Patient experience of symptoms and impacts of COVID-19: a qualitative investigation with symptomatic outpatients

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ABSTRACT

Objectives There is little in-depth qualitative evidence of how symptoms manifest themselves in outpatients with COVID-19 and how these in turn impact outpatients’ daily lives. The objective of the study was therefore to explore the experience of outpatients with COVID-19 qualitatively, concerning the symptomatic experience and its subsequent impact on daily life.

Setting Qualitative research study comprising virtual in-depth, open-ended interviews with outpatients and clinicians.

Participants Thirty US adult patients with COVID-19 were interviewed within 21 days of diagnosis. Patients were 60% female and 87% white, who had to self-report one of the following: fever, cough, shortness of breath/difficulty breathing, change/loss of taste/smell, vomiting/diarrhoea or body/muscle aches. Five independent clinicians were also interviewed about their experience treating outpatients.

Primary and secondary outcome measures Transcripts were analysed thematically to organise symptoms and impacts of daily life into higher-order overarching categories, and subsequently propose a conceptual model. The adequacy of the sample size was assessed by conceptual saturation analysis.

Results Patient-reported concepts were organised into six symptom themes (upper respiratory, lower respiratory, systemic, gastrointestinal, smell and taste, and other) and seven impact themes (activities of daily living, broad daily activities, leisure/social activities, and physical, emotional, professional and quarantine-specific impacts). Symptom type, severity, duration and time of onset varied by patient. Clinicians endorsed all patient-reported symptoms.

Conclusions The manifestation of symptoms in outpatients is heterogeneous and affects all aspects of daily life. Outpatients offered new detailed insights into their symptomatic experiences, including heterogeneous experiences of smell and taste, and the impacts that symptoms had on their daily lives. Findings of this research may be used to supplement existing knowledge of the outpatient experience of mild-to-moderate COVID-19, to further inform treatment guidelines and to provide an evidence base for evaluating potential treatment benefits.

INTRODUCTION

COVID-19 is caused by SARS-CoV-2. Initial reports of common COVID-19 symptoms included fever, cough and shortness of breath,1 but current Center for Disease Control (CDC) guidelines include loss of smell/taste, chills, fatigue, sore throat, nasal congestion and gastrointestinal symptoms. While our understanding of COVID-19 is evolving,2 most of the data used to inform its presentation are based on hospitalised patients3 4 and remain focused on those initial symptoms. However, data from broader samples also confirm fatigue, loss of appetite and chills as predictive of a positive test for SARS-CoV-2.5

Symptom profiles in COVID-19 are largely based on community and hospitalised patient-reported quantitative data.5 To date, qualitative research has largely focused on the experiences of those hospitalised by COVID-199 and of the healthcare
professionals who treat them. However, the majority of patients with COVID-19 do not require hospitalisation; little is known about the qualitative experiences of these patients. A recent qualitative meta-synthesis demonstrates the limited research involving outpatients who experienced mild-to-moderate COVID-19 symptoms. It is important to conceptualise the patient experiences of symptoms and the impacts those symptoms have on their daily lives in this population to help us better understand and adequately address their needs, facilitate dialogue with healthcare professionals and support the development of patient-reported outcome instruments for clinical trials. Therefore, this qualitative research aimed to explore the patient experience of COVID-19 in daily life from the perspective of outpatients based in the USA. The perspectives of clinicians who treat outpatients were also captured to support the clinical understanding of symptomology.

METHODS
This was a cross-sectional, applied qualitative research study comprising in-depth, open-ended interviews with patients with a confirmed diagnosis of COVID-19. Clinicians provided insights on the clinical experience. Interviews were conducted in September and October 2020.

Participants
The sample comprised adults in the USA with a diagnosis of COVID-19, confirmed by positive PCR test 21 days prior to the interview, who self-reported one of the following: fever ($\geq 100^\circ$F, or feeling feverish or chills), cough, shortness of breath or difficulty breathing, change in or loss of taste or smell, vomiting or diarrhoea, or body or muscle aches. Patients were excluded if they had been hospitalised in the past 30 days. A healthcare research firm coordinated participant recruitment; potentially eligible patients were identified via patient databases and physician referrals and invited to take part via email invitation. Fifty-two interested patients were screened for their eligibility and had the opportunity to discuss the study before providing written consent; of those, 30 met the inclusion criteria. A sample of this size was considered to be sufficient for reaching conceptual saturation; in the event that this was not the case, additional interviews would be planned until saturation was reached. A convenience sample of five clinicians who regularly treated patients with COVID-19 ($\geq 5$ a week) were also interviewed. Clinicians were recruited through the same healthcare research firm, with additional support from Regeneron Pharmaceuticals.

