ORIGINAL RESEARCH

Impact of Primary Chronic Immune Thrombocytopenia and Thrombopoietin Receptor Agonists Treatment Instructions on Daily Living: Results of a Multinational Cross-Sectional Survey

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Purpose: Thrombopoietin receptor agonists (TPO-RAs) are second-line treatments for people with immune thrombocytopenia (ITP). A survey was conducted to evaluate the understanding of and adherence to TPO-RA treatment instructions, and to determine the impact of ITP and TPO-RAs on daily living.

Patients and Methods: Cross-sectional, self-administered, online survey conducted from September 2023 to April 2024. Respondents were aged ≥18 years, diagnosed with primary chronic ITP, and prescribed a TPO-RA in the last 12 months and for ≥3 months.

Results: In total, 221 respondents were voluntarily recruited by patient organizations and completed the survey. Over one-third (37%) of respondents were given ≥5 specific instructions on medication use (eltrombopag 58%; avatrombopag 24%; romiplostim 9%). Taking treatment at the same time each day/week was most common. Eltrombopag-treated respondents were given the most instructions about food: timing of medication relative to meals (72%), timing of meals relative to medication (65%), and the restriction (44%) or avoidance (69%) of certain foods. Despite this, nearly one-third (32%) of eltrombopag-treated respondents ate when/what they wanted at times, and 64% would prefer to have a TPO-RA with no food/drink restrictions. Compared to before ITP diagnosis, living with ITP negatively impacted ≥1 daily activity or mental health in 89% of respondents, most commonly travelling (for pleasure [69%]). Approximately one-third (36%) experienced an improvement or no change in ≥1 daily activity or mental health after TPO-RA treatment initiation. Eating habits, sleeping, exercise/sport and mental health were markedly worsened by treatment with a TPO-RA. Avatrombopag and eltrombopag had the highest rates of any reported improvements across daily activities/mental health.

Conclusion: This real-world international survey showed that people with ITP may experience a negative impact on their daily activities and mental health from their condition. Treatment with some TPO-RAs may also impair specific activities, likely influenced by administration routes and dietary restrictions.

Keywords: daily life, immune thrombocytopenia, healthcare burden, medication instructions, real-world evidence, thrombopoietin receptor agonists

Introduction

Immune thrombocytopenia (ITP) is a rare autoimmune disorder resulting from the destruction and impaired production of platelets.[1,2] Although current guidelines still categorize ITP by disease duration (newly diagnosed [0–3 months], persistent [3–12 months], or chronic [>12 months], a longer duration of ITP is not considered another immune mechanism but consequently is associated with more relapses, increasingly cumulative and severe bleeding symptoms, and the need for second and further line treatments.[2–4] Additionally, ITP can be classified as primary (~80% of adult cases, occurring without a clearly identifiable source of immune dysregulation) or secondary (~20% of adult cases,

triggered by for example autoimmune diseases, lymphomas, infections or drug treatments);[1,2] treatments for secondary ITP should target the cause.

People living with ITP experience increased susceptibility to bleeding and typically present with skin hemorrhages (petechiae), mucosal bleeding, and bruising with minor trauma.[2] Rarely, serious or life-threatening intracranial hemorrhage occur (1–2% of cases).[2] Less known, and important to acknowledge, is that people living with ITP commonly experience fatigue, which is often severe.[5–7] Hence, ITP can have a substantial negative impact on overall health-related quality of life (HRQoL), including energy, physical functioning, daily activities and mental health.[5–11] However, the incidence and severity of bleeding and fatigue can vary and may be associated with non-disease-specific factors.[12]

Intravenous immunoglobulin (IVIg) and oral corticosteroids (OCS) are the standard first-line treatments for people with newly diagnosed ITP with bleeding symptoms that occur most often with platelet counts of $<30 \times 10^9$/L.[2–4,13] Despite their efficacy for increasing platelet count, responses to IVIg typically last only a few weeks, while later relapse and toxicity typically occur with OCS.[2–4,13,14] Indeed, although OCS achieve an initial rise in platelet counts in 60–80% of adults with ITP, platelet counts decline with dose reduction or cessation, and steroid-free remission is only maintained in 30–50%.[2] Furthermore, surveys indicate that >95% of people with ITP treated with OCS report related adverse events (AEs),[15] and OCS are considered to be significantly more bothersome than other therapeutic alternatives, with frequent side effects of weight gain/increased appetite and changes in face shape/bloating/swelling.[15,16]

Relapse to first-line treatment requires second and subsequent lines of therapy.[2–4,13,17] Consequently, treatment for persistent or chronic ITP are most frequently thrombopoietin receptor agonists (TPO-RAs), but treatment options also include fostamatinib (indicated for adults who are refractory to other treatments in Europe), and immune suppressive drugs such as off-label rituximab, azathioprine and mycophenolate mofetil.[2–4,13] TPO-RAs increase the production of platelets by acting on the thrombopoietin receptor on megakaryocytes and their precursors, stimulating their proliferation and differentiation and compensating the effects of splenic and liver clearance of platelets by bound platelet autoantibody and T-cell mediated apoptosis.[1,18–23]

Three TPO-RAs are currently approved for the treatment of people with ITP in most global countries: romiplostim (Nplate®, Amgen), eltrombopag (Revolade®/Promacta®, Novartis) and avatrombopag (Doptelet®, Sobi).[18–23] Several network meta-analyses (NMAs) of randomized trials in ITP have been conducted, which show that the three TPO-RAs are effective (improving platelet counts with lower bleeding rates) and provide a similar tolerability/safety profile compared to placebo.[24–31] The real-world efficacy and safety of TPO-RAs have also been demonstrated in routine clinical practice.[32–38]

The administration profiles of currently available TPO-RAs however differ, allowing physicians with their patients to choose between treatments. Romiplostim is administered by subcutaneous injection at an initial dose of 1 μg/kg once weekly, with dose adjustments up to 10 μg/kg per week according to platelet response.[18,19] Romiplostim is typically given by a healthcare professional in a medical setting, although self-administration is permitted in some countries such as those in the EU. Eltrombopag is administered orally at an initial dose of 25 or 50 mg once daily (depending on patient age, Asian ancestry and hepatic impairment), up to a maximum of 75 mg/day.[20,21] The tablets must be taken 4 hours before or 2 hours after any products such as antacids, dairy products (or other calcium-containing food products), or mineral supplements containing polyvalent cations, as these reduce drug exposure. Avatrombopag is administered orally at a starting dose of 20 mg once daily, with dose adjustments from 20 mg/week to 40 mg/day depending on subsequent platelet counts.[22,23] Avatrombopag in contrast should be administered with food and can be taken without dietary and time restrictions.

