HURON

SOCIAL MEDIA AND MOBILE HEALTH:

Communicating Benefit-Risk in a Connected Society

By Richard Huckle

Beyond the buzzwords, digital communication is impacting healthcare at all levels. From policy makers' Tweets, patient experiences on Facebook to smartphone gaming apps altering our behaviours. Here we review the benefits and risks associated with this 'new' way of communicating and in turn, how stakeholders can communicate benefits and risks in ways they have never been able to before. The past twelve years has seen the advent of smartphones, the expansion of their use and influence of the internet and social media in our daily lives. Consequently, the means by which we interact with each other and with the world's information have fundamentally changed.

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Connected Society

Social media is a communication tool to engage with the public and has the potential to debate health care policy, promote healthy behaviours, educate and interact with patients, caregivers and colleagues.

As social networking has evolved, medically focused communities have been established[1].

Uses for social media in healthcare include:

- Professional networking
- Education
- Organizational promotion
- Patient care
- Public health programmes
- Evidence gathering and dissemination

Regulatory Networking

Ultimately, all these uses share common goals, to better manage healthcare benefits and to communicate any risks.

There is an increasing awareness by regulators, industry and health care professionals (HCPs) of the possible value of various forms of digital communication (including social media, eHealth and mHealth) on the both effectiveness and safety of medicines. But, regulation of Internet and social

media platforms was not specifically addressed (by any of the regulators) until 2014, with the U.S. Food and Drug Administration (FDA) being first out of the blocks to propose draft guidances. Noting that patients and healthcare providers regularly receive information about medical products online via social media, these guidances shared the agency's thinking about how drug and medical device manufacturers can accurately communicate information about their products online (see FDA draft guidances[2,3,4]).

The European Medicines Agency (EMA) held a 2016 workshop[5] (September 2016) on the impact of social media on stakeholders and concluded that social media can ultimately be seen as an enabler of EMA's key goal, which is to put the patient at the centre of its activities. But more work needs to be done on how best to use the tools of the digital world, and EMA will follow developments very closely through various means, including a dedicated focus group to develop a social media strategy with the aim of broadening stakeholders' engagement. The EMA Committee for Medicinal Products for Veterinary Use has issued a reflection paper (on non-spontaneous adverse event reports including – reviewed literature, internet and social media), but there has not been any corresponding reflection paper or subsequent guidance on any social media usage by other EMA committees.

The need to obtain real-world data over the life-cycle of a medicine for both safety and effectiveness is another challenge that social media could transform. Social media may be a way to gather such real-life post-approval information and transfer information back to the patients. These techniques present great opportunities but also great challenges for both the industry and the regulators. Social media has limitations which includes delivery of complex, technical information to suit homogeneous audiences. Also, the open platform nature of the internet presents challenges for companies trying to maintain correct information about their products online and data privacy concerns.

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The regulator (FDA in this case) has become a blogger (on Twitter, the micro-blog app)

Post-Marketing Surveillance

Patient-generated data via digital platforms is being explored as a primary basis for capture and analysis of possible adverse drug reactions (ADRs). The Medicines and Healthcare products Regulatory Agency (MHRA) is leading a consortium of organisations (including European medicines regulators, academics and the pharmaceutical industry) in a three-year project to develop new ways of gathering information on suspected ADRs[6]. The project, known as WEB-RADR, aims to develop a mobile app for HCPs and patients or caregivers to report suspected ADRs to regulators. In addition to reporting suspected ADRs, the app could also serve as a platform to send accurate, timely and up to date medicines information to patients, clinicians, and caregivers.

Social media (particularly microblog sites such as Twitter) are seeing patients use them to describe adverse experiences with medical products (see

Figure). Patients reporting adverse events on Twitter showed a range of sophistication describing their experiences, despite the public availability of this information[7]. The nature of social media, ranging from specific vocabulary used amongst its specific communities, to inconsistent content in posts, makes data analysis from posts difficult. Consequently, several methods have been developed and launched to solve technical challenges associated with gathering and analysing data collected from social media. Researchers have developed tools including data mining by topic, assessing outliers based on either unusual side effects or misinformation. However, with the Facebook–Cambridge Analytica data scandal[8] when it was revealed that Cambridge Analytica had harvested the personal data of millions of people's Facebook profiles without their consent and used it for political purposes, users are increasingly aware as to what personal information they share and likely consequences (e.g., insurance companies validating injury claims[9]).

a) #**Schizophrenia**indication #**Seroquel** did not suit me at all. Had severe **tremors**ADR and weight **gain**ADR

b) I felt awful, it made my **stomach hurt**ADR with bad **heartburn**ADR too, **horrid taste in my mouth**ADR tho it does tend to clear up the **infection**indication.