Research team
The research was led by the lead author, a chartered health psychologist and experienced patient-centred outcomes researcher with a PhD in health psychology and expertise in qualitative and clinical research. The research team comprised experienced qualitative researchers and practicing clinicians with research expertise. The interviewers were unknown to the patients prior to the conduct of the interview and were not involved in any aspect of the patients’ healthcare. By involving all authors, with diverse academic and clinical backgrounds, we ensured that a multi-disciplinary approach was taken inclusive of different perspectives during analysis and interpretation.

Interview conduct
Patient interviews (~60 min) were conducted remotely via audio calls using Microsoft Teams software by experienced qualitative researchers who received specific training for this study. A semi-structured interview guide was developed, comprising open-ended questions informed by the research objectives and insights gained from the conduct of the clinician interviews, as well as structured prompts for all common symptoms of COVID-19 not spontaneously mentioned. Targeted probes were used if patients did not spontaneously detail how the symptom changed from day to day (ie, improved/worsened) or its duration (within-day and across the day), severity, and/or resolution. The impacts of symptoms and diagnosis were explored, including how patients were impacted emotionally and socially, as well as any disruption to daily activities due to COVID-19 symptoms.

Clinicians were asked about symptoms observed in outpatients, clinical presentations and symptomatic profiles of COVID-19, improvement/worsening in symptoms over time, onset/resolution of symptoms, and any clinical hierarchy of symptoms.

Data analysis
Interviews were audio-recorded, transcribed and anonymised. A data-driven approach was adopted whereby transcripts were coded in ATLAS.ti software using an open, inductive, thematic coding approach. The first transcript was independently coded by three researchers; any coding inconsistencies were discussed and reconciled. Researchers met regularly to discuss and adjust coding guidelines when necessary. Following coding, a conceptual model was developed; this was a visual representation of aspects of their experience living with COVID-19 using standard analytical techniques. Codes and quotations were compared with the rest of the data and inductively categorised into higher-order overarching categories including themes and subthemes, reflecting their conceptual underpinning. This involved an iterative process of cross-referencing and comparison between the different analytical categories, which was reviewed and fine-tuned.

Saturation analysis, the point at which no new concept-relevant information is being elicited from individual interviews, was conducted by grouping interviews chronologically and comparing the emerging subthemes that reflected the conceptual categorisation of the codes.
Patient and public involvement

While neither patients nor the public were involved in the design, conduct, reporting or dissemination of the study, the main focus of this study was on in-depth interviews with outpatients.

RESULTS

Patient interviews

All recruited outpatients were interviewed and included in the analysis (n=30). Patients were 45.0±19.4 years old (range 18–76), 60% female and 87% white. The interview was conducted an average of 19 days after symptoms began, and an average of 12 days (median 9.5, range 6–21) after COVID-19 diagnosis. Most patients (83%) were still experiencing at least one symptom during the time of the interview; of those, 68% described the overall severity of their symptoms in the past 24 hours as ‘mild’ and 32% as ‘moderate’. See table 1 for full patient demographic and health information.

The interviews yielded two overarching domains: symptoms and impacts on daily life. Thus, conceptual saturation was achieved for reported symptoms.

Symptoms

Symptoms were categorised into six major themes: upper respiratory tract, lower respiratory tract, systemic, gastrointestinal, smell and taste, and other. Each theme was further broken down into subthemes, as outlined in figure 1. Categorisation was created to summarise the data but was not indicative of an underlying common theoretical underpinning.

