Selection and Implementation of Sensors and Wearable Devices for Use in Clinical Trials to Support Labelling Claims

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Introduction

Due to the increased miniaturization of sensors and circuitry, the health and wellness industry is seeing rapid proliferation in the number and diversity of wearable sensors and devices to provide personal wellness applications. This provides opportunity to collect greater and richer data during clinical trials and post-marketing studies to better understand intervention effects and to support labelling claims for new drug applications.

Selection of a sensor or wearable device to capture clinical endpoints in clinical trials that may support labelling claims requires the demonstration of evidence to support device selection and endpoint validity. This poster reviews criteria and associated evidence required to demonstrate optimal device selection including safety, suitability and feasibility based on recent recommendations by the Critical Path Institute’s Electronic Patient-Reported Outcome Consortium (ePRoC) and the Clinical Trials Transformation Initiative (CTTI). We illustrate a number of device features with reference to a blood glucose meter developed specifically for clinical research and contrast features important for trials in comparison with typical features of consumer devices. We present appropriate models for data acquisition in clinical trials. Finally, we explore the evidence needed to support device reliability, validity and usability to satisfy regulators in the robustness and validity of data collected, and approaches required to validate derived clinical endpoints generated from wearable data.

Study objectives

The sensor or wearable must measure a concept of interest as defined by the study protocol objectives. Clinical outcome measurement is a concept related to a concept of interest, which must represent a meaningful health aspect (see Figure 1, for example).

Device safety and suitability

Sufficiency of safety data should be available from the manufacturer including as applicable: mechanical, electrical, and biologiological engineering performance, such as fatigue, wear, tensile strength, and compression; electrical safety and electromagnetic compatibility; sterility; and stability/hall life.

Suitability/Usability

(a) Study design factors

This includes: consideration of wear/use interval with battery length and data storage capacity; wear locations supported; whether data collected should be visible to the patient; data acquisition methodology – is real-time monitoring required?

(b) Patient population considerations

Is the sensor or wearable acceptable to the patient population including: ease of use, wear location, wear interval, form factor and design, and operational instructions? Certain patient populations, for example, may find the wrist straps or belts provided by some devices too short (e.g., obese patients) or too long (e.g., gaunt older adults) to wear comfortably, and young people may be unwilling to wear a visible device if they feel it is unfashionable or may draw unwanted attention to them.

Sensor/wearable vendor characteristics

Access and control of source data is of vital importance. In particular, safeguarding that data collected and stored on the device or within a vendor cloud cannot be changed or modified from its original form. In addition, ensuring that device updates can be controlled to ensure data collected are consistent across the study. Vendor risk assessment should be performed to ensure data access can be maintained for the duration of the trial, and processes are in place to enable data access in the case of device withdrawal.

Feasibility

Small feasibility studies are important assessments that may help to identify and address unanticipated potential technology issues when used in the context of the specific trial.

Example: MyGlucoHealth meter

Display/Handset size

Usable across a broad range of patients.

Configurable firmware

Turn on and off features as required by the clinical protocol.

Time/Date control

Double time/date-editing and synchronise with central server.

Country approvals

High number of market approvals to meet global trial needs.

Figure 2: MyGlucoHealth Blood Glucose Meter

Device reliability and validity

Content validity

Ensuring that the device measures a meaningful aspect of the disease/condition or assessment from a patient’s perspective. The reliability and accuracy requirements of this measure are detailed below. Content validity may be given, or may require qualitative research involving the target patient population, a representative group, or other reporters to establish whether the clinical outcomes provided by the sensor or wearable are able to provide an appropriate measure of their intended concept of interest.

Intra-device and inter-device reliability

Devices must demonstrate suitable intra- and inter-device reliability through validation studies including test human subjects. In addition, to ensure reliability is maintained, the device manufacturer should follow a quality system to ensure appropriate equivalence between batches within the production process.

Concurrent (criterion-related) validity

Concurrent validity is important evidence that the clinical outcome measures produced by the sensor or device correlate well with another measurement approach regarded as a “gold standard” approach. This may, for example, include assessment of gap parameters from a triaxial accelerometer against a camera-based motion capture system. Concurrent validity provides evidence that the sensor or wearable is faithfully measuring what is intended. This evidence may need to be repeated in specific patient populations – for example gait pattern differences associated with certain disease indications, e.g., Parkinson’s disease.

Ability to detect change

Outcome assessments provided by wearable devices or sensors should, when used in a clinical trial, be seen to be sensitive enough to detect change when a change exists. This is normally demonstrated by controlled studies involving an intervention that is understood to cause a change in the outcome of interest.

Consumer devices: considerations

Consumer vs. Research-grade devices

Any device, whether consumer or research oriented, that meets the requirements for selection (device safety and suitability, and device reliability and validity) should be regarded suitable for use in a clinical trial to support labelling claims. However, some consumer devices may have properties making them unsuitable including: accuracy concerns, data privacy considerations, lack of control over firmware and software updates. However, consumer devices typically have superior form factors which may improve patient acceptance.

Marketing approval (e.g., FDA 510(k) / CE mark)

US market clearance or European market approval is not a pre-requisite for device selection in clinical trials. In many cases, devices can be imported to countries using an importation license waiving marketing approval in the case of clinical trials use.

Endpoint validity

Meaningful change

Meaningful change can be considered to represent the smallest difference in an endpoint measure that would be perceived by patients as beneficial. Ensuring that changes detected in a clinical endpoint are of a clinically relevant magnitude, in addition to reaching statistical significance, is of vital importance when endpoints are included in new drug applications and in support of labelling claims. Meaningful change can be represented as a minimally clinically important difference (MCID) in group means, or by the minimal individual change that distinguishes a responder (an individual exhibiting a meaningful improvement) from a non-responder. Estimating meaningful change, where unknown, can be achieved in Phase II trials by including a number of well understood anchor measures. Relating changes observed in the new endpoint to the degree of change understood to be meaningful in each anchor measure provides a means of providing interpretation around the new endpoint. In general, meaningful change may be different for different patient populations. See [3] for more details and examples.

Responsiveness

It is important to ensure that a clinical endpoint derived from sensor or wearable device can identify differences in outcomes over time in individuals or groups (similar to those in the clinical trial) who have changed with respect to the measurement concept.

Data acquisition

Data storage and transmission must be secure and encrypted. While in some cases data upload during site clinic visits is acceptable, there is a drive to increase our ability to remotely monitor trial participants outside scheduled appointments. Typically this is achieved via central acquisition of sensor/wearable data into the trial database, from where it can be reported and reviewed. Some devices operate via a vendor cloud database (Figure 3a) and data acquired by the study database via direct transfer – usually via available Application Programming Interfaces (APIs). Alternatively, APIs on the device itself may provide a means to directly access data via Bluetooth or Near Field Communication protocols (Figure 3b). In these cases, a study app may provide the means to transmit data to the trial database, and this app may also be used by the patient for other purposes – for example recording of patient reported outcome data throughout the study.

Discussion and conclusions

There is a growing interest in leveraging sensor and wearable devices to collect richer data to understand intervention effects in clinical trials. When data collected will support new drug applications and labelling claims, it is important to ensure that device safety and suitability and validity can be evidenced, and that meaningful change in new derived endpoints is understood.

References