Treatment guidelines recommend considering patient preferences, and shared decision-making with healthcare professionals (HCPs) is encouraged.[2–4] While the patient perspective and HRQoL burden of ITP have been evaluated in several real-world studies,[6,8–11] studies of patients' perspectives on daily life relating to the administration and adherence of TPO-RA treatments are limited. This multinational survey was conducted with the following objectives: 1) evaluate the education of, understanding of, and adherence to TPO-RA treatment instructions by people with ITP, and 2) determine the impact of both ITP and TPO-RA treatment on daily life, including the extent to which support is sought.

Materials and Methods

Study Design and Recruitment

This was a non-interventional study with cross-sectional data collected retrospectively using an online survey of people living with ITP. Eligibility criteria (determined from the screening questions) were as follows: aged ≥18 years, diagnosed with primary chronic ITP by a physician, and treated with a TPO-RA (romiplostim, eltrombopag or avatrombopag) in the last 12 months and for ≥3 months.

People with ITP living in Germany, Finland, Norway, the Netherlands, the UK or the USA were recruited voluntarily by patient organizations via direct mail, email, and/or online platforms. The self-administered online survey was conducted between September 2023 and April 2024. The survey was designed by the study sponsor in collaboration with local patient organizations and two hematologists practicing in Europe and the USA, and was programmed using the web platform SurveyXact (Ramboll).[39] The survey included eight sections: introduction, screening, demographics, impact of ITP and TPO-RA medication on daily life, treatment patterns, TPO-RA medication adherence, previous ITP medication, and ITP support (Supplementary Appendix 1). It was translated into local languages (without linguistic validation) and required approximately 15 minutes to complete; no reward/remuneration was provided.

Data Analysis and Statistical Methods

Anonymous patient-level data were inputted into the online surveys directly by respondents and aggregated summary data presented using descriptive statistics. Continuous variables were summarized by mean, standard deviation (SD), median, quartiles, minimum and maximum values; categorical variables were summarized by counts and percentages. As this is a non-interventional study without pre-specified hypotheses, no formal statistical comparisons were undertaken.

Survey data collection was programmed to ensure that all respondents were required to answer all relevant questions, so there were no missing data. All data analyses were performed using Microsoft Excel and SAS statistical software. Sample size was based on feasibility of data collection to obtain a representative sample appropriate to the research approach and analytical method.

Ethics

The study protocol was reviewed by the WMO (Wet medisch-wetenschappelijk onderzoek met mensen) review board in the Netherlands (registration number: W23.263, NWMO23.11.025) who determined that ethical approval was not required due to the non-interventional study design and collection of anonymous data. Similarly, the study design did not meet the criteria for ethics committee approval in Norway,[40] Finland,[41] the UK,[42] Germany,[43,44] and the United States[45] (Supplementary Appendix 2). The study was conducted in accordance with the principles of the Declaration of Helsinki.

All respondents provided informed consent for study participation prior to starting the screening questions. Participation was voluntary and respondents had the right to opt-out at any time without having to give any reason(s). Respondents were not asked to input any personal or identifying information and therefore could not be identified directly; they were made aware of the intention to publish the results, and the role of the sponsor. The complete survey is available from the corresponding author on request.

Results

Patient Characteristics

In total, 221 respondents completed the survey across the six participating countries (Figure 1). The mean (SD) age was 57.4 (15.5) years, most were female (n=153; 69%) and from the Netherlands (n=77; 35%), the USA (n=72; 33%) or the UK (n=53; 24%) (Table 1).

TPO-RA Treatment Patterns

Respondents reported they were currently (n=204) or recently (n=17) treated with eltrombopag (n=118; 53%), romiplostim (n=65; 29%) or avatrombopag (n=38; 17%) at the time of survey completion (Table S1). The most common
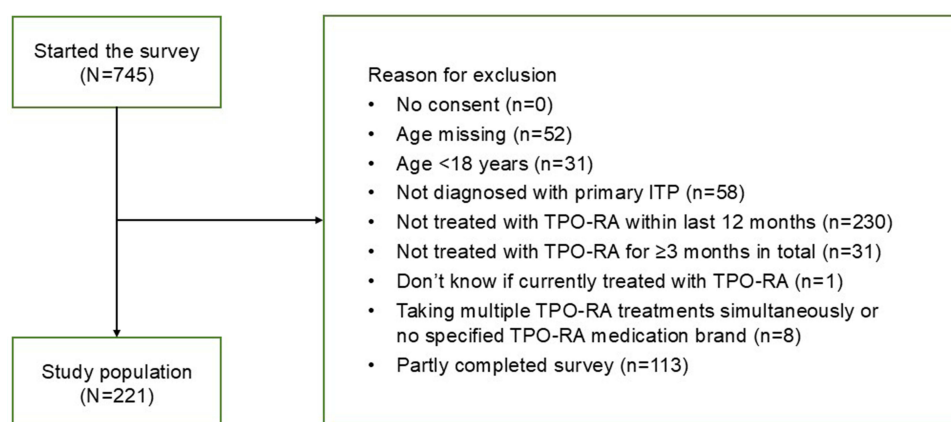
Figure 1 Patient disposition.
Abbreviations: ITP, immune thrombocytopenia; TPO-RA, thrombopoietin receptor agonist.

starting year for first treatment with a TPO-RA was 2019 (SD 4.0 years) and the average longest consecutive period on any TPO-RA treatment was 3.8 (SD 3.5) years.

Most respondents (85%) received information regarding different ITP treatment options, including those treated with avatrombopag (97%), romiplostim (85%) or eltrombopag (81%). Information about treatment was most commonly received via a doctor (80%), written information (for example, a leaflet) (62%), an online source (32%) or a nurse (27%). The majority of respondents (83%) reported they had discussed their personal preferences with a physician before making treatment decisions (shared decision-making), including those receiving avatrombopag (92%), romiplostim (85%) or eltrombopag (80%). There were, however, differences between countries in the proportion of respondents discussing these preferences (58% in Germany, Finland, Norway and the Netherlands combined [grouped due to missing responses, n=19], 79% in the UK [n=53] and 93% in the US [n=72]).

