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Consumer concerns about paracetamol: a retrospective analysis of a medicines call centre

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ABSTRACT

Objectives To identify consumer information needs about paracetamol, the most commonly used analgesic and antipyretic worldwide.

Design Retrospective analysis of medicines questions from the public.

Setting Australian consumer medicines call centre.

Participants Callers to National Prescribing Service *Medicines Line* between September 2002 and June 2010 (n=123 217).

Main outcome measures: Enquiry profile: demographics, enquiry type and concurrent medicines included in paracetamol calls; question themes derived from subset of call narratives.

Results Paracetamol comprised part of the enquiry in 5.2% of calls (n=6367). The caller age distribution for paracetamol calls was skewed towards a younger cohort, with 45.2% made by the 25-44 age group versus 37.5% in rest of calls. Significantly more paracetamol-related calls were made for a child (23.7%) compared to rest of calls (12.7%, p<0.001). The most frequent concurrently asked about medicines were codeine (11%, n=1521) and ibuprofen (6.4%, n=884).

While the most frequent paracetamol enquiry type was efficacy; interaction, administration and pregnancy/lactation related calls were more frequent for paracetamol versus rest of calls (21.5% vs. 14.8%, 15.5% vs. 11%, 13.75% vs. 8.3%, all p < 0.001). The frequency of enquiry types also varied by patient age group, with questions about administration more common in younger groups and about efficacy dominating in those over 45. Narrative analysis of over-represented paracetamol enquiry types showed specific concerns relevant to life stages: young children, those of reproductive age and the elderly. However, across age groups, callers overestimated paracetamol risk and sought strategies to reduce perceived risks.

Conclusions Consumers have many concerns about the use of paracetamol that are under-recognised by healthcare providers, with the nature of enquiries differing across life stages. These concerns are not adequately addressed by available consumer information. Improving access to targeted information about paracetamol would promote the safe and effective use of this common medicine.

Article Summary

Strengths and Limitations

- Our database of over one hundred thousand calls made over eight consecutive years by the Australian help-seeking public represents an untapped resource for identifying consumer medicines information gaps and concerns.
- The large sample size of paracetamol calls enabled unique questions for various patient life stages to be identified.
- Collected data permitted both quantitative and narrative analysis, giving detailed insight into consumer concerns, particularly in the areas of interactions and administration of paracetamol.
- Limitations include sampling bias; people who contact medicines call centres may have different information needs from the wider population.

INTRODUCTION

Paracetamol is the most commonly used analgesic and antipyretic worldwide and is widely available over-the-counter (OTC) in the United Kingdom (UK) and Australia.[1, 2] Although its mechanism of action is poorly understood, paracetamol remains popular due to tolerability and safety when taken at recommended doses. However, in overdose, whether by a large single dose or repeated supra-therapeutic dosing,[3] irreversible hepatotoxicity represents a global source of morbidity.[4-7] The serious health ramifications of the potential and proven misuse of paracetamol demonstrates opportunity for improvement in the provision of consumer-oriented resources and justifies research into consumer information needs.

Despite its widespread use, consumer information needs about paracetamol have not been well characterised in the literature. This is highlighted by a recent BMJ editorial stating that "important questions remain unanswered".[2] While the editorial sought to address three broad questions about this common medicine, paracetamol is used by distinct populations spanning across life stages. Young children,[8] pregnant women[9] and the elderly[10] have varying information-seeking priorities. For instance, as paracetamol is commonly administered to infants, queries from parents may differ in nature from the general population.[11] Furthermore, paracetamol is available in various combination formulations such as codeine for acute pain, with proven analgesic synergism.[12] The diverse side effect profiles and indications for combination products may result in unidentified differences in consumers' information needs.

Consumers may seek information about medicines from a variety of sources,[6] including medical practitioners, pharmacists, the Internet, medicines labelling and information leaflets. For paracetamol, written information plays a significant role due to its OTC availability. Health and medicines call centres are also used as a resource in Australia[12] and internationally.[14-16] Studies of queries handled by such helplines represent a largely untapped repository for researching consumer medicines information gaps or concerns. This study aims to characterise consumer information needs about paracetamol through analysis of medicines call centre data. This may serve to guide the practice of health professionals when prescribing or providing information about this frequently used medicine, to promote its safe and effective use.

METHODS

Data collection

We used data from the National Prescribing Service (NPS) MedicineWise (formerly NPS *Medicines Line*), operated by clinical pharmacists of Mater Health Services, Brisbane, between September 2002 and June 2010. This call centre was available to consumers Australia-wide for medicine-related questions. As data from our observational study was originally routinely collected as part of a health service without specific *a priori* research goals; research was conducted and reported in accordance with REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) guideline[17], an extension of the STROBE guidelines.[18]

Details of each call were captured on a standardised form and entered into a Microsoft Access® database. These included demographics, enquiry type, relationship of caller to patient and motivation for calling. For each call, up to three generic medicines relating to the question were recorded and categorised by the Anatomical Therapeutic Classification (ATC) of medicines.[19] Caller location was identified by postal code and grouped by state/territory and Accessibility Remoteness Index of Australia (ARIA), a measure of the remoteness of areas from service centres.[20] Relative population ratio was determined by dividing percentage of paracetamol calls from each ARIA category by percentage of population living in each ARIA category. Narrative for calls between January 2009 and June 2010 were also recorded electronically. Calls involving paracetamol in the question were extracted for analysis. Remaining calls were classified as 'rest of calls'. We excluded calls that only involved a voicemail request for consumer medicines information (CMI) leaflets.

Quantitative analysis

We conducted a retrospective quantitative analysis on all paracetamol-related calls. Comparisons between paracetamol and rest of calls were performed using a t-test for continuous data and a chi-square test for categorical data. Each call was originally coded for one of 25 enquiry types; these were collapsed into seven categories. Enquiry types were compared by patient age groups and other life stages e.g. during pregnancy or breastfeeding. Concurrent medicines included in paracetamol calls were also compared by age groups and a special population, pregnant women. A two-sided p-value <0.05 was considered significant. The data was exported to SPSS Statistics version 21 for analysis.[21]

Narrative analysis

Three highly ranked enquiry types where paracetamol calls were overrepresented compared to rest of calls ('interaction', 'administration and 'pregnancy/lactation') were selected for narrative analysis. Common themes were identified independently by two investigators, with subsequent discussion to resolve discrepancies. Interactions were further explored based on whether the call was: 1) directed towards a specific indication (pain, cough and cold, etc.); 2) sourcing information on potential interactions for their medicines list including paracetamol; or 3) incidental, where paracetamol was not part of the enquiry.

RESULTS

A total of 123 217 calls were available for analysis. Of these, 5.2% (n=6367) had paracetamol recorded as a medicine directly relating to the question. Whether paracetamol statistics were compared with rest of calls longitudinally (annually) or collectively for the eight year period, enquiry demographics were remarkably consistent. Calls originated from all Australian states and territories, with metropolitan, rural and remote dwellers all well represented (relative population ratio living in each ARIA category ranged between 0.6 and 1.09). The majority of paracetamol calls were from females (80.5%), which was not significantly greater than for the rest of calls (76.5%, p=0.05). There was a bimodal distribution for caller age, with peaks at 30 and 70 years. Contrastingly, patient age distribution was trimodal, with an additional peak at <1 year. Compared to rest of calls, the distribution of caller age for paracetamol calls was skewed towards a younger cohort, with 45.2% made by the 25-44 age group versus 37.5% in rest of calls. Paracetamol calls were significantly more often for patients aged 14 and under (22.1%) versus rest of calls (10.3%, p<0.001). Correspondingly, significantly more paracetamol-related calls were made for a child (23.7%) compared to rest of calls (12.7%, p<0.001). Within calls made about paracetamol, callers for children were much more likely to be female (92.1%) than calls made for themselves or others (76.8%, p<0.001). Over 90% of paracetamol calls were prompted by one of three reasons: inadequate information (47.9%), second opinion (27.2%) or a worrying symptom (15%). Compared to rest of calls, more calls were made for a second opinion (27.2% vs. 23.3%, p<0.001).

The most frequent concurrently asked about medicines (ATC5) in paracetamol calls were codeine (11%, n=1521) and ibuprofen (6.4%, n=884), with the remainder of concurrent medicines each comprising <2% of paracetamol calls (in rank order: tramadol, dextropropoxyphene, oxycodone, pseudoephedrine, meloxicam, diclofenac, celecoxib, aspirin). Of the top ten medicines, nine are indicated for analgesia, with pseudoephedrine (a decongestant) the only exception. Codeine and

ibuprofen were ranked first or second across all life stages except in those 65 year or older, where tramadol ranked second (Table 1).

Table 1. Top five ATC5 medicines included in paracetamol calls by age group

<1 year	1-4 years	5-24 years	25-44 years	45-64 years	65+ years	Pregnancy/lactation
Codeine Ibuprofen Pseudoephedrine Oxymetazoline Chlorpheniramine	Ibuprofen Codeine Amoxicillin Brompheniramine Chlorpheniramine	Codeine Ibuprofen Promethazine Pseudoephedrine Dextropropoxyphene	Codeine Ibuprofen Pseudoephedrine Doxylamine Tramadol	Codeine Ibuprofen Oxycodone Meloxicam Dextropropoxyphene	Codeine Tramadol Celecoxib Meloxicam Glucosamine	Codeine Ibuprofen Pseudoephedrine Doxylamine Oxymetazoline

Most commonly, therapeutic classes (ATC3) included in paracetamol calls were non-steroidal anti-inflammatory and anti-rheumatic medicines (12.8%, n=1778), followed by cough suppressants (11.4%, n=1578). These were in the top three ATC3 classes across all patient age groups. The third ranked class in the younger age groups (<1, 1-4, 5-24 years) was antihistamines, with opioids filling the third position in older age groups.

The most frequent paracetamol enquiry type was efficacy, followed by interaction, other safety concerns, and administration. In particular, interaction, administration and pregnancy/lactation related calls were much more frequent for paracetamol versus rest of calls (Table 2).

