REAL-WORLD EVIDENCE IN CLINICAL TRIALS

NOVEMBER 2020 **EXECUTIVE BRIEF**

Recent technological innovations have expanded the potential for the collection of real-world evidence (RWE) in clinical trials. Through patients' personal devices, fixed in-home sensors, or third-party wearable devices (e.g., Fitbit) and biological sensors, researchers can now collect ecologically valid data representing a wide array of constructs (e.g., geolocation, activity, sleep quality, air quality). Data collected in this manner can be less subjective than traditional patient reported outcome (PRO) measure completion. Operationally, incorporating RWE technology can reduce costs associated with clinical research by allowing for data collection standardization and the decentralization of trial management.[1] Such technologies are well tolerated by clinicians, hospital staff, and patients.[2,3] For example, patients participating in a clinical trial using smartphone geolocation to alert clinicians to emergency room visits reported increased reassurance regarding their care quality and access.[4] Clinicians and caregivers of individuals with Alzheimer's disease report overwhelming interest in wearables and sensors to facilitate care management and maintain patient safety.[2]

RWE technology has applications in a wide range of patient populations and clinical indications including cancer, cardiology, and diabetes. Through wearables and sensors, cancer researchers can gather real-time data representing biomarkers of patient health (e.g., blood pressure, glucose, weight, heart rate, fatigue) and quality of life (e.g., sleep quality, activity)[1,5]. Cardiology researchers can integrate 'smart', highly portable devices to facilitate remote conduct of critical clinical tests such as ECGs, reducing data loss and patient risk associated with missing clinical visits.[6] Recently, smart watches (e.g., Apple Watch, Fitbit) have shown promise as tools for proactively identifying abnormalities in heart function, such as atrial fibrillation.[7] Similarly, smart inhalers and insulin pumps can facilitate asthma and diabetes research, respectively.[8,9] A diverse selection of sensors and wearables now allows for precise, quantitative investigation of variables of interest in many clinical domains, such as sleep abnormalities, gait, speech, and environmental variables (e.g., air quality).[10]

SMARTPHONE RWE COLLECTION

Through Datacubed Health's Linkt app, researchers can easily and accurately collect passive RWE data using sensors embedded in a patient's own smartphone or a provisioned device. Linkt can automatically collect patient step counts and screen time; indicators of quality of life which may interest researchers in a range of clinical areas. More advanced geo-positioning data can be used to extract daily time spent walking, riding and bicycling while guarding patient privacy. Datacubed Health also has leveraged the standard on-phone accelerometry systems to provide precise measures of movement quality using the Linkt app (for example, gait abnormalities).

Datacubed Health also offers an advanced geofencing module. Unlike more invasive geolocation options, Datacubed Health's geofencing module stores patient location data only when patients cross a designated virtual boundary, known as a geofence (e.g., a boundary around a hospital or clinic). This mitigates ethical concerns associated with collecting and storing a large amount of patient location data. The Linkt system alerts study staff when a geofencing event occurs, facilitating clinical investigation of potential adverse events.

WEARABLES AND BIOSENSOR INTEGRATION

Datacubed Health has integrated a variety of medical-grade and consumer third-party wearables and biosensors. Using the RESTful API standard, data readouts from most of these devices are directly integrated into Datacubed Health's cloud server and databases, using fully automated data pushes. In many cases, SDK integration can be used to fully automate sensor set-up within the Linkt app, supporting the collection of RWE with minimal set up.

Datacubed Health has facilitated collection of RWE using wearables that represent a wide range of constructs, including heart rate, body temperature, sleep, skin conductivity, and activity. Linkt supports secure, mobile data collection with a diverse array of biosensors, including mobile electrocardiograms (ECGs), blood oxygen saturation and respiration rate monitors, smart scales, smart sharps containers, under-mattress sleep monitors, and air quality sensors in the home.

CASE STUDIES

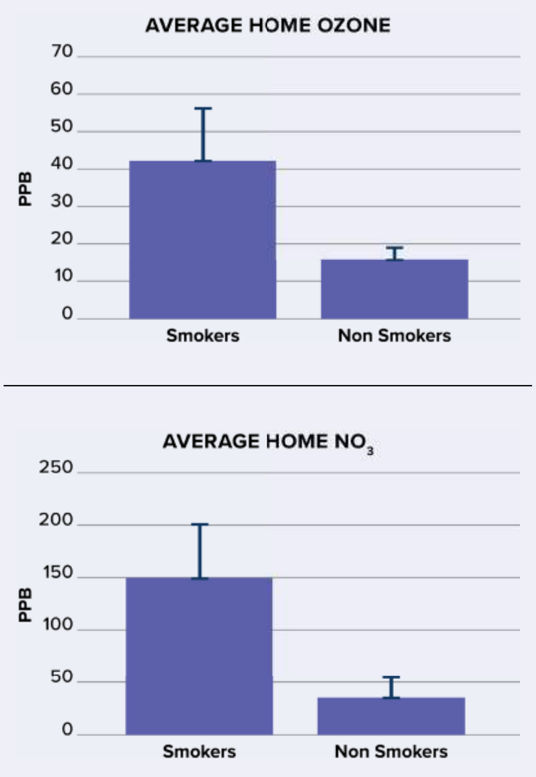
Below are two particularly powerful examples of Datacubed Health RWE integrations. Many other integrations are already available, including fitness trackers, smart scales, smart sharps containers and other medication adherence devices, as well as Bluetooth 'beacons' which can be used to determine time-in-bathroom or within-house movement, inexpensively. Dozens of new sensors are introduced each month. To accommodate this rapidly changing landscape, the Datacubed Health cloud has been designed for efficient connectivity with any RESTful, FHIR-capable, or Bluetooth-enabled device.

