

ADDRESS

(The ADverse Drug Reaction/Event Screening System)

Matthew M. Murawski, R.Ph., Ph.D.

President and CEO, M-Cubed, LLC

EXECUTIVE SUMMMARY

The ADDRESS system is an advanced, innovative software application incorporating the top 480 prescription drugs, as ranked by prescription volume. The application is deliberately structured in such a way as to closely approximate the essentially linear process of preparing a prescription in a community pharmacy. This approach was chosen to make it possible from all pharmacists, no matter what their level of training or education, to easily adapt to using the ADDRESS application to provide clinically-focused, valued added services to patients without stress or requirements for extensive training. The interface is simple, intuitive, and can easily be used by clerks or technicians to initiate the screening process. ADDRESS permits pharmacists in busy community pharmacies to add a clinically and economically important service that can dramatically improve patient quality of life with a minimum of effort and in a very short period of time.

The system is designed to discern the existence of ongoing ADRs and ADEs (side effects) in the ambulatory patient population. ADRs are not only problematic in and of themselves, it has also been established that ADRs are a driver of non-adherence to medications (an important issue in Medicare reimbursement rates). Previously, ADRs were detected and rated based on clinician judgement. It is likely, now that ADDRESS provides a valid, reliable, dependable and, most importantly, repeatable metric of ADR severity, that it can be shown ADRs actually drive non-adherence much more powerfully than previously assumed, through conditioning of the patient's behavior. (Briefly: Operant conditioning occurs when the subject is exposed to various schedules of reward or punishment in response to a given behavior. A patient diagnosed with a life-threatening chronic disease will strive to be adherent to what are clearly life-saving medications. Unfortunately, at some point, they will forget to take a medication on some random day. Should that medication be one that is causing a noisome, objectionable ADR, for that day they will feel much better than on average. Over time, they will forget, randomly, to take that medication once again, simply due to basic human limitations. The single strongest reinforcing conditioning schedule is intermittent positive reward. So, over time, the patient becomes conditioned to become non-adherent. And, because the entire process occurs subconsciously, when challenged, the patient will be unable to give a reason for their non-adherence, and will offer their best guess that they simply "forgot". And forgetfulness is a problem without any straightforward solution).

ADDRESS offers the opportunity to change this dynamic. All of the drugs on the patient's regimen are entered into the application as now programmed (eventually, it can be easily integrated with the dispensing system and auto-populated). For each drug, five pre-prepared questions are added to a queue, which on average will describe the symptoms of 60-70% of all known ADR/ADEs for a given medication. The application sorts the queue, looking for any duplicate questions across drugs (which occur with some regularity across drug classes) and shall only ask any duplicate questions once. The intent is to

make the process as psychometrically efficient as possible- to limit the time and the number of questions to the absolute minimum.

For each question presented, the patient is asked to indicate whether they have experienced the symptoms described in the question at any point in the past month. If the answer is no, the application moves on to the next question. If they patient responds that they have experienced such symptoms, they are then asked to indicate how severe the symptom was, on a six point scale from not really a problem to almost intolerable. They are also asked to indicate how frequently the symptom has occurred, on a five point scale from only once or twice to almost every day. The product of the integer values of these scales is used to calculate a concept called "IMPACT", which is an accepted means of stating the experienced burden of a given symptom. As any single drug may cause multiple ADRs, IMPACT can be added to calculate individual drug ADR burden, as well as ADR burden across the entire regimen. This quickly identifies those patients who are arguably suffering for ADR burdens of sufficient severity that their cases are actionable.

The justification for taking the time and making the effort to perform these screenings could be justified as a means of optimizing the patient's pharmacotherapy and quality of life. However, there are substantial economic and competitive issues at play as well. This summary shall limit consideration to the economic factors to be considered.