Table 2. Frequencies of enquiry types for paracetamol and rest of calls and enquiry types by age groups for paracetamol calls

Paracetamol calls versus rest of calls						
Enquiry type	**Paracetamol calls (%)** n=6367		**Rest of calls (%)** n=116850			***p*-value**
Efficacy	24.9		22.8			< 0.001
Interaction	21.5		14.8			< 0.001
Other safety	20.6		32.6			< 0.001
Administration	15.5		11.0			< 0.001
Pregnancy/Lactation	13.7		8.3			< 0.001
Logistics	3.3		5.8			< 0.001
Miscellaneous	0.5		4.4			< 0.001
Missing	0		0.3			
Paracetamol calls by age groups (years) (n=6367)						
Enquiry type	**<1 (%)**	**1-4 (%)**	**5-24 (%)**	**25-44 (%)**	**45-64 (%)**	**65+ (%)**
Efficacy	15.8	24.1	19.6	17.7	31.9	31.3
Interaction	10.5	28.2	29.3	22.2	21.7	20.0
Other safety	9.3	9.5	15.3	17.2	27.4	27.7
Administration	17.5	29.4	24.6	9.0	13.8	14.7
Pregnancy/Lactation	45.3	7.9	8.3	31.6	0.2	0.4
Logistics	1.5	0.7	2.9	1.7	4.3	5.4
Miscellaneous	0.2	0.2	0	0.6	0.6	0.5

The frequency of enquiry types also varied when compared by age groups. Administration enquiries were more common in younger groups, comprising approximately one-quarter of calls for patients under 24 years old (Table 2). Conversely, efficacy predominated in older age groups, at nearly one-third of enquiries in those over 45. Logistics questions were more common in this group, comprising 4.3 to 5.4% of enquiries in the over 45s versus 1.1 to 2.9% in younger groups. Calls about safety also increased in incidence with age. Enquiries about pregnancy and lactation were frequent in age groups 0-4 and 25-44, likely representing infant and mother patient groups.

There were some differences in the call profile for questions involving paracetamol alone versus those involving a concurrently enquired about analgesic (codeine or ibuprofen). Female callers predominated for questions about efficacy, interactions or safety. For paracetamol and ibuprofen calls, the caller was commonly of reproductive age (25-44 years) and asking on behalf of a child in 39.0% of calls, which was significantly greater than for paracetamol calls alone (21.3%, $p<0.001$). In contrast, paracetamol alone versus paracetamol and codeine questions were more evenly distributed across caller age range and were less frequently made on behalf of a child (22.9% and 17.3%, respectively).

Narrative analysis

The enquiry types 'interaction', 'administration' and 'pregnancy/lactation' were selected for narrative analysis, with 65%, 58.7% and 57.5% of calls in these categories respectively available for exploration of themes. A summary of narrative themes is given in Appendix 1.

Interaction calls

Fifteen themes were identified from the 895 interaction calls. These could broadly be grouped as relating to a therapeutic strategy or safety concern, with safety more common. Across all age groups, the most common themes focused on risk minimisation strategies: asking about the safety of prospectively administering paracetamol with another medicine (*Can I take Panadol® with Mobic®?*) or whether paracetamol could be used shortly after taking another medicine (*Can I take paracetamol if I had tramadol 50mg six hours ago?)*. While there was no specific theme identified for patients <1 year, callers for the 1-4 year group were concerned about combining medicines prior to administration (*Can I combine Dimetapp® Elixir and Panadol® to give to my two year old?)*. Calls for patients aged 5-24 concerned potential interactions with lifestyle products, such as alcohol or supplements (*Can I drink alcohol after taking Phenergan® and Panadol®?)*. For groups aged 25-44, 45-64 and 65+, a common theme was the appropriate choice of medicine for a particular purpose,

based on current medication (*What analgesics are safe to take with Zoloft® and Xanax®?)*. Lastly, both the 25-44 and 65+ groups asked about the potential for a worrying symptom being caused by a medicine interaction (*Could paracetamol and esomeprazole have caused stomach cramps*?).

When interaction calls were further categorised, enquiries directed towards a specific indication comprised the majority in the <1 and 1-4 age groups (59.0-64.6%). For all other age groups, calls sourcing information on potential interactions for a medicines list, including paracetamol, dominated.

Administration calls

For the 990 administration enquiries, 22 themes were identified. They could be broadly grouped as enquiries relating to dose, therapeutic strategy, medicine contents and safety concerns. Of these, dose-related questions were the most common. More specifically, the appropriate quantity (*What dose can I give of Panadol® for my son?*) or requesting a safety check of a proposed dose (*Is it okay to take 4-6 tablets of paracetamol per day?)* were common themes across all age groups.

Two age specific themes in the <1 year group were related to therapeutic strategy, specifically where callers sought to achieve the best therapeutic outcome. Firstly, callers sought to verify the appropriateness of administration in a specific setting, usually for a specified age (*Can I give Children's Panadol® to my 10 month old baby?)* or indication (*Can I give Children's Panadol® 500mg tablets for fever to my three year old?*). Management of re-dosing paracetamol after vomiting or diarrhoea was also common (*Can I give my child another dose of Panadol® if she immediately vomited it up after I administered it?)*. These two themes were replicated in the 1-4 age group. In addition, callers for those aged 1-4 asked about paracetamol administration with food or drink (*Can Painstop® be given with juice?*) and the action to take or outcomes after an unintentional overdose (*My one year old has swallowed at least 1/2 a paracetamol tablet - will she be okay?*).

Two age specific themes were identified for 5-24 year olds, with dose questions predominating. These included dose calculation (*Should you dose paracetamol by weight or age in children?*), verifying dose timing (*Is it okay to give my five year old 9.5mls of Panadol® syrup every four hours for a fever?*) and repeating a dose (*Can I repeat the dose of Panadol® from my child's fever after the last dose 5 hours ago?*). As for the 0-4 age group, outcome after an unintentional overdose was also a common theme (*Have I given too much Painstop® to my ten year old child?)*.

In the 25-44 age group, use of multiple paracetamol-containing medicines was a focus (*Can I take Mersyndol® one hour after taking 1000mg of Panamax®?)*. In contrast, callers aged 45-64 were interested in alternative analgesic options (*Is it okay to take Panadeine Forte® instead of Endone®?*) and medicine constituents, whether excipient or active (*Can you tell me the gluten content for Panamax®, Tramal® and Mobic®?).*

Several age specific themes were identified in the 65+ group. Medicine constituent questions predominated, with callers commonly asking for a direct comparison between medicines (*What is the difference between Panadol® and Panadol® Osteo?)*. Enquiries about the maximum permissible dose were prevalent (*What is the maximum dose of paracetamol that I can take for osteoarthritis pain?*). The concomitant use of a second paracetamol medicine was another common theme, as with the 25-44 age group. The final theme related to safety, where callers had a specific health concern about paracetamol (*Will taking four paracetamol a day harm my liver?)*.

Pregnancy / Lactation calls

There were broadly two types of questions related to paracetamol in pregnancy or breast feeding. Callers, usually the patient themselves, were either seeking reassurance of safety after exposure to paracetamol (*Will it matter if I've taken Di-Gesic® while breastfeeding?)* or trying to minimise risk prior to medicine exposure. Risk aversion questions included safety of use at a particular gestation or while breastfeeding (*Can I take paracetamol if I am* [a specified number of weeks] *pregnant/breast feeding?)* or seeking to quantifying medication risk (*What are the effects of paracetamol on my baby when breastfeeding?*).

DISCUSSION

We found that consumers have many unanswered questions about paracetamol. The nature of their concerns varied with the profiles of the caller and patient. Previous research has investigated patient, carer and/or health professional knowledge and attitudes about the use (dosing and unintentional risks) of paracetamol.[22-24] These studies identified paracetamol knowledge gaps in many consumers, as well as health care providers having varied knowledge of appropriate use. While "greater education of health care workers is required in order to provide families with appropriate information"[24] was recommended, little research has addressed health professional responses to the information gaps consumers have about paracetamol. Our data show that consumers tend to overestimate paracetamol risk. Conversely, health care providers underestimate consumer concerns about medication risk [25-27] and do not adequately acknowledge these concerns.[26, 28, 29] This

mismatch was also highlighted in the recent BMJ editorial[2] that addressed only three broad questions as important to paracetamol consumers (efficacy, adverse effects and dose).

The primary prompt for paracetamol calls was inadequate information, which highlights the lack of information provided with OTC medicines. In the UK, general sales list medicines[30] are freely available in supermarkets, thus come without advice from health professionals. Mandatory information supplied with OTC medicines varies between countries. Pharmaceutical companies in the UK must supply approved Patient Information Leaflets with all medicines unless all necessary information specified by the Medicines and Healthcare products Regulatory Agency (including indications, contraindications, general dosing instructions and side effects) is included on the label.[31] The electronic Medicines Compendium,[32] targeted at health professionals, provides additional Summaries of Product Characteristics. The equivalent Australian documents are Consumer Medicines Information (CMI) leaflets and Product Information, neither of which is mandatory for OTC medicines. Aside from Panamax®,[33] there are no accessible CMI for common paracetamol-only formulations. Importantly none of these resources provided strategies to prevent or reduce risk from predictable, real world occurrences such as re-dosing after vomiting. Addressing consumer concerns requires accessible, targeted and comprehensible information for OTC medicines; improving these aspects for paracetamol should be a focus of future research.

While written information is available to varying standards in the UK and Australia, medical professionals remain the most trusted information source.[34] Consumers are, however, unlikely to consult their GP about OTC medicine use.[35] Pharmacists may therefore play a pivotal role in providing information as the first and potentially only face-to-face contact.[36] Australian research has shown that the majority of OTC medicines for children are still sourced from pharmacies rather than supermarkets,[34] with many considering pharmacists medicines experts and preferring spoken over written information.[37] Consideration could also be given to changing the OTC status to pharmacist-only or prescription status, as has been called for in research and the media.[38, 39]

Medicines most commonly enquired about in combination with paracetamol were analgesics, especially codeine and ibuprofen, despite concomitant use in adults being safe and effective for additive analgesia at recommended doses.[40, 41] The differing caller and question profile for concurrent analgesia involving paracetamol is important for clinicians to know. Health professionals should also be aware that parents are concerned about interactions between the various medicines, including paracetamol, antihistamines, and ibuprofen. While both UK and Australian written

medicines information contain limited details about medicines with potential for interactions;[26, 28] consideration to include a similar list of safe medications would provide reassurance where there is common concurrent use.

This study has several strengths. A large number of calls made to *Medicines Line* were available over eight consecutive years. Paracetamol call distribution approached relative population frequency. The data also permitted both quantitative and narrative analysis, giving detailed insight into consumer concerns. Age groups were well represented in the enquiry type subsets for both interaction and administration so can be considered a representative sample for thematic analysis by age. Limitations include sampling bias; people who contact medicines call centres may have different information needs from the wider population. The calls are also from an Australian population and may not accurately reflect concerns held by consumers in other countries.

Consumers have many concerns about the use of paracetamol that are likely to be under-recognised by healthcare providers, with different patient age groups having unique questions that should be considered when targeting paracetamol information towards patients. Therapeutic strategies to minimise paracetamol risk are not adequately addressed by available information. Improving information may be challenging due to the OTC status of paracetamol and the diversity of commercial brands. Strategies such as increasing pharmacist involvement with paracetamol supply may be useful, but may necessitate a change in its availability in other places such as supermarkets. Ultimately, the accessibility of information that the public wants to know needs to be targeted to optimise the safe and effective use of paracetamol.