More than half of respondents (60%) previously used another type of ITP medication (beside their most recent TPO-RA) designed to increase platelet production, including 41% who previously used a non-ITP treatment (Table S1). Switching from other types of ITP medication was reported in a higher proportion of respondents taking avatrombopag (84%), followed by romiplostim (72%) and eltrombopag (45%). Reasons for switching to the TPO-RA taken at the time of the survey are summarized in Table S2. Across all treatments, the most common reason why respondents and physicians decided to switch TPO-RA medication was that their previous therapy was not working as expected (66–79%). Physician's suggestion was the second common reason for switching (to avatrombopag 38%; to eltrombopag 32%; to romiplostim (28%).

Education on Instructions for TPO-RA Use

Overall, 95% of respondents received instructions on how to take their TPO-RA medication and the majority received these instructions from a physician (80%) or a printed document (62%) (Figure S1). Over one-third of respondents (37%) were given ≥5 specific instructions to follow regarding their TPO-RA medication (eltrombopag 58%; avatrombopag 24%; romiplostim 6%) (Figure S2). Taking treatment at the same time each day/week was the most common instruction to consider for all TPO-RAs (eltrombopag 86%; avatrombopag 84%; romiplostim 68%) (Figure 2). Of the three TPO-RAs, eltrombopag-treated respondents reported the most instructions regarding food, including timing of medication relative to meals (72%) and meals relative to medication (65%), and the restriction (44%) or avoidance (69%) of certain foods (Figure 2). In general, respondents treated with romiplostim and avatrombopag had to follow fewer specific instructions.

Table I Baseline Demographics for People with ITP Completing the Survey

Characteristic*	Romiplostim (n=65)	Eltrombopag (n=118)	Avatrombopag (n=38)	Total (N=221)
Sex, n (%)				
Female	45 (69.2)	81 (68.6)[†]	27 (71.1)	153 (69.2)[†]
Male	20 (30.8)	36 (30.5)[†]	11 (28.9)	67 (30.3)[†]
Age, years, mean (SD)	58.9 (14.7)	56.3 (15.7)	58.2 (16.6)	57.4 (15.5)
Time since ITP diagnosis, years, mean (SD)	10.4 (10.4)	10.6 (10.8)	11.4 (11.0)	10.7 (10.6)
Country, n (%)				
Finland	2 (3.1)	4 (3.4)	1 (2.6)	7 (3.2)
Germany	0	1 (0.8)	0	1 (0.5)
Netherlands	27 (41.5)	41 (34.7)	9 (23.7)	77 (34.8)
Norway	0	7 (5.9)	4 (10.5)	11 (5.0)
UK	15 (23.1)	29 (24.6)	9 (23.7)	53 (24.0)
USA	21 (32.3)	36 (30.5)	15 (39.5)	72 (32.6)
Employment status, n (%)[‡]				
Working full-time[§]	15 (23.1)	36 (30.5)	8 (21)	59 (26.7)
Working part-time	11 (16.9)	22 (18.6)	8 (21)	41 (18.6)
Retired	26 (40.0)	41 (34.7)	14 (37)	81 (36.7)
Student	3 (4.6)	4 (3.4)	4 (10.5)	11 (5.0)
Wanting to work, but unemployed due to health-related reason(s)	5 (7.7)	4 (3.4)	3 (7.9)	12 (5.4)
Receiving/awaiting approval for disability payments	5 (7.7)	11 (9.3)	2 (5.3)	18 (8.1)
Homemaker	2 (3.1)	4 (3.4)	1 (2.6)	7 (3.2)
Temporarily laid off	0	0	1 (2.6)	1 (0.5)
Unemployed and looking for work	1 (1.5)	0	0	1 (0.5)
None of the above	2 (3.1)	2 (1.7)	0	4 (1.8)
Identify as a person with a disability, n (%)				
Yes	20 (30.8)	36 (30.5)	10 (26.3)	66 (29.9)
No	45 (69.2)	81 (68.6)	28 (73.7)	154 (69.7)
Prefer not to answer	0	1 (0.8)	0	1 (0.5)

Notes: *Proportions may exceed 100% due to rounding. [†]Excludes one (0.5%) patient who preferred not to answer. [‡]Maximum of two answers were allowed. [§]Working ≥32 hours/week. No formal statistical comparisons were undertaken and aggregated summary data are presented using descriptive statistics.
**Abbreviations**: ITP, immune thrombocytopenia; SD, standard deviation.

## Adherence to and Understanding of TPO-RA Treatment Restrictions

Approximately three-quarters of respondents (74%) understood completely why they needed to adhere to TPO-RA medication instructions (eltrombopag 75%; romiplostim 75%; avatrombopag 69%); an additional 21% of respondents (23%, 13% and 29%, respectively) reported that they understood a little why they needed to adhere (Figure S3). Nearly one-third (32%) of eltrombopag-treated respondents at times did not abide by food restrictions and ate when/what they wanted, contrary to instructions for taking this TPO-RA medication (Figure 3). Additionally, 64% of eltrombopag-treated respondents confirmed they would prefer to take a TPO-RA medication without restrictions related to food and drinks.

