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Corresponding Author:	Joseph Tay Wee Teck, MB BCh BAO MSc University of St Andrews School of Medicine St Andrews, Fife UNITED KINGDOM
Corresponding Author Secondary Information:	
Corresponding Author's Institution:	University of St Andrews School of Medicine
Corresponding Author's Secondary Institution:	
First Author:	Joseph Tay Wee Teck, MB BCh BAO MSc
First Author Secondary Information:	
Order of Authors:	Joseph Tay Wee Teck, MB BCh BAO MSc
	Alberto Oteo
	Alexander Baldacchino
Order of Authors Secondary Information:	

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Rapid opioid overdose response system technologies

Joseph Tay Wee Teck* [1,2]
Alberto Oteo[1]
Alexander Baldacchino[1]

[1] DigitAS Project, Population and Behavioural Science Division, School of Medicine, University of St Andrews, St Andrews, UK
[2] Forward Leeds and Humankind Charity, Durham, UK

* Corresponding author: jbtwt1@st-andrews.ac.uk

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Abstract

Purpose of review:

Opioid overdose events are a time sensitive medical emergency, which is often reversible with naloxone administration if detected in time. Many countries are facing rising opioid overdose deaths and have been implementing Rapid Opioid Overdose Response Systems (ROORS). We describe how technology is increasingly being used in ROORS design, implementation and delivery.

Recent findings:

Technology can contribute in significant ways to ROORS design, implementation, and delivery. Artificial intelligence-based modelling and simulations alongside wastewater-based epidemiology can be used to inform policy decisions around naloxone access laws and effective naloxone distribution strategies. Data linkage and machine learning projects can support service delivery organizations to mobilize and distribute community resources in support of ROORS. Digital phenotyping is an advancement in data linkage and machine learning projects, potentially leading to precision overdose responses. At the coalface, opioid overdose detection devices through fixed location or wearable sensors, improved connectivity, smartphone applications and drone-based emergency naloxone delivery all have a role in improving outcomes from opioid overdose. Data

driven technologies also have an important role in empowering community responses to opioid overdose.

Summary:

This review highlights the importance of technology applied to every aspect of ROORS. Key areas of development include the need to protect marginalized groups from algorithmic bias, a better understanding of individual overdose trajectories and new reversal agents and improved drug delivery methods.

Introduction

Opioid use disorder (OUD) is a globally impactful condition with significant mortality, morbidity, and economic impact (1). Worldwide, roughly 27 million people have OUD, and opioids accounts for two thirds of direct drug related deaths, mostly from fatal overdose(2) . Many more non-fatal versus fatal opioid overdoses occur (3), and multiple factors influence progression to fatality including opioid potency, polysubstance use including of sedatives such as benzodiazepines, and the availability of medications for opioid use disorder and rapid opioid overdose response systems (3,4). Individual characteristics which may predispose to an opioid overdose include an older age, associated co-morbid conditions such as respiratory or cardiovascular disease, solitary drug use and using an intravenous route of administration(5).

The rapid opioid overdose response system.

An opioid overdose is a time-sensitive medical emergency which relies heavily on an appropriate response from bystanders in the community (6). Following the identification of an opioid overdose, and the triggering of emergency services response, trained ambulance crews and/or clinicians can administer naloxone which is an opioid reversal agent(7). Unfortunately, inevitable delays in the arrival of emergency service responders results in a delay of the reversal of opioid related respiratory depression through naloxone administration, prolonged tissue anoxia, and poor outcomes including death (7). The rapid opioid overdose response system (ROORS) consists of recognition of an opioid overdose by a witness, initiation of basic life support and rapid provision of naloxone, activation of the emergency response system and emergency medical services assessment and aftercare (7,8) (Figure 1). An effective rapid opioid overdose response system has three main components (Figure 1):

1. A framework for implementation
2. A multi-stakeholder network to design and deliver the service.

3. The people witnessing and responding to an opioid overdose.

Rapid opioid overdose response system technologies.

A paradigm shift within healthcare towards the use of technologies such as big data analytics(3), artificial intelligence(1) and digital health interventions(6), and novel monitoring and detection methods (7) has increasingly influenced the development and delivery of ROORS. Big data analytics in healthcare describes the integration and analysis of large volumes of data from diverse sources such as electronic health records, biometric sensors, administrative datasets, results of clinical investigations, smartphone geolocation and social media interactions into actionable information (9).