UHOO AIR QUALITY SENSOR

The uHoo external sensor provides a suite of environmental air quality measures (e.g., CO/CO2/O3 Concentration, Air Pressure, Humidity, Temperature, etc.), and after setup, transmits this data via Wi-Fi, to

FIGURE 1

Differences in Smoking vs Non-Smoking Home Ozone and NO3



Datacubed Health's database. In the data presented here, six volunteers, including three smokers and three non-smokers, installed uHoo sensors in their homes. The uHoo sensors identified elevated ozone and nitrate in the smokers' homes, relative to the non-smoker's homes, demonstrating the sensitivity of these sensors (Figure 1). Relative humidity data was used to determine the times at which participants bathed. CO data was used to identify the times at which participants were cooking. The PM2.5 data was used to identify when windows were opened and closed, and to evaluate indoor air quality in real-time. The potential applications for these data in clinical research and treatment of respiratory disorders (e.g., COPD, asthma) are manifold.

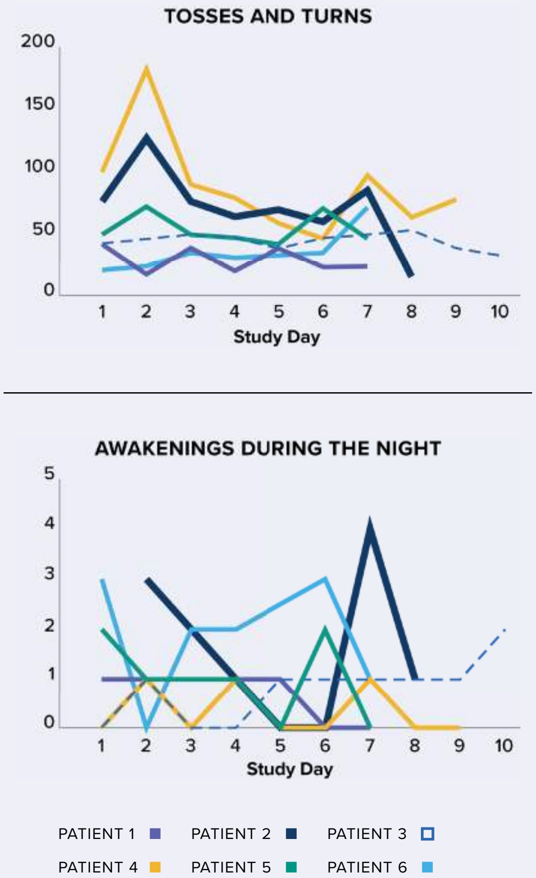
EMFIT QUANTIFIED SLEEP TRACKER

The Emfit device is a strip, fitted under the participants' mattress, that gathers motion-related variables specific to sleep quality (e.g., time asleep, bedtime, tosses and turns, REM sleep cycles), and more general physiological variables (heart rate and respiratory rate).

This data, captured in the Datacubed Health cloud, indicated that the Emfit device can be effectively used to gather RWE variables representing participant sleep quality, including number of bed exits and overall sleep quality. On the participant level, variable trends in these constructs were observed (Figure 2).

FIGURE 2

Participant Tosses and Turns, and Awakenings During the Night Over Time



CONCLUSIONS

Smartphones, wearables, and biosensors represent a profound opportunity for clinical researchers to gather real-world data that quantifies participant health, habits, treatment adherence, and overall quality of life. When used with Datacubed Health's Linkt platform, this data is gathered with minimal-to-no action required of participants, resulting in complete and accurate data, and maximum study retention and compliance. Wearable and biosensor integration with Linkt and the Datacubed Health cloud server via API, Bluetooth or, where appropriate, SDK, is seamless, easy, and secure. These sensors can even be used as minimally invasive approaches for generating case alerts associated with potential adverse events in clinical trials. Datacubed Health's robust tools for the collection of RWE data using smartphones, wearables, and biosensors, can maximize data completeness, participant retention and compliance, and researcher satisfaction while minimizing participant data security risk.

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