Impact of ITP

Mean (SD) time since ITP diagnosis to survey completion was 10.7 (10.6) years. Compared to before ITP diagnosis, living with ITP was reported to negatively impact ≥1 daily activity or mental health in 89% of respondents, including 33% affected by ≥7 activities (Figure S4). Across all respondents, travelling (for pleasure [69%]), mental health (66%), exercise/sport (62%), sleeping (49%) and socializing (49%) were most commonly affected by ITP, compared with pre-diagnosis (Figure 4). Conversely, commuting (to school or work) and eating habits were least affected by ITP diagnosis. Overall, 21–58% of respondents reported that daily activities were not affected by a diagnosis of ITP (Figure 4).
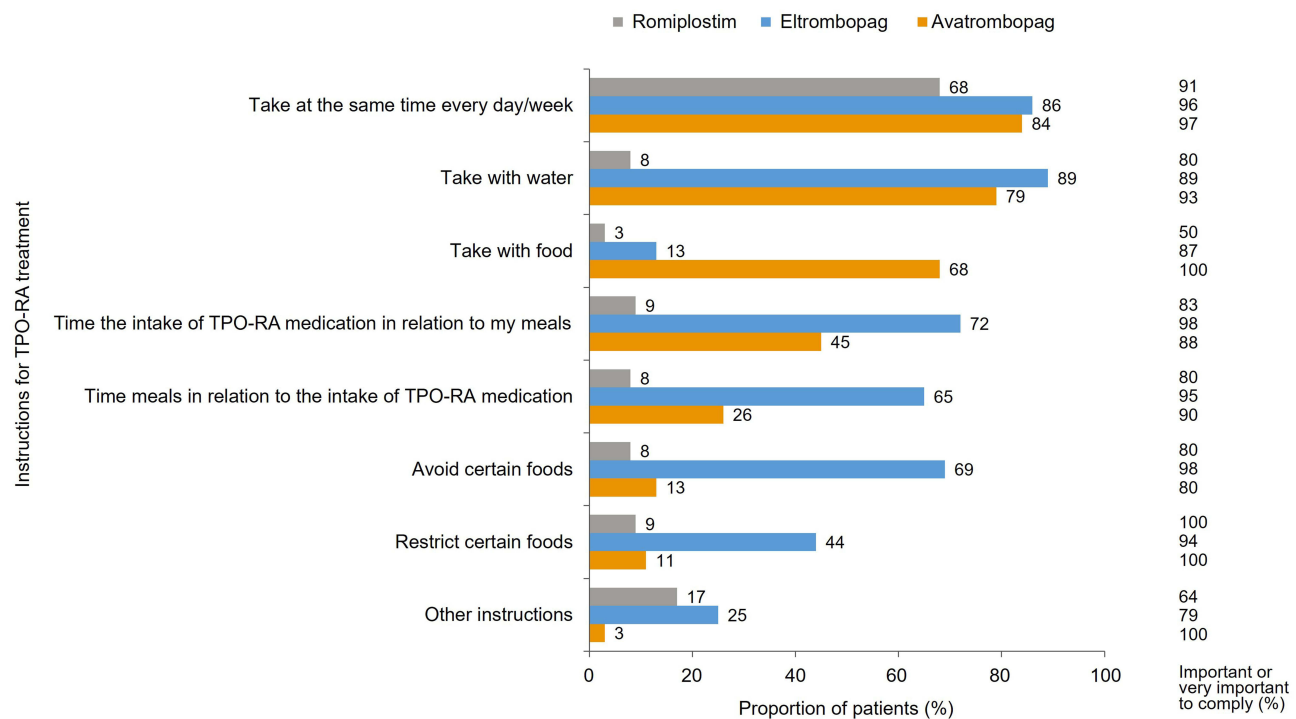
Figure 2 Specific instructions respondents reported they should follow when taking TPO-RA medication.
Notes: Respondents were asked: *Which of the following instructions should you follow when taking TPO-RA medication?* Figure shows proportion of respondents per treatment who found it important or very important to follow each instruction category. Question completed by N=221 (romiplostim, n=65; eltrombopag, n=118; and avatrombopag, n=38). No formal statistical comparisons were undertaken and aggregated summary data are presented using descriptive statistics.
Abbreviations: TPO-RA, thrombopoietin receptor agonist.
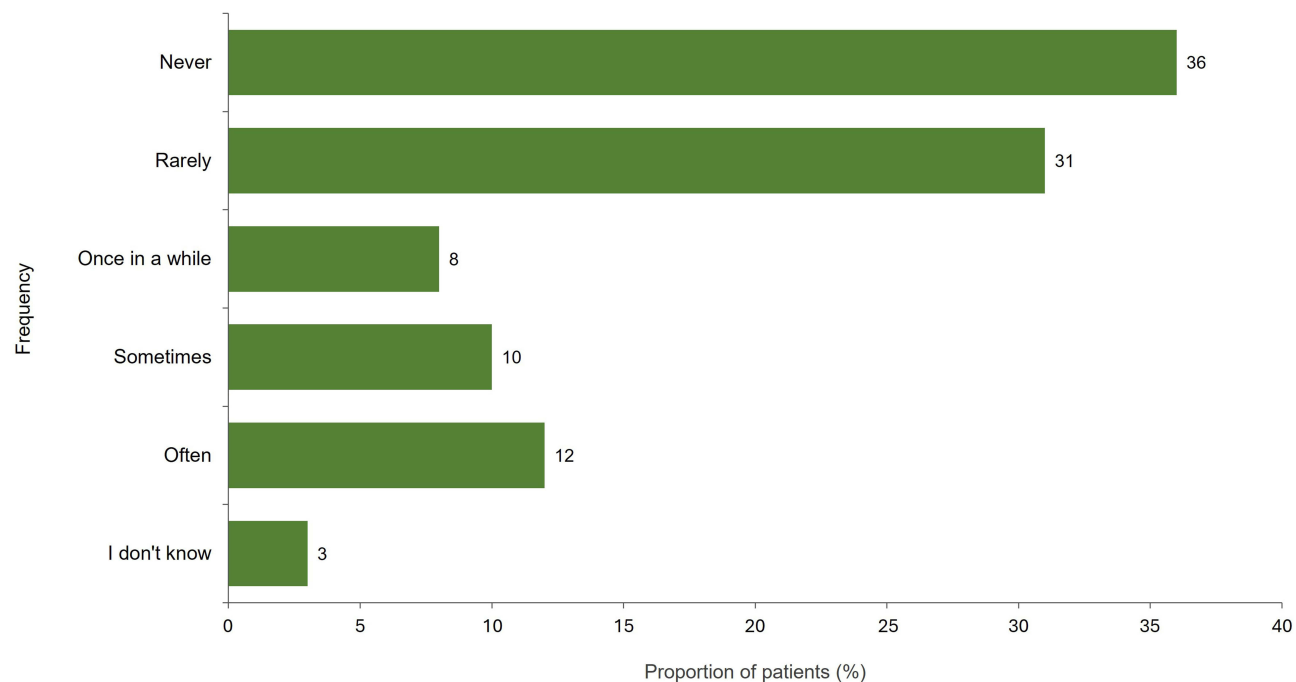