Artificial intelligence (AI) is often needed to process and analyze these data due to the volume, complexity, and dynamic nature of healthcare data. The term AI has been coined to describe the technological reproduction, through advanced statistical and programming tools, of the creative, inductive, and reasoning capabilities of the human mind(8). Practical examples of AI include algorithms which use large, linked datasets to make and refine predictions around an issue of concern such as identifying individuals at risk of an opioid overdose or geographical areas in greater need of first responders(3). Table 1 defines some of the terms used in relation to big data analytics and artificial intelligence. This review explores the impact of these technologies on each of the three components of ROORS.

Technology supporting ROORS implementation through surveillance and intelligence.

The framework for ROORS implementation provides the foundational legislative and regulatory requirements determining naloxone availability and use, and public health intelligence to support appropriate policy and resource allocation.

Artificial intelligence-based modelling and simulation

Naloxone, an opioid reversal agent is a prescription only medication (10). Jurisdictions wishing to adopt ROORS have therefore needed to introduce legal exemptions to enable bystander administration and distribution of naloxone rescue kits. Exemptions include Good Samaritan Laws (GSL) which provide legal protection against arrest and liability for bystanders who administer naloxone when witnessing an overdose(11), and Naloxone Access Laws (NAL) which allow members of the public to possess, distribute and administer naloxone to people not directly related to them without legal repercussions(12). AI in data analytics provides advanced statistical techniques to examine large datasets and can provide an understanding of the potential implications of these laws. Several such statistical and modelling studies have been used to explore NAL and GSL to provide supporting evidence to policymakers (12–14). For example, Sabounchi et al. used a system dynamics modeling approach to examine the impact of GSL on overdose deaths, emergency department visits for overdose and behavioral changes of bystanders(15).

Several distribution models for naloxone rescue kits have been used to maximize the impact of this intervention in a cost-efficient way(16). Examples include through community-based services targeting at risk populations and their close networks, through over the counter or vending machine purchasing, peer distribution, or co-prescribing alongside opioid prescribing (16). Zang et al. carried out a spatial microsimulation model comparing different options and identified that distributing naloxone according to people who inject drugs according to geographic need was both the most cost-effective model but also most likely to reduce geospatial health inequality(17). Irvine et al., performed a counterfactual modelling study to guide policy makers in each US state on future naloxone rescue kit investment according to opioid epidemic type and optimum naloxone distribution model(16). The authors produced the first US wide estimate of naloxone need, highlighted that current naloxone access pathways and distribution models were underdeveloped and critically, included data on the toxicity of the illicit drug supply (16).

It is essential to understand the opioid crisis faced in many countries as a dynamic series of epidemics determined by the mix of substances used and their toxicity(4). The modelling studies mentioned earlier around NAL and GSL effectiveness have not tended to show consistent improvements in opioid related deaths in every jurisdiction prompting calls for more complex data driven models (12–14). Critical to this complexity must be an improved understanding of the substances implicated in each overdose death (4).

Wastewater based epidemiology.

Epidemiological surveillance of the drugs implicated in an opioid overdose is often incomplete as it relies on people who use illicit drugs presenting to healthcare settings and disclosing behavior which is usually actively criminalized. Understanding the toxicity of the substances underpinning opioid overdose hotspots is critical however, as evidence is growing of different epidemic “waves” which have included synthetic opioids such as fentanyl and piperidine-based analogues (18), increasing co-use of opioids and stimulants such as methamphetamine (19) and depressants such as xylazine, a non-opioid veterinary tranquilizer (20). In situations where the toxicity of a substance requires a higher dosage or is simply not reversible by naloxone, it is very likely that modelling studies will be inaccurate if robust drug surveillance data is absent.

Wastewater based epidemiology (WBE) allows for the sampling of the sewage of a defined area to detect and quantify drug metabolites using highly sensitive and specific methods such as liquid Chromatography with tandem mass spectrometry (21). WBE can be used as an early warning sentinel surveillance system by detecting the presence of new substances into an areas' drug supply which are of greater toxicity, compound the toxicity of the established opioid supply or are resistant to being reversed by naloxone (22). Further, communities with high opioid overdose rates, yet with WBE indicating low quantities of naloxone exposure may be effective sites for a targeted overdose education and naloxone distribution program(23).

