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Initiation of aripiprazole once-monthly using a two-injection start in adult patients diagnosed with schizophrenia: real-world views and experiences of Italian healthcare professionals

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Summary. Aim. In Italy, aripiprazole once-monthly 400 mg (AOM 400) can be initiated using a two-injection start (TIS) in adult patients diagnosed with schizophrenia who are stabilised with oral aripiprazole. With this approach, treatment initiation is completed in a single day, without the need for 14 days of concurrent oral aripiprazole supplementation. This study examined how healthcare professionals (HCPs) view and use the AOM 400-TIS in real-world clinical practice in Italy, a country where uptake of the AOM 400-TIS has been relatively high. **Methods.** Responses were analysed for Italian physicians and nurses who participated in a pan-European, non-interventional, cross-sectional online survey that explored perspectives and attitudes towards prescribing and/or administering AOM 400-TIS in patients diagnosed with schizophrenia. Responses were collected across two waves and were analysed descriptively. **Results.** Responses were available for 108 Italian HCPs, representing 47.2% of all survey participants. Common reasons for using the AOM 400-TIS were poor treatment adherence (81.5%), patient preference (50.0%), and disease relapse (42.6%), while common barriers to its use were patient reluctance to receive two injections (36.1%), concerns about tolerability (24.1%), and concerns about safety (23.1%). Most HCPs agreed or strongly agreed that the AOM 400-TIS resulted in satisfactory patient outcomes (85.2%), was easy to administer (82.4%), and had a safety/tolerability profile similar to the traditional one-injection start (69.4%). **Discussion.** The results confirm the favourable clinical opinions, perspectives, and experiences of Italian HCPs who prescribe and/or administer the AOM 400-TIS in clinical practice.

Key words. Aripiprazole once-monthly, clinical practice, long-acting injectable, real-world perspectives, survey, two-injection start, 1-day initiation regimen.

Inizio di aripiprazolo una volta al mese tramite due iniezioni in pazienti adulti con schizofrenia: prospettive ed esperienze cliniche di professionisti sanitari italiani.

Riassunto. Obiettivo. In Italia, la terapia con aripiprazolo 400 mg una volta al mese (AOM 400) può essere iniziata con la somministrazione di due iniezioni (TIS) in pazienti adulti diagnosticati con schizofrenia e stabilizzati con aripiprazolo orale. Con questo approccio, il trattamento raggiunge livelli ematici efficaci in un solo giorno, senza necessitare di 14 giorni di integrazione concomitante con aripiprazolo orale. Questo studio ha esaminato come i professionisti sanitari (HCP) percepiscono e utilizzano l'AOM 400-TIS nella loro pratica clinica in Italia, un Paese dove l'adozione dell'AOM 400-TIS è stata relativamente elevata. **Metodi.** Le risposte analizzate sono state fornite da medici e infermieri italiani che hanno partecipato a un'indagine online paneuropea, non interventistica e trasversale che ha esplorato prospettive e attitudini nei confronti della prescrizione e/o somministrazione di AOM 400-TIS in pazienti diagnosticati con schizofrenia. Le risposte sono state raccolte in due tempi e analizzate in maniera descrittiva. **Risultati.** Sono state raccolte e analizzate le risposte di 108 operatori sanitari italiani, che rappresentano il 47,2% di tutti i partecipanti al sondaggio. Frequenti motivazioni per l'uso dell'AOM 400-TIS sono state: scarsa aderenza al trattamento (81,5%), preferenza del paziente (50,0%) e ricaduta della malattia (42,6%). Ostacoli comuni al suo utilizzo sono invece risultati: riluttanza del paziente a ricevere due iniezioni (36,1%) e preoccupazioni riguardo tollerabilità (24,1%), e preoccupazioni riguardo sicurezza (23,1%). La maggior parte degli operatori sanitari concorda, o concorda fortemente, che l'AOM 400-TIS sia facile da somministrare (82,4%), abbia un profilo di sicurezza/tollerabilità simile a quello tradizionale di avvio con una sola iniezione (69,4%) e porti a risultati soddisfacenti per i pazienti (85,2%). **Discussione.** I risultati confermano le opinioni cliniche positive, le prospettive e le esperienze degli operatori sanitari italiani che prescrivono e/o somministrano l'AOM 400-TIS nella pratica clinica.

Parole chiave. Aripiprazolo una volta al mese, avvio con due iniezioni, iniettabile a lunga durata, pratica clinica, prospettive cliniche, sondaggio, regime di avvio di 1 giorno.

Introduction

Aripiprazole monohydrate long-acting injectables (LAIs) include a once-monthly formulation (aripiprazole once-monthly 400 mg [AOM 400]), which is approved in Europe for the maintenance treatment of adult patients diagnosed with schizophrenia who are stabilised with oral aripiprazole[1]. More recently, a once-every-2-months formulation has been approved (aripiprazole 2-month ready-to-use 960 mg [Ari

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2MRTU 960])[1], which has a similar pharmacokinetic, safety/tolerability, and efficacy profile to AOM 400 in people diagnosed with schizophrenia[2-4].

AOM 400 has been available and reimbursed in Italy since July 2014. At the time of its approval, treatment initiation comprised a single injection of AOM 400 plus 14 consecutive days of oral aripiprazole. In October 2020, a simplified initiation regimen for AOM 400 was approved by the European Medicines Agency. This regimen, variously referred to as the two-injection start (TIS) or the 1-day initiation regimen[5,6], involves two injections of AOM 400 administered at separate injection sites (deltoid or gluteal muscle) plus a single dose of oral aripiprazole 20 mg[1]. With the AOM 400-TIS, all treatments are administered on the same day during a single clinic visit. Therapeutic drug levels are achieved on the first day of treatment[7], removing the need for 14 days of oral aripiprazole supplementation.

Based on the authors' own experience, uptake of the AOM 400-TIS was rapid in Italy, with a rate of adoption that exceeded that in other European countries. Potential reasons for this include the familiarity of Italian psychiatrists with AOM 400 and the perception that the AOM 400-TIS is a practical alternative to the traditional one-injection start. Notably, removing the requirement for 14 days of overlapping oral aripiprazole reduces the risk of adherence-related under-treatment and subsequent relapse during the initiation of therapy[7]. Related to this, the AOM 400-TIS reduces the burden on patients to remember to take oral medication for 14 days with their first injection of AOM 400, as well as any associated oversight needed from families or other caregivers[7,8]. In an inpatient setting, the AOM 400-TIS may allow for an earlier discharge, since the requirement for healthcare professionals (HCPs) to supervise multiple days of oral medication intake is removed[7].