ADR/ADEs are a very real, very serious, and enormously expensive aspect of the health care system. The estimated cost of ADRs to the US health care system is has been estimated to be at least \$140 billion each year, via mechanisms such as treatment of ADR reactions, hospital readmission, and in some cases, long-term patient harm and mortality. As previously mentioned, ADRs are strongly linked with non-adherence to prescribed therapy, which itself has been estimated to result in costs to the US health care system exceeding \$170 billion/yr. (Another set of estimates places the cost of both ADRs and non-adherence at \$180 billion *each*). In either case, the total estimates of costs to the Health Care System exceed the total spend on ALL prescription medications. These figures approach one-sixth the total U.S. Health Care Spend. Any entity in a position to efficiently and effectively address these problems using a low-cost intervention is clearly in a position to justify enormous amounts of revenue, it fact Kiely to far exceed any possible margin from the sale of the medications themselves. In addition, it has been recently estimated that non-adherence to prescription drugs results in a loss to the pharmaceutical industry in the range of approximately \$495 billion/yr. In short, clearly the opportunity exists to save substantial amounts of resources, and, as a direct consequence, the possibility of significant additional revenue in the community pharmacy industry cannot be ignored.

Of course, screening alone will not result in the fullest return of developing the opportunity this technology represents. Pharmacists will have to develop relationships with primary prescribers to inform them of the results of such screenings, or to provide printouts of the results to patients. A preferable option is for the pharmacist to work with the provider to de-challenge the patient (stop use of the mostly likely drug for a period agreeable to the prescriber to determine if the ADR resolves) in order to establish causation and create billable function within the Pharmacy. Under collaborative practice arrangements, such practices could become widespread. Options then range from changes in dose, dose frequency, extended-release formulations, or therapeutic substitution of another member of the same therapeutic class with a lower incidence of the problematic ADR. Patients can be screened for ADRs in the Pharmacy, and, once the practice is established, their pharmacotherapy can optimized in the Pharmacy, minimizing ADR burden to the extent possible, while optimizing adherence. The use of ADDRES will create a strong justification for a new stream of revenue that shall far exceed drug inventory in magnitude.

AN ANALYSIS OF THE COMPETITIVE ADVANTAGE OF AN ADDRESS INITIATIVE

As noted above, there are competitive advantages that accrue through full adoption of the ADDRESS application that may be of even greater significance than the economic potential of this technology as described above. As a participant, observer, and scientist whose field is the study of Pharmacy *in situ*, (A Ph.D. in Pharmacy Administration) it is not difficult for the writer to determine that Independent Community Pharmacy (to some extent), and, especially the Chain Industry, is approaching a nexus. A nexus past which the Chain Industry's survival is a legitimate question. The reference, of course, is to Amazon's recent acquisition of PillPack and their stated intention of becoming a major player in the prescription drug market for ambulatory care.

Historically, Independent Community Pharmacy has managed to compete and to remain viable at a smaller scale by specializing in service to that market segment of customers willing to pay a premium to obtain higher levels of attention and service. To the Chain Industry, Amazon's play must be construed as a major, even possibly terminal threat, as it challenges the Chain Industry's long-time and massively successful business model of location, convenience, and prompt service. Unfortunately, as difficult as this is to say, it seems highly unlikely that a chain- any chain- even CVS- can compete head to head with the single most efficient, most successful wish-fulfillment company on the face of the planet. CVS has slowly and methodically staked out the optimal store sites in cities and towns across the United States, ensuring rapid, professional service is only a few minutes' drive from the patient's home. Innovations like drive through service, guaranteed fill times, and additional staffing as needed has allowed CVS to reach a point of dominance in the industry.

And yet, it is difficult to see that business model successfully competing with one where the patient need never leave home at all. A few seconds with a cell-phone, and for a relatively reasonable fee the patient's prescription will appear *on their doorstep*- without them ever having to leave the comfort of their home at all. This is a true game changer. It might take five years. It might take ten years- optimistically, perhaps even fifteen years. But eventually, if CVS continues to compete on the basis of location, convenience, and prompt service with Amazon and their PillPack subsidiary, the outcome is very likely inevitable. And that slight possibility that the outcome might not be inevitable is dependent on Amazon/PillPack committing a massive, possibly large-scale error resulting in extensive patient mortality/morbidity.

There is only one area where CVS is in a position to compete with Amazon/PillPack from a position of advantage. It will require some reassessment of the business model, but the advantage is there. Basically, CVS needs to take a page from the Independent Community Pharmacy, and seek to leverage the relationship between the patient and the pharmacist. Amazon/PillPack can offer call centers, just as in the manner of mail-order Pharmacy. Brief, unsatisfying interactions with pharmacists in the CVS Pharmacy will not be sufficiently competitive with the convenience of call-centers to maintain a substantial advantage long term in the market segment that has sought out CVS's mix of services. It would seem that the only way in which Amazon/Pillpack cannot compete is in the existence of and nature of the therapeutic relationship between the pharmacist and the patient.

