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SHORT COMMUNICATION

A Comparison of the Reliability of Smartphone Apps for Opioid Conversion

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Abstract
Background Many medical professionals use smartphone applications (apps) on a daily basis to support clinical decision making. Opioid switching (conversion of one opioid to another at equianalgesic dose) is common in clinical practice and often challenging for doctors. Apps providing an opioid conversion tool can therefore be a useful resource. Despite rapid growth in the use of medical apps, the lack of robust regulation and peer review to ensure the accuracy and reliability of app content is currently an area of concern.
Method We searched major online app stores for apps providing an opioid dose conversion tool. We assessed output variability between apps in the dose calculation of seven opioid switches, as well as assessing the level of professional medical involvement in the authorship, creation and design of the apps.
Results Of 23 different apps identified, more than half ($n = 12$; 52 %) had no stated medical professional involvement and only 11 (48 %) apps provided direct references to primary sources for their opioid conversion ratios. Conversion of 1 mg of oral morphine to oral codeine demonstrated the largest conversion output range (median 6.67 mg, range 3.333–12 mg). Conversion of 1 mg of oral morphine to methadone ranged from 0.05–0.67 mg, with only 44 % of methadone-converting apps ($n = 4$) commenting that the conversion ratio changes with magnitude of methadone dose. Overall, 35 % of apps ($n = 8$) did not warn the user about the standard practice of dose reduction when opioid switching. There was a statistically significant difference in the mean conversion output for hydromorphone (oral) between apps with and without medical professional involvement (0.2256 vs 0.2536; $p = 0.0377$).
Conclusions There are significant concerns with regard to the reliability of information provided by apps offering opioid dose conversion, with lack of information regarding evidence-based content and peer review in many cases. It is crucial that better regulation of medical apps is instigated in order to ensure that patient safety is maintained.

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1 Introduction

Opioid analgesics are integral to both the management of acute pain and the treatment of pain associated with malignancy [1]. The process of opioid switching (conversion of one opioid to another, with the aim of achieving the same, or an improved, analgesic effect) [2] is common in clinical practice. It is required when there are adverse effects, poor analgesic control, drug-drug interactions, the need for an alternative route of administration, a change in clinical status (i.e. worsening renal function), or cost and drug availability considerations [3, 4]. As difficulties in calculating equivalent doses of opioids can arise, equianalgesic tables are widely used by clinicians to aid in opioid conversion.

Equianalgesic tables were created more than 40 years ago, and have undergone little modification in the interim

[2]. As such, there may be significant limitations in their reliability [2, 5, 6]. Tables can demonstrate large variation in opioid conversion doses, with conversion ratios ranging from 2:1 to 10:1 for the same opioid switch [5]. Reports also demonstrate that the potency of opioids can vary depending on the direction of the switch, a factor not commonly integrated into equianalgesic tables [6]. In spite of these concerns, equianalgesic tables continue to be used routinely as a reference tool in clinical practice.

Advances in mobile technology have brought many opportunities for reference material software to be accessed in a variety of formats, including as applications (apps) on smartphones [7]. Ownership of smartphones by medical professionals is now in the range of 81–85 %, with the most commonly used apps amongst medical trainees being drug guides (79 %) and medical calculators (18 %) [8].

Studies have demonstrated that junior doctors feel underprepared for prescribing [9]. They have a prescribing error rate of around 10 % (this is significantly higher than the 5.9 % error rate demonstrated by consultants) [10], and junior doctors have particular difficulty in calculating drug dosages [11]. This cohort is also likely to be the most frequent user of smartphones [12], and probable user of apps to support prescribing decisions.

The aims of this study were (i) to evaluate the current availability of medical calculator apps for smartphones which provided a dose-conversion tool for commonly used opioids; (ii) to assess the inter-app variability in opioid dose conversion ratios; and (iii) to assess the proportion of these apps claiming to involve medical professionals in their creation.