Figure 3 Eltrombopag-treated respondents who reported how often they ate when and/or what they wanted despite the instructions provided regarding taking TPO-RA medication.
Notes: Respondents were asked: *Overall, how often do/did you eat when and/or what you want despite the instructions given regarding taking TPO-RA medication?* Figure shows proportions of respondents who answered by response category. Question completed by n=118; question not directed to respondents treated with avatrombopag or romiplostim. No formal statistical comparisons were undertaken and aggregated summary data are presented using descriptive statistics.
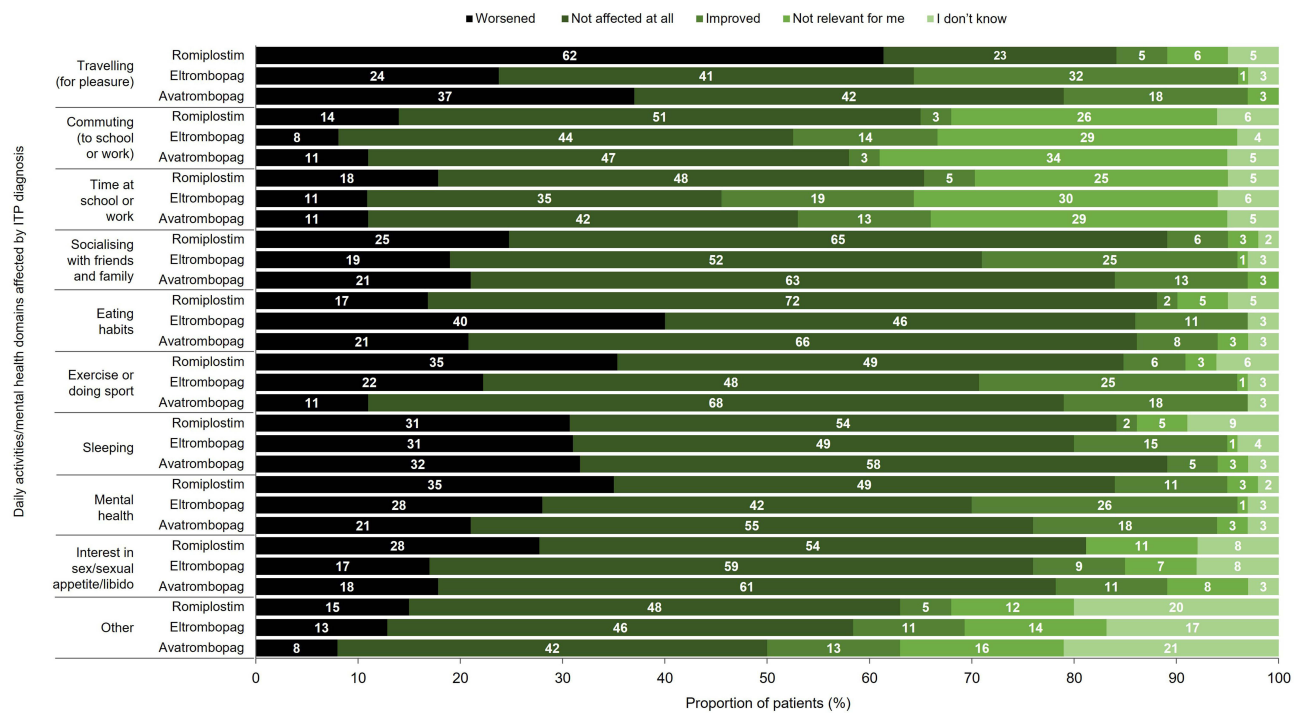**Abbreviations**: TPO-RA, thrombopoietin receptor agonist.
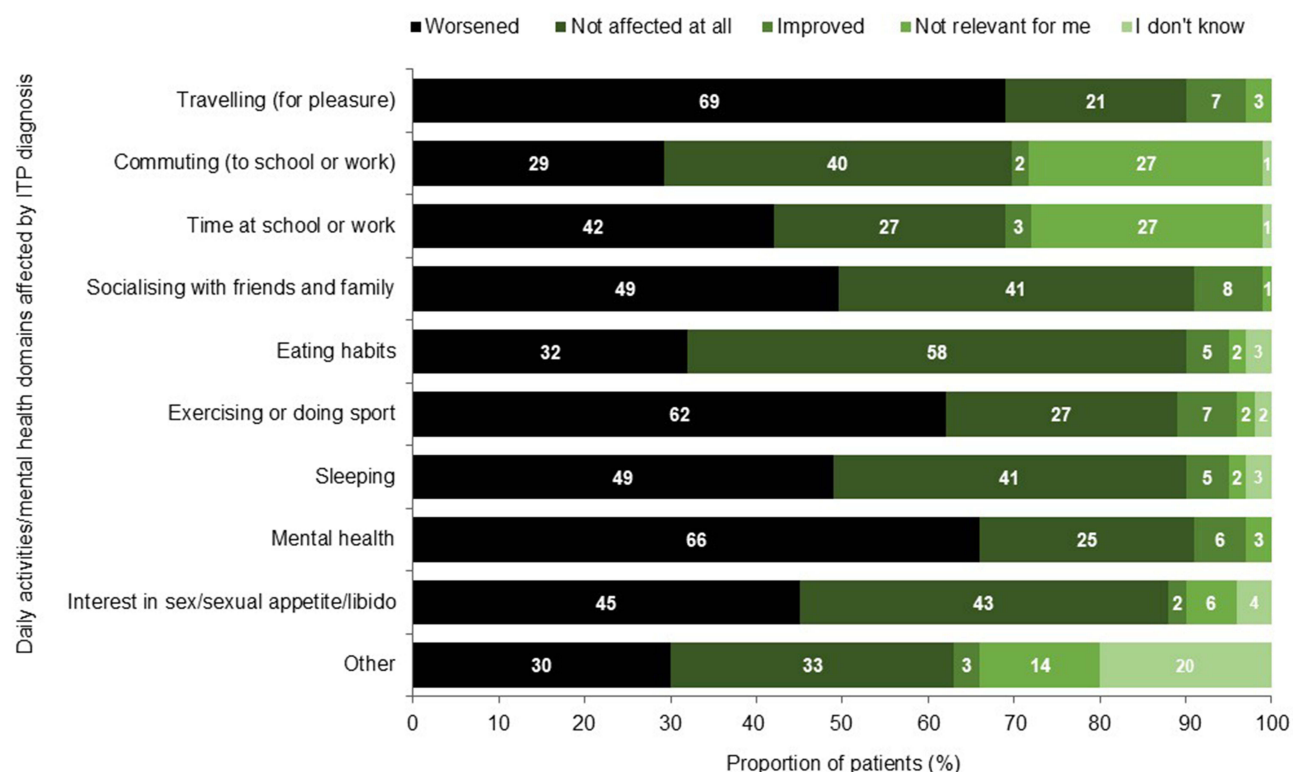
Figure 4 Daily activities/mental health domains affected by ITP diagnosis.
Notes: Respondents were asked: *To what extent are the following everyday activities affected by your ITP in general compared to life before you were diagnosed with ITP?* Figure shows proportion of respondents per treatment who answered by response category; proportions may exceed 100% due to rounding. Question completed by N=221 (romiplostim, n=65; eltrombopag, n=118; and avatrombopag, n=38). No formal statistical comparisons were undertaken and aggregated summary data are presented using descriptive statistics.
Abbreviations: ITP, immune thrombocytopenia.

