Consumers’ questions about antipsychotic medication: revealing safety concerns and the silent voices of young men

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Title: Consumers’ questions about antipsychotic medication: revealing safety concerns and the silent voices of young men

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Abstract

**Purpose:** Little is known about consumer information needs regarding antipsychotic medicines. Medicines call centre (MCC) derived data are underutilised; and could provide insight into issues of importance to consumers. This study aimed to explore consumers’ information needs about antipsychotic medication sought from a national MCC in Australia.

**Methods:** Questions received by the National Prescribing Service (NPS) Medicines Line relating to antipsychotic medication from September 2002 to June 2010 were examined by antipsychotic subclass and in relation to other medication queries.

**Results:** We identified 6,295 calls related to antipsychotic medication. While female callers predominated, the percentage of males with antipsychotic questions was statistically significantly higher than for other medication calls (33.9% vs 22.6%; p<0.001). There were distinct gender differences in medicines information seeking across age ranges. Younger men asked about second-generation antipsychotics, shifting towards first-generation antipsychotics after 45 years of age. Female interest in both subclasses was comparable, irrespective of age. Most callers asking about antipsychotics sought information for themselves (69.4%). Callers were primarily concerned about safety (57.0%), especially adverse drug reactions (28.8%), and were more often prompted by a worrying symptom (23.8%) compared with the rest of calls (17.2%). Trends of antipsychotic questions received corresponded with antipsychotic prescription data.

**Conclusions:** The number of calls received by this MCC over time reveals an ongoing consumer need for additional, targeted information about antipsychotics. Noticeable was the relatively high frequency of young male callers asking about antipsychotics, indicating that call centres could be a way to reach these traditionally poor users of health services.

**Keywords:** antipsychotic agents, information seeking behaviour, consumer health information, medicines call centre, health information seeking, medicines information seeking
Introduction

Mental illness constitutes a large and increasing burden of disease in Australia and worldwide [1]. Psychotic disorders, in particular schizophrenia that requires lifelong treatment, contribute significantly to health burden and costs [2]. Prescribing of antipsychotics has increased markedly in Europe, North America and Australia in recent years [3-5]. It is therefore not surprising that consumers’ need for information about antipsychotics is also growing.

When looking for information about medicines, consumers use a diverse range of information sources such as their doctor, pharmacist, the internet or consumer medication information (CMI) leaflets [6-8]. Another valuable resource is a medicines call centre (MCC) [9-11]. Information provided with prescription medicines is often perceived as inadequate by consumers [12]; and a MCC can be helpful to fill the information gap. Although there is extensive literature covering the area of health information seeking behaviour [13-15]; studies about medicines information seeking are limited. There is, specifically, a lack of studies about consumers’ antipsychotic medication information needs. Data derived from a MCC is an underutilised resource and could provide insight into antipsychotic-related issues of concern to consumers. The aim of this study was to profile antipsychotic medication information seekers and explore their information needs, as presented to a national MCC in Australia.
Methods

Study site

*Medicines Line* is a national MCC, funded by the National Prescribing Service (NPS), to promote quantity use of medicines by providing information that is independent, evidence-based and safe. Consumers could access the service for information about prescription, over-the-counter or complementary medicines for the cost of a local call, Monday to Friday 9am to 6pm, from anywhere in Australia, or leave a voicemail for a return call or to request consumer medicines information leaflets. Callers were also encouraged to discuss the information provided with their doctor or pharmacist. While marketing was primarily via the NPS website, the service was promoted in the media as part of National Medicines Week in 2007 and 2008. Between its launch in September 2002 and 30 June 2010, the service was operated by experienced clinical pharmacists at Mater Health Services, Brisbane.

Information collected during the call was recorded by the pharmacist on a standardised, scannable form, with the call narrative entered into a Microsoft Access™ database, linked by the unique scanform number. Information included demographic data of the caller, the patient and the relationship between caller and patient. Details of questions were collected, such as enquiry type and motivation for calling.

Medicines involved in the call were recorded and categorised into major groups, based on the Anatomical Therapeutical Chemical (ATC) classification of the World Health Organization [16]. Major groups were further divided into minor therapeutic classes, based on the Monthly Index of Medical Specialties (MIMS) Australia classification [17]. MIMS is a source for medicine’s product information, available for Australian healthcare professionals.

Data extraction
Calls in the database were classified as ‘antipsychotic-related calls’, where the question concerned a medication from the minor group ‘antipsychotic agents’. The remainder of calls about medication from all other minor and major groups were classified as ‘rest of calls’.