Recently, the results of a non-interventional, cross-sectional survey were published, offering an insight into the views and experiences of HCPs from 5 European countries who prescribe and/or administer the AOM 400-TIS.[9] The survey included a notable number of participants from Italy, which could provide a unique opportunity to examine study outcomes from an Italian perspective. However, individual country-level data were not previously published. The results of an Italian-specific analysis are reported here, with author interpretation that places the findings in the context of Italian clinical practice.

Materials and methods

Survey objectives and design

A full and thorough description of the non-interventional, cross-sectional online survey has been reported previously[9,10]. In brief, HCPs from Germany, Italy, Denmark, Sweden, and the United Kingdom (UK) participated in the survey, which was conducted in two waves between February and November 2024[9]. The primary aim of the survey was to assess HCPs' experiences and satisfaction with the AOM 400-TIS[10]. Secondary aims were to: 1) examine the characteristics of HCPs who prescribe AOM 400-TIS; 2) identify patient and clinical factors that influence their decision to initiate treatment using the AOM 400-TIS; 3) assess their perceptions of the efficacy, safety, and tolerability of the AOM 400-TIS; and 4) gather broader insights into their views and experiences with the AOM 400-TIS[10]. The survey was developed with input from a steering committee of clinical experts to ensure that the content reflected real-world European practice and captured the relevant settings and specialities involved in prescribing or administering AOM 400-TIS[10].

The survey comprised 28 questions and was designed to be completed in 15-20 minutes[10]. In most cases, participants were instructed to select one or more predefined response options depending on the nature of the question[10]. In answering the survey questions, participants were directed to reflect on their past experience with the AOM 400-TIS (administered according to their local label) in adult patients diagnosed with schizophrenia[10]. Full versions of the survey have been published previously in the supplementary appendices accompanying Fagiolini et al.[10] and Beckham et al[9].

The survey was conducted online and hosted on a secure web-based platform[10]. Participants completed the survey in their local language and received a modest and appropriate payment in their local currency as compensation for their time[10]. Data collection was pseudonymised, with each participant assigned a unique identification number to ensure confidentiality[10]. The survey underwent internal and external user testing prior to launch, including checks of a dummy dataset to confirm correct programming of filters and quotas. Data quality was monitored during the survey period using predefined quality control measures (e.g., identification of duplicate respondents, speeders, and flatliners), with formal data checks conducted at soft launch (5-10% of completers), at 50% completion, and once the full study sample had been achieved.

The study followed the ethical principles set out in the Declaration of Helsinki and met the requirements of the European Union General Data Protection Regulation[10]. Since the study involved only physician surveys and did not include patients or access to patient medical records, it was deemed exempt from Institutional Review Board (IRB) review (SALUS IRB; 14 January 2024)[10]. The completed Checklist for Reporting of Survey Studies can be found in the supplementary material.

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Participant population and recruitment

Eligible participants were licensed physicians or nurses who were involved in the treatment and management of schizophrenia and who had prescribed and/or administered the AOM 400-TIS to patients diagnosed with schizophrenia on at least three occasions[10]. Employment by a pharmaceutical company was an exclusion criterion[10].

Participant recruitment in Wave 1 of the study (1 February-21 March 2024 [participants from Germany, Italy, and the UK]) was via online panels of individuals who had been independently preselected by a recruiting agency, based on their likelihood to meet the study criteria and their prior interest in participating in research studies[10]. Participants were invited to participate until the pre-planned sample size was achieved. HCPs from the panels were randomly selected and provided a unique link to the survey information sheet[10]. Those meeting all study requirements and eligibility criteria, including provision of electronic consent, were invited to complete the survey[10]. All ineligible respondents were directed away from the survey[10]. Recruitment via online panels was also adopted in Wave 2 of the study (18 September-27 November 2024 [participants from Denmark, Sweden, and Italy]), with extra Italian participants recruited on a voluntary basis via email from the local network of the Italian member of the steering committee[9].

Statistical analysis

Data were analysed descriptively on an item-by-item basis using Microsoft® Excel® 365[10]. The descriptive design of the study meant that a formal power calculation was not required[10]. Within the Italian sample, planned recruitment was 110 HCPs (Wave 1, n=30; Wave 2, n=80 [with up to n=50 recruited via online panels and up to n=30 recruited via the Italian steering committee member's professional network])[9]. The target distribution of HCPs recruited via online panels across Waves 1 and 2 combined was approximately two physicians for every one nurse (i.e., 55 physicians [Wave 1, n=20; Wave 2, n=35] and 25 nurses [Wave 1, n=10; Wave 2, n=15])[9]. For HCPs recruited on a volunteer basis (Wave 2 only), there was no preplanned distribution of physicians versus nurses[9]. No formal inferential testing (e.g., chi-square or t-tests) was conducted.

Results

In total, 1501 HCPs based in Italy were invited to take part in the survey, 241 were screened (1260 did not respond), and 108 completed the survey; 133 HCPs were excluded; the main reasons for exclusion included screen failure (n=69) or incomplete survey (n=60). Of the 108 HCPs who completed the survey from Italy, 31 participated in Wave 1 and 77 participated in Wave 2 (recruited via online panels, n=51; recruited via email invite, n=26). The characteristics of the Italian participants are detailed in table 1. The two most prevalent job roles were physician psychiatrist (68.5%) and psychiatric nurse (23.1%), while the two most common work environments were specia-

Table 1. Characteristics of Italian HCP survey participants.