Upper respiratory tract symptoms included stuffy/congested nose, runny nose, postnasal drip, phlegm, sneezing, sore throat (accompanied by lost voice), sinus pressure/pain, head congestion, swollen glands and earache. Symptoms were grouped into this theme if they referred to experiences affecting the head, nose or throat. Patients often reported experiencing multiple upper respiratory tract symptoms simultaneously, as one patient stated:

My sinus congestion. I would sneeze a lot, and I was just very stuffy to where my voice didn’t sound normal. It felt like a sinus infection. Most days I had to have a humidifier to try to get it to go away. I still have some stuffiness and runny nose. (Female, 18–24 years age range)

Themes were created based on the way that patients described their symptom experience (eg, patients described stuffy/congested nose differently than head congestion):

It was a little bit of a nasal drip and I was sniffling. (Male, 60–69)

I had head congestion from the very beginning. That lasted the entire time, but I felt like I didn’t have mucus in my head that was making me congested. It felt like it was swollen tissues. (Female, 40–49)

Lower respiratory tract symptoms were cough, chest pressure/tightness, chest pain, shortness of breath and difficulty breathing (ie, symptoms related to lung functioning). Cough was commonly described as dry and non-productive.

When I cough, it’s coming from my chest really deep. But I haven’t coughed up anything. (Female, 25–30)

Similar to upper respiratory symptoms, patients reported multiple lower respiratory symptoms at once (eg, cough and chest pain or chest pressure and difficulty breathing).

I did have that pain because I was coughing a lot. (Male, 50–59)

It just feels like a pressure on my chest where I can’t breathe very well. (Female, 60–69)

Gastrointestinal symptoms were nausea, vomiting, diarrhoea, constipation and stomachache. These symptoms

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Overview of patient sample characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=30</td>
<td></td>
</tr>
<tr>
<td>Age range, mean years, (SD)</td>
<td>18–76 (45.03, 19.39)</td>
</tr>
<tr>
<td>Gender, n (%)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>12 (40)</td>
</tr>
<tr>
<td>Female</td>
<td>18 (60)</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>26 (86.7)</td>
</tr>
<tr>
<td>Other</td>
<td>4 (13.3)</td>
</tr>
<tr>
<td>Number of days between diagnosis and interview, mean (SD)</td>
<td>12.40 (5.29)</td>
</tr>
<tr>
<td>Number of days since symptoms began, mean (SD)</td>
<td>19.17 (7.96)</td>
</tr>
<tr>
<td>Number of days between symptoms began and diagnosis, mean (SD)</td>
<td>6.77 (7.96)</td>
</tr>
<tr>
<td>General health ratings, n (%)</td>
<td></td>
</tr>
<tr>
<td>Excellent</td>
<td>6 (20)</td>
</tr>
<tr>
<td>Very good</td>
<td>8 (26.7)</td>
</tr>
<tr>
<td>Good</td>
<td>4 (13.3)</td>
</tr>
<tr>
<td>Fair</td>
<td>9 (30)</td>
</tr>
<tr>
<td>Poor</td>
<td>3 (10)</td>
</tr>
<tr>
<td>Comorbidities,* n (%)</td>
<td></td>
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<tr>
<td>17 (57)</td>
<td></td>
</tr>
</tbody>
</table>

*Comorbidities across sample include cardiovascular disease (eg, heart failure, coronary artery disease, cardiomyopathy, pulmonary hypertension, pulmonary fibrosis), hypertension, diabetes (eg, type 1, type 2, gestational), chronic obstructive pulmonary disease, chronic kidney disease, cancer, sickle cell disease, metabolic dysfunction-associated fatty liver disease, chronic liver disease (eg, cirrhosis), history of stroke and thalassaemia.
Figure 1  Patient experience of COVID-19. *Impacts reflect activities and health-related quality of life experiences affected as a result of having COVID-19. †Symptoms or impacts associated with experience of other symptoms or impacts. ADLs relate to routine activities including eating, bathing, dressing and independently moving within the home (eg, getting out of bed and from the bedroom to the shower). Broad daily activities relates to independent living and include preparing meals, shopping for groceries, performing household and caring for others. ADLs, activities of daily living.

were not reported as often as others but had a significant impact on the patients’ daily lives.

I actually had started vomiting. It was waking me up at 3 or 4 o’clock in the morning. (Male, 31–39)

The smell and taste theme comprised symptoms related to lost or altered sense of smell or taste. This was distinct from upper respiratory tract symptoms because the pathophysiological mechanisms underlying these symptoms are different from other common upper-respiratory illnesses where senses are more directly related to other respiratory symptoms (eg, stuffy nose impairing smell). Patients described their sense of taste/smell changing, being diminished or lost altogether; sense alterations often occurred together but could occur separately. Lost or altered taste or smell was the only common symptom reported as unchanging while present.