As the focus of the MCC was service provision, only three demographic variables relating to the caller and/or patient were requested: gender, age and postcode. Age was categorised into nine age groups, based on the Australian Bureau of Statistics National Health Survey [18]. Caller postcodes were grouped by state or territory, relative population frequency and by Accessibility/Remoteness Index of Australia (ARIA), i.e. a measure of remoteness (from service centres) for all places in Australia [19].

The following question characteristics were also extracted from the database:

- Date of call
- Enquiry type: Category of question asked by the caller. Only one of twenty options could be chosen by the pharmacist handling the call (e.g. administration, adverse drug reaction (ADR), interaction, dose, pregnancy). These items were collapsed into four main groups; safety, efficacy, judicious use and other.
- Prompt: Callers were asked what motivated them to contact the service. This response was categorised into one of nine drivers of medicines information seeking behaviour including inadequate information, conflicting information, second opinion and worrying symptom.
- Medicine(s) involved in the query: Although the patient may have been taking multiple medicines, a maximum of three were entered into the database in order of relevance to the question. While in some cases, e.g. interaction questions, all three medicines (including one or more antipsychotics) were equally relevant to the question, the first medicine entered was assigned as the ‘primary’ medicine. Antipsychotic-related calls were grouped into the subclasses of ‘first-generation antipsychotics’ and ‘second-generation antipsychotics’ based on this primary medicine. Lithium, also categorised as an antipsychotic according to the ATC and MIMS-classifications [16,17], was excluded from the group of antipsychotic-related calls as it has a
different and unique mechanism of action. Calls related to lithium have been included in the group ‘rest of calls’.

- Prior information source: Information source(s) the caller had consulted prior to contacting Medicines Line (e.g. doctor, pharmacist, other health professional, support group, media, internet or consumer medicines information (CMI)).

Analyses

The MCC service Access™ database was exported to SPSS® version 21 for statistical analyses. Frequency tables were computed for caller demographics and question characteristics; these were compared by antipsychotic subclass. Data from antipsychotic-related calls were also compared with the rest of calls in the database. A chi-square test was used to compare dichotomous and categorical variables and an independent sample t-test was used to compare continuous variables. A p-value of ≤0.05 was applied to indicate statistical significance.

In addition, for the primary medicine of interest, the temporal relationship between antipsychotic classes of interest to consumers in this cohort relative to the dispensing of antipsychotic prescriptions (actual medicine use) was explored. Comparisons were made between annual calls about antipsychotics (first- and second-generation antipsychotics) and national prescription data from the Australian Statistics on Medicines (ASM) which provides annual dispensed prescription totals for medicines, based on a combination of Pharmaceutical Benefits Scheme (PBS) data and community pharmacy data [20]. Percentages per antipsychotic subclass were calculated using the total number of Medicines Line calls and the sum of all dispensed item types for that class in ASM, for 2002 to 2010 inclusive, as denominators.

Ethical Approval
This study was undertaken as part of a program of research that has received ‘Low and Negligible Risk’ ethical approval from the Human Research Ethics Committee, Mater Health Services Brisbane Limited (HREC Protocol Ref No: LNR submission 2012-68).
Results

A total of 125,919 calls were available for analysis concerning 195,855 medications. Antipsychotic-related calls accounted for 5.0% (n=6,295) of total calls. Of these calls, most (89.1%) involved a question about a single antipsychotic while the remaining 10.9% included two or more antipsychotics. This equates to an average of 1.1 (mode 1; range 1-3) antipsychotic medications per enquiry.

Among the 6,295 calls involving at least one antipsychotic, an antipsychotic was the primary medicine in 4,398 calls. This primary medicine of interest was a second-generation antipsychotic in 81.0% (n=3,564) of these calls, most commonly olanzapine, quetiapine and risperidone. Of the 834 calls (19.0%) where a first-generation antipsychotic was the primary medicine, the focus was on chlorpromazine, haloperidol and pericyazine.

In Figure 1, the calls received by Medicines Line for subgroups of antipsychotics (first- and second-generation) per year is compared to the sum of all prescriptions dispensed for these subgroups in Australia. This comparison shows a similar trend over time between the percentage of calls per antipsychotic subgroup (medicine of interest in this cohort) and the percentage of prescriptions dispensed per antipsychotic subgroup from 2002 to 2010 (national medication use) [20].

Besides antipsychotics, other medications frequently involved in antipsychotic-related questions were sodium valproate (5.6% of antipsychotic calls), diazepam (4.6%) and lithium (4.0%) – all these agents act on the nervous system.

