ELSEVIER

editorial

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Serendipitous drug repurposing through social media

Conception of a plan

The path leading to a new drug becoming commercially available is long and expensive, involving an average of 13 years [1] and estimated costs from US$618 million to US$2.6 billion [1–3]. Drug repurposing, the use of an existing drug for a new indication, has emerged as a viable alternative to traditional *de novo* drug discovery. Drug repurposing allows investigators to bypass or streamline toxicity studies and should make these drugs more acceptable than early-phase drugs to providers, patients and families [4]. Drug repurposing has occurred by serendipity [4,5] when a patient has two medical conditions that, apparently by chance, turn out to be treatable by the same drug. This has been an inefficient process that has relied heavily on individual observant clinicians or patients to identify seminal cases for further study.

Almost one out of every two adults in the USA has been reported to have at least one chronic physical illness such as cardiovascular disease, arthritis, diabetes, asthma or cancer (https://www.healthypeople.gov/2020/about/foundation-health-measures/General-Health-Status). Among children, the prevalence of chronic disorders such as asthma, obesity, behavior and learning problems or food allergies is ~25% [6]. As many as one in five people of all ages are said to have serious mental health issues (http://www.nimh.nih.gov/health/statistics/prevalence/any-mental-illness-ami-among-adults.shtml#sthash.FhVGS2uS.dpuf). Thus, it should not be surprising that roughly one-third of Americans now are said to be living with multiple chronic conditions [7], not to mention acute illnesses. Many are taking one or more medicines. In this era of social media, including the consumer as a partner in drug discovery through self-report of serendipitous benefits from medications could identify some with potential for repurposing.

The Facebook survey

As a preliminary test of the feasibility of this approach and after approval by our institutional Investigational Review Board (IRB), we administered a brief Facebook-disseminated survey of user-reported experiences with prescription, over-the-counter and/or homeopathic agents. This asked whether adult responders or their children had taken any substance which they believed had helped treat a problem other than the one for which it had been intended and, if so, to name the drug, what problem it had been taken for and what secondary problem it seemed to help. Responders were encouraged to think about even minor ailments such as transient viral illnesses (e.g., colds). In an effort to understand who is likely

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to respond to this type of survey, individuals were asked to provide information relating to their age, gender and race.

Surveys were sent with an introductory explanation via Facebook to Friends of one of the authors (D.P.K.) along with users who 'like' and/or 'follow' the Facebook accounts of our institutional Hospitals and Cancer Center (total $n = 40\,308$). To what extent Facebook users who 'liked' or 'followed' more than one of these mailers was not examined. Individuals were given 1 month to respond to a single mailer. Two months later, the response report was examined again to assess the likelihood of getting additional responses to a single mailer if Friends were given additional time. Surveys were returned by 49 Friends. All responses came within 1 week of sending the mailer. From this, 15/49 claimed to have used one or more drugs that had unintended beneficial consequences, although, in 13 of these cases, the 'unintended' response was actually an effect of the medicine that could have been anticipated by the prescriber. For example, amitryptilline, gabapentin, lyrica, tramadol and benadryl prescribed for accepted indications such as pain or anxiety helped with insomnia; hydrochlorothiazide prescribed for hypertension also reduced passage of kidney stones; ciprofloxacin and keflex prescribed for cystitis or 'bacterial infections' were also perceived to have improved coughing or acne symptoms. We considered two of the responses to be of potential interest. One 41-year-old woman was treated with Zoloft® (sertraline) for depression. She also had a diagnosis of psoriasis and noticed clearer skin with some lesions disappearing for several months before recurring. A PubMed review of 'Zoloft, psoriasis' identified another case in which psoriatic skin disease appeared to have resolved in temporal association with Zoloft® [8]. However, that patient had been started simultaneously on isoniazid which has been anecdotally associated with improvement of psoriasis when given as monotherapy [9], perhaps another example of serendipity. Thus, the credibility of our responder's observation remains to be substantiated. A 78-year-old man reported that Equate® (tolnaftate) athlete's foot spray relieved his neuropathy, even at a time when he had no obvious *tinea pedis*. There is no literature to address the credibility of this claim, and we have no information as to the accuracy or cause of a neuropathy diagnosis. It is not likely that the responder's athlete's foot caused pain so that we can only guess that the neuropathy truly was a secondary diagnosis. This observation also requires additional evaluation.

Reflections and concluding remarks

Social media has been used to look at adverse events from drugs and drug interactions [10]. Our experience could be the first exploration of applying social media to drug repurposing. Although our exploratory results were not earth-shattering, we found that with almost no effort – the minimal time to develop a survey and the touch of several buttons to release the survey once to several thousand Facebook users – we identified two agents with possible repurposing potential. Other systematic approaches have been taken to find drugs with the potential for repurposing. These usually have included mining large drug and drug-use databases. However, population-based ways of looking for drugs that unexpectedly mitigate more than one ailment are probably not granular enough to provide details with which to support claims. At the very least, database studies do not take into account problems too minor to generate medical interventions that nevertheless might be significant annoyances (e.g., the common cold), and which might improve by serendipitous treatment. Moreover, most medical databases do not routinely monitor non-prescription medications that might have unexpected repurposing potential.

Our approach had a few limitations, some of which might be inherent to queries through social media. For example, to minimize nonresponse owing to privacy concerns, we did not ask for information that would have allowed us to recontact specific individuals to refine their answers. All of the responses came within 1 week of the mailer, and we made no attempt to resend the survey. Although we obtained 49 responses, reasons for nonresponse could not be ascertained. For the majority of surveys that provided information, responders were Caucasian and female; there were no African American responders. We do not know how well the responder demographics reflected all users who saw the posted survey, and we inadvertently might have targeted specific consumer types. The mailer was sent to Facebook users who 'like' and/or 'follow' the Facebook pages of our medical facility. Thus, recipients might have been more interested in health issues than is the general Facebook community. Although we had hoped to reach larger numbers and a more diverse group by having users forward our link to their Friends, we have no way of knowing to what extent this actually happened.

Our small survey nevertheless did demonstrate feasibility. Social media avenues – email, tweets and other shared social media sites in addition to Facebook – potentially have an audience of many millions of individuals. More-focused queries about specific disorders could be directed to members of relevant patient, family or provider groups. With appropriate scientific curating, credible reports of serendipitous benefits could be posted online and held open for refutation, confirmatory reports and possibly for large-scale scientific testing. Consumers and social media organizations could help to systematize serendipity.

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