FOOTNOTES

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Contributors: TMM and MLVD provided supervision, conceived and designed the study. SL conducted the literature review and data analysis. SL, TMM and MLVD interpreted the data, drafted and critically revised the manuscript. SL, TMM and MLVD as guarantors accept full responsibility for the work and/or the conduct of the study, had access to the data, and controlled the decision to publish.

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Ethical approval: This study was approved by Mater Health Services Brisbane, Human Research Ethics Committee (LNR submission 2012-68) and University of Queensland School of Medicine Low Risk Ethical Review Committee (2014-SOMILRE-0098).

Transparency: The authors (SL, MLVD, TMM) affirm that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

Data sharing statement: No additional data are available.

REFERENCES

1 Sood S, Howell J, Sundararajan V, et al. Paracetamol overdose in Victoria remains a significant health-care burden. *J Gastroenterol Hepatol* 2013;28:1356-60.
2 Dear JW, Antoine DJ, Park BK. Where are we now with paracetamol? *BMJ* 2015;351:3705.
3 Daly FFS, O'Malley GF, Heard K, et al. Prospective evaluation of repeated supratherapeutic acetaminophen (paracetamol) ingestion. *Ann Emerg Med* 2004;44:393-8.

4 McGill M, Jaeschke H. Metabolism and Disposition of Acetaminophen: Recent Advances in Relation to Hepatotoxicity and Diagnosis. *Pharm Res* 2013;30:2174-87.
5 Office for National Statistics. Deaths related to drug poisoning in England and Wales, 2014 registrations [Internet]. Newport: Office for National Statistics; 2015 [cited 2015 Oct 31]. Available from: http://www.ons.gov.uk/ons/dcp171778_414574.pdf.
6 Australian Institute of Health and Welfare. Drugs in Australia 2010: tobacco, alcohol and other drugs [Internet]. Canberra: Australian Institute of Health and Welfare; 2011 [cited 2015 Sep 15]. Available from: http://www.aihw.gov.au/WorkArea/DownloadAsset.aspx?id=10737420455.
7 Australian Bureau of Statistics. Deaths collection: Drug Related Deaths by Type of Drug (Total Drug Related Deaths) [Internet]. Canberra: Commonwealth of Australia; 2007 [cited 2015 Oct 31]. Available from: http://www.drugfree.org.au/fileadmin/Media/Reference/DFA_DrugRelatedStats.pdf.
8 Holappa M, Ahonen R, Vainio K, et al. Information sources used by parents to learn about medications they are giving their children. *Res Social Adm Pharm* 2012;8:579-84.
9 Hameen-Anttila K, Nordeng H, Kokki E, et al. Multiple information sources and consequences of conflicting information about medicine use during pregnancy: a multinational Internet-based survey. *J Med Internet Res* 2014;16:60.
10 Grymonpre RE, Steele JW. The medication information line for the elderly: an 8-year cumulative analysis. *Ann Pharmacother* 1998;32:743-8.
11 Khoo K, Bolt P, Babl FE, et al. Health information seeking by parents in the Internet age. *J Paediatr Child Health* 2008;44:419-23.
12 Gatti A, Sabato E, Di Paolo AR, et al. Oxycodone/paracetamol: a low-dose synergic combination useful in different types of pain. *Clin Drug Investig* 2010;30 Suppl 2:3-14.
13 National Prescribing Service Limited. Medicines Line [Internet]. Sydney: National Prescribing Service; 2012 [cited 2015 Jul 28]. Available from: http://www.nps.org.au/contact-us/medicines-line.
14 Pohjanoksa-Mäntylä MK, Antila J, Eerikäinen S, et al. Utilization of a community pharmacy-operated national drug information call center in Finland. *Res Soc Adm Pharm* 2008;4:144-52.
15 Marvin V, Park C, Vaughan L, et al. Phone calls to a hospital medicines information helpline: analysis of queries from members of the public and assessment of potential for harm from their medicines. *Int J Pharm Pract* 2011;19:115-22.
16 Government of Ontario. Telehealth Ontario [Internet]. Ontario: Government of Ontario; 2015 [cited 2015 Jul 28]. Available from: https://www.ontario.ca/page/get-medical-advice-telehealth-ontario.
17 Benchimol EI, Smeeth L, Guttmann A, et al. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement. *PLoS Med* 2015;12:e1001885.
18 von Elm E, Altman DG, Egger M, et al. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *BMJ* 2007;335:806-8.
19 WHO Collaborating Centre for Drug Statistics Methodology. Guidelines for ATC classification and DDD assignment, 2015 [Internet]. Oslo: Norwegian Institute of Public Health; 2014 [cited 2015 Oct 31]. Available from: http://www.whocc.no/filearchive/publications/2015_guidelines.pdf.
20 Australian Bureau of Statistics. Families in regional, rural and remote Australia 2006 Census Data [Internet]. Canberra: Australian Government; 2010 [cited 2015 Nov 3]. Available from: http://www.abs.gov.au/AUSSTATS/abs@.nsf/Lookup/1379.0.55.001Explanatory%20Notes12002-2006?OpenDocument
21 IBM Corp. SPSS Statistics for Windows, 23 ed. New York: IBM Corp; 2015.

22 Wolf MS, King J, Jacobson K, et al. Risk of unintentional overdose with non-prescription acetaminophen products. *J Gen Intern Med* 2012;27:1587-93.
23 Herndon CM, Dankenbring DM. Patient perception and knowledge of acetaminophen in a large family medicine service. *J Pain Palliat Care Pharmacother* 2014;28:109-16.
24 Karwowska A, Nijssen-Jordan C, Johnson D, et al. Parental and health care provider understanding of childhood fever: a Canadian perspective. *CJEM* 2002;4:394-400.
25 DeWitt JE, Sorofman BA. A model for understanding patient attribution of adverse drug reaction symptoms. *Drug Inf J* 1999; 33: 907–20.
26 Britten N. Medication errors: the role of the patient. *Br J Clin Pharmacol* 2009;67:646-50.
27 Knapp P, Gardner PH, Carrigan N, et al. Perceived risk of medicine side effects in users of a patient information website: A study of the use of verbal descriptors, percentages and natural frequencies. *Br J Health Psychol* 2009 14: 579-94.
28 Berry DC, Michas IC, Gillie T, et al. What do patients want to know about their medicines and what do doctors want to tell them? A comparative study. *Psychol Health* 1997;12:467-80.
29 Hoffmann TC, Del Mar C. Patients' expectations of the benefits and harms of treatments, screening, and tests: a systematic review. *JAMA Intern Med* 2015;175:274-86.
30 National Health Service Choices. Medicines Information [Internet]. London: National Health Service; 2014 [cited 2015 Oct 31] Available from: http://www.nhs.uk/conditions/Medicinesinfo/Pages/Introduction.aspx.
31 Medical and Healthcare Products Regulatory Agency. Best practice guidance on the labelling and packaging of medicines [Internet]. London: Government of the United Kingdom; 2014 [cited 31 Oct 2015] Available from: https://www.gov.uk/government/publications/best-practice-in-the-labelling-and-packaging-of-medicines.
32 Electronic Medicines Compendium. About the eMC [Internet]. Leatherhead (UK): Datapharm; 2015 [cited 2015 Oct 31]. Available from: http://www.medicines.org.uk/emc/about-the-emc.
33 Sanofi. Panamax: Consumer Medicines Information [Internet]. Sydney: Sanofi; 2014 [cited 2015 Sep 8]. Available from: http://www.sanofi.com.au/products/aus_cmi_panamax.pdf
34 Hesse B, Nelson DE, Kreps GL, et al. Trust and sources of health information: The impact of the internet and its implications for health care providers: findings from the first health information national trends survey. *Arch Intern Med* 2005;165:2618-24.
35 Sleath B, Rubin RH, Campbell W, et al. Physician-patient communication about over-the-counter medications. *Soc Sci Med* 2001;53:357-69.
36 Simoens S, Lobeau M, Verbeke K, et al. Patient experiences of over-the-counter medicine purchases in Flemish community pharmacies. *Pharm World Sci* 2009;31:450-7.
37 Hamrosi K, Raynor D, Aslani P. Enhancing provision of written medicine information in Australia: pharmacist, general practitioner and consumer perceptions of the barriers and facilitators. *BMC Health Serv Res* 2014;14:183.
38 Jozwiak-Bebenista M, Nowak JZ. Paracetamol: mechanism of action, applications and safety concern. *Acta Pol Pharm* 2014;71:11-23.
39 Collins N. Paracetamol 'should be prescription-only' [Internet]. London: The Telegraph; 2012 [cited 2014 Jul 14]; Available from: http://www.telegraph.co.uk/news/uknews/9134065/Paracetamol-should-be-prescription-only.html.
40 Merry AF, Gibbs RD, Edwards J, et al. Combined acetaminophen and ibuprofen for pain relief after oral surgery in adults: a randomized controlled trial. *Br J Anaesth* 2010;104:80-8.
41 Barkin RL. Acetaminophen, Aspirin, or Ibuprofen in Combination Analgesic Products. *Am J Ther* 2001;8:433-42.

APPENDIX 1

Themes from interaction and administration calls (by age group) and pregnancy calls

Age group	<1 year	1-4 years	5-24 years	25-44 years	45-64 years	65+ years
Interaction narrative (n=895 calls)						
Enquiry subgroup (% of calls for age group)						
Directed	59.0	64.6	44.0	39.5	32.4	34.8
Interaction	38.5	33.3	48.8	53.4	59.5	55.8
Incidental	2.6	2.1	7.2	7.1	8.1	9.4
Common theme across ages	Safety of medicines to be administered Safety of using a second medicine after recent administration of the first					
Specific themes	None	Safety of combining medicines prior to administration	Interactions between paracetamol and lifestyle products	Attributing a worrying symptom to a medication interaction Appropriate medicine choice, based on current medication	Appropriate medicine choice, based on current medication	Appropriate medicine choice, based on current medication Attributing a worrying symptom to a medication interaction
Administration narrative (n=990 calls)						
Common theme across ages	Appropriate dose (quantity or safety check)					
Specific themes	Appropriate-ness of paracetamol administration Management of re-dosing	Appropriate-ness of paracetamol administration Management of re-dosing Outcome after unintentional overdose Administration with food/drink	Dosing questions (timing, calculations, repeat dose) Outcome after unintentional overdose	Safety of concomitant use of a different paracetamol medicine	Medicine constituents (excipient & active) Alternative analgesic options	Maximum recommended dose Comparison between two medicines Medicine constituents (excipient & active) Safety of concomitant use of a different paracetamol medicine Specific safety concern
Pregnancy/Lactation narrative (n=501 calls)						
Common themes	Is it safe to take paracetamol in pregnancy/breastfeeding? Quantifying the risk or clarifying a safe dose of paracetamol to take in pregnancy/breastfeeding					

The RECORD statement – checklist of items, extended from the STROBE statement, that should be reported in observational studies using routinely collected health data.