Characteristics of callers

Table 1 lists characteristics of callers to the service. While females were the predominant caller, the percentage of male callers with questions about antipsychotics (33.9%) was significantly higher compared with the 22.6% of males calling for other medication (p<0.001). The mean age of callers for antipsychotic-related queries was 46.0 years (SD 14.6; range 16-98). They were significantly younger (p<0.001) than callers for the ‘rest of calls’ (mean age 50.8 years, SD 17.9; range 5-100).
Approximately 70% of callers for both antipsychotic and other medication information rang on behalf of themselves. The remainder called for a significant ‘other’, mostly a family member. Calls originated from all states and territories in Australia. Postcode classification by relative call frequency and ARIA [21,22] revealed that service uptake was equally distributed across all areas of accessibility and remoteness, with people calling from ‘remote’ areas approaching the relative population frequency.

Age and gender of callers for antipsychotic-related questions (per subgroup) were compared with those of callers for other medication (Figure 2). The mean caller age for first-generation antipsychotics agents was 48.5 years (SD 14.8) compared to 45.4 years (SD 14.5) for second-generation antipsychotics (p<0.001). However, even though the ratio of female to male callers asking about second-generation or first-generation antipsychotics remained fairly consistent (approximately 65%:35%; p=0.934), there were distinct gender differences in medicines information seeking across age ranges. Younger men, 15 to 44 years, displayed a strong interest in second-generation antipsychotics, shifting towards first-generation antipsychotics after 45 years of age.

Female interest in both subclasses was comparable, irrespective of age.

When comparing data from the subgroups of antipsychotics with the rest of calls (Figure 2), several key issues emerged. For the rest of calls, the majority of callers were female for each age group. This is in contrast with antipsychotic-related calls, in particular with calls about second-generation antipsychotics. The main difference was in the 25-34 year age group, where the proportion of males with second-generation antipsychotic queries was 10.9% compared with the 3.2% of males asking about other medication. Female callers requesting antipsychotic information were generally older, most often 45-54 years old.

Reasons for calling

Table 2 lists the motivation for calling the MCC. Across all calls, the major reasons were inadequate information, a worrying symptom or requiring a second opinion. Antipsychotic-related
calls were more often prompted by a worrying symptom (23.8%; n=1,491) than the rest of calls (17.2%; n=20,442) (p<0.001). There was no difference in the information needs of people calling for themselves or for another person.

**Prior information source**

Callers ringing about antipsychotic medication (n=6,295) cited 7,645 information sources used before contacting Medicines Line compared with the remaining 119,624 callers who nominated 143,271 sources. This suggests that consumers frequently use more than one source when seeking medicines information. In both cohorts, health professionals were important ‘prior information sources’, consulted in more than half of calls. The doctor was the main prior information source (40.6% for antipsychotic-related calls (n=2,557) and 33.2% for rest of calls (n=39,681)).

**Narrative of enquiries**

Medication safety was the main caller concern, accounting for almost 60% of calls (n=3,578) about antipsychotics (Table 2). Noticeable from individual enquiry types was the high number of calls received about adverse drug reactions (ADRs), with a frequency of 28.8% (n=1,810) for antipsychotic-related calls versus 18.7% (n=22,280) for rest of calls (p<0.001). The frequencies of other individual enquiry types were reasonably consistent compared to other medicines.

When call narrative was explored for key themes, safety-related questions focused on side-effects, risks in special populations and interactions. Some examples:

- ‘Are any of my medicines (sertraline, haloperidol) causing my drowsiness and bleeding nose?’
- ‘Will I get addicted to Zyprexa (olanzapine)?’
- ‘What should I do to treat the constipation caused by my chlorpromazine and quetiapine?’
- ‘How long will my side effects of pain in the legs and sedation due to paliperidone last?’

Questions about the risks in special populations included ‘Would I be able to breastfeed my new born baby if I have been on olanzapine throughout my pregnancy and will most likely continue on it after..."
baby is born?; while interaction questions often involved another psychiatric medication, complementary or lifestyle drug e.g. ‘Can my son take Aurorix (moclobemide) if he is on Zyprexa (olanzapine)?’ or ‘Do my complementary medicines interact with olanzapine?’ Safety concerns about antipsychotics were followed by a desire for information on medication effectiveness. For instance: ‘How quickly will Neulactil (pericyazine) start to work?’, or ‘Would ziprasidone be a better drug than olanzapine with regards to weight gain and diabetes?’
Discussion

Our study profiled antipsychotic medication information seekers and identified an apparent unmet need for information about antipsychotic medicines, particularly in young males.