Characteristics	n=108
Primary job role/specialty, n (%)	
Physician	
General practitioner/primary care practitioner	1 (0.9)
Psychiatrist	74 (68.5)
Other[a]	2 (1.9)
Nurse	
Psychiatric	25 (23.1)
Community	4 (3.7)
Other[b]	2 (1.9)
Primary work setting, n (%)[c]	
Specialist mental health clinic/centre	83 (76.9)
Hospital inpatient	28 (25.9)
Hospital outpatient	14 (13.0)
General practitioner	3 (2.8)
Other[d]	6 (5.6)
Time working professionally in clinical practice, median (IQR) [range], years	20.0 (10.0-29.3) [1.0-69.0]
Proportion of patients in caseload diagnosed with schizophrenia, median (IQR) [range], %	30.0 (20.0-46.3) [3.0-100]
Proportion of patients in caseload diagnosed with schizophrenia and treated with LAIs, median (IQR) [range], %	40.0 (20.0-65.0) [2.0-100]
Main responsibility regarding the AOM 400-TIS, n (%)	
Prescribing	50 (46.3)
Administration	27 (25.0)
Both	31 (28.7)

[a]Other responses included: medical resident (n=1) and psychiatry resident (n=1).
[b]Other responses included: ward physician (n=1) and hospital (n=1).
[c]Participants could select all response options that applied, meaning percentages could total >100%.
[d]Other responses included: *'private clinic'* (n=1); *'mental health centre'* (n=1); *'outpatient clinic, rehabilitation facilities'* (n=1); *'psychiatric diagnosis and treatment unit (Servizio Psichiatrico di Diagnosi e Cura)'*[e] (n=1); *'psychosocial centre'* (n=1); and *'university psychiatry department'* (n=1).
[e]Servizio Psichiatrico di Diagnosi e Cura is an Italian hospital unit where voluntary and mandatory inpatient psychiatric treatment is provided; it is based within hospital facilities and it is part of the mental health department.
Legend: AOM 400-TIS= aripiprazole once-monthly 400 mg two-injection start; HCP= healthcare professional; IQR= interquartile range; LAI= long-acting injection.

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list mental health clinics/centres (76.9%) and hospital inpatient settings (25.9%). The Italian HCPs had worked professionally in clinical practice for a mean (standard deviation [SD]) of 19.7 (12.2) years. Within the HCP caseload, the mean (SD) proportion of patients with a diagnosis of schizophrenia was 35.5% (22.5%); of these, a mean (SD) of 43.7% (25.8%) were treated with LAI antipsychotics.

Table 2 outlines factors related to use of the AOM 400-TIS by Italian HCPs. Nearly one-half of participants (45.4%) reported that they had been prescribing and/or administering the AOM 400-TIS for a period exceeding 24 months. The AOM 400-TIS was most frequently used in patients with moderate symptoms (68.5%), with no notable variation in use between those aged 18-35 years (67.6%) and those aged 36-64 years (69.4%).

The most frequently reported reasons that Italian HCPs chose to initiate treatment with the AOM 400-TIS in patients diagnosed with schizophrenia are shown in figure 1. Of the available responses, '*Poor treatment adherence*' was selected most frequently (81.5%), followed by '*patient preference (i.e., patient not willing to take oral medication)*' (50.0%) and '*relapse(s) of disease*' (42.6%).

The primary objectives cited by Italian HCPs when choosing to prescribe the AOM 400-TIS are outlined in figure 2, with the most common being '*to improve adherence*' (74.1%), '*to prevent relapses*' (67.6%), '*to improve patient quality of life*' (QoL, 60.2%), and '*to prevent re-hospitalisations*' (59.3%). When HCPs were prompted to identify the single most important objective when choosing to prescribe the AOM 400-TIS, '*to improve adherence*' was selected most often (35.3%), followed by '*to improve patient QoL*' (27.1%), '*to prevent relapses*' (17.6%), and '*to improve symptoms*' (11.8%).

The most frequently cited reasons and/or barriers to not use the AOM 400-TIS are displayed in figure 3. The most commonly selected response was '*patients*

Table 2. Italian HCP use of the AOM 400-TIS initiation regimen in a maintenance treatment setting.

	n=108
Approximate time since HCP started to prescribe/administer the AOM 400-TIS, n (%)	
<6 months ago	15 (13.9)
6-12 months ago	17 (15.7)
13-24 months ago	27 (25.0)
>24 months ago	49 (45.4)
Average time spent by patient on oral aripiprazole prior to nitiating AOM via the AOM 400-TIS, n (%)	
<14 days	50 (46.3)
14-28 days	41 (38.0)
>28 days	17 (15.7)
Average severity of symptoms of typical patients whose treatment with AOM was initiated via the AOM 400-TIS, n (%)[a]	
Mild	25 (23.1)
Moderate	74 (68.5)
Severe	40 (37.0)
Age of typical (adult) patients whose treatment with AOM was initiated via the AOM 400-TIS, n (%)[a]	
18-35 years	73 (67.6)
36-64 years	75 (69.4)
≥65 years	6 (5.6)
Treatment setting in which the AOM 400-TIS is typically prescribed, n (%)[a]	
Inpatient	64 (59.3)
Outpatient	74 (68.5)
Otherb,c	2 (2.6)

[a]Participants could select all response options that applied, meaning percentages could total >100%.
[b]This response option was only included in Wave 2 of the survey (n=77).
[c]Other response included: *'both'* (n=2).
Legend: AOM= aripiprazole once-monthly; AOM 400-TIS= aripiprazole once-monthly 400 mg two-injection start; HCP= healthcare professional.

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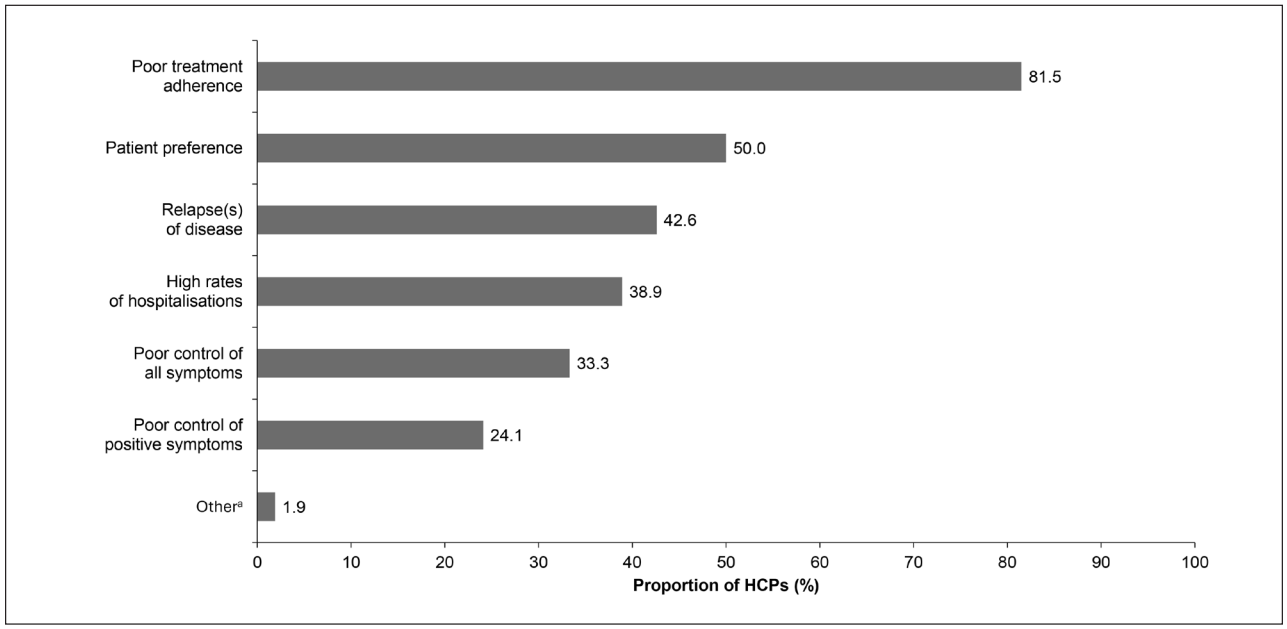

