo B, et al. Efficacy of guselkumab in subpopulations of patients with moderate-to-severe plaque psoriasis: a pooled analysis of the phase III VOYAGE 1 and VOYAGE 2 studies. Br J Dermatol. 2018;178:132–9.
27. Sbidian E, Chaimani A, Afach S, Doney L, Dressler C, Hua C, et al. Systemic pharmacological treatments for chronic plaque psoriasis: a network meta-analysis. Cochrane Database Syst. Rev. 2020;CD011535.
28. Reich K, Gooderham M, Thaçi D, Crowley JJ, Ryan C, Krueger JG, et al. Risankizumab compared with adalimumab in patients with moderate-to-severe plaque psoriasis (IMMvent): a randomised, double-blind, active-comparator-controlled phase 3 trial. Lancet. 2019;394:576–86.
29. Reich K, Papp KA, Blauvelt A, Tyring SK, Sinclair R, Thaçi D, et al. Tildrakizumab versus placebo or etanercept for chronic plaque psoriasis (reSURFACE 1 and reSURFACE 2): results from two randomised controlled, phase 3 trials. Lancet. 2017;390:276–88.

30. Papp KA, Leonardi CL, Blauvelt A, Reich K, Korman NJ, Ohtsuki M, et al. Ixekizumab treatment for psoriasis: integrated efficacy analysis of three double-blinded, controlled studies (UNCOVER-1, UNCOVER-2, UNCOVER-3). Br J Dermatol. 2018;178:674–81.
31. Menter A, Papp KA, Gooderham M, Pariser DM, Augustin M, Kerdel FA, et al. Drug survival of biologic therapy in a large, disease-based registry of patients with psoriasis: results from the Psoriasis Longitudinal Assessment and Registry (PSOLAR). J Eur Acad Dermatol Venereol. 2016;30:1148–58.
32. Hampton JR. Evidence-based medicine, opinion-based medicine, and real-world medicine. Perspect Biol Med. 2002;45:549–68.
33. MacKinnon RJ. Evidence based medicine methods (part 1): the basics. Pediatr Anesth. 2007;17:918–23.
34. NICE. Systemic biological therapy for psoriasis—NICE Pathways. https://pathways.nice.org.uk/pathways/psoriasis#path=view%3A/pathways/psoriasis/systemic-biological-therapy-for-psoriasis.xml&content=view-index. Accessed 31 July 2020.
35. NICE. Etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis. https://www.nice.org.uk/guidance/ta199. Accessed 31 July 2020.
36. NICE. Crohn's disease: management NICE guideline. Available from: http://www.nice.org.uk/guidance/ng129. Accessed 31 July 2020.
37. NICE. Ulcerative colitis: management NICE guideline. Available from: http://www.nice.org.uk/guidance/ng130. Accessed 31 July 2020.
38. Mistry J, Hill D, Kaul A. CCG biologics pathways: re-introduction of the postcode lottery by stealth. Rheumatology. 2020;59(Suppl. 2):87.
39. Hänsel Petersson G, Åkerman S, Isberg PE, Ericson D. Comparison of risk assessment based on clinical judgement and Cariogram in addition to patient perceived treatment need. BMC Oral Health. 2016;17:13.
40. Jones J, Hunter D. Qualitative research: consensus methods for medical and health services research. BMJ. 1995;311:376.
41. Hasson F, Keeney S, McKenna H. Research guidelines for the Delphi survey technique. J Adv Nurs. 2000;32:1008–15.
42. Raine R, Sanderson C, Black N. Developing clinical guidelines: a challenge to current methods. BMJ. 2005;331:631–3.
43. ICER. ICER Value Assessment Framework. https://icer-review.org/methodology/icers-methods/icer-value-assessment-framework-2/. Accessed 27 Nov 2020.
44. Angelis A, Kanavos P, Phillips LD. ICER value framework 2020 update: recommendations on the aggregation of benefits and contextual considerations. Value Health. 2020;23:1040–8.
45. Sculpher M, Claxton K, Pearson SD. Developing a value framework: the need to reflect the opportunity costs of funding decisions. Value Health. 2017;20:234–9.
46. Monaghan N. Human nature and clinical freedom, barriers to evidence-based practice? Br Dent J. 1999;186:208–9.
47. Mehta NN, Shin DB, Joshi AA, Dey AK, Armstrong AW, Duffin KC, et al. Effect of 2 psoriasis treatments on vascular inflammation and novel inflammatory cardiovascular biomarkers: a randomized placebo-controlled trial. Circ Cardiovasc Imaging. 2018;11:e007394.
48. Puchner A, Gröchenig HP, Sautner J, Helmy-Bader Y, Juch H, Reinisch S, et al. Immunosuppressives and biologics during pregnancy and lactation: a consensus report issued by the Austrian Societies of Gastroenterology and Hepatology and Rheumatology and Rehabilitation. Wien Klin Wochenschr. 2019;131:29–44.