I never completely lost my taste, it remained altered until I began to be able to smell again. (Female, 60–69)

The systemic theme reflected symptoms that affect the entire body, rather than a single organ or body part. This theme comprised fever, chills, sweating, body aches, muscle aches, joint pain, headache/migraine, back pain, physical fatigue/sleepiness, mental fatigue, weakness, dizziness/lightheadedness, heart palpitations, loss of appetite and not feeling like oneself. The duration of systemic symptoms was variable; fever, body aches and headache persisted from 1 day to several weeks, which was similarly described in other themes. Fatigue also varied but typically lasted over 1 week. Varying experiences were also reported in fluctuation of symptoms across all themes but particularly within systemic symptoms, with patients reporting consistency across days, variation within a day (ie, worse in the morning) and variation across days (ie, absent 1 day but present the next day).

I’m having a good day like, I’m not aching as much, and then, the next day, I would be very sore and achy. (Female, 60–69)

Other less common symptoms reported were skin rash, skin redness, red eyes, watery eyes and numb feet.

Impacts on daily life

Impacts on daily life referred to any COVID-19 related effects on activities of daily living (ADLs), broad daily activities, leisure and social life, professional impacts, psychological/emotional impacts, physical impacts and impacts specific to quarantine (figure 1). Most impacts on daily life were not attributed to any singular symptom—which were reportedly short-lived—but rather to the holistic experience of COVID-19 infection.

The ADL theme referred to changes in patients’ performance of self-care tasks (ie, hygiene and dressing), eating habits, mobility or daily routine. Broad daily activities encompassed changes in activities not necessary for fundamental functioning, but which allow patients to live independently, including shopping, meal preparation, home maintenance and care of dependents. Each of these activities was reported as central to patients’ lives pre-COVID-19, and patients emphasised the disruption caused by their illness.
I couldn’t get anything done that I normally get done. Doing any kind of housework, laundry—I couldn’t do anything. (Female, 40–49)

Activities related to exercise, hobbies/leisure activities and socialising with friends or family were categorised under leisure and social life. This theme referred specifically to social/leisure impacts caused by COVID-19 symptoms, not by mandated quarantine due to infection. This theme also included impacts on relationships with those within the patients’ households.

It’s still really, really difficult not being able to hug my kids and my wife and having to stay away from them. (Male, 31–39)

Professional impacts referred to any effects on the patient’s work or schooling. Similarly, this theme comprised only changes due to COVID-19 and its symptoms, not due to quarantine (eg, working from home or virtual class).

I still have school to do, all of my online courses, and so I would do those for about 3 hours each day and then after that I felt like I just had to be asleep, and I just didn’t really have any motivation to do anything. (Male, 18–24)

Physical impacts comprised physical changes related to COVID-19, specifically weight loss and sleep disruption. Though these may be considered symptoms themselves, patients described them as secondary to other symptoms.

I actually lost like 8 pounds during my 2 weeks of quarantine [due to infection]. (Female, 18–24)

The emotional/psychological theme encompassed changes in the patients’ psyche or mood, including depression, anxiety, irritability, frustration, feelings of isolation and worries about the symptoms and meaning of a COVID-19 diagnosis. Patients used a breadth of language to describe their emotional response to COVID-19 and its symptoms; subthemes reflect patients’ words with as much granularity as possible without over-emphasising the emotional impact.

I was a little bit worried because you hear stories on the news and whatnot that some people took a turn for the worse after a week. (Male, 60–69)

Patient experiences due to a mandatory quarantine period (typically 2 weeks), were classified within their own theme. These impacts included being housebound, having to stay away from others, and boredom.

Clinic interviews

Five clinicians were interviewed (n=4 in the USA; n=1 in South Korea, where all patients with COVID-19 are hospitalised regardless of symptom severity). The Korean clinician was informed of the focus of this study and asked to comment specifically on their experience treating mild-to-moderate cases. See table 2 for full clinician backgrounds.

Clinicians confirmed all symptoms reported by patients and described three distinct symptomatic presentations of COVID-19: (1) fever-dominant presentation (high fevers and associated symptoms eg, headache, malaise, fatigue and muscle aches); (2) respiratory presentation (cough, shortness of breath and difficulty breathing) and (3) gastrointestinal presentation (diarrhoea, vomiting and nausea). Clinicians agreed that patients often experience symptoms across presentations during their time with COVID-19.