The key will be to take the steps necessary to be able to provide a truly *therapeutic* relationship. Independent Community Pharmacy relies on familiarity, service, and caring. With adoption and full development of the ADDRESS technology, CVS can position itself to provide optimization of the patient's

pharmacotherapy in a true, meaningful therapeutic relationship wherein the patient ends up happier, healthier, living a longer life in which they enjoy a higher quality of life than has hitherto been possible. By moving quickly, CVS is in a position to relegate Amazon/Pillpack to a limited supply function not terribly differentiated from mail order firms than have been in business for decades.

The key in bringing ADDRESS online, first to market, established as the gold standard, and establishing trust with the patient base. At that point, no ersatz facsimile that Amazon might attempt to create would be competitive. This is a technology that has taken more than 20 years of theoretical and technical development. Its recreation by individuals without the unique combinations of requisite scientific knowledge and skills involved would be extremely unlikely in any time frame that would offer immediate competition. And even then, that scenario would have to assume that the development and expansion of the ADDRESS technology would come to a standstill- which shall not be the case. The technology exists today to integrate ADDRESS with the dispensing system, populating the patients screening; the technology exists to extend the screening past the first visit to the next five questions, and the next five questions, until all possible ADRs have been exhausted. The technology exists to accomplish this by placing the technology in a machine much like the popular blood pressure kiosk, using patient identification cards issued by CVS (You could even include a discount club) allowing patients to complete ADDRESS screening for ongoing ADRs at their leisure, and at their own speed. The application is specific to the level of indication, and creates a HIPPA complaint identifier to protect patient anonymity.

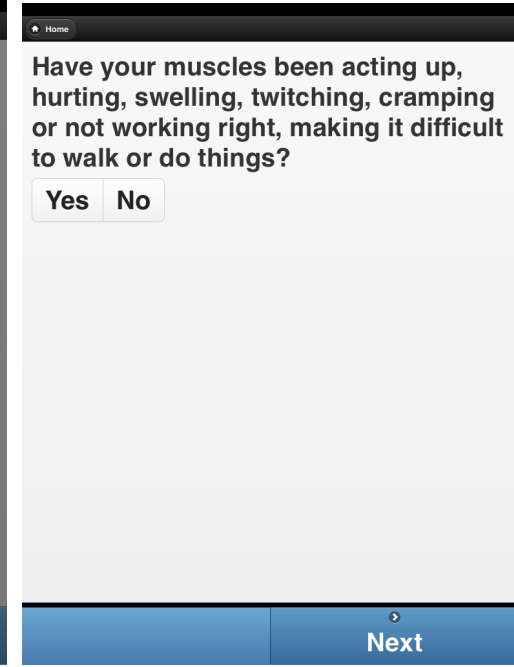
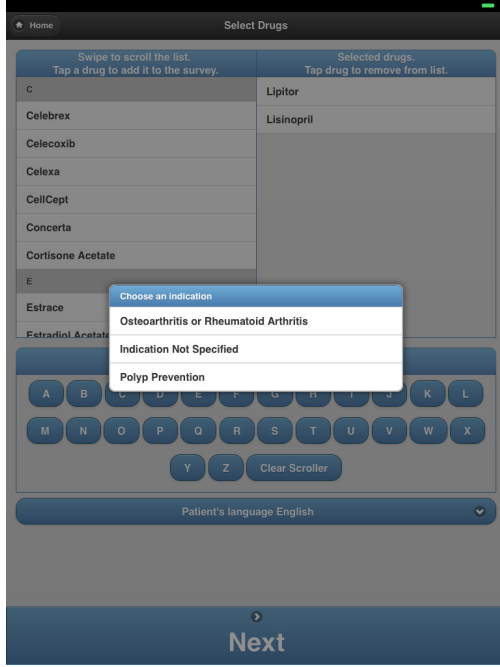
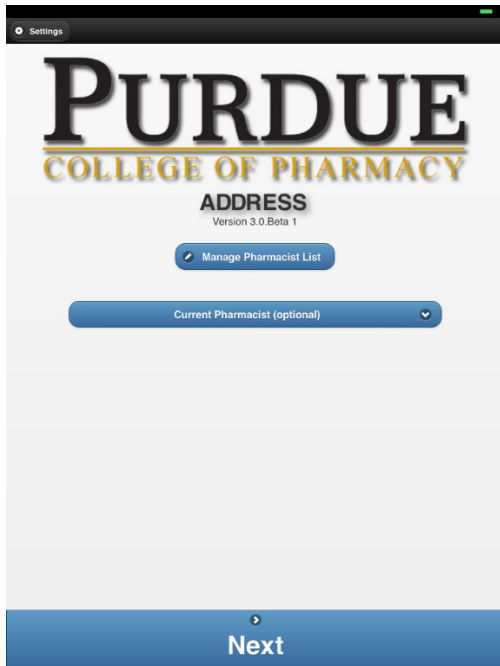
There's theoretically no limit to the degree which this technology can be applied, and its impact on the nation's overall health is difficult, if not impossible to overstate. With proper deployment, it creates a competitive advantage over every other player in the market, enhances the bottom line to an extent limited only by the company's ability to negotiate, and, with some luck, allows CVS to make the legitimate claim that it has played a major role in reducing the cost of health care in the United States. And it shall certainly be less expensive to deploy and develop to its fullest extent than drones or similar problematic technology. All that is required is the ability to see the potential and the willingness to make a play.