2 Methods

Between 28 January and 5 February 2012, the major online app stores (Android ‘Google Play’ store, iOS ‘App Store’, BlackBerry ‘Blackberry App World’, Windows Phone ‘Marketplace’, Symbian ‘Ovi (Nokia)’ store and Bada ‘Samsung Apps’ store) were searched using relevant terms (opioid, morphine, medical calculator, conversion) to identify apps that had opioid dose/formulation conversion capabilities. We included any app which explicitly stated that they contained an opioid conversion tool on the app store description prior to download or purchase. The apps we identified all provided a tool or reference table for conversion of one opioid to another, or the same opioid but different formulation, at equianalgesic dose. Apps varied in the number of different opioid conversions they offered. Some apps also offered a calculator adjustment to account for opiate cross-tolerance, whilst others simply suggested that the calculated dose should be reduced accordingly. Online app store descriptions, author’s associated web pages and content within apps were analysed to source information on user ratings, price, author and author qualification. Those apps priced in US dollars (USD) were converted to pounds sterling (GBP) as per the exchange rate on 12 February 2012 (1 USD = 0.634719 GBP). Data on app ratings were taken from information supplied on individual app pages on the online app stores. For apps that were found in more than one store, average price, user rating and number of raters across the stores were calculated. For each individual app we analysed content and associated web pages for evidence of medical involvement in their creation, design or review.

Table 1 Equianalgesic conversions used in app analysis

Drug to be converted	Formulation of drug 1	Dose of drug 1 (mg)	Drug converted to	Formulation of drug 2
Morphine	Oral	1	Codeine	Oral
Morphine	Oral	1	Morphine	IM/IV/SC
Morphine	Oral	1–100	Fentanyl	IV
Morphine	Oral	1	Oxycodone	Oral
Morphine	Oral	1	Hydromorphone	Oral
Morphine	Oral	1–100	Fentanyl	Transdermal patch
Morphine	Oral	1	Methadone	Oral

app application, *IV* intravenous, *IM* intramuscular, *SC* subcutaneous

Seven equianalgesic opioid conversions that are commonly required in clinical practice were selected for the purpose of comparing the outputs generated by the apps (Table 1). Those apps that provided a tool for adjustment of cross-tolerance were set to 0 % dose reduction. One mg of oral morphine was used as a standard where possible; however, conversions with high potency opioids (for example intravenous and transdermal fentanyl) required an input value of 100 mg oral morphine to produce a conversion ratio in some cases. Some apps provided a dose-conversion range; in these instances the median value in the dose range was taken for the purpose of statistical analysis.

3 Results

The preliminary search identified 26 apps with opioid-conversion tools, six of which were duplicated across stores (Table 2). Of these 26 apps, three were excluded: one app crashed on opening, another was written in French and therefore the accuracy of our data input could not be guaranteed, and a third app converted patient-controlled analgesia rather than simple opioid switching. This left a total of 23 apps for full analysis. Six apps (26 %) had the

Table 2 Opioid conversion apps by store

	App store (operating system)					
	App Store (iOS)	Play Store (Android)	BlackBerry App World (Blackberry)	Marketplace (Windows Phone)	Ovi Store (Symbian)	Samsung Apps (Bada)
No. of unique apps (n = 20)	16	4	0	0	0	0
No. of duplicated apps (n = 6)	6	6	1	5	0	0

apps applications

sole function of opioid conversion, whilst the remaining 17 apps (74 %) included an opioid conversion tool as part of a wider range of medical calculators.

4 Details of Application (App) Price, Rating and Most Recent Update

Five apps (22 %) offering opioid conversion were free to download, whilst the remaining 18 apps (78 %) charged an average price of £2.64 (range £0.69–£6.67). Seventeen apps (74 %) were rated by users out of a score of 5. Average app rating was 3.0, with a median number of 7 raters and range of 0.33–919 raters per app. Nineteen apps (83 %) had been updated within the last 2 years, the earliest in May 2010 and the most recent in January 2012. The remaining four apps (17 %) made no mention of their most recent update.