Figure 1. Most common reason(s) selected by Italian HCPs for initiating maintenance treatment with the AOM 400-TIS (n=108).

Data are ranked from the most to the least selected response options. Participants could select all response options that applied, meaning percentages could total >100%.
Other responses included *'simplification of the dosage scheme'* (n=1) and *'improved medication efficacy and tolerability'* (n=1).
AOM 400-TIS=aripiprazole once-monthly 400 mg two-injection start; HCP=healthcare professional.

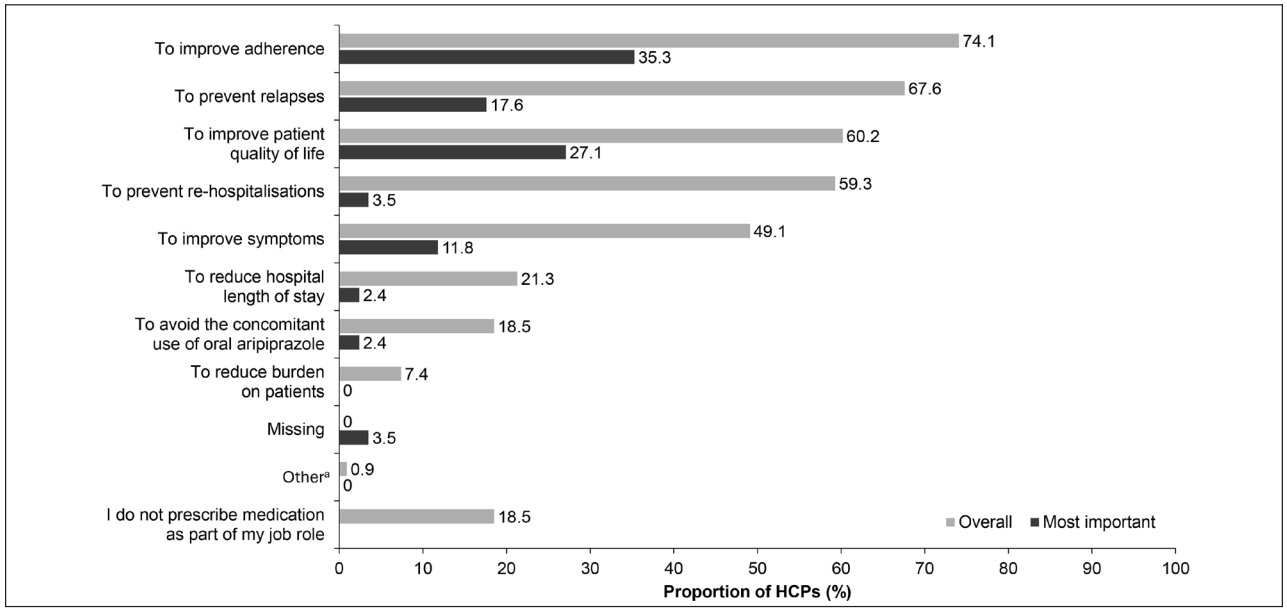

Figure 2. Main objective(s) selected by Italian HCPs when choosing to prescribe the AOM 400-TIS initiation regimen (overall category, n=108; most important category, n=85).

Participants were asked to select all response options that applied (overall category), and to select one response option that they considered the most important (most important category). The denominator was n=108 for the overall category (all participants) and n=85 for the most important category (all participants [n=108] minus those who did not prescribe as part of their job role [n=20] and those with missing responses [n=3]).
Data are ranked from the most to least selected response options in the overall category. In the overall category, participants could select all response options that applied, meaning percentages could total >100%.
[a]The 'Other' response was *'improving tolerability'* (n=1).
AOM 400-TIS=aripiprazole once-monthly 400 mg two-injection start; HCP=healthcare professional.

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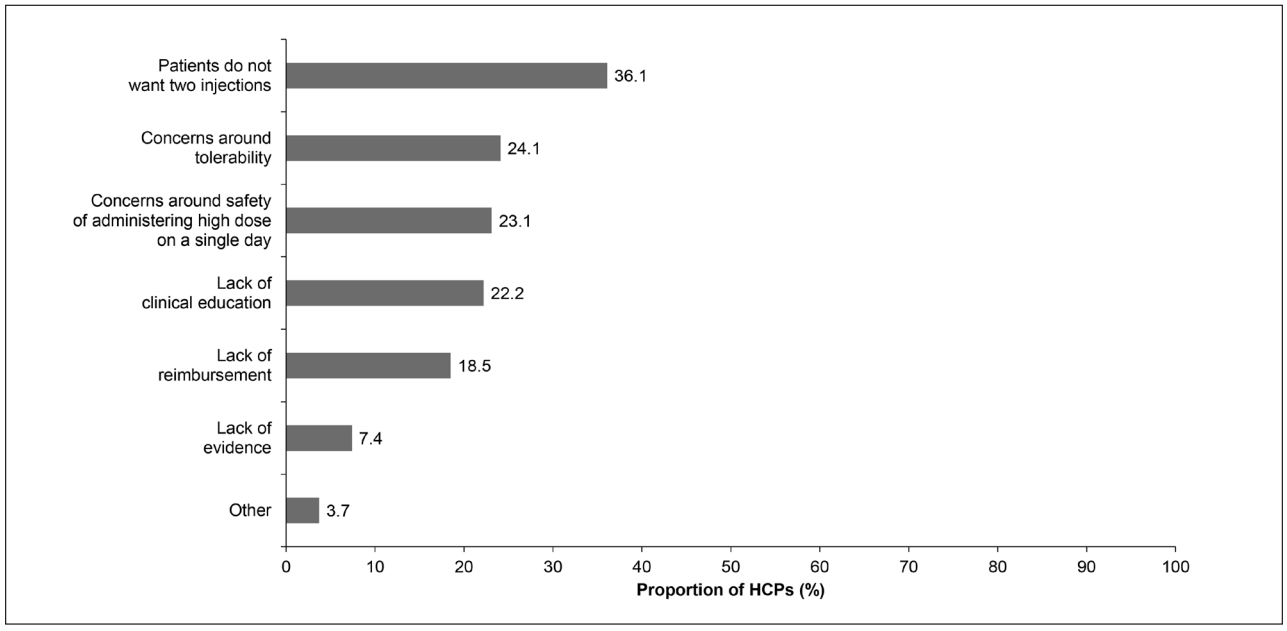

