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Measuring free-living physical activity in COPD patients: Deriving methodology standards for clinical trials through a review of research studies

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ABSTRACT

This article presents a review of the research literature to identify the methodology used and outcome measures derived in the use of accelerometers to measure free-living activity in patients with COPD. Using this and existing empirical validity evidence we further identify standards for use, and recommended clinical outcome measures from continuous accelerometer data to describe pertinent measures of sedentary behaviour and physical activity in this and similar patient populations. We provide measures of the strength of evidence to support our recommendations and identify areas requiring continued research. Our findings support the use of accelerometry in clinical trials to understand and measure treatment-related changes in free-living physical activity and sedentary behaviour in patient populations with limited activity.

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1. Introduction

Chronic obstructive pulmonary disease (COPD) is a chronic, poorly reversible respiratory disease characterised by airflow limitation and deterioration of lung function. According to The World Health Organisation, COPD affects around 64 million people globally and killed more than 3 million people in 2004 [1]. The total annual cost of COPD to the UK National Health Service is estimated to be over £800 million [2]. Respiratory symptoms of COPD include dyspnea, cough and production of sputum. Difficulty breathing can cause COPD patients to have reduced ability to exercise and perform routine activity such as standing up and walking.

Physical activity reduces the risk of many chronic diseases through a number of mechanisms including, for example, improved weight control, enhanced lipid profiles, improved glycaemic control and lower blood pressure [3]. Psychological effects of physical activity include reductions in stress, depression and anxiety [3]. Increased physical activity is also associated with improvements in quality of life [4]. In COPD, inactive patients are reported to exhibit worse exercise capacity, more dyspnea and a trend for worse functional status which can lead patients into a vicious cycle of increased dyspnea, exacerbations, deconditioning, declining lung function and mortality [5,6]. Increasing physical activity in COPD is associated with improved health outcomes including reductions in hospital admissions and respiratory mortality [7].

In clinical trials of COPD treatment, improvements in physical activity and mobility are important secondary outcomes and these are routinely estimated using in-clinic controlled assessments of exercise capacity such as treadmill tests and the six minute walking test (6MWT). In the 6MWT, the distance that a patient can walk in 6 min is recorded, using either a treadmill or an empty corridor circuit. This provides a controlled assessment of functional capacity [8]. For many reasons, 6MWT distance may not always relate to the amount of physical activity and the degree of mobility that the patient actually achieves in their daily living. For drug treatments that improve lung function in COPD patients, increased activity and mobility and the associated improvements in quality of life may be expected. This increased willingness and motivation to conduct discretionary non-essential tasks requiring levels of physical activity may be better measured in the home context using an activity monitor.

Despite this, there has been limited usage of activity monitors to measure physical activity endpoints in clinical drug development programmes for COPD and related indications. Reasons for this are likely due to a number of perceived barriers including: (i) regulatory acceptance of the validity of devices and the data management assumptions made; (ii) scientific understanding of the data recorded and how to derive meaningful summary outcome measures; and (iii) a lack of standards for implementing activity data collection in clinical trial protocols.

Research grade activity monitors retail from $200 to $300 per unit, prices that are not prohibitive within the budget of many pharmaceutical clinical trials. Overall numbers required may be reduced by recycling and re-using devices within an individual study. The logistics associated with device provision and management is a source of additional resource and expenditure when employing activity monitors in a global, multicentre clinical trial.

1.1. Regulatory acceptance

Miniaturisation of sensors and circuitry has enabled huge proliferation in the development and commercialisation of wearable and external monitoring devices in the areas of wellness and health. Examples include cardiac and ECG monitoring devices and sleep and activity monitors. Activity monitors and their associated apps and software are growing in popularity for those wanting to improve fitness or manage weight through regular exercise regimens. High accuracy and precision of these devices is less important in the personal health monitoring arena, yet vital in the area of clinical research if the data from these devices are to be used in the accurate characterisation of treatment related effects [9]. Not all commercial devices may have the degree of accuracy and precision that would warrant their use in clinical trials, but some manufacturers have invested significantly into the scientific validation of their devices and associated algorithms, and validation evidence has been published in peer reviewed journals. This provides good evidence of device validity, accuracy and precision that can support the use of such devices in clinical trials. This may be associated with European CE marking approval and/or US 510(k) approval as additional device quality credentials.

In addition to the ability of the device to accurately measure activity and mobility in terms of continuously recorded accelerometer data, regulators will be concerned with how the recorded data were cleaned and summarised, what assumptions were made in doing so, and the relevance of the outcome measures derived.

A growing number of commercial devices provide the raw accelerometry data, but all summarise raw signals into counts and/or estimates of energy expenditure such as METs and kcals. Firmware on the device is responsible for translating raw accelerations into these summary measures, and activity intensity thresholds (e.g. moderate, vigorous) and energy expenditure is then determined with reference to published doubly labelled water calibration curves or VO_2/HR regression lines. Usually the specific details of the preliminary data processing algorithms are contained within the device and proprietary to the device manufacturer and not disclosed. This firmware is also responsible for filtering noise out of the signal — for example routine vibrations picked up as small accelerations during motor vehicle travel. The extent of published validation work should provide a measure of confidence in the scientific validity of this firmware, although a growing number of accelerometers are beginning to provide access to the raw data enabling researchers to apply standard open algorithms to interpret the accelerometry signals.

Aside from this, regulators will have an interest in how valid data is identified amongst the continuous stream of data recorded. This will include, for example, reviewing the assumptions that were made to determine whether a period where no activity was recorded was due to lack of movement or due to removal of the device, and how missing data were dealt with — arising, for example, from periods of non-wear during a day, or missing days of data.

1.2. Scientific understanding of the data

Activity monitors provide a variety of variables associated with activity. For pedometers, the most basic measure is the number of steps over a period of time. The equivalent for accelerometers is the number of counts, which measure not just the presence of a movement but also the magnitude of force (acceleration) generated by movement. As indicated above, activity monitors also often use these to estimate energy expenditure in the form of kcals and METs.

There are many different ways in which continuous activity data can be summarised to create relevant summary statistics. As opposed to total counts/steps or total energy expenditure, increased mobility in