Impact of TPO-RA Medication

Impact on Daily Life/Mental Health

Overall, the integration of TPO-RA medication into daily life was reported to be not difficult/very difficult (including 56% easy/very easy) for 82% of respondents and difficult/very difficult for 18% of respondents (Figure S5). Overall, 36% of respondents reported an improvement or no change in ≥1 daily activity or mental health after TPO-RA treatment initiation, including either no impact (23–72%) or an improvement (2–32%) in individual domains (Figure 5). Treatment with avatrombopag and eltrombopag was associated with the highest rates of improvements across the different daily activity/mental health domains. However, all individual domains were reported to be negatively impacted to some extent by treatment with TPO-RAs (Figure 5); travelling (for pleasure) was impacted to the greatest extent (romiplostim 62%; avatrombopag 37%; eltrombopag 24%). Other domains affected by at least one TPO-RA treatment in ≥30% of respondents were eating habits, exercise/sport, sleeping and mental health. (Figure 5). In 33% of respondents overall, TPO-RA treatment was reported to impact ≥3 daily activities negatively (42% for respondents receiving romiplostim, 31% for eltrombopag and 21% for avatrombopag) (Figure S6). In addition, 78% of the respondents were satisfied/very satisfied with their TPO-RA medication (Figure S7).

Impact on Eating and Drinking

Among respondents whose eating habits were affected to some extent by treatment with TPO-RAs (n=66), the majority were receiving eltrombopag (n=47); the most substantial impact among the eltrombopag-treated respondents was on when (70%) and what (74%) they eat/ate (Figure 6A). Among respondents reporting that eltrombopag affected when they eat/ate (n=43), 76% responded that the timing of their meals was affected every or most days per week (Figure 6B), with

Figure 5 Daily activity/mental health domains affected by at least one TPO-RA treatment.
Notes: Respondents were asked: *To what extent are the following everyday activities affected by TPO-RA medication use compared to before you took the medication?* Figure shows proportion of respondents per treatment who answered by response category; proportions may exceed 100% due to rounding. Question completed by N=221 (romiplostim, n=65; eltrombopag, n=118; and avatrombopag, n=38). No formal statistical comparisons were undertaken and aggregated summary data are presented using descriptive statistics.
Abbreviations: TPO-RA, thrombopoietin receptor agonist.

breakfast and dinner being most impacted (49% of respondents had breakfast earlier/later than preferred or skipped this meal altogether, and 42% had dinner earlier than they would have preferred). Of eight respondents receiving avatrombopag who reported that their medication affected their eating habits, six reported that it affected when they ate; eight of 11 respondents treated with romiplostim reported that it affected what they ate.

Among respondents who reported TPO-RA medication use affected what or how much they ate (n=51), more respondents were treated with eltrombopag (n=38) than with romiplostim (n=10) or avatrombopag (n=3). Among the eltrombopag-treated respondents, dairy products were most often avoided or restricted (76–87%), followed by vitamins or supplements (containing iron, calcium, aluminum, magnesium, selenium or zinc [55%]), or alcohol (34%) ([Figure S8](#)). More than half (56%) of respondents treated with eltrombopag were bothered to some or a large extent by the food/drink restrictions. Overall, 76% of respondents treated with eltrombopag rarely or never consumed restricted foods or drinks in the time span from 4 hours before to 2 hours after treatment.

Discussion

The TPO-RAs romiplostim, eltrombopag and avatrombopag provide effective and well-tolerated treatment options for chronic ITP in routine clinical practice as demonstrated by pivotal Phase 3 studies[46–48] and multiple real-world evidence studies.[32–38] This survey, conducted in five European countries and the USA, aimed to provide detailed information on the real-world experiences of people living with ITP and who are treated with TPO-RAs. On average, respondents had been diagnosed for 11 years and received TPO-RA medication for up to 5 years at the time of survey. The cross-sectional study results therefore provide valuable long-term insights regarding the impact of both the condition and treatment on daily life.

The three TPO-RAs have drug-specific differences in their administration instructions. Our survey found that almost all respondents received and understood the importance of adherence to medication instructions. Those treated with

romiplostim received the fewest instructions and the highest proportion of respondents who received ≥5 medication instructions were treated with eltrombopag. The latter was associated with more medication instructions related to the timing of food intake and food types than the other TPO-RAs; these data most likely relate to that eltrombopag tablets must be taken 4 hours before or 2 hours after specific foods or supplements.[20,21] As expected, these restrictions affected the eating habits of eltrombopag-treated respondents taking part in the survey, particularly what and when they wanted to eat. Notwithstanding the latter, about one-third of respondents did not always adhere to the recommendations and instead ate when/what they wanted occasionally. Although administration of eltrombopag with high–calcium-containing food or antacids can reduce bioavailability by up to 70%,[49] our study did not identify what was consumed during the times respondents ate when/what they wanted, and neither if non-compliance affected their platelet number. Further investigation on these aspects would be of interest. The survey surprisingly found that a small subpopulation of romiplostim-treated respondents (8–9%) reported they followed treatment instructions related to food/drink despite the fact that there are no formal food-related prescribing instructions for this once-weekly subcutaneously administered TPO-RA. Additionally, some romiplostim-treated respondents reported a negative impact on their eating habits (once or twice per week), including when and what they eat/ate. The reason for these findings is unclear.