	Item No.	STROBE items	Location in manuscript where items are reported	RECORD items	Location in manuscript where items are reported	COMMENTS
Title and abstract						
	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found	Title p.1 & Abstract p.2	RECORD 1.1: The type of data used should be specified in the title or abstract. When possible, the name of the databases used should be included. RECORD 1.2: If applicable, the geographic region and timeframe within which the study took place should be reported in the title or abstract. RECORD 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract.	Title & Abstract Abstract – Setting & participants Not applicable – our dataset was not linked -	Observational study: retrospective analysis of calls to an Australian medicines call centre i.e. National Prescribing Service (NPS) Medicines Line between September 2002 and June 2010
Introduction						
Background rationale	2	Explain the scientific background and rationale for the investigation being reported	Introduction p.4 – *Paragraphs 1 & 2*			
Objectives	3	State specific objectives, including any pre-specified hypotheses	Introduction p.4 – *Paragraph 3*			
Methods						
Study Design	4	Present key elements of study design early in the paper	Methods pp.5-6 – Quantitative Analysis & Narrative Analysis subsections			
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Methods p.5 – Data Collection subsection			
Participants	6	*(a) Cohort study* - Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	Methods p.5 – Data Collection subsection, with eligibility criteria, and the sources and methods of selection of participants provided	RECORD 6.1: The methods of study population selection (such as codes or algorithms used to identify subjects) should be listed in detail. If this is not possible, an explanation should be	Methods – Data Collection subsection, with eligibility criteria, and the sources and methods of selection of participants provided	Study population consisted of all callers to NPS *Medicines Line* between September 2002 and June

		Case-control study - Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study* - Give the eligibility criteria, and the sources and methods of selection of participants *(b) Cohort study* - For matched studies, give matching criteria and number of exposed and unexposed *Case-control study* - For matched studies, give matching criteria and the number of controls per case		provided. RECORD 6.2: Any validation studies of the codes or algorithms used to select the population should be referenced. If validation was conducted for this study and not published elsewhere, detailed methods and results should be provided. RECORD 6.3: If the study involved linkage of databases, consider use of a flow diagram or other graphical display to demonstrate the data linkage process, including the number of individuals with linked data at each stage.	N/A N/A	2010. As data was collected as part of a health-related service at a single time point, our study is neither case-control, cohort or cross-sectional. However, of these options, cross-sectional would be the closest study type.
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.	Data from this observational study were routinely collected as part of a health service without specific *a priori* research goals	RECORD 7.1: A complete list of codes and algorithms used to classify exposures, outcomes, confounders, and effect modifiers should be provided. If these cannot be reported, an explanation should be provided.	N/A	
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Methods p.5 – Data Collection			All data obtained from NPS Medicines Line
Bias	9	Describe any efforts to address potential sources of bias	To validate consistency of population characteristics over time, longitudinal analysis of demographics (gender, age, geographical location by ARIA, enquiry type, medicines in question & motivation to call was conducted Bias in analysis managed through double analysis of narrative			
Study size	10	Explain how the study size	Methods p.5: Study population			

		was arrived at	consisted of all callers to NPS Medicines Line between September 2002 and June 2010			
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	Methods p.5 – Data Collection (Paragraph 2) & Quantitative Analysis – groupings chosen based on topic of interest (e.g. therapeutic class or drug, caller or patient cohort e.g. by age)			
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) *Cohort study* - If applicable, explain how loss to follow-up was addressed *Case-control study* - If applicable, explain how matching of cases and controls was addressed *Cross-sectional study* - If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses	a) Methods p.5 – Quantitative Analysis b) Methods p.5 – Quantitative Analysis for sub-groups c) Calls with missing data were included in totals and any data exclusions (e.g. voicemail requests for CMI only) were made explicit. d) N/A e) N/A			
Data access and cleaning methods		..		RECORD 12.1: Authors should describe the extent to which the investigators had access to the database population used to create the study population.	Study approved by Mater Health Services Brisbane, Human Research Ethics Committee (LNR submission 2012-68) & University of Queensland School of Medicine Low Risk Ethical Review Committee (2014-SOMILRE-0098). Data access by authors is clearly defined in the HREC application .Mater Pharmacy Services (Dr T McGuire) is joint data	

				RECORD 12.2: Authors should provide information on the data cleaning methods used in the study.	custodian with NPS MedicinesWise Extensive data cleaning undertaken in conversion of data from Access to SPSS e.g. codes to identify voicemail CMI requests were excluded as they did not involve a medicines question.	
Linkage		..		RECORD 12.3: State whether the study included person-level, institutional-level, or other data linkage across two or more databases. The methods of linkage and methods of linkage quality evaluation should be provided.	N/A	
Results						
Participants	13	(a) Report the numbers of individuals at each stage of the study (*e.g.*, numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed) (b) Give reasons for non-participation at each stage. (c) Consider use of a flow diagram	a) Results p.6 – *Paragraph 1 &* The number of participants for each aspect of demographics was reported, often as a quantitative table including missing data. b) N/A *c) -*	RECORD 13.1: Describe in detail the selection of the persons included in the study (i.e., study population selection) including filtering based on data quality, data availability and linkage. The selection of included persons can be described in the text and/or by means of the study flow diagram.	Results – Paragraph 1 The number of participants for each aspect of demographics was reported, often as a quantitative table including missing data. *Flow chart provided as an Appendix*	
Descriptive data	14	(a) Give characteristics of study participants (*e.g.*, demographic, clinical, social) and information on exposures and potential confounders (b) Indicate the number of participants with missing data for each variable of interest (c) *Cohort study* - summarise follow-up time (*e.g.*, average and total amount)	a) Results p.6 – Paragraph 1 b) pp.6-7 The number of participants for each aspect of demographics reported (as a quantitative table including missing data or with missing data noted as a footnote). c) N/A			
Outcome data	15	*Cohort study* - Report numbers of outcome events or summary measures over time	As data was collected at a single time point we did not measure outcome events			

		Case-control study - Report numbers in each exposure category, or summary measures of exposure *Cross-sectional study* - Report numbers of outcome events or summary measures				
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	a) Results section pp.6-8 Confounder-adjusted estimates not applicable b) N/A - no continuous variables c) N/A			
Other analyses	17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	Methods pp.5-6– Quantitative Analysis & Narrative Analysis Results section pp.6-10			
Discussion						
Key results	18	Summarise key results with reference to study objectives	Discussion p.11-12– *Paragraphs 1, 2, 4*		Discussion – *Paragraphs 1, 2, 4*	
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Discussion p.13 – *Paragraph 5:* Population derived by calls to a MCC. We do not know if people who do not contact a MCC have similar medicines information gaps and concerns.	RECORD 19.1: Discuss the implications of using data that were not created or collected to answer the specific research question(s). Include discussion of misclassification bias, unmeasured confounding, missing data, and changing eligibility over time, as they pertain to the study being reported.	Discussion – *Paragraph 5*	
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant	Discussion p.13– *Paragraph 6*			

		evidence				
Generalisability	21	Discuss the generalisability (external validity) of the study results	Discuss (strengths & weaknesses paragraph) p.13– *"Because of the large number of calls made, the duration over which data collection ran, and the geographical distribution of calls, these results may be generalised to the Australian public. As UK and Australian usage and availability of paracetamol are similar, we believe our findings are also applicable to the UK".*			
Other Information						
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	p.13 Funding statement			
Accessibility of protocol, raw data, and programming code				RECORD 22.1: Authors should provide information on how to access any supplemental information such as the study protocol, raw data, or programming code.	Raw data is held at MPS Mater Pharmacy Services (Dr T McGuire) is joint data custodian with NPS. Data access by authors is limited and clearly defined in the HREC application.	

[1] Reference: Benchimol EI, Smeeth L, Guttmann A, Harron K, Moher D, Petersen I, Sørensen HT, von Elm E, Langan SM, the RECORD Working Committee. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement. *PLoS Medicine* 2015; in press.

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Consumer concerns about paracetamol: a retrospective analysis of a medicines call centre

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Consumer concerns about paracetamol: a retrospective analysis of a medicines call centre

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ABSTRACT

Objectives To identify consumer information needs about paracetamol, the most commonly used analgesic and antipyretic worldwide.

Design Retrospective analysis of medicines questions from the public.

Setting Australian consumer medicines call centre.

Participants Callers to National Prescribing Service *Medicines Line* between September 2002 and June 2010 (n=123 217).

Main outcome measures: Enquiry profile: demographics, enquiry type and concurrent medicines included in paracetamol calls; question themes derived from subset of call narratives.

Results Paracetamol comprised part of the enquiry in 5.2% of calls (n=6367). The caller age distribution for paracetamol calls was skewed towards a younger cohort, with 45.2% made by those aged 25-44 versus 37.5% in rest of calls. Significantly more paracetamol-related calls were made for a child (23.7%) compared to rest of calls (12.7%, p<0.001). The most frequent concurrently asked about medicines were codeine (11%, n=1521) and ibuprofen (6.4%, n=884).

Questions underpinned by paracetamol risk (interaction, use in pregnancy/lactation or other safety concerns) predominated (55.8%). When individual paracetamol enquiry types were compared with rest of calls, efficacy was most frequent (24.9% vs. 22.8%); however, interaction (21.5% vs. 14.8%), administration (15.5% vs. 11%) and pregnancy/lactation (13.8% vs. 8.3%) categories were more prevalent for paracetamol calls (all p < 0.001). Enquiry type frequency also varied by patient age group, with questions about administration more common in younger groups and efficacy dominating in those over 45. Narrative analysis of over-represented paracetamol enquiry types showed specific concerns relevant to life stages: young children, those of reproductive age and the elderly.

Conclusions Consumers have many concerns about the use of paracetamol that may be under-recognised by healthcare providers, with the nature of enquiries differing across life stages. These concerns are not adequately addressed by available consumer information. Improving access to targeted information about paracetamol would promote the safe and effective use of this common medicine.

Article Summary

Strengths and Limitations

- Our database of over one hundred thousand calls made over eight consecutive years by the Australian help-seeking public represents an untapped resource for identifying consumer medicines information gaps and concerns.
- The large sample size of paracetamol calls enabled unique questions for various patient life stages to be identified.
- Collected data permitted both quantitative and narrative analysis, giving detailed insight into consumer concerns, particularly in the areas of interaction and administration of paracetamol.
- Limitations include sampling bias; people who contact medicines call centres may have different information needs from the wider population.

INTRODUCTION

Paracetamol is the most commonly used analgesic and antipyretic worldwide and is widely available over-the-counter (OTC) in the United Kingdom (UK) and Australia.[1, 2] Although its mechanism of action is poorly understood, paracetamol remains popular due to tolerability and safety when taken at recommended doses. However, in overdose – whether by a large single dose or repeated supra-therapeutic dosing –[3] irreversible hepatotoxicity represents a global source of morbidity.[4-7] The serious health ramifications of the potential and proven misuse of paracetamol demonstrates opportunity for improvement in the provision of consumer-oriented resources and justifies research into consumer information needs.