Clinicians confirmed patient reports regarding the varied nature of symptom severity and duration. Lingering symptoms were fatigue, weakness, shortness of breath, fever, joint pain, cough, loss of taste/smell and mental fatigue. Clinicians indicated that most patients returned to baseline health once symptom-free, but a minority took longer to return to pre-COVID-19 health due to changes in mental clarity (eg, mental fatigue) or energy levels.

Table 2 Overview of clinician sample characteristics

<table>
<thead>
<tr>
<th>Current position(s)</th>
<th>Specialty/training</th>
<th>Number of years practicing</th>
<th>Experience with patients with COVID-19</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assistant professor and attending physician at an academic medical centre</td>
<td>Pulmonary and critical care</td>
<td>8–9</td>
<td>Treats patients in person and remotely, hospitalised and non-hospitalised, prediagnosis and postdiagnosis</td>
</tr>
<tr>
<td>Attending physician in infectious diseases at an urban federally qualified health centre</td>
<td>Internal medicine</td>
<td>10</td>
<td>Treats patients in person and remotely. Sees patients with and without symptoms (patients are screened at the door to the clinic), about 10 patients with COVID-19-positive per week</td>
</tr>
<tr>
<td>Infectious disease department</td>
<td>Infectious disease</td>
<td>Not stated</td>
<td>Treats only hospitalised patients, as all patients with COVID-19 are hospitalised in Korea</td>
</tr>
<tr>
<td>Pulmonary critical care physician at a community teaching hospital and director of the sleep centre</td>
<td>Pulmonary critical care, internal medicine and sleep medicine</td>
<td>16</td>
<td>Treats patients who have had COVID-19 in the past, but are not recovering (eg, retained shortness of breath or cough). Sees 4–5 patients in the office per week. Generally performs second-line treatment only</td>
</tr>
<tr>
<td>Fellow internist, private practitioner at a community hospital, and internal medicine director of a rehab hospital</td>
<td>Internal medicine</td>
<td>25</td>
<td>Treats 50/50 hospitalised and non-hospitalised patients. Sees 4–5 people per week who are concerned about COVID-19. Conducts visits remotely and in person</td>
</tr>
</tbody>
</table>
This study provides novel insight into the conceptualisation of the patient experience of COVID-19 and adds to the limited research investigating the experience of patients with mild-to-moderate COVID-19 symptoms who are required to self-care at home, often in isolation from others. While others have investigated the long-term experiences of patients with COVID-19, to the best of our knowledge this is the first study to explore the experiences of non-hospitalised patients who are in the acute phase of disease and still experiencing symptoms.

Symptoms were consistent with those reported by the CDC, and we collected and summarised those symptoms in a conceptually grounded conceptual model containing the following groups: upper and lower respiratory, systemic, gastrointestinal, and loss of or alteration in taste or smell. We consider this model to be a comprehensive representation of COVID-19 symptoms based on patients’ heterogeneous symptom profiles and the achievement of conceptual saturation, indicating the adequacy of the sample size; therefore, it is a basis to determine which symptoms to consider when evaluating treatment benefits in COVID-19.

Although the symptoms in the conceptual model can be considered comprehensive at a group level, the individual combination of symptoms per patient varied greatly. The individual patient experience also varied in terms of symptom duration, severity and timing of onset, culminating in the lack of one clear symptomatic COVID-19 profile. This key finding is supported by clinician feedback, and is consistent with the current medical knowledge of COVID-19 manifestations and recently published narratives describing the variability with which people experience this disease.

Heterogeneity of altered senses of smell and taste was a key finding not described by clinicians, who commonly reported that both senses would be lost completely, often in conjunction with one another. However, patients described experiencing changes in only one of these senses or both senses non-concurrently; patients also described alterations in senses, rather than loss. This symptom was commonly reported in this study and is one of the strongest predictors of a COVID-19 infection in mild-to-moderate cases. Although frequent in influenza infections, the manifestation of this symptom without other upper-respiratory symptoms is distinctive in COVID-19.