More than half of respondents treated with eltrombopag were bothered by the food-related restrictions and reported that they would prefer a medication without such restrictions. These data are consistent with other real-world studies, which reported that people with ITP expressed a strong preference for a therapy without food restrictions over one with food restrictions.[9–11] Conversely, avatrombopag is recommended to be taken with food but has no other dietary restrictions regarding specific food types or polyvalent cations;[22] only around one in ten respondents treated with avatrombopag reported food avoidance or restrictions. In the absence of existing data in the literature, future studies are required to determine whether the different recommendations regarding food for the oral administration of eltrombopag and avatrombopag also leads to differences in compliance.

The survey found that living with ITP affected multiple areas of life, most significantly travelling (for pleasure), eating habits, exercise/sport, sleeping and mental health. Previous real-world studies (including TRAPeze and I-WISh) have also demonstrated the profound impact of ITP symptoms on HRQoL, particularly fatigue, work and productivity, and mental health, including anxiety/depression.[5–7,9–11] Moreover, the effects of living with ITP (and/or treatment) on HRQoL and daily activities might be under-reported.[50]

With respect to the TPO-RAs, it was encouraging that the beneficial effects of TPO-RA on platelet counts and bleeding were not offset, indicated by no worsening of at least one daily activity/mental health domain in 36% of respondents. Travelling (for pleasure) was the individual daily activity most impacted by treatment with TPO-RAs (reported in 62% of romiplostim-treated respondents). This effect on travel may be anticipated as romiplostim is a weekly subcutaneous injection, usually reconstituted and administered in a healthcare setting although self-administration may be possible with training.[51] While some people with ITP may find subcutaneous delivery of romiplostim challenging in contrast to oral administration of eltrombopag and avatrombopag, others may prefer once-weekly administration[9,10] (for example, those less suited to daily compliance required for oral TPO-RAs). Previous studies have suggested that in general, people with ITP express a strong preference for orally versus subcutaneous TPO-RA treatment administration;[9–11] although the overall body of evidence from these studies is largely based on comparisons between romiplostim and eltrombopag, owing to the later approval and availability of avatrombopag (June 2019 in the USA and January 2021 in Europe.[22,23]

Despite the medication instructions and the potential impact of treatment on HRQoL, more than 80% of respondents in our study did not find it difficult/very difficult to integrate TPO-RA medication into their daily life, and almost 80% were satisfied/very satisfied with their TPO-RA. High levels of satisfaction (in over two-thirds of study participants with chronic ITP in Europe) to TPO-RAs (romiplostim or eltrombopag) were also reported in other real-world studies.[7,9–11] Reported reasons for treatment satisfaction included effectiveness for maintaining platelet count, treating symptoms, preventing bleeding events, lack of dietary restrictions, oral (versus subcutaneous) administration and less frequent dosing.[9,11]

Aligned to treatment guidelines recommending that people with ITP are involved in the selection of therapy,[3] 83% of respondents to our survey reported that their physician or another HCP did take their personal preferences into account,
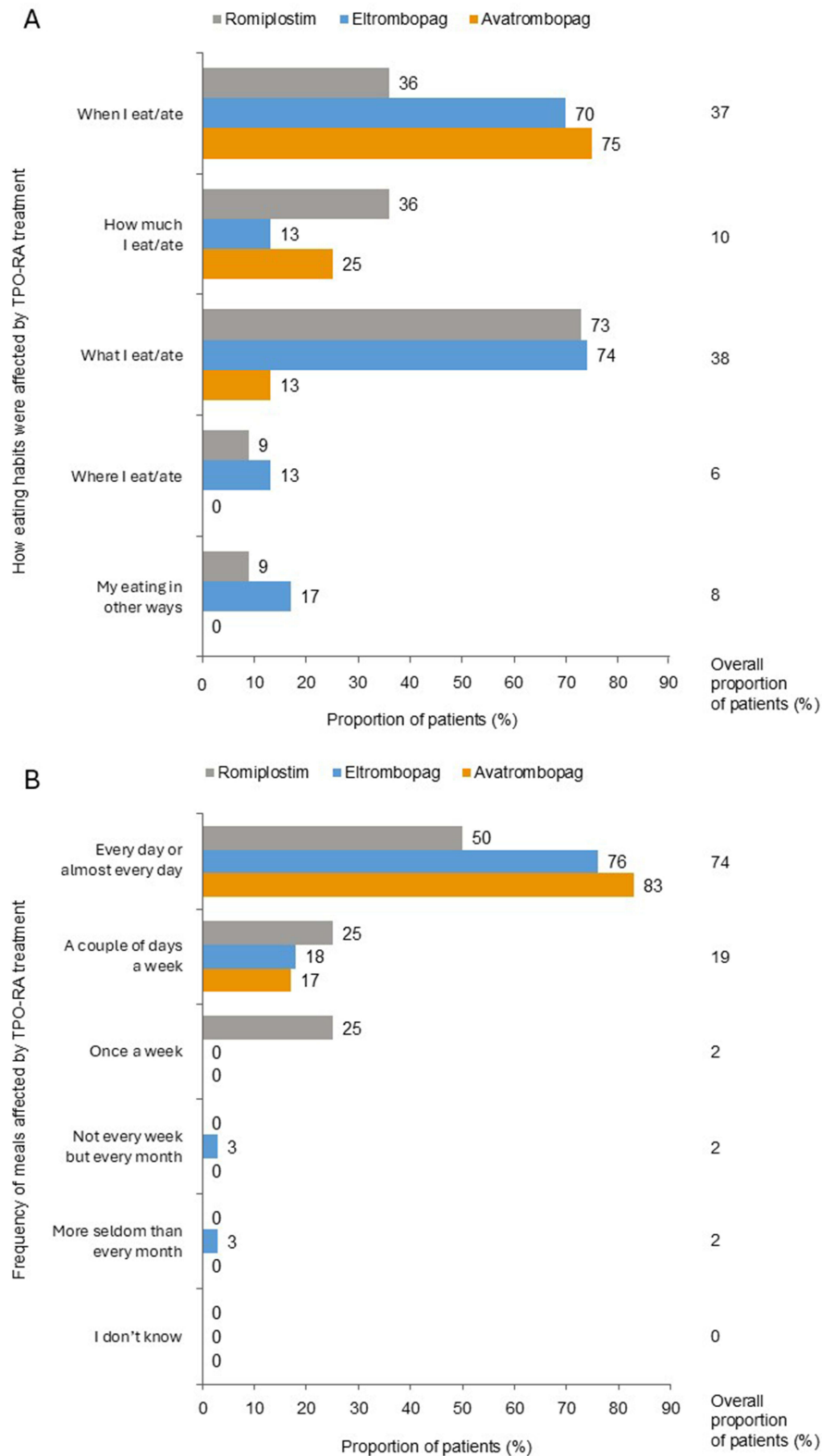
Figure 6 Impacts of TPO-RA medication on (**A**) eating habits and (**B**) timing of meals.