Figure 3. Reasons and/or barriers selected by Italian HCPs that might lead them to not use the AOM 400-TIS initiation regimen (n=108).

Data are ranked from the most to least selected response options. Participants could select all response options that applied, meaning percentages could total >100%.
[a]Other responses included: *'based on how the question is phrased, I have no obstacles but other colleagues may not prescribe due to lack of specific training'* (n=1); *'none'* (n=1); *'I do not prescribe'* (n=1); and *'I administer by prescription'* (n=1).
AOM 400-TIS=aripiprazole once-monthly 400 mg two-injection start; HCP=healthcare professional.

don't want two injections' (36.1%), followed by '*concerns around tolerability'* (24.1%), '*concerns around safety of administering high dose on a single day'* (23.1%), and a '*lack of clinical education*' (22.2%).

Patient and clinical factors that influenced HCPs' decision to prescribe the AOM 400-TIS are shown in figure 4. The top three responses were '*adherence to prior treatment*' (55.6%), '*efficacy*' (41.7%), and '*safety/*

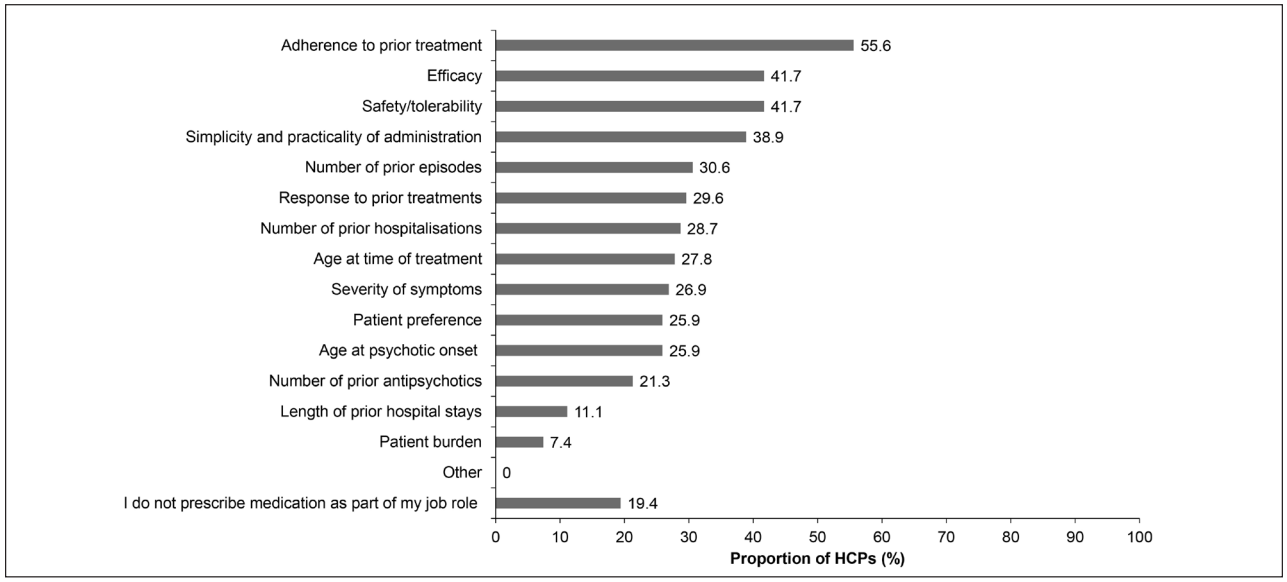

Figure 4. Important patient and clinical factors that influence Italian HCPs' decision to prescribe the AOM 400-TIS initiation regimen (n=108).

Data are ranked from the most to least selected response options. Participants could select all response options that applied, meaning percentages could total >100%. AOM 400-TIS= aripiprazole once-monthly 400 mg two-injection start; HCP= healthcare professional.

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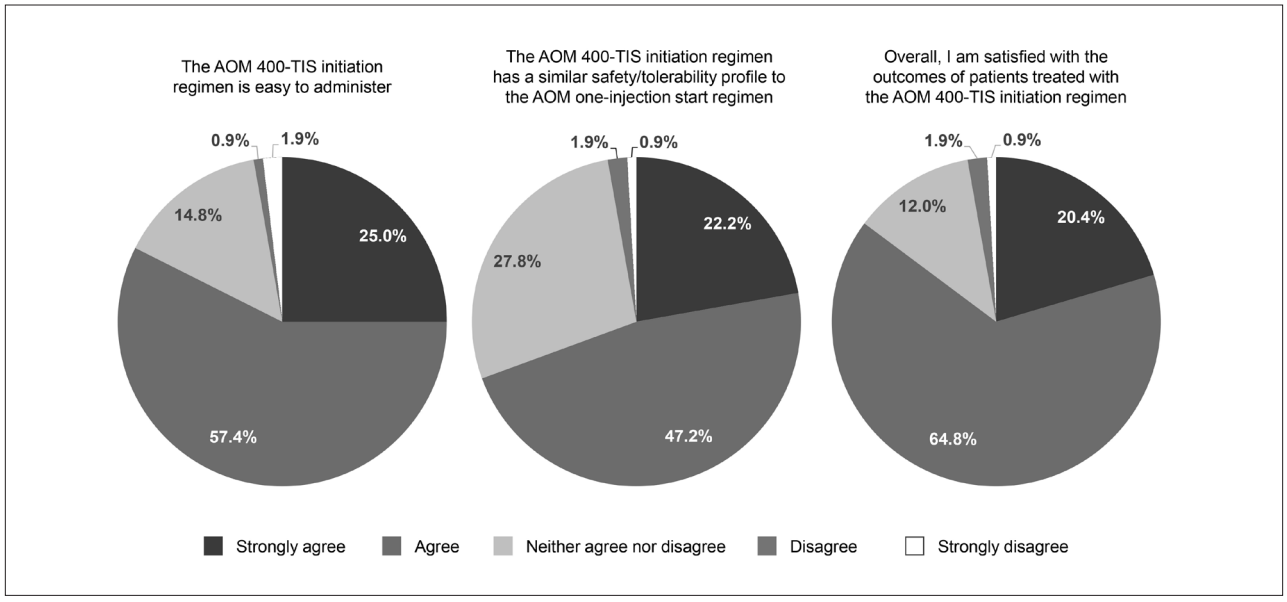