5 Medical Involvement in App Development and Referencing of Primary Sources

Five apps (22 %) described the involvement of a named anaesthetist, palliative care consultant or other physician in the app development or content. One app was identified as having physician authorship by using a search engine to reach the developer's website, and a second app was produced by a health informatics company under the direction of a consultant physician. Three app authors (13 %) were individuals with a medical doctoral degree (MD) and one further app was produced as an evidence-based resource by the faculty of a medical centre in the US. In the remainder (n = 12; 52 %), neither the author's qualifications nor the individuals involved in the development of the app were stated.

Only 11 (48 %) apps provided direct references for their opioid conversions. Ten (43 %) of these apps provided reference materials that ranged from journal articles relating to opioid conversion to clinical practice guidelines and pharmacology or pain management textbooks. One app developed by a training grade doctor based its opioid dosing conversions on a website that has certification with a code of ethical conduct pertaining to the distribution of reliable medical information. The remaining 12 (52 %) apps provided no direct references. One of these apps, created by an individual with a doctoral degree, stated its conversions were based on the 'clinical practice' of the author, whilst the remaining 11 (48 %) gave no information on a primary source for their opioid conversion ratios. One of these apps used 'sources believed to be authoritative in the subject of pharmacological treatment options', whilst a further 5 of these 11 apps, all with unknown authors but produced by the same company, stated that the information they contained was based on 'public medical literature'. None provided reference to support these claims.

Table 3 Conversion of 1-mg oral morphine by opioid

Conversion (route of administration; units)	No. of apps	Median (mg)	Range (mg)
Codeine (PO; mg)	21	6.67	3.333–12
Morphine (IV/IM/SC; mg)	23	0.33	0.3–0.5
Fentanyl (IV; μg)	16	3.33	3–3.333
Oxycodone (PO; mg)	23	0.67	0.5–1
Hydromorphone (PO; mg)	23	0.25	0.13–0.27

apps applications, *PO* oral, *IV* intravenous, *IM* intramuscular, *SC* subcutaneous

6 Evaluation of App Capabilities

Analysis of opioid conversions between apps for oral morphine to intravenous, intramuscular and subcutaneous morphine, oral codeine, oral oxycodone, oral hydromorphone and intravenous fentanyl can be seen in Table 3. All apps converted more than one opioid. Nine apps (39 %) converted oral morphine to oral methadone, with the results seen in Table 4. Nine apps (39 %) also converted oral morphine to fentanyl transdermal patch (Table 5).

7 Analysis of App Outputs

Codeine demonstrated the largest conversion ratio range (median 6.67 mg, range 3.333–12 mg). The conversions of oral morphine to intravenous/intramuscular/subcutaneous morphine, oral hydromorphone, oral oxycodone and

Table 4 Equianalgesic conversions of morphine to methadone according to app

App	Conversion of 1 mg oral morphine to oral methadone (mg)
1	0.1
2	0.67
3	0.066–0.6
4	0.1
5	0.067–0.667
6	0.083–0.25
7	0.05–0.333
8	0.1
9	0.67

app application

Table 5 Equianalgesic conversions of oral morphine to fentanyl transdermal patch

App	Conversion of morphine 100 mg (PO) to fentanyl transdermal patch
1	0.667 mg (= 27.8 μg/h)
2	25 μg/h
3	25 μg/h
4	25 μg/h
5	42–60 μg/h
6	50 μg/h
7	50 μg/h
8	90 mg PO morphine = 37 μg/h 120 mg PO morphine = 50 μg/h
9	50 μg/h

app application, PO oral

intravenous fentanyl showed less variation between apps (Table 3). In the conversion of 100 mg of oral morphine to a transdermal fentanyl patch the range was 25 μg/h–60 μg/h (Table 5). Conversions of 1 mg of oral morphine to methadone ranged from 0.05–0.67 mg (Table 4) but the large variation may have been due to the dose-dependent nature of the conversion ratio. Four apps (44 %) specified a different conversion ratio depending on morphine dose; dose ranges are therefore seen in Table 4. Only four out of the nine apps (44 %) providing a methadone conversion tool warned the user about the impact of the magnitude of methadone dose on the conversion ratio.