Technology supporting ROORS design through metadata acquisition.

A challenge to ROORS providers is in obtaining accurate real-time data to make informed resource and service design decisions (4).

Data linkage and machine learning

Data linkage involves combining diverse sources and types of data which relate to the same person to create an enhanced, accessible data resource(24). Examples of data sources are electronic healthcare records, clinical investigations, administrative data, naloxone administration data from emergency services or law enforcement, accident and emergency attendances, opioid prescription records, socio-demographic information (25), spatial visualizations of the distance to naloxone distribution sites and other harm reduction services (26), and survival rates from an identified opioid overdose (27). Natural language processing, a form of machine learning which analyses free text and interprets it accurately and meaningfully, can support the robustness of coding of socio-demographic characteristics or risk factors relating to an opioid overdose when applied to healthcare records (28).

These enhanced data linked resources can then be analysed in several different ways in a variety of settings to provide the necessary community level intelligence to support ROORS delivery. Examples in the literature have included the use of data linked organisational tools to rapidly direct emergency services and community first responders to overdose hotspots and geolocation and time specific forecasts to ensure that communities are adequately resourced at time where there is most need (27). For example, through spatio-temporal data analysis using geographic information systems, machine learning, and AI, predictive models to identify neighbourhoods more likely to encounter opioid overdoses can be developed, supporting the appropriate redirection of ROORS resources (25). Another example is the Overdose Detection Mapping Application Program (ODMAP) which applies spatio-temporal data analysis to various connected first responder databases, giving ROORS providers and planners approximate real-time location data of suspected overdoses (29). Indeed, the efficacy of such data linkage projects in identifying communities of risk to support ROORS design is currently subject to a randomized, population-based, community intervention trial in the US (30).

Digital phenotyping and precision medicine

Digital phenotyping and precision medicine are new data linkage and machine learning based clinical paradigms with great potential within ROORS (31). Digital phenotyping involves large scale data-linkage from many of the connected devices discussed later in this review such as wearables and smartphones and data discussed above such as medical records and administrative data (32). By combining these data sources, digital phenotyping may enable a deeper understanding of real-time and real-life physiological changes and the social context of an individual’s experience of illness, potentially facilitating person specific interventions (27,32).

People who experience opioid overdoses are not a homogenous group and will not have the same clinical trajectories, responsiveness to naloxone or outcomes. So far, modelling studies relating to Naloxone initiatives do not account for this variability(18). Marsch et al., have designed a digital phenotyping study to understand the clinical trajectory of people in treatment for opioid use disorder which may be the template for future studies examining trajectories of opioid overdose victims(32). Participants will be prompted to report on their sleep, stress levels, pain severity, cravings, withdrawal, substance use risk context, mood, substance use and treatment adherence through smartphone prompts three times a day (called Ecological Momentary Assessment, EMA), alongside social media and geolocation data and physiological measurements using mobile sensors (32). It is hoped that AI approaches will produce predictions from this data to design interventions tailored to the person’s needs and physiology (32).

Technology supporting ROORS delivery.

Included here are technologies for detection and response to an opioid overdose, technologies which digitally facilitate community empowerment to act on opioid overdoses (33) and drone delivery of naloxone (34).

Fixed location opioid overdose detection devices.

These devices are attached to fixed points in a physically enclosed area such as a public washroom, a bedroom, or a drug consumption room. The physical space would be pre-defined as one with increased traffic of people like to experience an opioid overdose. Examples include the South End Clinic AntiMotion sensor and the Brave sensor which uses ultra-sensitive radar in public washrooms and sets off an alert to staff should there be a reduction of movement (presumed to be due to an overdose) (20,34). Wilson et al., recently conducted a pilot controlled environment comparative study comparing three fixed location passive infrared sensors against standard electrode montage and respiratory equipment polysomnography (PSG) to detect increased movements due to pain and opioid withdrawal symptoms or decreased movements associated with apneic events (35). This study found that ambient sensors were activated in only two of the 118 apnea episodes identified by PSG indicating current limitations of this technology in detecting opioid overdose associated respiratory depression (35).