Despite its widespread use, consumer information needs about paracetamol have not been well characterised in the literature. This is highlighted by a recent BMJ editorial stating that "important questions remain unanswered".[2] While the editorial sought to address three generalised questions about this common medicine, paracetamol is used by distinct populations spanning across life stages, who have varying information-seeking priorities. These include young children,[8] pregnant women[9] and the elderly.[10] For instance, as paracetamol is commonly administered to infants, queries from parents may differ in nature from the general population.[11] Additionally, paracetamol is available in various combination formulations such as codeine for acute pain, with proven analgesic synergism.[12] The diverse side effect profiles and indications for combination products may result in unidentified differences in consumers' information needs.

Consumers may seek information about medicines from a variety of sources,[6] including medical practitioners, pharmacists, the Internet, medicines labelling and information leaflets. For paracetamol, written information plays a significant role due to its OTC availability. Health and medicines call centres are also used as a resource in Australia[13] and internationally.[14-16] Studies of queries handled by such helplines represent a largely untapped repository for researching consumer medicines information gaps or concerns. This study aimed to characterise consumer information needs about paracetamol through analysis of medicines call centre data. This may serve to guide the practice of health professionals when prescribing or providing information about this frequently used medicine, to promote its safe and effective use.

METHODS

Data collection

We used data from the National Prescribing Service (NPS) MedicineWise (formerly NPS *Medicines Line*), operated by clinical pharmacists of Mater Health Services, Brisbane, between September 2002 and June 2010. This call centre was available to consumers Australia-wide for medicine-related questions. As data from our observational study was originally routinely collected as part of a health service without specific *a priori* research goals; research was conducted and reported in accordance with REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) guideline[17], an extension of the STROBE guidelines.[18]

Details of each call were captured on a standardised form and entered into a Microsoft Access® database. These included demographics, enquiry type, relationship of caller to patient and motivation for calling. For each call, up to three generic medicines relating to the question were recorded and categorised by the Anatomical Therapeutic Chemical (ATC) classification system of medicines.[19] Of the five ATC levels, we examined medicine classes at ATC3 level, which labels medicines according to their pharmacological subgroup (e.g. antihistamines-systemic), as well as ATC5 level, which identifies the chemical substance (e.g. chlorpheniramine). Caller location was identified by postal code and grouped by state/territory and Accessibility Remoteness Index of Australia (ARIA), a measure of the remoteness of areas from service centres.[20] Relative population ratio was determined by dividing percentage of paracetamol calls from each ARIA category by percentage of population living in each ARIA category. Narrative for calls between January 2009 and June 2010 were also recorded electronically. Calls involving paracetamol in the question were extracted for analysis. Remaining calls were classified as 'rest of calls'. We excluded calls that only involved a voicemail request for Consumer Medicines Information (CMI) leaflets.

Quantitative analysis

We conducted a retrospective quantitative analysis on all paracetamol-related calls. Comparisons between paracetamol and rest of calls were performed using a chi-square test for categorical data. Each call was originally coded for one of 25 enquiry types. These were collapsed into seven question categories: 'efficacy' (indications for use, medicine comparisons, effectiveness for specific conditions or symptoms); 'interaction'; 'other safety' (side-effects or cautions for use), 'administration' (dose, administration, formulation or storage issues); safety in 'pregnancy and/or lactation'; 'logistics' (availability or cost) and 'miscellaneous'. Enquiry types were compared by patient age groups and

other life stages e.g. during pregnancy or breastfeeding. Concurrent medicines included in paracetamol calls were also compared by age groups and a special population, pregnant women. A two-sided p-value <0.05 was considered significant. The data was exported to SPSS Statistics version 21 for analysis.[21]

Narrative analysis

Three highly ranked enquiry types where paracetamol calls were overrepresented compared to rest of calls ('interaction', 'administration and 'pregnancy/lactation') were selected for narrative analysis. Two investigators (SL and TMM) independently coded the content of questions within each dataset and created categories, grouped under higher order headings or themes. Coding differences were resolved through discussion until consensus was reached. Themes for interaction and administration calls were compared by age group. Interactions were further explored based on whether the call was: 1) directed towards a specific indication (pain, cough and cold, etc.); 2) sourcing information on potential interactions for their medicines list including paracetamol; or 3) incidental, where paracetamol was not part of the enquiry.

RESULTS

A total of 123 217 calls were available for analysis. Of these, 5.2% (n=6367) had paracetamol recorded as a medicine directly relating to the question. Whether paracetamol statistics were compared with rest of calls longitudinally (annually) or collectively for the eight-year period, enquiry demographics were remarkably consistent. Calls originated from all Australian states and territories, with metropolitan, rural and remote dwellers all well represented (relative population ratio living in each ARIA category ranged between 0.6 and 1.09). The majority of paracetamol calls were from females (80.5%), which was not significantly greater than for the rest of calls (76.5%, p=0.05). There was a bimodal distribution for caller age, with peaks at 30 and 70 years. Contrastingly, patient age distribution was trimodal, with an additional peak at <1 year. Compared to rest of calls, the distribution of caller age for paracetamol calls was skewed towards a younger cohort, with 45.2% made by the 25-44 age group versus 37.5% in rest of calls. Paracetamol calls were significantly more often for patients aged 14 and under (22.1%) versus rest of calls (10.3%, p<0.001). Correspondingly, significantly more paracetamol-related calls were made for a child (23.7%) compared to rest of calls (12.7%, p<0.001). Within calls made about paracetamol, callers for children were much more likely to be female (92.1%) than calls made for themselves or others (76.8%, p<0.001). Over 90% of paracetamol calls were prompted by one of three reasons: inadequate information (47.9%), second

opinion (27.2%) or a worrying symptom (15%). Compared to rest of calls, more calls were made for a second opinion (27.2% vs. 23.3%, p<0.001).

The most frequent concurrently asked about medicines (ATC5) in paracetamol calls were codeine (11%, n=1521) and ibuprofen (6.4%, n=884), with the remainder of concurrent medicines each comprising <2% of paracetamol calls (in rank order: tramadol, dextropropoxyphene, oxycodone, pseudoephedrine, meloxicam, diclofenac, celecoxib, aspirin). Of the top ten medicines, nine are indicated for analgesia, with pseudoephedrine (a decongestant) the only exception. Codeine and ibuprofen were ranked first or second across all life stages except in those 65 year or older, where tramadol ranked second (Table 1).

Table 1. Top five ATC5 medicines included in paracetamol calls by age group

<1 year	1-4 years	5-24 years	25-44 years	45-64 years	65+ years	Pregnancy/lactation
Codeine Ibuprofen Pseudoephedrine Oxymetazoline Chlorpheniramine	Ibuprofen Codeine Amoxicillin Brompheniramine Chlorpheniramine	Codeine Ibuprofen Promethazine Pseudoephedrine Dextropropoxyphene	Codeine Ibuprofen Pseudoephedrine Doxylamine Tramadol	Codeine Ibuprofen Oxycodone Meloxicam Dextropropoxyphene	Codeine Tramadol Celecoxib Meloxicam Glucosamine	Codeine Ibuprofen Pseudoephedrine Doxylamine Oxymetazoline

The most common pharmacological classes (ATC3) included in paracetamol calls were non-steroidal anti-inflammatory and anti-rheumatic medicines (12.8%, n=1778), followed by cough suppressants (11.4%, n=1578) (Table 2). These were in the top three ATC3 classes across all patient age groups. The third ranked class in the younger age groups (<1, 1-4, 5-24 years) was antihistamines, with opioids ranking in the top three for older groups.

Table 2. Top three ATC3 levels included in paracetamol calls by age group

<1 year	1-4 years	5-24 years	25-44 years	45-64 years	65+ years
Cough suppressants Non-steroidal anti-inflammatory and anti-rheumatics Antihistamines - systemic	Non-steroidal anti-inflammatory and anti-rheumatics Cough suppressants Antihistamines - systemic	Cough suppressants Non-steroidal anti-inflammatory and anti-rheumatics Antihistamines - systemic	Cough suppressants Non-steroidal anti-inflammatory and anti-rheumatics Opioids	Non-steroidal anti-inflammatory and anti-rheumatics Cough suppressants Opioids	Non-steroidal anti-inflammatory and anti-rheumatics Opioids Cough suppressants

Overall, enquiry types underpinned by paracetamol risk predominated (interaction, use in pregnancy and/or lactation or other safety concerns), constituting 55.8% of calls (Table 3). When individual paracetamol enquiry types were compared with rest of calls, although efficacy was most frequent (24.9% vs. 22.8%); interaction (21.5% vs. 14.8%), administration (15.5% vs. 11%) and pregnancy/lactation (13.8% vs. 8.3%) calls occurred significantly more frequently for paracetamol calls (all $p < 0.001$).

Table 3. Frequencies of enquiry types for paracetamol and rest of calls and enquiry types by age groups for paracetamol calls

Paracetamol calls versus rest of calls						
Enquiry type	**Paracetamol calls (%)** n=6367		**Rest of calls (%)** n=116850			***p*-value**[1]
Efficacy	24.9		22.8			< 0.001
Interaction[2]	21.5		14.8			< 0.001
Other safety[2]	20.6		32.6			< 0.001
Administration	15.5		11.0			< 0.001
Pregnancy/Lactation[2]	13.7		8.3			< 0.001
Logistics	3.3		5.8			< 0.001
Miscellaneous	0.5		4.4			< 0.001
Missing	0		0.3			
Paracetamol calls by age groups (years) (n=6367)						
Enquiry type	**<1 (%)**	**1-4 (%)**	**5-24 (%)**	**25-44 (%)**	**45-64 (%)**	**65+ (%)**
Efficacy	15.8	24.1	19.6	17.7	31.9	31.3
Interaction	10.5	28.2	29.3	22.2	21.7	20.0
Other safety	9.3	9.5	15.3	17.2	27.4	27.7
Administration	17.5	29.4	24.6	9.0	13.8	14.7
Pregnancy/Lactation	45.3	7.9	8.3	31.6	0.2	0.4
Logistics	1.5	0.7	2.9	1.7	4.3	5.4
Miscellaneous	0.2	0.2	0	0.6	0.6	0.5

[1] *All statistical comparisons between paracetamol-related calls and rest of calls used chi-square analyses*
[2] *Enquiry types related to safety*

The frequency of enquiry types also varied when compared by age groups. Administration enquiries were more common in younger groups, comprising approximately one-quarter of calls for patients under 24 years old (Table 3). Conversely, efficacy predominated in older age groups, at nearly one-third of enquiries in those over 45. Logistics questions were more common in this group, comprising 4.3 to 5.4% of enquiries in the over 45s versus 1.1 to 2.9% in younger groups. Calls about safety also increased in incidence with age. Enquiries about pregnancy and lactation were frequent in age groups 0-4 and 25-44, likely representing infant and mother patient groups.