Figure 5. Italian HCPs' responses to statements on their recent experience with the AOM 400-TIS initiation regimen (n=108).
AOM= aripiprazole once-monthly; AOM 400-TIS= aripiprazole once-monthly 400 mg two-injection start; HCP= healthcare professional.

tolerability' (41.7%). When asked to rank their responses in order of importance, HCPs most often selected '*adherence to prior treatment*' (39.1%) and '*efficacy*' (12.6%) as being most important (figure S1).

Wider views and experiences with the AOM 400-TIS

HCP responses to statements on their recent experience with the AOM 400-TIS are shown in figure 5. Overall, 85.2% of HCPs agreed or strongly agreed that they were satisfied with the outcomes of patients who received the AOM 400-TIS, with 82.4% agreeing or strongly agreeing that the AOM 400-TIS was easy to administer. Collectively, 69.4% of HCPs agreed or strongly agreed that the AOM 400-TIS had a similar safety/tolerability profile to initiation with a single injection of AOM 400 plus 14 days of supplemental oral aripiprazole.

Discussion

The results of the current survey offer a valuable perspective on the real-world use of the AOM 400-TIS initiation regimen in Italy. Based on feedback from more than 100 physicians and nurses, data indicate that HCPs prescribe or administer the AOM 400-TIS to support treatment adherence, align with patient preferences, and reduce the risk of relapse. Reasons for not using the AOM 400-TIS include patient reluctance to receive two injections at the same time and safety or tolerability concerns.

Treatment adherence was a primary driver of AOM 400-TIS use. Specifically, poor treatment adherence was the most common reason that Italian HCPs used the AOM 400-TIS (81.5% of HCPs), improving adherence was the most common treatment objective (74.1%), and adherence to prior therapy was the most common patient/clinical factor influencing its use (55.6%). The survey did not collect data on the rationale behind HCPs' responses, so reasons for the focus on adherence are unclear. However, therapeutic drug levels are rapidly achieved with the AOM 400-TIS[6,7], without the need for 14 days of supplemental tablet taking. This removes the known vulnerability associated with missed oral doses in the early treatment phase, which could be advantageous in populations with known adherence challenges[6,11].

Patient preference ranked above disease relapse as a reason for initiating maintenance treatment with the AOM 400-TIS in the Italian cohort. The focus on patient preference in Italy aligns with recent findings from other pan-European and North American qualitative interview studies, in which prescribers identified patient preference and buy-in as an important factor when prescribing an LAI, and a critical determinant of LAI treatment success[12,13].

The most common reasons or barriers given for not using the AOM 400-TIS were that patients did not want two injections or that they had concerns around the tolerability or safety of administering a high dose on a single day. Based on the authors' own clinical experiences, potential approaches to overcoming barriers to the AOM 400-TIS regimen may include

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framing the regimen positively as a means of reducing patient anxiety or resistance, with communication focused on simplification, reassurance, and the long-term benefits of stability and relapse prevention. The regimen may be framed as a 'one-and-done' approach that ensures immediate long-acting coverage without the burden of daily pills, a message that resonates well with patients, particularly younger individuals and those with prior difficulty adhering to oral treatment. It may also resonate well with patients with early-phase disease, a population for whom functional recovery is considered an important and achievable long-term treatment goal[14]. For illustration, one way of presenting it might be: 'With this injection plan, you're protected starting today, without needing to remember any pills tomorrow'. Emphasis can also be placed on the regimen being well tolerated, while providing rapid therapeutic coverage without the need for follow-up oral medication; findings that are supported by the scientific literature[7,15]. At the same time, it is important that decisions regarding the AOM 400-TIS are not imposed, but are instead developed collaboratively, taking into account any views or concerns that a patient may have about the regimen. This aligns with the previously mentioned qualitative interview studies, in which researchers emphasised the importance of shared decision-making and the need for prescribers to engage patients in conversation to explore any preconceptions they might have about LAIs[12,13]. This same approach is also relevant to patient-prescriber conversations about a TIS with Ari 2MRTU 960, an LAI formulation of aripiprazole monohydrate that is administered once every 2 months.

The data reported here add to already published real-world findings on the use of the AOM 400-TIS in clinical practice in Italy specifically. A retrospective review of 133 patients living with schizophrenia treated at ten Italian clinics found no notable safety concerns with the AOM 400-TIS[15]. Adverse events (AEs) within the first month were mild or moderate, and the safety profile of AOM 400-TIS was similar to that for AOM 400 in clinical trials[15]. Separately, the results of a European database study, which included patients from Italy, showed that real-world incidence rates for extrapyramidal AEs with AOM were compatible with those reported in clinical studies[16], a finding that could alleviate any general hesitation in prescribing AOM. In a retrospective chart review of 24 inpatients in Italy who received the AOM 400-TIS, including 10 with psychosis or schizophrenia, most did not require hospital readmission (83.3%) or a subsequent emergency room visit (87.5%)[17]. Reporting on the AOM 400-TIS in Italy also extends to patients with concomitant substance use disorder (SUD). Investigators examined outcomes following initiation of AOM 400 using a one-injection start or the TIS in 152 patients with or without concomitant SUD[11]. No serious adverse events were reported, aside from one case of akathisia which resulted in treatment discontinuation in a patient without SUD who received the AOM 400-TIS; all other events were mild, transient, and required no intervention[11]. Although all patient groups showed improvements in psychopathology, the overall effect was greater with the AOM 400-TIS versus the one-injection start in those with concomitant SUD[11].

Fewer than 20% of Italian HCPs cited a lack of reimbursement as a reason and/or barrier that might lead them to not use the AOM 400-TIS. There appear to be few administrative obstacles to accessing the AOM 400-TIS in Italy, including those related to pricing or formulary inclusion. At the time the survey was conducted, AOM 400 was reimbursed under the national healthcare system, with the reimbursement conditions for the TIS regimen being essentially the same as for the original LAI formulation. In some regions in Italy, a therapeutic plan signed by a psychiatrist may be required, but this is considered generally straightforward.