Characteristics of (antipsychotic) medication information seekers

The profile of callers asking about medicines in general and antipsychotics in particular is predominantly female, seeking information for themselves or a significant other. This is consistent with the literature suggesting that women tend to seek health information more often than men [13,14,23], and for either themselves or a ‘family’ member [24]. It also aligns with data from other MCCs [25,26]. However, our study found a relatively high proportion of (young) males calling Medicines Line for information about antipsychotics. The literature is less clear in relation to caller age. Some studies about health seeking behaviour suggest that younger individuals are more likely to health seek [14,27,28] while others note a positive relationship with increasing age [13,29]. In our study, while callers seeking information on antipsychotics were spread across a wide age range supporting both paradigms, they were, on average, a younger cohort. This could be explained by the age of onset of psychosis, which is often in early adulthood [30]. This is also when affected individuals are having their first experiences of taking antipsychotic medications, potentially triggering information seeking behaviour.

Studies suggest that young males are less likely to help seek [13,29] or access health services [29], in particular for mental health disorders [29,31,32]. However, it is unlikely that they have fewer questions than, for instance, young women. Perhaps they are not getting the answers they need through conventional channels? It is possible that young men feel more comfortable contacting a call centre instead of directly facing a healthcare professional. This is in line with mental health patients’ preference for anonymous sources for health and medicines information [33-35]. Consultation via a telephone service could therefore be a way for them to voice questions about
their health and for health services to reach this group of consumers. Further research is needed to confirm and explore this finding.

**MCCs as a source for (antipsychotic) medication information**

In a country as vast as Australia, there are challenges of providing equitable access to quality health services in rural and remote areas. A medicines information service with direct phone access to a pharmacist has the potential to overcome the tyranny of distance and meet the needs of rural as well as urban consumers, independent of location. However, this does not always equate to actual service utilisation. In this study, calls relating to antipsychotics not only originated from all Australian states and territories, but also importantly, people calling from ‘remote’ areas approached the relative population frequency. This supports that the MCC service model had utility for mental health consumers in rural and remote areas where there is likely to be less access to mental health services.

Although the two variables in Figure 1 use different denominators, over an eight year period, there was a close parallel between the percentage of calls about antipsychotic subgroups (medicine of interest in this cohort) and the percentage of antipsychotic prescriptions dispensed annually (national medicine use). This longitudinal perspective, together with the quantum of calls received over time, reveals the ongoing need consumers have for quality information about (all subgroups of) antipsychotic medication. This need was also recognized in other MCC studies [25,26].

**Link between uncertainty and motivation to seek medicines information**

Uncertainty, related to an information gap or a symptom of concern, has been shown to drive health seeking behaviours such as seeking medicines information [13,14,36,37]. Inadequate information was the main reason for contacting this MCC, in both antipsychotic-related and the remainder of calls. Consumers receiving inadequate information tend to be dissatisfied with the
information available to them and want to know more, supporting the existence of a knowledge gap for almost half of those seeking information on antipsychotics [38-40].

The second main motivation for calling the MCC with antipsychotic medication questions was a ‘worrying symptom’. The higher number of questions prompted by a worrying symptom in relation to antipsychotics compared with ‘rest of calls’ is supported by the frequent occurrence of adverse effects with antipsychotics [41]. In almost half of total antipsychotic-related calls, the prior information source previously consulted was not a health care professional but, for instance, the internet. It is of concern that this cohort had not sought help from their health carers about this worrying symptom prior to contacting the service. The call, however, provided an opportunity for a MCC pharmacist to decrease caller uncertainty about their medication-related issue, and appropriately triage callers requiring review by their doctor. Another important prompt in both types of calls was ‘second opinion’. Studies that assessed the motivation of people to seek health information on the internet also highlighted ‘second opinion’ as a prompt for health seeking behaviour - the hope to find something ‘new’ [42,43]. Since there is limited literature available about motivation for health seeking behaviour, these findings could provide a foundation for further research.

**Narrative of medicine information seeking**

Safety was the main concern of callers with those asking for information about antipsychotics more frequently wanting information about adverse drug reactions than callers for other medication. Safety as a goal of medicines information seeking is in agreement with literature about medicines information needs of consumers [8,44] and with findings from other MCCs [9,26,45]. Medicines information provided by healthcare professionals or accompanying medication, such as the Consumer Medicines Information (CMI) leaflet, should therefore focus more on safety issues, in particular strategies to minimise or monitor risk. Antipsychotics are medications with a high side-effect burden [41], which can be worrying and trigger health seeking behaviour. Qualitative studies
involving mental health patients revealed a knowledge gap among patients, especially about adverse drug reactions from antipsychotics [38-40]. Patients experiencing these tend to be less compliant with their therapy [46,47]. It is, therefore, important that such questions from consumers are answered before their concerns escalate and they cease their therapy. Further research should be aimed at assessing the specific information needs of consumers about adverse effects of antipsychotics and their preferences for receiving this information.