There were some differences in the call profile for questions involving paracetamol alone versus those involving a concurrently enquired about analgesic (codeine or ibuprofen). Female callers

predominated for questions about efficacy, interactions or safety. For paracetamol and ibuprofen calls, the caller was commonly of reproductive age (25-44 years) and asking on behalf of a child in 39.0% of calls, which was significantly greater than for paracetamol calls without ibuprofen (21.3%, p<0.001). In contrast, paracetamol and codeine questions were more evenly distributed across caller age range and were less frequently made on behalf of a child (17.3% versus 22.9% for paracetamol calls without codeine).

Narrative analysis

The enquiry types 'interaction', 'administration' and 'pregnancy/lactation' were selected for narrative analysis, with 65%, 58.7% and 57.5% of calls respectively available for exploration of themes. A summary of narrative themes and question examples by life stage is provided in Appendix.

Interaction calls

Fifteen themes were identified from 895 interaction calls. The major theme was safety (85.1%, n=762), with a small percentage addressing therapeutic strategy (6.1%, n=55). The remainder did not primarily address paracetamol interactions. Across all age groups, the most common objective was minimising medication risk, asking about the safety of prospectively administering paracetamol with another medicine (*Can I take Panadol® with Mobic®?*). This comprised 73.6% of all interaction enquiries (n=659). Another question common to all age groups was whether paracetamol could be used shortly after taking another medicine (*Can I take paracetamol if I had tramadol 50mg six hours ago?)* (6.9%, n=62). While there was no specific theme identified for patients <1 year, callers for the 1-4 year group were concerned about combining medicines prior to administration (*Can I combine Dimetapp® Elixir and Panadol® to give to my two year old?)*. Calls for patients aged 5-24 concerned potential interactions with lifestyle products, such as alcohol or supplements (*Can I drink alcohol after taking Phenergan® and Panadol®?)*. For groups aged 25-44, 45-64 and 65+, a common theme was the appropriate choice of medicine for a particular purpose, based on current medication (*What analgesics are safe to take with Zoloft® and Xanax®?)*. Lastly, both the 25-44 and 65+ groups asked about the potential for a worrying symptom being caused by a medicine interaction (*Could paracetamol and esomeprazole have caused stomach cramps*?).

When interaction calls were further categorised, enquiries directed towards a specific indication comprised the majority in the <1 and 1-4 age groups (59.0-64.6%). For all other age groups, calls sourcing information on potential interactions for a medicines list, including paracetamol, dominated.

Administration calls

For the 582 administration enquiries, 22 themes were identified. They could be broadly grouped as enquiries relating to dose (37.6%, n=219), therapeutic strategy (21.2%, n=124), medicine constituents (10.1%, n=59) and safety concerns (9.6%, n=56), with the remainder not targeting paracetamol as the primary medicine or addressing issues such as pharmacokinetics. Common dose related questions asked across all age groups were the appropriate amount or volume (45.7% of dose questions, n=100) (*What dose can I give of Panadol® for my son?*) and a safety check of a proposed dose (14.2%, n=31) (*Is it okay to take 4-6 tablets of paracetamol per day?).*

Two age specific themes in the <1 year group were related to therapeutic strategy, specifically where callers sought to achieve the best therapeutic outcome. Firstly, callers sought to verify the appropriateness of administration in a specific setting, usually for a specified age (*Can I give Children's Panadol® to my 10 month old baby?)* or indication (*Can I give Children's Panadol® 500mg tablets for fever to my three year old?*). Secondly, management of re-dosing paracetamol after vomiting or diarrhoea was a common concern (*Can I give my child another dose of Panadol® if she immediately vomited it up after I administered it?)*. These two themes were replicated in the 1-4 age group. In addition, callers for those aged 1-4 asked about paracetamol administration with food or drink (*Can Painstop® be given with juice?*) and the action to take or outcomes after an unintentional overdose (*My one year old has swallowed at least 1/2 a paracetamol tablet - will she be okay?*).

Age specific themes identified for 5-24 year olds were largely dose-related. These included dose calculation (*Should you dose paracetamol by weight or age in children?*), verifying dose timing (*Is it okay to give my five year old 9.5mls of Panadol® syrup every four hours for a fever?*) and repeating a dose (*Can I repeat the dose of Panadol® from my child's fever after the last dose 5 hours ago?*). As for the 0-4 age group, outcome after an unintentional overdose was also a common theme (*Have I given too much Painstop® to my ten year old child?)*.

In the 25-44 age group, use of multiple paracetamol-containing medicines was a focus (*Can I take Mersyndol® one hour after taking 1000mg of Panamax®?)*. In contrast, callers aged 45-64 were interested in alternative analgesic options (*Is it okay to take Panadeine Forte® instead of Endone®?*) and medicine constituents, whether excipient or active (*Can you tell me the gluten content for Panamax®, Tramal® and Mobic®?).*

Several age specific themes were identified in the 65+ group. Medicine constituent questions predominated, with callers commonly asking for a direct comparison between medicines (*What is the difference between Panadol® and Panadol® Osteo?)*. Enquiries about the maximum permissible dose were prevalent (*What is the maximum dose of paracetamol that I can take for osteoarthritis pain?*). The concomitant use of a second paracetamol medicine was another common theme, as with the 25-44 age group. The final theme related to safety, where callers had a specific health concern about paracetamol (*Will taking four paracetamol a day harm my liver?)*.

Pregnancy / lactation calls

There were broadly two types of questions related to paracetamol in pregnancy or breast feeding. Callers, usually the patient themselves, were either seeking reassurance of safety after exposure to paracetamol (*Will it matter if I've taken Di-Gesic® while breastfeeding?)* or trying to minimise risk prior to medicine exposure. Risk aversion questions included safety of use at a particular gestation or while breastfeeding (*Can I take paracetamol if I am* [a specified number of weeks] *pregnant/breast feeding?)* or seeking to quantifying medication risk (*What are the effects of paracetamol on my baby when breastfeeding?*).

DISCUSSION

We found that consumers have many unanswered questions about paracetamol. The nature of their concerns varied with patient age or life stage. Safety was the major area of enquiry across ages, with interest in interaction and side-effect risk increasing with age. Effectiveness of the medicine was an issue for all, but especially for pre-school children and older adults. Pregnancy or lactation questions focused on minimising paracetamol risk prior to maternal, foetal or infant exposure or seeking a risk management strategy after inadvertent exposure, while administration was an issue in young patients where dosing can be difficult.

Previous research has investigated patient, carer and/or health professional knowledge and attitudes about the use (dosing and unintentional risks) of paracetamol.[22-24] These studies identified paracetamol knowledge gaps for many consumers, as well as health care providers having varied knowledge of appropriate use. However, it was difficult to identify a question pattern about paracetamol use from these publications due to diversity in study design. Participants were commonly recruited from a general practice waiting room where they generally responded to questions constructed by the investigators. This is not the same sample frame as our database of spontaneous calls. In general, misinformation about risks was a recurring theme; and this is what our

paper also shows. While "greater education of health care workers is required in order to provide families with appropriate information"[24] was recommended, little research has addressed health professional responses to the information gaps consumers have about paracetamol. Generally, health care providers underestimate consumer concerns about medication risk [25-27] and do not adequately acknowledge these concerns.[26, 28, 29] This mismatch was also highlighted in the recent BMJ editorial[2] that addressed only three broad questions as important to paracetamol consumers (efficacy, adverse effects and dose). Our study provides the consumer perspective to this issue.

The primary prompt for paracetamol calls was inadequate information, which highlights the lack of information provided with OTC medicines. In the UK, general sales list medicines[30] are freely available in supermarkets, thus come without advice from health professionals. Mandatory information supplied with OTC medicines varies between countries. Pharmaceutical companies in the UK must supply approved Patient Information Leaflets with all medicines unless all necessary information specified by the Medicines and Healthcare products Regulatory Agency (including indications, contraindications, general dosing instructions and side effects) is included on the label.[31] The electronic Medicines Compendium,[32] targeted at health professionals, provides additional Summaries of Product Characteristics. The equivalent Australian documents are CMI leaflets and Product Information, neither of which is mandatory for OTC medicines. Aside from Panamax®,[33] there are no accessible CMI for common paracetamol-only formulations. Importantly, none of these consumer resources provide strategies to prevent or reduce risk from common occurrences such as re-dosing after vomiting or reassurance, where appropriate, when planned or inadvertent exposure to paracetamol occurs. Addressing consumer OTC medicine concerns requires information in CMI (or equivalent) to be comprehensible and actionable, targeted for life stage. Improving these aspects for paracetamol should be a focus of future research.

While written information is available to varying standards in the UK and Australia, medical professionals remain the most trusted information source.[34] Consumers are, however, unlikely to consult their GP about OTC medicine use.[35] Furthermore, research shows that health care professionals tend to drive and dominate communication about medicines in consultations, rendering it critical for deficiencies in patient knowledge to be brought to the forefront of health professional awareness.[36] Pharmacists may therefore play a pivotal role in providing information as the first and potentially only face-to-face contact.[37] Australian research has shown that the majority of OTC medicines for children are still sourced from pharmacies rather than

supermarkets,[34] with many considering pharmacists medicines experts and preferring spoken over written information.[38] Consideration could also be given to changing the OTC status to pharmacist-only or prescription status, as has been called for in research and the media.[39, 40]

Medicines most commonly enquired about in combination with paracetamol were analgesics, especially codeine and ibuprofen, despite concomitant use in adults being safe and effective for additive analgesia at recommended doses.[41, 42] The differing caller and question profile for concurrent analgesia involving paracetamol is important for clinicians to know. Health professionals should also be aware that parents are concerned about interactions between the various medicines, including paracetamol, antihistamines, and ibuprofen. While both UK and Australian written medicines information contain limited details about medicines with potential for interactions;[26, 28] consideration to include a similar list of safe medications would provide reassurance where there is common concurrent use.

This study has several strengths. A large number of calls made to *Medicines Line* were available over eight consecutive years. Paracetamol call distribution approached relative population frequency. The data also permitted both quantitative and narrative analysis, giving detailed insight into consumer concerns. Age groups were well represented in the enquiry type subsets for both interaction and administration so can be considered a representative sample for thematic analysis by age. Limitations include sampling bias; people who contact medicines call centres may have different information needs from the wider population. This study highlighted those consumers who had sufficient concerns about paracetamol use to seek information, but fails to capture the reverse – consumers who assume that paracetamol is safe due to its OTC status.[43]The calls are also from an Australian population and may not accurately reflect concerns held by consumers in other countries.