Ten apps (43 %) allowed the user to account for cross-tolerance through a dose-reduction tool. Thirteen apps (57 %) did not provide this tool and only five (38 %) of these informed the user about cross-tolerance with a suggestion to reduce the calculated dose as the user felt necessary.

Analysis was undertaken to compare the conversion outputs between apps that had medical input versus no medical input and those apps with referenced work from those without. The results demonstrated no significant difference in the mean conversion outputs between apps with or without medical involvement or referenced work for codeine, morphine, fentanyl, oxycodone or hydromorphone conversions ($p > 0.05$), with one exception. The mean conversion output for hydromorphone was significantly different between apps with and without medical professional involvement (0.2256 vs 0.2536; $p = 0.0377$). Analysis was not undertaken for buprenorphine given the small numbers of apps.

8 Discussion

This study has a number of novel findings relating to opioid conversion apps. Firstly, the calculated dosages are highly variable, with statistically significant differences in conversion outputs between apps with stated medical involvement and those without in some cases. Secondly, few apps appear to identify the primary data source underlying their calculation algorithm. Thirdly, there is a lack of information as to whether there has been involvement in app creation or content of individuals who have practical experience in or insight into the undertaking of these high-risk prescribing decisions.

Opioid prescribing is a key theme in patient safety [13] and adverse incidents with opioid analgesics are common [14]. Prescription error, either at drug initiation, conversion or dose titration, is a significant risk factor for opioid-related death [15]. The National Institute for Health and Clinical Excellence has recently released guidelines regarding opioid prescription in palliative care, with the aim of improving patient safety through clearer recommendations [16]. Studies have suggested that because of the complexity of opioid switching, an electronic medium for opioid dosing may help to improve patient safety [17]. The advantages of smartphone apps over a standard textbook for opioid switching are clear: they are smaller, more accessible and offer greater portability, offering faster access at the point of care. Smartphone apps can also be updated quickly in line with new developments in research or changes to clinical guidelines.

The rapid growth in Internet content offers a powerful tool to efficiently deliver clinical guidelines and practice to a global audience. However, the volume and diversity of health-related information available via the worldwide web results in logistical difficulties in quality control and professional peer review of materials in order to ensure the delivery of correct and accurate information. Nevertheless, the role of the Internet and personal digital assistants in medical education has increased exponentially over recent years, with a significant proportion of undergraduate teaching being achieved through e-learning programmes and initiatives [18, 19]. Furthermore, smartphone apps are beginning to demonstrate their potential as an e-learning tool in medical education [20]. Electronic opioid calculators have shown to decrease prescribing errors and the time taken for dose calculation by both medical students and consultants, when compared with manual calculation using a dosing table or drug formulary [17, 21]. Nevertheless, variation in individual patient factors such as pharmacokinetic handling and pharmacodynamic responsiveness, pharmacogenetics and drug interactions mean that even proper use of conversion calculators can only provide general guidance. Those using numerical conversion apps should receive training in numeracy skills related to dose calculations since this has also been shown to reduce prescribing error [22].

Other reports have highlighted low levels of medical professional involvement in the design and content of medical apps (i.e. dermatology (36 %) [23], microbiology (34 %) [7], coloproctology (32 %) [24]) and in pain management [25]. Our data therefore highlights important issues regarding the reliability, peer review and evidence base of medical apps aimed at use by medical professionals and patients. Medical calculators are the second most frequent app downloaded by doctors [8]; it is possible that the use of inaccurate or poor-quality apps for opioid dose conversion could lead to greater risk of prescription error, particularly by less experienced members of the medical team.