Novel remote sensing methods are being actively evaluated, for example using active sonar transmission and detection via a mobile phone placed near the person at risk of overdose (7). The sonar waveforms are processed by cloud-based software to identify a reduction in chest wall movements corresponding to an opioid induced overdose, triggering an emergency response (7). Another system makes use computer vision whereby an analysis of sequential video frames and pixel intensity variation identifies a drop of chest wall movements signaling possible respiratory depression. Both these approaches, while viable currently, have moderate sensitivity and specificity and response time compared to other available options and so may need further development and research (7).

Wearable technology

Wearable technology has been evaluated as potential opioid detection or naloxone delivery devices since 2016 at least(20) with concerns around obtrusiveness, privacy, accuracy, the need to be connected via mobile internet or WIFI, the ability of users to keep devices secure or charged and motion artifact interference being key considerations (20). There are currently three commercially available wristwatch type devices which are functionally similar in what they do, detecting physiological measures such as locomotion, skin temperature and electrodermal activity, sending this data via a smartphone for analysis, and signalling a response to a nominated first responder where appropriate (20).

A proof-of-concept device which identifies physiological evidence of an opioid overdose and triggers the automated subdermal release of naloxone has been proposed and prototyped (36). Issues around such a product are that it requires implantation into the person’s tissues, reduces the degree of autonomy and control in terms of the extent of sedation someone may wish to experience before naloxone is administered, and the cost to deliver this technology at scale(36,37).

The development of novel composite nanomaterials and microstructures has enabled a paradigm shift in how we define wearable devices(38,39). Specifically, these materials have enabled the production of flexible and stretchable strain sensors which can measure chest wall movement, pulse, ECG or temperature and can be incorporated into clothing fibre or on a skin adhesive patch (38,39). Such materials introduce a level of unobtrusiveness in monitoring and high scalability owing to industry-comparable performance, low cost, and accessibility (38,39). The challenge of powering these devices is being actively addressed, including through stretchable fibre-shaped nanogenerators which can harvest human-body mechanical energy to produce a self-powered system (40).

Internet of things

Internet of things (IoT) is a relatively new conceptual paradigm describing the potential of internet connected computing devices contained in everyday objects and technologies, allowing regular data exchange (41). Indeed, the limitations of fixed location opioid overdose detection devices and wearable technologies mentioned above may be somewhat circumvented were there to be cross-validation between these different data sources to build a picture of the individuals health status in relation to overdose risk or occurrence (7,42,43). Verma et al., describe the potential of the IoT paradigm to increase the individuals' involvement in their health, heightened and more efficient health monitoring and response by service providers, connecting internet enabled devices such as clothing embedded sensors, other wearables, smart-beds, fixed location sensors, mobile phones and associated applications, and devices which may increasingly be embedded in or infrastructure as part of the smart city concept (43).

The potential of IoT is highly dependent on the increased worldwide implementation of the fifth-generation technology standard for broadband cellular networks (5G), with faster, more efficient, and greater capacity to accommodate new devices, services and while remaining cost neutral (43). As 5G becomes ubiquitous, devices will be able to remain connected with greater capacity for data exchange and privacy with lower energy expenditure (43). Security and ethical issues remain the greatest concern, with the possibilities of hackers holding personal health information hostage, or governments or private industry using data to undermine individual human rights.

The technology to detect opioid induced respiratory depression discussed here focusses on oxygen saturation, respiratory or heart rate measures. Singh et al., note that capnography, measuring ventilation by detecting exhaled CO2 volume via an infrared sensor, is more sensitive, specific and potentially enables a faster response time than the other sensors discussed here(7). Unfortunately, current options require expensive and uncomfortable specialized equipment limiting capnography as a viable, scalable community based overdose detection technology(7).

Smartphone applications

Smartphone applications are perhaps the commonest form of ROOST (20,44). Smartphones are a pre-requisite to the functionality of several other ROORS technologies, for example, in providing connectivity to wearable sensors, to collect EMA data, and geolocating individuals at risk of an opioid overdose (45). Specific to ROORS delivery, smartphone applications have been used to identify locations where naloxone is available, to provide training in the use of naloxone, and to link people who are at risk of an opioid overdose to volunteer community based first responders and emergency services (20,44,46).

Digital empowerment of community led overdose responses.