With regards to the daily life impacts associated with COVID-19, the emotional/psychological impacts for patients is of interest, consistent with existing qualitative research and in line with research priorities to collect data on the mental health and psychological impacts experienced by patients with COVID-19 at all clinical stages of infection and illness. The current study builds on existing research by drawing attention to the wide range of impacts experienced by outpatients with COVID-19, including physical, leisure, routine and broad ADLs. Despite interviewing outpatients with mild-to-moderate cases of COVID-19 (at the time of interviewing), patients reported all aspects of their daily lives as being impacted while experiencing COVID-19 symptoms. The ways in which patients’ daily lives were impacted while they were experiencing symptoms played a significant role in the experience that patients depicted. Given that the impacts of daily living occurred concomitantly with symptoms, we can hypothesise that a reduction in symptoms should reduce at least some impacts described by patients. Further qualitative research should aim to understand the relationship between specific symptoms of COVID-19 and associated impacts of daily living.

This study had some limitations. First, there was a time-lapse between the onset of COVID-19 symptoms and the interview. Patients, on average, completed the interview 12 days after their positive diagnosis. Further studies could explore the symptom trajectory at an earlier stage of the acute COVID-19 experience, but recruitment challenges may make this difficult, such as the time between being tested and receiving the results. Second, the participants were not of a representative racial/ethnic background, and therefore further research in a more diverse population is required as racial/ethnic disparities in illness severity have been identified across all age groups. The relatively young average age of the study sample is also a limitation; age is a documented risk factor for COVID-19 infection, and older patients have been disproportionately affected by COVID-19 symptoms. However, younger patients did report a range of symptoms and daily life impacts, emphasising the importance of infection prevention measures in younger adults. Moreover, the types of symptoms experienced by patients did not differ by participant age; further research should be conducted to confirm the differentiation of symptoms by age groups. Finally, almost half of participants described their general health as excellent or good. It is likely that patients were responding to this question based on how they perceive their health outside of the study. It would be of interest to explore the experiences of those patients with additional health concerns. Additional research should explore the symptom experience quantitatively, including long-term effects of COVID-19, through non-interventional observational studies and clinical trials.

This study provides unique and valuable insights from the patient perspective into the symptom experience in outpatients with COVID-19 and how it could impact their lives more broadly, including physical, emotional, and psychological functioning. Symptom reporting using patient-reported outcome instruments can facilitate tracking of those with mild-to-moderate COVID-19 symptoms that can be managed at home, and to monitor patients within clinical trials and over a longer term. The current study could contribute to existing knowledge on the patient experience of symptoms and help to inform the development of...
a new patient-reported outcome instrument, which captures symptoms relevant to outpatients. Existing clinical guidelines for treating outpatients with mild- to-moderate COVID-19 are limited; as of April 2022, the National Institute of Health provides guidelines for those at high risk of clinical progression but does not suggest treatment methods for the remainder of the outpatient population. By providing insights on the patient experience, the current study elucidates the extent to which patients’ lives are impacted by having even mild-to-moderate experiences of COVID-19. Increased understanding of outpatient needs could supplement existing knowledge in informing treatment guidelines for those patients who self-manage symptoms at home.

CONCLUSION
This study revealed unique insights about the symptomatic experience of outpatients with COVID-19 and its impacts on daily life. It provides an evidence base for selecting symptoms and impacts important for evaluating the benefit of treatment in outpatients. While reported symptoms were in line with expectations, evaluating the benefit of treatment in outpatients. While reported symptoms were in line with expectations,5 15 38 the design, or conduct, or reporting, or dissemination plans of this research.

REFERENCES

Patient consent for publication Not applicable.

Ethics approval This study involves human participants. The protocol, demographic and health information form, interview guide, screener and informed consent form received ethical approval from the New England Independent Review Board (study number: 1291666) prior to any contact with patients. Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer-reviewed.

Data availability statement All data relevant to the study are included in the article.

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Competing interests DR is a Regeneron Pharmaceuticals employee/stockholder and former Roche employee, and current stockholder. SS and VM are Regeneron Pharmaceuticals employees/stockholders. AJP has received consulting fees from Regeneron Pharmaceuticals, honoraria from NACE (CME), and has participated in an advisory board for Boehringer Ingelheim. NM, AR and KP are employees of Modus Outcomes. PM is the cofounder and CEO of Modus Outcomes. NM, AR, KP and PM consulted for Regeneron Pharmaceuticals.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.


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