If what I have shared here has piqued your interest, I would be most willing to pay a visit, give a full demonstration, and answer any question you might have. In fact, I'd prefer it. It has been my experience people can read my explanations of the technology, yet despite my best efforts, they seem to have some difficulty grasping such an out of the box concept. Let them see it, play with it, and sit through a demonstration, and the enthusiasm is palatable.

With consideration of just how innovative this approach is, I have decided to dispense with further text and descriptions, and provide you with a few screen shots of the manner in which the application presents to the patient, as well as a sample of the kind of data presented to the pharmacist for assessment on the following few pages. It is my hope you will see the full potential this working prototype already has to impact the industry, as well as just how much further it can be taken, with us working together.

My Sincere Regards-

Matthew M. Murawski, R.Ph. Ph.D.



Home

Have your muscles been acting up, hurting, swelling, twitching, cramping or not working right, making it difficult to walk or do things?

Only once or twice

Almost every week

Weekly

More than once a week

Daily

Next

Not a real problem

Barely noticeable

Mildly troublesome

Rather bothersome

Very bothersome

Almost intolerable

Next

Home

You can now either submit the checklist by pushing the button marked "Submit", or if you would like, you can help our research effort by creating a simple code that will be your identifier, but will not let anyone know who you are. We just need you to tell us:

The first two letters of your mother's first name.
Example: **RU**th

The day of month of your birthday.
Example: June **19**

The first two letters of your father's first name.
Example: **CH**arles

The last two digits of your HOME phone number.
Example: 555-23**30**

A B C D E F G H
I J K L M N O P Q
R S T U V W X Y Z

Next

Home

Thank you for completing this checklist. Please return this tablet to the pharmacy staff.

Display results

Home

Metformin, Lipitor

Have you experience unusual or distressing stomach gas and/or diarrhea/loose stools?
 Frequency: Weekly
 Severity: Rather bothersome

- Possible side effect of more than one drug - tap to view incidence

+ 56.2% of patients experience this side effect with Metformin - tap for treatment hints

+ 13.6% of patients experience this side effect with Lipitor - tap for treatment hints

Metformin

Have you felt as if you just don't have enough energy to get the things done that you need to that you have felt drowsy, tired, or almost asleep?
 Frequency: Weekly
 Severity: Mildly troublesome

+ 8.449999999999993% of patients experience this side effect with Metformin - tap for t...

Lipitor

Have your joints been especially painful, swollen, hard to move or stiff and sore?
 Frequency: More than once a week
 Severity: Very bothersome

+ 14.05% of patients experience this side effect with Lipitor - tap for treatment hints

Lisinopril

Have you felt dizzy, lightheaded, or felt as if the room is spinning, especially when standing up, or actually fainted and fell down?
 Frequency: Only once or twice
 Severity: Mildly troublesome

+ 7.8% of patients experience this side effect with Lisinopril - tap for treatment hints

Celebrex

Submit results