49. Lichtenstein GR, Feagan BG, Mahadevan U, Salzberg BA, Langholff W, Morgan GJ, et al. Pregnancy outcomes reported during the 13-year TREAT registry: a descriptive report. Am J Gastroenterol. 2018;113:1678–88.
50. British National Formulary. Golimumab. https://bnf.nice.org.uk/drug/golimumab.html#pregnancy. Accessed 27 Nov 2020.
51. British National Formulary. Adalimumab. https://bnf.nice.org.uk/drug/adalimumab.html#pregnancy. Accessed 27 Nov 2020.
52. British National Formulary. Certolizumab pegol. https://bnf.nice.org.uk/drug/certolizumab-pegol.html#pregnancy. Accessed 27 Nov 2020.
53. British National Formulary. Etanercept. https://bnf.nice.org.uk/drug/etanercept.html#pregnancy. Accessed 27 Nov 2020.
54. NICE. Adalimumab for the treatment of adults with psoriasis. http://www.nice.org.uk/guidance/ta146. Accessed 06 Aug 2020.
55. NICE. Certolizumab pegol and secukinumab for treating active psoriatic arthritis after inadequate response to DMARDs. http://www.nice.org.uk/guidance/ta445. Accessed 06 Aug 2020.
56. NICE. Adalimumab, etanercept and infliximab for the treatment of rheumatoid arthritis. https://www.nice.org.uk/guidance/ta130. Accessed 06 Aug 2020.
57. NICE. Ustekinumab for treating active psoriatic arthritis. https://www.nice.org.uk/guidance/ta340. Accessed 06 Aug 2020.
58. NICE. Risankizumab for treating moderate to severe plaque psoriasis. https://www.nice.org.uk/guidance/ta596. Accessed 06 Aug 2020.
59. NICE. Ustekinumab for moderately to severely active Crohn's disease after previous treatment. https://www.nice.org.uk/guidance/ta456. Accessed 06 Aug 2020.
60. NICE. Vedolizumab for treating moderately to severely active ulcerative colitis. https://www.nice.org.uk/guidance/ta342. Accessed 06 Aug 2020.
61. NICE. Infliximab, adalimumab and golimumab for treating moderately to severely active ulcerative colitis after the failure of conventional therapy. https://www.nice.org.uk/guidance/ta329. Accessed 06 Aug 2020.
62. NICE. Vedolizumab for treating moderately to severely active Crohn's disease after prior therapy. https://www.nice.org.uk/guidance/ta352. Accessed 06 Aug 2020.
63. NICE. Brodalumab for treating moderate to severe plaque psoriasis. http://www.nice.org.uk/guidance/ta511. Accessed 06 Aug 2020.
64. NICE. Ixekizumab for treating moderate to severe plaque psoriasis. Available at: https://www.nice.org.uk/guidance/ta442. Accessed 06 Aug 2020.
65. NICE. Costing statement : Ustekinumab for the treatment of adults with moderate to severe psoriasis. https://www.nice.org.uk/guidance/ta180. Accessed 06 Aug 2020.
66. NICE. Golimumab for the treatment of psoriatic arthritis. http://www.nice.org.uk/guidance/ta220. Accessed 06 Aug 2020.
67. NICE. Guselkumab for treating moderate to severe plaque psoriasis. http://www.nice.org.uk/guidance/ta521. Accessed 06 Aug 2020.
68. NICE. Infliximab for the treatment of adults with psoriasis. http://www.nice.org.uk/guidance/ta134. Accessed 06 Aug 2020.
69. NICE. Ixekizumab for treating active psoriatic arthritis after inadequate response to DMARDs. http://www.nice.org.uk/guidance/ta537. Accessed 06 Aug 2020.
70. NICE. Secukinumab for treating moderate to severe plaque psoriasis. http://www.nice.org.uk/guidance/ta350. Accessed 06 Aug 2020.
71. NICE. Tildrakizumab for treating moderate to severe plaque psoriasis. http://www.nice.org.uk/guidance/ta575. Accessed 06 Aug 2020.
72. Conroy M, Shannon W. Clinical guidelines: their implementation in general practice. Br J Gen Pract. 1995;45:371–5.
73. Hampton JR. The end of clinical freedom. BMJ. 1983;287:1237–8.
74. Williams A. Health economics: the end of clinical freedom? BMJ. 1988;297:1183–6.

75. Schimpf K. Should clinical freedom be constrained in the name of self-sufficiency? Blood Coagul Fibrinol. 1994;5:S47–50.
76. Ayala F, Lambert J, TANGO Study Group. Efficacy, tolerability and safety of switching from etanercept to infliximab for the treatment of moderate-to-severe psoriasis: a multicenter, open-label trial (TANGO). J Dermatolog Treat. 2015;26:304–311.
77. Amin M, No DJ, Egeberg A, Wu JJ. Choosing first-line biologic treatment for moderate-to-severe psoriasis: what does the evidence say? Am J Clin Dermatol. 2018;19:1–13.
78. Tarallo M, Onishchenko K, Alexopoulos ST. Costs associated with non-medical switching from originator to biosimilar etanercept in patients with rheumatoid arthritis in the UK. J Med Econ. 2019;22:1162–70.