Consumers have many concerns about paracetamol use that are likely to be under-recognised by healthcare providers, with different patient age groups and life stages having unique questions that should be considered when targeting information towards patients. Therapeutic strategies to minimise paracetamol risk are not adequately addressed by available information. Improving information may be challenging due to the OTC status of paracetamol and the diversity of commercial brands. Strategies such as increasing pharmacist involvement with paracetamol supply may be useful, but may necessitate a change in its unrestricted availability in other places such as supermarkets. Ultimately, the accessibility of information that the public wants to know needs to be targeted to optimise the safe and effective use of paracetamol.

FOOTNOTES

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Contributors: TMM and MLVD provided supervision, conceived and designed the study. SL conducted the literature review and data analysis. SL, TMM and MLVD interpreted the data, drafted and critically revised the manuscript. SL, TMM and MLVD as guarantors accept full responsibility for the work and/or the conduct of the study, had access to the data, and controlled the decision to publish.

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Ethical approval: This study was approved by Mater Health Services Brisbane, Human Research Ethics Committee (LNR submission 2012-68) and University of Queensland School of Medicine Low Risk Ethical Review Committee (2014-SOMILRE-0098).

Transparency: The authors (SL, MLVD, TMM) affirm that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

Data sharing statement: No additional data are available.

REFERENCES

1 Sood S, Howell J, Sundararajan V, et al. Paracetamol overdose in Victoria remains a significant health-care burden. *J Gastroenterol Hepatol* 2013;28:1356-60.
2 Dear JW, Antoine DJ, Park BK. Where are we now with paracetamol? *BMJ* 2015;351:3705.
3 Daly FFS, O'Malley GF, Heard K, et al. Prospective evaluation of repeated supratherapeutic acetaminophen (paracetamol) ingestion. *Ann Emerg Med* 2004;44:393-8.
4 McGill M, Jaeschke H. Metabolism and Disposition of Acetaminophen: Recent Advances in Relation to Hepatotoxicity and Diagnosis. *Pharm Res* 2013;30:2174-87.
5 Office for National Statistics. Deaths related to drug poisoning in England and Wales, 2014 registrations [Internet]. Newport: Office for National Statistics; 2015 [cited 2015 Oct 31]. Available from: http://www.ons.gov.uk/ons/dcp171778_414574.pdf.
6 Australian Institute of Health and Welfare. Drugs in Australia 2010: tobacco, alcohol and other drugs [Internet]. Canberra: Australian Institute of Health and Welfare; 2011 [cited 2015 Sep 15]. Available from: http://www.aihw.gov.au/WorkArea/DownloadAsset.aspx?id=10737420455.
7 Australian Bureau of Statistics. Deaths collection: Drug Related Deaths by Type of Drug (Total Drug Related Deaths) [Internet]. Canberra: Commonwealth of Australia; 2007 [cited 2015 Oct 31]. Available from: http://www.drugfree.org.au/fileadmin/Media/Reference/DFA_DrugRelatedStats.pdf.
8 Holappa M, Ahonen R, Vainio K, et al. Information sources used by parents to learn about medications they are giving their children. *Res Social Adm Pharm* 2012;8:579-84.
9 Hameen-Anttila K, Nordeng H, Kokki E, et al. Multiple information sources and consequences of conflicting information about medicine use during pregnancy: a multinational Internet-based survey. *J Med Internet Res* 2014;16:60.
10 Grymonpre RE, Steele JW. The medication information line for the elderly: an 8-year cumulative analysis. *Ann Pharmacother* 1998;32:743-8.
11 Khoo K, Bolt P, Babl FE, et al. Health information seeking by parents in the Internet age. *J Paediatr Child Health* 2008;44:419-23.
12 Gatti A, Sabato E, Di Paolo AR, et al. Oxycodone/paracetamol: a low-dose synergic combination useful in different types of pain. *Clin Drug Investig* 2010;30 Suppl 2:3-14.
13 National Prescribing Service Limited. Medicines Line [Internet]. Sydney: National Prescribing Service; 2012 [cited 2015 Jul 28]. Available from: http://www.nps.org.au/contact-us/medicines-line.
14 Pohjanoksa-Mäntylä MK, Antila J, Eerikäinen S, et al. Utilization of a community pharmacy-operated national drug information call center in Finland. *Res Soc Adm Pharm* 2008;4:144-52.

15 Marvin V, Park C, Vaughan L, et al. Phone calls to a hospital medicines information helpline: analysis of queries from members of the public and assessment of potential for harm from their medicines. *Int J Pharm Pract* 2011;19:115-22.
16 Government of Ontario. Telehealth Ontario [Internet]. Ontario: Government of Ontario; 2015 [cited 2015 Jul 28]. Available from: https://www.ontario.ca/page/get-medical-advice-telehealth-ontario.
17 Benchimol EI, Smeeth L, Guttmann A, et al. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement. *PLoS Med* 2015;12:e1001885.
18 von Elm E, Altman DG, Egger M, et al. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *BMJ* 2007;335:806-8.
19 WHO Collaborating Centre for Drug Statistics Methodology. Guidelines for ATC classification and DDD assignment, 2015 [Internet]. Oslo: Norwegian Institute of Public Health; 2014 [cited 2015 Oct 31]. Available from: http://www.whocc.no/filearchive/publications/2015_guidelines.pdf.
20 Australian Bureau of Statistics. Families in regional, rural and remote Australia 2006 Census Data [Internet]. Canberra: Australian Government; 2010 [cited 2015 Nov 3]. Available from: http://www.abs.gov.au/AUSSTATS/abs@.nsf/Lookup/1379.0.55.001Explanatory%20Notes12002-2006?OpenDocument
21 IBM Corp. SPSS Statistics for Windows, 23 ed. New York: IBM Corp; 2015.
22 Wolf MS, King J, Jacobson K, et al. Risk of unintentional overdose with non-prescription acetaminophen products. *J Gen Intern Med* 2012;27:1587-93.
23 Herndon CM, Dankenbring DM. Patient perception and knowledge of acetaminophen in a large family medicine service. *J Pain Palliat Care Pharmacother* 2014;28:109-16.
24 Karwowska A, Nijssen-Jordan C, Johnson D, et al. Parental and health care provider understanding of childhood fever: a Canadian perspective. *CJEM* 2002;4:394-400.
25 DeWitt JE, Sorofman BA. A model for understanding patient attribution of adverse drug reaction symptoms. *Drug Inf J* 1999; 33: 907–20.
26 Britten N. Medication errors: the role of the patient. *Br J Clin Pharmacol* 2009;67:646-50.
27 Knapp P, Gardner PH, Carrigan N, et al. Perceived risk of medicine side effects in users of a patient information website: A study of the use of verbal descriptors, percentages and natural frequencies. *Br J Health Psychol* 2009 14: 579-94.
28 Berry DC, Michas IC, Gillie T, et al. What do patients want to know about their medicines and what do doctors want to tell them? A comparative study. *Psychol Health* 1997;12:467-80.
29 Hoffmann TC, Del Mar C. Patients' expectations of the benefits and harms of treatments, screening, and tests: a systematic review. *JAMA Intern Med* 2015;175:274-86.
30 National Health Service Choices. Medicines Information [Internet]. London: National Health Service; 2014 [cited 2015 Oct 31] Available from: http://www.nhs.uk/conditions/Medicinesinfo/Pages/Introduction.aspx.
31 Medical and Healthcare Products Regulatory Agency. Best practice guidance on the labelling and packaging of medicines [Internet]. London: Government of the United Kingdom; 2014 [cited 31 Oct 2015] Available from: https://www.gov.uk/government/publications/best-practice-in-the-labelling-and-packaging-of-medicines.
32 Electronic Medicines Compendium. About the eMC [Internet]. Leatherhead (UK): Datapharm; 2015 [cited 2015 Oct 31]. Available from: http://www.medicines.org.uk/emc/about-the-emc.
33 Sanofi. Panamax: Consumer Medicines Information [Internet]. Sydney: Sanofi; 2014 [cited 2015 Sep 8]. Available from: http://www.sanofi.com.au/products/aus_cmi_panamax.pdf
34 Hesse B, Nelson DE, Kreps GL, et al. Trust and sources of health information: The impact of the internet and its implications for health care providers: findings from the first health information national trends survey. *Arch Intern Med* 2005;165:2618-24.

35 Sleath B, Rubin RH, Campbell W, et al. Physician-patient communication about over-the-counter medications. *Soc Sci Med* 2001;53:357-69.
36 Stevenson FA, Cox K, Britten N, Dundar Y. A systematic review of the research on communication between patients and health care professionals about medicines: the consequences for concordance. *Health Expect.* 2004;7:235-45.
37 Simoens S, Lobeau M, Verbeke K, et al. Patient experiences of over-the-counter medicine purchases in Flemish community pharmacies. *Pharm World Sci* 2009;31:450-7.
38 Hamrosi K, Raynor D, Aslani P. Enhancing provision of written medicine information in Australia: pharmacist, general practitioner and consumer perceptions of the barriers and facilitators. *BMC Health Serv Res* 2014;14:183.
39 Jozwiak-Bebenista M, Nowak JZ. Paracetamol: mechanism of action, applications and safety concern. *Acta Pol Pharm* 2014;71:11-23.
40 Collins N. Paracetamol 'should be prescription-only' [Internet]. London: The Telegraph; 2012 [cited 2014 Jul 14]; Available from: http://www.telegraph.co.uk/news/uknews/9134065/Paracetamol-should-be-prescription-only.html.
41 Merry AF, Gibbs RD, Edwards J, et al. Combined acetaminophen and ibuprofen for pain relief after oral surgery in adults: a randomized controlled trial. *Br J Anaesth* 2010;104:80-8.
42 Barkin RL. Acetaminophen, Aspirin, or Ibuprofen in Combination Analgesic Products. *Am J Ther* 2001;8:433-42.
43 Bennin F, Rother HA. "But it's just paracetamol": Caregivers' ability to administer over-the-counter painkillers to children with the information provided. *Patient Educ Couns*. 2015;98:331-7.

APPENDIX

Table 1. Themes from interaction and administration calls (by age group) and pregnancy/lactation calls

Age group	<1 year	1-4 years	5-24 years	25-44 years	45-64 years	65+ years
Interaction narrative (n=895 calls)						
Common theme across ages	Safety of medicines to be administered Safety of using a second medicine after recent administration of the first					
Specific themes	None	Safety of combining medicines prior to administration	Interactions between paracetamol and lifestyle products	Attributing a worrying symptom to a medication interaction Appropriate medicine choice, based on current medication	Appropriate medicine choice, based on current medication	Appropriate medicine choice, based on current medication Attributing a worrying symptom to a medication interaction
Administration narrative (n=582 calls)						
Common theme across ages	Appropriate dose (quantity or safety check)					
Specific themes	Appropriateness of paracetamol administration Management of re-dosing	Appropriateness of paracetamol administration Management of re-dosing Outcome after unintentional overdose Administration with food/drink	Dosing questions (timing, calculations, repeat dose) Outcome after unintentional overdose	Safety of concomitant use of a different paracetamol medicine	Medicine constituents (excipient & active) Alternative analgesic options	Maximum recommended dose Comparison between two medicines Medicine constituents (excipient & active) Safety of concomitant use of a different paracetamol medicine Specific safety concern
Pregnancy/Lactation narrative (n=501 calls)						
Common themes	Is it safe to take paracetamol in pregnancy/breastfeeding? Quantifying the risk or clarifying a safe dose of paracetamol to take in pregnancy/breastfeeding					

Table 2. Age specific themes for interaction and administration calls.