Figure - Examples of user-posted drug reviews in Twitter (DailyStrength) [10]

From a regulatory context, apps are standalone software and must in no way promote the use of any associated medicine per se.

The Rise of Mobile Apps

Apps informing and consenting the user (such as WEB-RADR), could be the solution to these social media privacy concerns whilst still providing a convenient vehicle to real-time communication.

Advances in the use of mobile health (mhealth) technologies and apps for portable electronic devices, such as tablets and smartphones have been brought about by several contributing factors, including increased processing power, greater memory storage, a reduction in size of components, and lower costs to consumers. In addition, mobile signal coverage and data transfer speed has greatly increased accessibility along with the availability of internet connections through Wi-Fi networks, allowing greater access to information. Furthermore, most smart devices now incorporate sensors such as accelerometers, global positioning satellite components and cameras, which have greatly improved their functionality, expanding their usability into areas such as healthcare. Consequently, app developers have been producing software that falls into the "medical applications" and "healthcare" categories. Some could fall into categories which will be regulated as medical devices, others as diagnostic devices, while yet others will fall outside the scope of these definitions or even be classed as borderline, between classifications.

Despite the potential risks associated with mobile medical apps, most do not undergo formal review or evaluation before entering the market. Currently, developers must first submit their program for review by the app store (e.g., iTunes, Google Play). Although, this review process is conducted to ensure the app is functional on that particular platform (e.g., Apple iOS or Android OS) and has no major technical issues, the clinical content in medical apps is not assessed. As such, many apps of lesser quality can slip through the review process. While this lack of review by those responsible for the app marketplace is concerning, there is also a general lack of oversight. In fact, regulation of most software products has proven to be difficult due to their

complexity and diversity (and global availability and exposure).

From a regulatory context, apps are standalone software and must in no way promote the use of any associated medicine per se. As with all media sources, rules on promotional activity are governed by codes including: IFPMA Code of Practice (2012), EFPIA Code on the Promotion Of Prescription-Only Medicines to, and Interactions with Healthcare Professionals (HCP - 2014) and PhRMA - Code on Interactions with Healthcare Professionals (2009).

Regulators have released some guidance for developers to implement such technologies which has helped clarify expectations and draw attention to the need for governance of the growing mhealth market. But, regulation of medical apps was not specifically addressed until 2011, when the FDA released a draft guidance on the topic. The guidance was updated, finalised and issued in February 2015, outlining how the FDA will apply its regulatory authority to mobile medical apps. The FDA has already recognised some of the challenges outlined previously and has released two main categories of guidance to clarify how these applications should be categorised: 1) "mobile medical applications" (MMAs)[11] and; 2) "general wellness products"[12].

The regulation of medical devices differs from that of drugs since it is based on a step or tier classification system. Specifically, devices are designated as either Class I, II, or III, depending on their potential risk. Class I devices are the lowest risk and are generally exempt from review. Class II devices, however, are considered an intermediate level of risk and developers are usually required to submit a premarket notification (or 510(k) notification). Under this process, developers must show that the product is "substantially equivalent" to a similar device already on the market. Class III devices are the highest risk level and must generally undergo a more complex, time-consuming and expensive premarket approval process.

The MMA guidance also discusses the types of apps for which the FDA plans to exercise "enforcement discretion," meaning that their regulatory authority would not be applied except in special circumstances.

The MMA guidance also discusses the types of apps for which the FDA plans to exercise "enforcement discretion," meaning that their regulatory authority would not be applied except in special circumstances. This category mainly includes patient-oriented apps, such as those that help patients track and manage health information.

For example, the FDA will not regulate apps that provide contextually relevant access to medical information used in clinical practice (e.g., apps that check for drug–drug or drug–allergy interactions). Similarly, the FDA will not review apps that provide clinicians with a summary of best practice guidelines or other therapy recommendations for a medical condition (e.g., an app presenting a contextually relevant antibiotic treatment algorithm based on site of infection). Mobile medical calculators are another type of commonly used app for which the FDA will exercise enforcement discretion.

Historically, software products intended for use in disease diagnosis or treatment have been classified as a medical devices. Wide-ranging changes to the overall medical devices and in vitro diagnostics regulatory framework are now in force with the new EU Regulations. The regulation of medical devices in the EU is governed by the CE Marking process. The EU has attempted to provide guidance for MMAs, including the MHRA's guidance "Medical device stand-alone software including apps (including IVDMDs)" released in 2014 and the EU's guidance document on "Medical Devices - Scope, field of application, definition - Qualification and Classification of stand-alone software – MEDDEV 2.1/6" released in 2016. However, these are far less comprehensive than guidance provided by the FDA

and arguably leaves a degree of ambiguity as to their scope, demonstrating that the EU has work to do in terms of regulating digital healthcare.