79. Rezk MF, Pieper B. Treatment outcomes with biosimilars: be aware of the nocebo effect. Rheumatol Ther. 2017;4:209–18.
80. Gecse KB, Cumming F, D'Haens G. Biosimilars for inflammatory bowel disease: how can healthcare professionals help address patients' concerns? Expert Rev Gastroenterol Hepatol. 2019;13:143–55.
81. Gibofsky A, Skup M, Mittal M, Johnson SJ, Davis M, Chao J, et al. Effects of non-medical switching on outcomes among patients prescribed tumor necrosis factor inhibitors. Curr Med Res Opin. 2017;33:1945–53.
82. Nguyen E, Weeda ER, Sobieraj DM, Bookhart BK, Piech CT, Coleman CI. Impact of non-medical switching on clinical and economic outcomes, resource utilization and medication-taking behavior: a systematic literature review. Curr Med Res Opin. 2016;32:1281–90.
83. Dolinar R, Kohn CG, Lavernia F, Nguyen E. The non-medical switching of prescription medications. Postgrad Med. 2019;131:335–41.
84. Chapman MA, Charles D, Loaiza-Bonilla A. The role of biosimilars in patient access to therapeutic antibodies for immune mediated inflammatory diseases. Curr Pharm Des. 2018;23:6779–83.
85. Gharia M, Sudhakar A. Reduced injection site pain with succinate buffer-based adalimumab biosimilar (ZRC-3197) Injection (SUFFER study): an observational study. Indian J Rheumatol. 2019;14:151.
86. Heerschap C, Nicholas A, Whitehead M. Wound management: investigating the interprofessional decision-making process. Int Wound J. 2019;16:233–42.
87. NHS South, Central and West Commissioning Support Unit. Individual funding requests (IFR). http://www.fundingrequests.cscsu.nhs.uk/. Accessed 31 July 2020.
88. British Association of Dermatologists. Independent funding request (IFR). http://www.bad.org.uk/healthcare-professionals/clinical-services/specialised-services/independent-funding-request. Accessed 31 July 2020.
89. NICE. NICE technology appraisal guidance. https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance. Accessed 06 Aug 2020.
90. NHS Specialist Pharmacy Service. RMOC Advisory statement: Sequential Use of Biologic Medicines. https://www.sps.nhs.uk/articles/rmoc-advisory-statement-sequential-use-of-biologic-medicines/. Accessed 31 July 2020.
91. Jeffery MM, Bellolio MF, Wolfson J, Abraham JM, Dowd BE, Kane RL. Validation of an algorithm to determine the primary care treatability of emergency department visits. BMJ Open. 2016;6:e011739.
92. Ijaz M, Khan MJ, Khan J, Usama. Association of clinical characteristics of patients presenting with influenza like illness or severe acute respiratory illness with development of acute respiratory distress syndrome. Monaldi Arch Chest Dis. 2017;87:18–21.
93. Goldsworthy S, Leslie-Dakers M, Higgins S, Barnes T, Jankowska P, Dogramadzi S, et al. A pilot study evaluating the effectiveness of dual-registration image-guided radiotherapy in patients with oropharyngeal cancer. J Med Imaging Radiat Sci. 2017;48:377–84.
94. Hunter RJ, Buckley N, Fitzgerald EL, MacCormick AD, Eglinton TW. General surgery prioritization tool: a pilot study. ANZ J Surg. 2018;88:1279–83.
95. Coates LC, Tillett W, Chandler D, Helliwell PS, Korendowych E, Kyle S, et al. The 2012 BSR and BHPR guideline for the treatment of psoriatic arthritis with biologics. Rheumatology. 2012;52:1754–7.
96. Shah VV, Lee EB, Reddy S, Lin EJ, Wu JJ. Comparison of guidelines for the use of TNF inhibitors for psoriasis in the United States, Canada, Europe and the United Kingdom: a critical appraisal and comprehensive review. J Dermatolog Treat. 2018;29:586–92.
97. Whitehead SJ, Ali S. Health outcomes in economic evaluation: the QALY and utilities. Br Med Bull. 2010;96:5–21.
98. Garrison LP, Kamal-Bahl S, Towse A. Toward a broader concept of value: identifying and defining elements for an expanded cost-effectiveness analysis. Value Health. 2017;20:213–6.
99. Pettitt DA. The limitations of QALY: a literature review. J Stem Cel Res Ther. 2016;6:334.
100. Perfetto EM, Oehrlein EM, Boutin M, Reid S, Gascho E. Value to whom? The patient voice in the value discussion. Value Health J Int Soc Pharmacoecon Outcomes Res. 2017;20:286–91.
101. Akins RB, Tolson H, Cole BR. Stability of response characteristics of a Delphi panel: application of bootstrap data expansion. BMC Med Res Methodol. 2005;5:37.
102. Fink-Hafner D, Dagen T, Doušak M, Novak M, Hafner-Fink M. Delphi Method: strengths and weaknesses. Metod Zv. 2019;16:1–19.

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