Age range (years)	Age-specific themes	Example questions
Interaction narrative (n=895 calls)		
<1	None	
1-4	Safety of combining medicines prior to administration	*Can I combine Dimetapp® Elixir and Panadol® to give to my two year old?*
5-24	Interactions between paracetamol and lifestyle products	*Can I drink alcohol after taking Phenergan® and Panadol®?*
25-44	Attributing a worrying symptom to a medication interaction	*Could paracetamol and esomeprazole have caused stomach cramps*
	Appropriate medicine choice, based on current medication	*What analgesics are safe to take with Zoloft® and Xanax®?*
45-64	Appropriate medicine choice, based on current medication	
65+	Appropriate medicine choice, based on current medication	
	Attributing a worrying symptom to a medication interaction	*Could paracetamol and esomeprazole have caused stomach cramps?*
Administration narrative (n=582 calls)		
<1	1. Appropriateness of paracetamol administration	*Can I give Children's Panadol® to my 10 month old baby?*
	2. Management of re-dosing	*Can I give my child another dose of Panadol® if she immediately vomited it up after I administered it?*
1-4	1. Appropriateness of paracetamol administration	*Can I give Children's Panadol® to my 10 month old baby?*
	2. Management of re-dosing	*Can I give my child another dose of Panadol® if she immediately vomited it up after I administered it?*
	3. Outcome after unintentional overdose	*My one year old has swallowed at least 1/2 a paracetamol tablet - will she be okay?*
	4. Administration with food/drink	*Can Painstop® be given with juice?*
5-24	1. Dosing questions (timing, calculations, repeat dose)	*Should you dose paracetamol by weight or age in children?* *Is it okay to give my five year old 9.5mls of Panadol® syrup every four hours for a fever?* *Can I repeat the dose of Panadol® from my child's fever after the last dose 5 hours ago?*
	2. Outcome after unintentional overdose	*Have I given too much Painstop® to my ten year old child?*
25-44	1. Safety of concomitant use of a different paracetamol medicine	*Can I take Mersyndol® one hour after taking 1000mg of Panamax®?*
45-64	1. Medicine constituents (excipient & active)	*Can you tell me the gluten content for Panamax®, Tramal® and Mobic®?*
	2. Alternative analgesic options	*Is it okay to take Panadeine Forte® instead of Endone®?*
65+	1. Medicine constituents (excipient & active), particularly comparison between two medicines	*What is the difference between Panadol® and Panadol® Osteo?*
	2. Maximum recommended dose	*What is the maximum dose of paracetamol that I can take for osteoarthritis pain?*
	3. Safety of concomitant use of a different paracetamol medicine	*Can I take Mersyndol® one hour after taking 1000mg of Panamax®?*
	4. Specific safety concern	*Will taking four paracetamol a day harm my liver?*

The RECORD statement – checklist of items, extended from the STROBE statement, that should be reported in observational studies using routinely collected health data.

	Item No.	STROBE items	Location in manuscript where items are reported	RECORD items	Location in manuscript where items are reported	COMMENTS
Title and abstract						
	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found	Title p.1 & Abstract p.2	RECORD 1.1: The type of data used should be specified in the title or abstract. When possible, the name of the databases used should be included. RECORD 1.2: If applicable, the geographic region and timeframe within which the study took place should be reported in the title or abstract. RECORD 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract.	Title & Abstract Abstract – Setting & participants Not applicable – our dataset was not linked -	Observational study: retrospective analysis of calls to an Australian medicines call centre i.e. National Prescribing Service (NPS) Medicines Line between September 2002 and June 2010
Introduction						
Background rationale	2	Explain the scientific background and rationale for the investigation being reported	Introduction p.4 – *Paragraphs 1 & 2*			
Objectives	3	State specific objectives, including any pre-specified hypotheses	Introduction p.4 – *Paragraph 3*			
Methods						
Study Design	4	Present key elements of study design early in the paper	Methods pp.5-6 – Quantitative Analysis & Narrative Analysis subsections			
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Methods p.5 – Data Collection subsection			
Participants	6	*(a) Cohort study* - Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	Methods p.5 – Data Collection subsection, with eligibility criteria, and the sources and methods of selection of participants provided	RECORD 6.1: The methods of study population selection (such as codes or algorithms used to identify subjects) should be listed in detail. If this is not possible, an explanation should be	Methods – Data Collection subsection, with eligibility criteria, and the sources and methods of selection of participants provided	Study population consisted of all callers to NPS *Medicines Line* between September 2002 and June

		Case-control study - Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study* - Give the eligibility criteria, and the sources and methods of selection of participants *(b) Cohort study* - For matched studies, give matching criteria and number of exposed and unexposed *Case-control study* - For matched studies, give matching criteria and the number of controls per case		provided. RECORD 6.2: Any validation studies of the codes or algorithms used to select the population should be referenced. If validation was conducted for this study and not published elsewhere, detailed methods and results should be provided. RECORD 6.3: If the study involved linkage of databases, consider use of a flow diagram or other graphical display to demonstrate the data linkage process, including the number of individuals with linked data at each stage.	N/A N/A	2010. As data was collected as part of a health-related service at a single time point, our study is neither case-control, cohort or cross-sectional. However, of these options, cross-sectional would be the closest study type.
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.	Data from this observational study were routinely collected as part of a health service without specific *a priori* research goals	RECORD 7.1: A complete list of codes and algorithms used to classify exposures, outcomes, confounders, and effect modifiers should be provided. If these cannot be reported, an explanation should be provided.	N/A	
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Methods p.5 – Data Collection			All data obtained from NPS Medicines Line
Bias	9	Describe any efforts to address potential sources of bias	To validate consistency of population characteristics over time, longitudinal analysis of demographics (gender, age, geographical location by ARIA, enquiry type, medicines in question & motivation to call was conducted Bias in analysis managed through double analysis of narrative			
Study size	10	Explain how the study size	Methods p.5: Study population			

		was arrived at	consisted of all callers to NPS Medicines Line between September 2002 and June 2010			
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	Methods p.5 – Data Collection (Paragraph 2) & Quantitative Analysis – groupings chosen based on topic of interest (e.g. therapeutic class or drug, caller or patient cohort e.g. by age)			
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) *Cohort study* - If applicable, explain how loss to follow-up was addressed *Case-control study* - If applicable, explain how matching of cases and controls was addressed *Cross-sectional study* - If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses	a) Methods p.5 – Quantitative Analysis b) Methods p.5 – Quantitative Analysis for sub-groups c) Calls with missing data were included in totals and any data exclusions (e.g. voicemail requests for CMI only) were made explicit. d) N/A e) N/A			
Data access and cleaning methods		..		RECORD 12.1: Authors should describe the extent to which the investigators had access to the database population used to create the study population.	Study approved by Mater Health Services Brisbane, Human Research Ethics Committee (LNR submission 2012-68) & University of Queensland School of Medicine Low Risk Ethical Review Committee (2014-SOMILRE-0098). Data access by authors is clearly defined in the HREC application .Mater Pharmacy Services (Dr T McGuire) is joint data	

				RECORD 12.2: Authors should provide information on the data cleaning methods used in the study.	custodian with NPS MedicinesWise Extensive data cleaning undertaken in conversion of data from Access to SPSS e.g. codes to identify voicemail CMI requests were excluded as they did not involve a medicines question.	
Linkage		..		RECORD 12.3: State whether the study included person-level, institutional-level, or other data linkage across two or more databases. The methods of linkage and methods of linkage quality evaluation should be provided.	N/A	
Results						
Participants	13	(a) Report the numbers of individuals at each stage of the study (*e.g.*, numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed) (b) Give reasons for non-participation at each stage. (c) Consider use of a flow diagram	a) Results p.6 – *Paragraph 1* The number of participants for each aspect of demographics was reported, often as a quantitative table including missing data. b) N/A *c) -*	RECORD 13.1: Describe in detail the selection of the persons included in the study (i.e., study population selection) including filtering based on data quality, data availability and linkage. The selection of included persons can be described in the text and/or by means of the study flow diagram.	Results – Paragraph 1 The number of participants for each aspect of demographics was reported,	
Descriptive data	14	(a) Give characteristics of study participants (*e.g.*, demographic, clinical, social) and information on exposures and potential confounders (b) Indicate the number of participants with missing data for each variable of interest (c) *Cohort study* - summarise follow-up time (*e.g.*, average and total amount)	a) Results p.6 – Paragraph 1 b) pp.6-7 The number of participants for each aspect of demographics reported c) N/A			
Outcome data	15	*Cohort study* - Report numbers of outcome events or summary measures over time	As data was collected at a single time point we did not measure outcome events			

		Case-control study - Report numbers in each exposure category, or summary measures of exposure *Cross-sectional study* - Report numbers of outcome events or summary measures				
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	a) Results section pp.6-8 Confounder-adjusted estimates not applicable b) N/A - no continuous variables c) N/A			
Other analyses	17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	Methods pp.5-6– Quantitative Analysis & Narrative Analysis Results section pp.6-10			
Discussion						
Key results	18	Summarise key results with reference to study objectives	Discussion p.11-12– *Paragraphs 1, 2, 4*		Discussion – *Paragraphs 1, 2, 4*	
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Discussion p.13 – *Paragraph 6:* Population derived by calls to a MCC. We do not know if people who do not contact a MCC have similar medicines information gaps and concerns.	RECORD 19.1: Discuss the implications of using data that were not created or collected to answer the specific research question(s). Include discussion of misclassification bias, unmeasured confounding, missing data, and changing eligibility over time, as they pertain to the study being reported.	Discussion – *Paragraph 5*	
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant	Discussion p.13– *Paragraph 6*			

		evidence				
Generalisability	21	Discuss the generalisability (external validity) of the study results	Discuss (strengths & weaknesses paragraph) p.13–Paragraph 6			
Other Information						
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	p.14 Funding statement			
Accessibility of protocol, raw data, and programming code				RECORD 22.1: Authors should provide information on how to access any supplemental information such as the study protocol, raw data, or programming code.	Raw data is held at MPS Mater Pharmacy Services (Dr T McGuire) is joint data custodian with NPS. Data access by authors is limited and clearly defined in the HREC application.	

[1] Reference: Benchimol EI, Smeeth L, Guttmann A, Harron K, Moher D, Petersen I, Sørensen HT, von Elm E, Langan SM, the RECORD Working Committee. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement. *PLoS Medicine* 2015; in press.