Empowered communities are at the core of successful ROORS delivery. Jayawardene et al., are investigating the feasibility of a network of trained (through online interactive and asynchronous modules) citizen responders to overdose events linked to emergency response services through a smartphone application (46). The key mechanism underpinning the effectiveness of this initiative does not lie in the technology, rather in the efforts used to mobilize communities through a shared identity and diversify recruitment through social media and community groups (46). A more targeted form of digital community empowerment is demonstrated by Claborn et al., in their development of an integrated dashboard to support local overdose responses (47). Such dashboards would bring together data from community-based harm reduction services such as overdose incidents, non-fatal overdoses and drug-checking results and help to direct peer to peer availability of naloxone rescue kits and harm reduction advice to where it is most needed (47). Collating this data on a shared digital platform, available to community organizations, people who use drugs, and embedding it within conventional ROORS may support more effective grassroots level responses while also filling critical data gaps that cannot be covered by statutory services (4,47).

Drone-based emergency naloxone delivery

Reducing the time for critical medications to reach the site of a medical emergency has been a longstanding focus of prehospital medicine research (34). Roberts et al., reviewed the current literature on the use of unmanned aerial vehicles, or drones to address a critical link in the chain of survival and found that this technology could significantly improve patient outcomes including for patients in need of naloxone to reverse an opioid overdose (34). As with most of the technologies discussed above however, real-world implementation will expose barriers and knowledge gaps which will need to be addressed, and ROORS will need to adapt accordingly to embed drone technology for it to reach its full potential (34).

Conclusion

We have summarized the ways in which technology is currently being used in planning and delivery of ROORS including new applications making use of cutting edge of technology. Ongoing developments which will contribute to the improvement of ROORS include addressing algorithmic bias reflecting societal prejudices permeating organizational and administrative systems and structures and systematically incomplete data which disadvantages marginalized groups (48)(. Extended use of digital phenotyping will enable a precision medicine approach to patients at risk of opioid overdose such that we are able to tailor the ROORS first responder approach according to the individual's co-morbidities and physiological status. Finally, our increased understanding of the "waves" of the opioid epidemic will support the development of new reversal agents and drug delivery systems which addresses powerful new synthetic opioids and co-consumed depressants and tranquillizers.

Key points:

- The rapid opioid overdose response system (ROORS) consists of recognition of an opioid overdose, the initiation of basic life support and rapid provision of naloxone, activation of the emergency response system and emergency medical services assessment and aftercare.
- Technologies such as big data analytics, machine learning and artificial intelligence, smartphone applications, and novel monitoring and detection methods have increasingly influenced the development and delivery of ROORS.
- Real-world implementation will expose barriers and knowledge gaps and ROORS will need to adapt accordingly to maximize the potential of these new technologies.
- Key areas of development include protecting against algorithmic bias, tailoring overdose responses to individual vulnerabilities and novel overdose reversal agents and delivery methods.

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(*) special interest and two bullets (**) outstanding interest.

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Table 1

Table 1. Definition of terms in relation to artificial intelligence and big data analytics.

Artificial intelligence	AI is a multidisciplinary field which uses science and engineering to develop machines capable of solving complex problems for which there is typically a need for human input.
Big data	Big data analytics is characterized by the integration and analysis of a large volume of heterogenous and complex data. Examples of the content within healthcare datasets which contribute to its enormous volume include electronic health records, clinical trial data, anthropometrics, demographics and socioeconomic information, lifestyle and clinical phenotyping (for example, diagnoses, medication use, medical imaging and procedure results).
Machine learning	Machine learning is statistical modelling driven by advanced complex data. It is a tool to automatically optimise multidimensional data to produce a predictive model which does not presuppose an a-priori hypothesis. In other words, it is the ability of a computer to learn without explicitly being programmed
Deep learning	Deep learning makes use of multiple unsupervised learning models, each of which identifies patterns from raw unlabelled data. The learning model is continuously refined to produce generalized representations of the data. These data are then fed into a predictive model to improve predictions a process called back propagation. Consequently, a DL model can evaluate and improve upon its own predictive accuracy with no human input at all.
Natural language processing	This refers to computer algorithms which can be trained to automatically and accurately categorise human free text input to reflect its intended meaning based on context or other language nuances. This can be useful for example when trying to determine features of opioid use disorder or to identify if someone is homeless based on free text clinical notes within an electronic health record as opposed to specific pre-determined codes.

Figure with legend black and white

Figure 1. Components of a Rapid Opioid Overdose Response System (ROORS)