While the results presented here are specific to the AOM 400-TIS, they may offer insight into how Italian HCPs perceive a TIS involving Ari 2MRTU 960, the once-every-2-month LAI formulation of aripiprazole monohydrate. Ari 2MRTU 960 was approved in Europe in March 2024 for the maintenance treatment of schizophrenia in adult patients stabilised with aripiprazole[1,18] (either oral aripiprazole or AOM), and can also be initiated using a TIS initiation regimen (i.e., one injection of Ari 2MRTU 960, one injection of AOM 400, and a single 20 mg dose of oral aripiprazole)[1]. Although real-world data on the Ari 2MRTU 960 TIS are currently lacking – reflecting the recency of the drug's approval – it is plausible that the drivers and barriers identified for the AOM 400-TIS may also be relevant for the Ari 2MRTU 960 TIS. That said, between-treatment differences in the dosing interval and related follow-up schedule may shape initiation decisions differently.

General limitations of the survey have been reported previously[9,10]. Of note, participants comprised a convenience sample of HCPs recruited from existing panels who voluntarily participated in the survey, which introduces selection bias[10]; since invitations were not drawn from a national registry of Italian HCPs, the sample does not approximate a random sample of the underlying clinician population. Added to this, approximately one-quarter of Italian participants were recruited via the professional network of the Italian member of the steering committee, which may introduce further selection bias and limit the diversity and generalisability of responses.

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Conclusions

The results of the current survey provide an insight into the views and experiences of more than 100 Italian HCPs who prescribe and/or administer the AOM 400-TIS in adults diagnosed with schizophrenia in real-world practice. Treatment adherence was a primary driver of AOM 400-TIS use, along with relapse prevention, and alignment with patient preferences. Perceived barriers to use of the AOM 400-TIS were patient reluctance to receive two injections at the same time and safety/tolerability concerns. Most HCPs agreed that the AOM 400-TIS was easy to administer, had a safety/tolerability profile similar to the one-injection start, and led to satisfactory patient outcomes.

Prior presentation: results have been published previously in poster format: Beckham C et al. Use and experience of Italian healthcare professionals with aripiprazole once-monthly 400mg two-injection start initiation regimen in adult patients with schizophrenia. Poster presented at: the 33rd European Congress of Psychiatry (EPA); 2025 Apr 5-8; Madrid, Spain [Poster EPV1559].

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Conflicts of interest: Murat Yildirim is an employee of H. Lundbeck A/S, Valby, Denmark. Clodagh Beckham was an employee of Otsuka Pharmaceutical Europe Ltd., Berkshire, United Kingdom, at the time the research was conducted. Sofia Pappa has acted as a consultant, speaker, or has received research grants from Lundbeck, Janssen, Otsuka, Recordati, Rovi, Gedeon Richter, Sunovion, and Teva. Karolina Leopold has participated on advisory boards and/or as a speaker, and/or has received research grants from Boehringer Ingelheim, Lundbeck, Janssen, Otsuka, Recordati, and Rovi. Joe Hickey is an employee of OPEN Health, London, United Kingdom, the contract research organisation that conducted the study. William J. Cottom and Olivia Rogerson were employees of OPEN Health, London, United Kingdom at the time the research was conducted. Andrea Fagiolini is a consultant and/or speaker and/or has received research grants from Angelini, Boehringer Ingelheim, Idorsia, Italfarmaco, Lundbeck, Janssen, Medicamenta, Mylan, Otsuka, Pfizer, Recordati, Rovi, Sunovion, Teva, and Viatris.

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Supplementary material

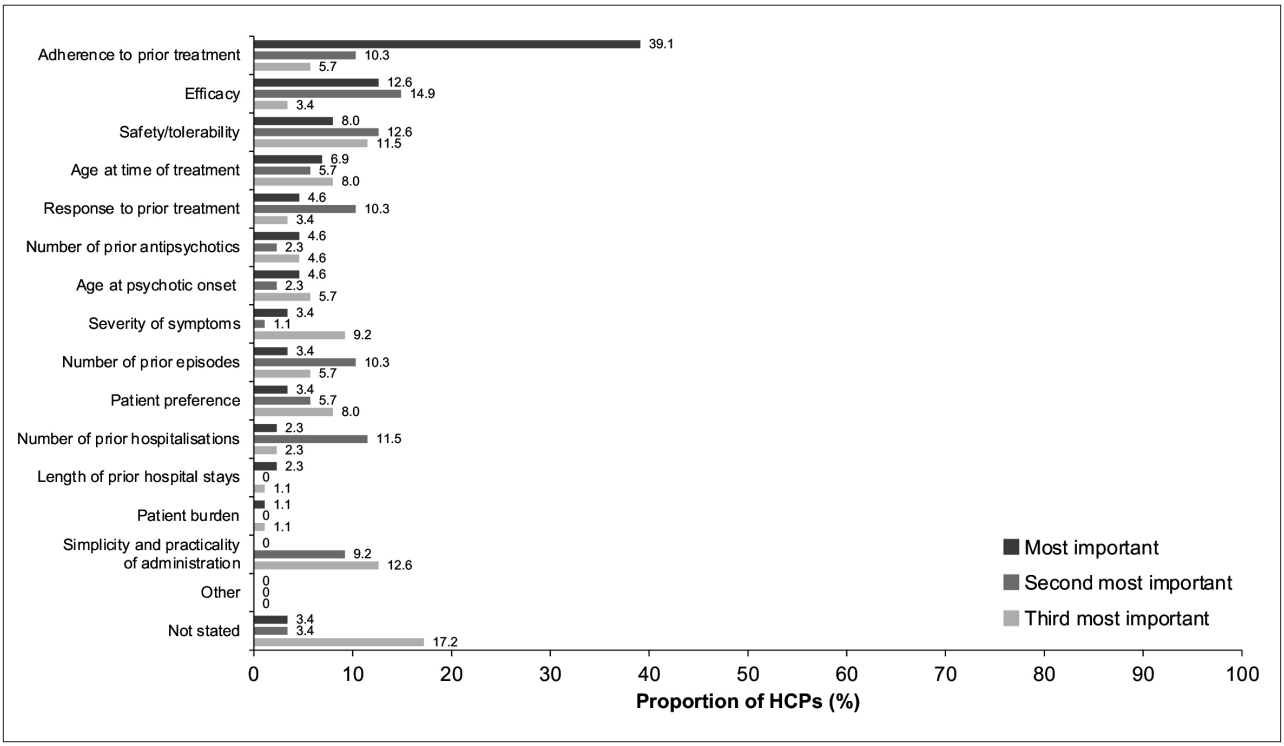

Figure S1. Top three most important patient and clinical factors that influenced Italian HCPs' decision to prescribe the AOM 400-TIS initiation regimen (n=87).