Limitations

The Medicines Line service model was developed as a cost-effective strategy to meet the medicines information needs of Australian consumers; it was not created as a data repository for research. As a result, there are missing data, especially in relation to the voicemail requests for CMI leaflets. The percentage of missing data is however not more than 5% for every characteristic and is reasonably comparable for both antipsychotic-related calls and rest of calls.

An addition, callers to a MCC are only part of the total group of medicine users. We do not know if the non-health information seeking consumer wants more or different information about their medicines. However, our study includes a significant proportion of questions from young males (often direct users of the antipsychotic medicines), who are known to be infrequent users of health services.

Conclusion

The number of calls received by this MCC reveals an ongoing need for additional information on antipsychotics from consumers. Noticeable was the relatively high frequency of young males contacting the MCC for safety information about antipsychotic medication, a cohort known to be poor users of health services. Acknowledging their preference for telephone consultation can help reach this group. Overall, MCCs are a valuable and underutilised repository for research on consumer medicines information seeking behaviour.
Acknowledgements

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Conflict of Interest

The sponsors had no role in study design; in the collection, analysis and interpretation of data; in the writing of the report; and in the decision to submit the paper for publication. On behalf of all authors, the corresponding author states that there is no conflict of interest.


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Fig. 1 Comparison of the distribution of subgroups of antipsychotics (first-generation and second-generation) per year for calls received by Medicines Line and the sum of all prescriptions dispensed for these subgroups in Australia. Percentages of calls were calculated using the total number of calls per year where an antipsychotic was the primary drug. For prescription data, percentages were calculated using the annual total of defined daily dose (DDD) per 1000 population per day per the Australian Statistics on Medicines [20]. AP = antipsychotic
Fig. 2 Caller gender and age range compared for calls about first-generation antipsychotics, second-generation antipsychotics and rest of calls.

\* Missing data for gender and/or age is omitted from these total number of calls: \(n=34\) (4.1% of 834) in first-generation antipsychotic-related calls, \(n=104\) (2.9% of 3,564) in second-generation antipsychotic-related calls and \(n=2,163\) (1.8% of 119,624) for rest of calls.
# Tables

## Table 1 Comparison of caller characteristics of antipsychotic-related and rest of calls

<table>
<thead>
<tr>
<th></th>
<th>Antipsychotic-related calls</th>
<th>Rest of calls</th>
<th>Statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>%</td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Gender (%)</td>
<td></td>
<td></td>
<td></td>
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<tr>
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<tr>
<td>Male</td>
<td>33.9</td>
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<tr>
<td>Total (missing omitted)</td>
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<td>100.0</td>
</tr>
<tr>
<td>Missing$^a$</td>
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<td>0.1</td>
</tr>
<tr>
<td>Age (years)</td>
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<tr>
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<tr>
<td>5-14</td>
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<tr>
<td>15-24</td>
<td>4.2</td>
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<td>25-34</td>
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<td>55-64</td>
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<td>65-74</td>
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<td>≥75</td>
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<td>Total (missing omitted)$^a$</td>
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<tr>
<td>Mean age (SD)</td>
<td>46.0 (14.6)</td>
<td>50.8 (17.9)</td>
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<td>Relationship (% self)</td>
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<td>4,365/6,286</td>
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<tr>
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<td>df=1 p&lt;0.001</td>
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<tr>
<td>Missing$^b$</td>
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<td>9</td>
<td>0.3</td>
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</tbody>
</table>

$^a$ Percentages are total of data available per variable. These may not add exactly to 100.0 due to rounding.

$^b$ Number and percentage of missing data per variable for total antipsychotic-related and rest of calls. Total missing data in rest of calls for gender and/or age = 2163 with data about both gender and age missing for 141 callers.
Table 2 Comparison of the motivation for contacting the MCC and the enquiry type, classified by relationship of the caller to the patient

<table>
<thead>
<tr>
<th></th>
<th>Antipsychotic-related calls</th>
<th>Rest of calls</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Self</td>
<td>Other</td>
<td>Self</td>
</tr>
<tr>
<td></td>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>%</td>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>Prompt</td>
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<td>Inadequate information</td>
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<tr>
<td></td>
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<td>Worrying symptom</td>
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<td></td>
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<td>Other</td>
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<td>Forgot information</td>
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a Percentages are total of data available per variable. These may not add exactly to 100.0 due to rounding.

b Number and percentage of calls where the relationship of the caller to the patient (self/other) and/or the prompt/enquiry type of the call is missing.

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