Notes: Respondents were asked: (**A**) *You answered that your eating habits are/were affected by TPO-RA medication use. Compared to when you had ITP but were not receiving TPO medication, how does/did the medication affect your eating habits?* Figure shows the proportion of patients per treatment who answered that their eating habits had worsened (**B**) *You answered that TPO-RA medication use affects/affected when you eat/ate. How often is/was the timing of your meals affected by TPO-RA medication?* Question A completed by n=66 (romiplostim, n=11, eltrombopag, n=47 and avatrombopag, n=8) and question B by n=43 (romiplostim, n=4, eltrombopag, n=33 and avatrombopag, n=6). Both figures show proportion of respondents per treatment who answered by response category; proportions may exceed 100% due to rounding. No formal statistical comparisons were undertaken and aggregated summary data are presented using descriptive statistics.

Abbreviations: TPO-RA, thrombopoietin receptor agonist.

emphasizing shared decision-making. The latter should include discussions not only on the route of administration (subcutaneous vs oral) and dosing frequency (once daily vs once weekly) but also food restrictions (none vs dietary/timing limitations). Additionally, 85% of respondents received information about different ITP treatment options. Consultation between HCPs and patients is important, particularly as they may have different perceptions and priorities regarding treatment for ITP.[50] Other factors to consider when selecting between TPO-RAs may include comorbidities and drug cost-effectiveness.[4]

The three TPO-RAs have differences in mechanistic action, molecular structure and/or pharmacokinetic profile,[32,50] and consequently switching between TPO-RAs is advocated by treatment guidelines[3,4] based on improved outcomes in people with ITP who switched from the prior TPO-RA due to poor efficacy or AEs.[32,33,52–54] In our survey, 60% of respondents reported that they previously used another type of ITP medication (beside their most recent TPO-RA) designed to increase platelet production. Common reasons for respondents and physicians to switch TPO-RA treatment (n=132) were the prior drug did not work as expected or AEs; medication restrictions and bothersome administration were also reported to a lesser extent. The percentage of respondents who switched between TPO-RAs may appear to be quite high considering their documented efficacy in managing ITP, but this is potentially a consequence of the long time since diagnosis (increasing the likelihood of becoming refractory to treatment or experiencing AEs). The lowest rate of switching between TPO-RAs was reported in those treated with romiplostim, while the highest rate was reported in those treated with avatrombopag (lack of efficacy or physician suggestion were common reasons). However, switching data are skewed by the fact that only six respondents using eltrombopag or romiplostim had previously received avatrombopag at the time of the survey, potentially owing to later approval of avatrombopag. Differences in the timing of availability of the TPO-RAs may also affect other survey findings, such as the impact of medication on daily life.

The survey has several limitations. It was beyond the scope to capture in detail the number and type of prior therapies received (and in which line) for ITP, outcomes based on the line of therapy or switching (due to low sample sizes after switching) or longitudinal long-term outcomes. In addition, outcomes of effectiveness, tolerability, compliance with medication and HRQoL were not formally assessed, and it is possible that the burden of ITP and its treatment may vary by patient age. Although respondents were asked to carefully consider the impact of ITP and TPO-RA medication on their everyday activities and mental health, it may have been difficult for them to clearly separate out the effects of disease from the different medications received since diagnosis – the patient experience likely reflects a combination of both illness and medication use. There was an absence of formal statistical comparisons of the data between TPO-RA sub-populations and specific age groups, while the median duration of treatment with the individual TPO-RAs was not available in the dataset. There was also lack of representation due to imbalances in the number of respondents treated with the different TPO-RAs; this may have impacted some of the study results and additional analyses will be required. Similarly, the use of a self-administered online survey and recruitment via local patient organizations may have potentially introduced a disproportionately proactive or well-educated group of respondents. In addition, potential country-specific differences may have possibly impacted the results, but the study was not powered to make any statistical comparisons across countries or regions and it was not feasible due to low numbers in some countries. The study focused on the three TPO-RAs currently approved for ITP in most global countries but it is acknowledged that other TPO-RAs may be available in selected countries, such as recombinant human thrombopoietin and hetrombopag approved for use in China. Future studies may be implemented to help address some of the study limitations listed here.

In general, survey methods favor people with more disposable time, access to technology/competent using computers, and those who are highly motivated. Conversely, the survey has several strengths, particularly the acquisition of real-world data from several countries in Europe and the US, and the inclusion of the three TPO-RAs widely used in Europe. The results represent the patient perspective (self-reported) and recruitment was aided by patient organizations, resulting in a large sample size overall. The survey also had a broad scope, avoided missing data, and was able to provide valuable new insights into medication instructions and related adherence.

Conclusion

In this multinational survey, people living with ITP reported negative impact on their daily activities/mental health from their condition. Similarly, treatment with some TPO-RAs may additionally impair specific activities, likely influenced by

administration routes and dietary restrictions. These factors should be considered and discussed with people with ITP when selecting therapy. Nearly all survey respondents with ITP treated with a TPO-RA received and understood medication instructions, most found that implementation of TPO-RA medication into daily life was easy, and most were satisfied with their treatment. These real-world first-hand perspectives on ITP and TPO-RA treatment should help to inform optimal management in routine clinical practice.

Abbreviations

EU, European Union; HCP, healthcare professional; HRQoL, health-related quality of life; ITP, immune thrombocytopenia; IVIg, intravenous immunoglobulin, OCS, oral corticosteroids, SD, standard deviation; TPO-RA, thrombopoietin receptor agonist; WMO, Wet medisch-wetenschappelijk onderzoek met mensen.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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