Participants were asked to select the response option that they considered the first, second, and third most important.
Data are ranked from the most to least selected response options in the most important category. The denominator was n=87 (all participants [n=108] minus those that did not prescribe as part of their job role [n=21]).
AOM 400-TIS=aripiprazole once monthly 400 mg two-injection start; HCP=healthcare professional.

Checklist for Reporting of Survey Studies (CROSS)

Section/topic	Item	Item description	Reported on page #
Title and abstract			
Title and abstract	1a	State the word "survey" along with a commonly used term in title or abstract to introduce the study's design.	202 (abstract methods)
	1b	Provide an informative summary in the abstract, covering background, objectives, methods, findings/results, interpretation/discussion, and conclusions.	202
Introduction			
Background	2	Provide a background about the rationale of study, what has been previously done, and why this survey is needed.	202-203
Purpose/aim	3	Identify specific purposes, aims, goals, or objectives of the study.	203
Methods			
Study design	4	Specify the study design in the methods section with a commonly used term (e.g., cross-sectional or longitudinal).	203
	5a	Describe the questionnaire (e.g., number of sections, number of questions, number and names of instruments used).	203

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Segue **Checklist for Reporting of Survey Studies (CROSS)**

Section/topic	Item	Item description	Reported on page #
Data collection methods	5b	Describe all questionnaire instruments that were used in the survey to measure particular concepts. Report target population, reported validity and reliability information, scoring/classification procedure, and reference links (if any).	203-204
	5c	Provide information on pretesting of the questionnaire, if performed (in the article or in an online supplement). Report the method of pretesting, number of times questionnaire was pre-tested, number and demographics of participants used for pretesting, and the level of similarity of demographics between pre-testing participants and sample population.	203
	5d	Questionnaire if possible, should be fully provided (in the article, or as appendices or as an online supplement).	203, also published previously (Fagiolini et al.[10]).
Sample characteristics	6a	Describe the study population (i.e., background, locations, eligibility criteria for participant inclusion in survey, exclusion criteria).	203-204
	6b	Describe the sampling techniques used (e.g., single stage or multistage sampling, simple random sampling, stratified sampling, cluster sampling, convenience sampling). Specify the locations of sample participants whenever clustered sampling was applied.	203-204
	6c	Provide information on sample size, along with details of sample size calculation.	204
	6d	Describe how representative the sample is of the study population (or target population if possible), particularly for population-based surveys.	209
Survey administration	7a	Provide information on modes of questionnaire administration, including the type and number of contacts, the location where the survey was conducted (e.g., outpatient room or by use of online tools, such as SurveyMonkey).	203-204
	7b	Provide information of survey's time frame, such as periods of recruitment, exposure, and follow-up days.	204
	7c	Provide information on the entry process: –> For non-web-based surveys, provide approaches to minimize human error in data entry. –> For web-based surveys, provide approaches to prevent "multiple participation" of participants.	204
Study preparation	8	Describe any preparation process before conducting the survey (e.g., interviewers' training process, advertising the survey).	204
Ethical considerations	9a	Provide information on ethical approval for the survey if obtained, including informed consent, institutional review board [IRB] approval, Helsinki declaration, and good clinical practice [GCP] declaration (as appropriate).	203
	9b	Provide information about survey anonymity and confidentiality and describe what mechanisms were used to protect unauthorized access.	203
Statistical analysis	10a	Describe statistical methods and analytical approach. Report the statistical software that was used for data analysis.	204
	10b	Report any modification of variables used in the analysis, along with reference (if available).	n/a
	10c	Report details about how missing data was handled. Include rate of missing items, missing data mechanism (i.e., missing completely at random [MCAR], missing at random [MAR] or missing not at random [MNAR]) and methods used to deal with missing data (e.g., multiple imputation).	Reported in Fagiolini et al.[10]
	10d	State how non-response error was addressed.	204
	10e	For longitudinal surveys, state how loss to follow-up was addressed.	n/a
	10f	Indicate whether any methods such as weighting of items or propensity scores have been used to adjust for non-representativeness of the sample.	n/a
	10g	Describe any sensitivity analysis conducted.	n/a

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Segue **Checklist for Reporting of Survey Studies (CROSS)**

Section/topic	Item	Item description	Reported on page #
Results			
Respondent characteristics	11a	Report numbers of individuals at each stage of the study. Consider using a flow diagram, if possible.	Reported in Fagiolini et al.[10]
	11b	Provide reasons for non-participation at each stage, if possible.	Not reported
	11c	Report response rate, present the definition of response rate or the formula used to calculate response rate.	n/a
	11d	Provide information to define how unique visitors are determined. Report number of unique visitors along with relevant proportions (e.g., view proportion, participation proportion, completion proportion).	204
Descriptive results	12	Provide characteristics of study participants, as well as information on potential confounders and assessed outcomes.	204
Main findings	13a	Give unadjusted estimates and, if applicable, confounder-adjusted estimates along with 95% confidence intervals and p-values.	n/a
	13b	For multivariable analysis, provide information on the model building process, model fit statistics, and model assumptions (as appropriate).	n/a
	13c	Provide details about any sensitivity analysis performed. If there are considerable amount of missing data, report sensitivity analyses comparing the results of complete cases with that of the imputed dataset (if possible).	n/a
Discussion			
Limitations	14	Discuss the limitations of the study, considering sources of potential biases and imprecisions, such as non-representativeness of sample, study design, important uncontrolled confounders.	209
Interpretations	15	Give a cautious overall interpretation of results, based on potential biases and imprecisions and suggest areas for future research.	210
Generalizability	16	Discuss the external validity of the results.	208-209
Other sections			
Role of funding source	17	State whether any funding organization has had any roles in the survey's design, implementation, and analysis.	210
Conflict of interest	18	Declare any potential conflict of interest.	210
Acknowledgements	19	Provide names of organizations/persons that are acknowledged along with their contribution to the research.	210