When determining if a medical mobile app meets the definition of a medical device or accessory its the intended purpose (defined as the "use for which the device is intended according to the data supplied by the manufacturer on the labelling, in the instructions and/or in promotional materials") needs to be considered. The claims that the manufacturer makes within the app itself (labelling) and instructions for use provided with the app and in promotional materials (e.g., advertising, websites, brochures etc.) are used to determine whether an app is a medical device or not.

Diabetes iPhone and Android apps are available for smartphones and tablets to assist in diabetes management. These apps typically log blood glucose readings (directly via a sensor or manual input), although some allow you to log carbohydrate intake, food, medication, weight and more. These apps feature graphs displaying the blood glucose figures – or graphs displaying these plus food and medication, detailed tables of results, figures and various export functions such as the ability to email to email the results directly to directly to the patient's HCP. mySugr is an example of a company developing apps in this area and its products include educational and logging apps for patients with diabetes along with Scanner, an app that can transfer blood sugar values from the patient's glucometer to their iPhone and then logbook. This diabetes logbook with all transferred blood glucose values and clear data reports will help to facilitate HCP analysis and treatment optimisation.

The results can also be synchronized to webbased apps for analysis and interpretation, helping to spot patterns and maximize results by identifying weak spots in therapy and focusing on effective changes. The mySugr app is a registered risk class 1 (CE marked) medical device in the U.S. and EU, and mySugr (the company) is ISO 13485 certified. mySugr GmbH was acquired by Roche in June 2017[13].

Two examples from gamification and how this is revolutionising healthcare are Mango Health's compliance app and MindMaze's virtual reality gaming technology for stroke rehabilitation.

MyAsthma app available from the App Store®

Another example is the MyAsthma app (developed by GSK and the University of Nottingham)[14] for patients (or their carers) living with asthma. The app is designed to help patients understand their asthma by providing environmental and lifestyle information that may be relevant to their condition, together with data indicating the status of their asthma. Patients or their carers can check and track their asthma control by using the Asthma Control Test (ACT) or the Childhood-ACT (C-ACT) as appropriate within the app, and export information from the app to share with their HCP. The app is not intended to diagnose asthma or provide advice on medicines, but it is a Class I medical device with an Intended Use Statement.

Apps such as mySugr and MyAsthama could be part of a Patient Support Programme (PSP) along with gamification (social welfare wellness solutions) apps. Gamification is another mobile health area gaining

traction, recognising the fact that games can offer a fun way to boost user engagement. Gamification increases satisfaction and voluntary participation by incorporating interactive features, rewards and competition into the healthcare experience. Gamified apps could provide a potentially cost-effective platform for health promotion, drive consumer engagement and having a substantial public health impact[15].

Two examples of how gamification is revolutionising healthcare are Mango Health's compliance app and MindMaze's virtual reality gaming technology for stroke rehabilitation. Mango Health developed a smartphone app designed to motivate patients to take their medications on time. Users set the times when medications should be taken, the app then reminds them and provides information about the medications and any warnings about drug interactions and side effects. By taking the medications properly, users earn points towards gift cards or charitable donations in raffles held weekly (rules on promotional activity being observed). The company MindMaze, created devices such as MindMotion™ PRO, which offers a stimulating virtual environment tailored according to the user's preferences and needs, motivating them to get the most from their therapeutic exercise training regimen. With real-time multisensory feedback, patients can monitor their own performance. MindMotion™ PRO has been cleared by the FDA (501(k)) and is CE marked[16].

An example of an app which has not been developed as a class I medical device or MMA is the aforementioned WEB-RADR app. The pharmacovigilance reporting schemes (such as the Yellow Card Scheme) are vital in helping the regulators MHRA) monitor the safety of all healthcare products in the UK to ensure they are acceptably safe for patients. Through WEB-RADR, reports can be made from the app, installed on a handheld electronic device for all medicines including vaccines, blood factors and immunoglobulins, herbal medicines and homeopathic remedies, and all medical devices available on the UK market. The app enables consumers and caregivers to report side effects and review personalised information published by the MHRA related to treatment pathways.

The Digital Divide

A social and economic divide that restricts access to information and communication technology is another challenge. Healthcare organisations should be aware that whilst consumer feedback derived from social media networks and mobile health can be helpful, they should still seek other methods to confirm that information derived from offline sources matches information from digitally sources.

For digital communication solutions to work, marketing and regulatory departments need to work as a single team. The value of being able to interact with patients in in a real-time world cannot be ignored. But the structures and procedures need to be in place to allow the regulators to do their job. Mistakes will be made, but as long as there are robust procedures in place to deal with situations swiftly and efficiently, the damage can be controlled and any legal requirements satisfied.