The regulation of smartphone apps in the UK and the US is currently undergoing development. The Medical Device Directive (MDD) oversees the regulation of mobile devices within the EU, with each member state under its own competent authority [26]. There is currently a lack of consistency in legislation between the different member states, with ongoing debate about whether medical apps, or which medical apps, should be regarded as a medical device. The definition of a medical device varies between member states and, as such, apps falling outside these definitions are not required to meet medical requirements or undergo risk assessment before market. Providers of all apps that fall into the category of a medical device must gain CE (Conformité Européene) approval through their competent authority prior to marketing. The CE mark is a manufacturer's claim that his medical device meets the directive's 'essential requirements' and, where necessary, has been independently assessed by a 'notified body'. The MDD also includes a classification system to ensure that the level of regulatory control over a medical device is in accordance with the degree of risk associated with its use. In general, most medical apps fall into the lowest risk category (Class I) and as such can self-certify conformity to the essential requirements without the need for an independent body. None of the apps studied here explicitly stated CE certification; this may reflect difficulties regarding the definition of a medical device internationally. The Medicines and Healthcare products Regulatory Agency (MHRA) is the competent authority for the regulation of medical devices within the UK. However, apps with CE approval from any member state can be freely downloaded in the UK without undergoing further authorization with the MHRA. To date, only one UK-developed app has been given MHRA accreditation – 'Mersey Burns' produced by Medicapps Ltd, an app for prescribing intravenous fluids by estimating burns coverage, which is currently available on the iOS platform [27]. Many medical apps include disclaimers to help limit liability, with some large app stores placing the onus entirely on the app developer to ensure conformity to appropriate legal requirements. At the time of writing, global regulatory bodies have early plans and embryonic frameworks in place for their approach to addressing the regulation and legal responsibilities involved in medical app usage in practice. However, these approaches are currently highly diverse and undergoing rapid development [28, 29].

Within the US, the FDA has recently released guidance on its intentions to regulate mobile medical applications. They propose to regulate apps intended for the diagnosis, treatment or prevention of disease, apps that transform a mobile platform into a medical device, and apps that allow the user to input patient-specific data and, through the use of a formula or calculator, produce patient-specific results intended for use in clinical decision making [30]. This latter category will include dose calculators. However, this guidance currently serves as a recommendation only, until a time when full regulatory oversight is introduced.

The calculation of incorrect opioid doses may be associated with considerable potential for patient harm. We have demonstrated that the conversion ratios of opioids by apps are variable. As previously highlighted, there is variability in traditional textbook equianalgesic tables [5]. This is secondary to the challenge of defining a 'gold standard' that accounts for patient-specific factors (e.g. treatment of either acute or chronic pain). Furthermore, the heterogeneous nature of study design from which equianalgesic tables are derived may result in considerable inter-table variation. Consequently, variability in opioid conversion apps may be the result of direct translation of textbook conversion tables into apps, rather than errors in app ratios and data themselves. Variability is an inherent feature of equianalgesic tables; it is therefore important that, regardless of source, opioid conversion tables are used with caution and serve as a guide rather than an exact science. There are some important limitations of our work. Firstly, we did not compare variation seen in smartphone opioid apps with that seen in textbook equianalgesic tables.

Whilst absence of a gold standard table may make this difficult, there would be scope for comparison with a number of selected textbook tables. We note that this is an important area for further research. Secondly, apps with opioid converters were identified by app store descriptions prior to download. As such, some apps with converters may not have been identified in the initial search. Thirdly, the data used for analysis of authorship was based on available and sometimes limited information. This may not reveal the full extent of medical expertise in app creation and content.

9 Conclusion

We have demonstrated that opioid calculator conversion outputs are highly variable between apps. Evidence of medical involvement in app creation or referencing of primary sources is lacking in many cases, and a statistically significant difference was found in conversion outputs of hydromorphone in those apps with and without stated medical involvement. There is great potential for electronic reference tools and smartphone-delivered software to revolutionize and improve the efficiency of clinical practice and enhance medical education. However, it is essential that regulation and quality control is improved. This will ensure that only evidence-based, peer-reviewed medical apps with accurate and up-to-date information are available. Information available to consumers on app stores is often limited; better regulation could provide reassurance to purchasers of medical apps that the information they contain is reliable and correct, as well as strengthen trust within the sector. Crucially, better regulation in this rapidly growing market could reduce the potential for compromise to patient safety that apps offering opioid conversion may pose. We also recommend that doctors are further educated in the possible risk to patients associated with the use of such apps.

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