Software intended for use in a medical context can be classified as a medical device, and health apps therefore potentially fall within the regulators remit. However, the sheer volume of apps, and their rapid uptake by patients/consumers and HCPs, raises questions about the appropriate levels of regulation and oversight, and whether current and impending regulatory frameworks are fit for purpose.

Although apps are intended to help individuals improve their health and/or manage their disease, they all present different levels of potential risk of harm. Many of the apps that are currently available on the market and unregulated may present undetermined, or possibly higher risk to the user, due to lack of understanding by the user or machine error. Could regulation stifle innovation? While classification processes present additional work for app developers, these steps are essential to ensuring a device's quality, effectiveness, trust and above all, safety for end users.

Data collected from social media and mobile sources

offer pharma and biotech industries an opportunity to better communicate in real-time with and learn from patients. The key to a successful benefit-risk communication strategy is to involve regulatory experts from the outset to avoid inadvertently overstepping the many (and increasing) boundaries.

Terminology

Social media (and blog) – websites and applications that enable users to create and share content or to participate in social networking (e.g., Facebook, Twitter, Instagram, Snapchat, YouTube, WhatsApp etc.).

eHealth – (electronic (sometimes digital) health) promoting, empowering and facilitating health and wellbeing with individuals, families and communities, and the enhancement of professional practice using information management (e.g., SMS texting, email, telephone/ video conference support, remote monitoring applications etc.).

mHealth – (mobile health) is a general term for the use of mobile phones and other wireless technology (and can include eHealth). The most common application of mHealth is the use of mobile devices to educate consumers about preventive healthcare services.

Big Data – large or complex datasets. Data sets grow rapidly- in part because they are increasingly gathered from social media, eHealth and mHealth (e.g. As of Q3 2018, Facebook had 2.27 billion monthly active users (https:// www.statista.com/statistics/264810/number-of-monthly-active-facebook-users-worldwide/)

References

1. Fogelson NS et al, Beyond likes and tweets: an in-depth look at the physician social media landscape. Clin Obstet Gynecol 2013 56(3) 495–508
2. FDA Draft Guidance for Industry: Fulfilling Regulatory Requirements for Post-marketing Submissions of Interactive Promotional Media for Prescription Human and Animal Drugs and Biologics. January 1014
3. FDA Draft Guidance for Industry: Internet/Social Media Platforms with Character Space Limitations—Presenting Risk and Benefit Information for Prescription Drugs and Medical Devices. June 2014
4. FDA Draft Guidance for Industry: Internet/Social Media Platforms: Correcting Independent Third-Party Misinformation About Prescription Drugs and Medical Devices June 2014
5. EMA Report from a workshop on the impact of social media on patients, healthcare professionals and regulators 24 October 2016 EMA/625077/2016 Stakeholders and Communication Division
6. MHRA Press Release 5 September 2014: UK regulator leads innovative EU project on the use of smartphones and social media for drug safety information.
7. FreifeldJohn CC et al, Digital Drug Safety Surveillance: Monitoring Pharmaceutical Products in Twitter. Drug Safety 2014 37(5) 343–350
8. Cadwalladr C and Graham-Harrison E Revealed: 50 million Facebook profiles harvested for Cambridge Analytica in major data breach. The Guardian Mar 2018 https://www.theguardian.com/news/2018/mar/17/ cambridge-analytica-facebook-influence-us-election
9. Hickey S. Insurance cheats discover social media is the real pain in the neck. The Guardian 2016 18 Jul https://www.theguardian.com/money/2016/jul/18/ insurance-cheats-social-media-whiplash-false-claimants
10. Nikfarjam A et al, Pharmacovigilance from social media: mining adverse drug reaction mentions using sequence labeling with word embedding cluster features. J Am Med Inform Assoc 2015 22(3):671-81
11. FDA Guidance for Industry and Food and Drug Administration Staff: Mobile Medical Applications February 2015
12. FDA Guidance for Industry and Food and Drug Administration Staff: General Wellness: Policy for Low Risk Devices July 2016
13. Roche Media Release Roche acquires mySugr to form a leading open platform for digital diabetes management Basel, 30 June 2017 https://www.roche.com/media/releases/med-cor-2017-06-30.htm
14. Cross T How does the new asthma app work? The Telegraph June 2017 https://www.telegraph.co.uk/education/stem-awards/healthcare/ asthma-app/
15. Edwards EA et al, Gamification for health promotion: systematic review of behaviour change techniques in smartphone apps BMJ Open 2016;6:e012447. doi:10.1136/bmjopen-2016-012447
16. MindMaze Company Information. MindMotion Pro https://www.mindmaze.com/mindmotion/ accessed: 14 January 2019

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