

# Can actigraphy outcome measures from existing clinical trials provide a framework for future?



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## Introduction:

The term “wearables” is now ubiquitous, generating a growing interest in the potential of this technology in Clinical trials. Questions remain around its clinical value and the logistics of integration into clinical trials. Not widely known is that “wearables” have been used in research to study sleep and activity patterns since the 1970’s<sup>1</sup>, to study clinical sleep and sleep disorder<sup>2</sup> and track activity levels, steps and energy expenditure in large community based studies<sup>3</sup>. Wearables that generate objective Sleep and Activity data have also been used in drug development trials for over 20 years<sup>4</sup>. The majority of those trials have used the term “Actigraphy”; a term not well known outside of sleep, activity and circadian rhythm research.

## Background:

This retrospective analysis is designed to determine if there is a commonality among the existing Actigraphy endpoints and study designs that could provide a framework for future clinical trials.

## Methods:

ClinicalTrials.gov, EU Clinical Trials Register and The International Standard Randomised Controlled Trial Number Register (ISRCTN) were filtered for Industry Sponsors and mined for the following words: “Actigraphy”, “Actimetry”, and the names of the most commonly known devices and manufacturers “Actiwatch<sup>®</sup>”, “Actigraph Motionwatch<sup>®</sup>”, “Motionlogger<sup>®</sup>”, “Bodymedia”, “GT3x<sup>®</sup>”, “Fitbit<sup>®</sup>”. Data from the resultant studies were compiled into a database and cleaned to remove duplication and anomalies. Each Trial protocol was examined to identify the following parameters: Therapeutic Area, Phase, Outcome Measure, Wear Time, Recording timeframe and Device Location. Where the data was not complete in the primary data source, trials summary data if available was used.

## Results:

This retrospective analysis is designed to determine if there is a commonality among the existing Actigraphy endpoints and study designs that could provide a framework for future clinical trials.

### Therapeutic Areas Where Actigraphy was used:

- 80% of the trials were of the Central Nervous system (CNS)
- Sleep Disorder accounted for the majority of these trials followed by Pain, Alzheimer’s and Depression (Figure 1).

### Endpoints and Outcome Measures.

- Actigraphy data was used predominantly to generate primary and secondary endpoints (34% and 46% respectively) (Table 1) with only a small portion of the data being collected (2%) generating exploratory endpoints.
- 8% of the data generated by Actigraphy was used to qualify subjects as part of Inclusion and Exclusion criteria and used to verify the required sleeping, activity or Periodic Leg Movement (PLM) pattern.
- Sleep endpoints are most common. (Figure 2). However of those trials 42% used very non-specific terms such as “Actigraphy Data” or “Sleep” (Table 2). The remaining studies used either 1 specific endpoint such as Total Sleep Time or a combination of the Sleep parameters that are generated by Actigraphy devices such as Wake After Sleep Onset, Sleep Efficiency and Number of awakenings. A similar patterns emerged from the Activity endpoints with 66% using non-specific terms such as “Activity”, and those that were defined used either a single endpoints such as “Steps” or a combination of endpoints such as “Activity counts and Steps” (Table 2).

### Device Location, Wear time and Recording Timeframe:

- Only a third of trials identified the wear position of the device.
- 47% of trials recorded wear time, the majority of Psychiatric trials gathered Actigraphy data for more than 1 week (Figure 3). Restless Leg Syndrome (RLS)/PLM trials were analysed separately, as the nature of the disease determines that the devices are worn for discrete periods when the Periodic Leg Movement occurs.
- 22% of trials had incomplete or no data regarding the timeframe over which the devices were worn. However trends did emerge from the remaining data and the majority of the trials (52%) gathered data at baseline (screening, randomization or other time-point in the trial) (Figure 4) which was used as comparator with data gathering following therapeutic intervention, the remaining trials (26%) gathered data at discrete points with no reference to pre or post intervention. trials summary data if available was used.

## Conclusions

This analysis has shown that Wearables (Actigraphy) have been used for 20 years in Pharma sponsored trials. The majority of these trials are in the CNS therapeutic area and have been used to generate Primary and Secondary endpoints. The use of Actigraphy in this area is supported by a strong body of academic research articulating the value of this data in generating clinically relevant endpoints for Sleep<sup>2</sup>, Alzheimer’s disease<sup>4</sup> Pain<sup>5</sup> and Depression<sup>6</sup>.

There are significant gaps in the data which impedes definitive conclusions regarding device location, wear time and recording timeframes and precise endpoints that have clinical relevance. However the available data suggests that in the Psychiatric area wear time should be greater than 1 week and most trials collect activity and sleep data prior to and post intervention.

The use of non-specific terminology to describe the clinical endpoints diminishes the value of the published protocols in identifying the discrete endpoints that have clinical value.

Clinical Trial registries are a good though not complete source of data and can be used to help craft future trial protocols. In order for these data sources to be truly valuable and facilitate the greater use of wearables within clinical trials, conventions should be adopted around nomenclature of the technology, device location, wear time and trial design.

Table 1: Outcome Measures

Outcome Measure	Number of Trials
Primary	20
Secondary	38
Primary and Secondary	11
Primary and Inclusion	4
Primary and Exclusion	1
Inclusion	3
Exclusion	1
Exploratory	2
Translation Research	1
Other outcome measures	1
Safety Evaluation	1
Not stated	7
Total Number of Trials	90

Figure 1: Number of Trials per CNS Therapeutic Area

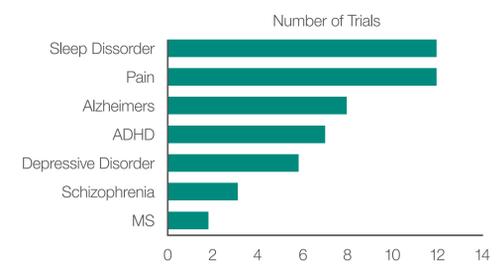


Figure 2: Actigraphy Endpoints used in Clinical Trials



Table 2 Sleep, Activity and PLM Endpoints used in Clinical Trials

Outcome Measure	Sleep Endpoints	Activity Endpoints	PLM Endpoints
Non-Specific Term	17	10	2
1 Parameter	9	4	10
>1 Parameter	15	4	1

Figure 3: Device Wear Time by Therapeutic area

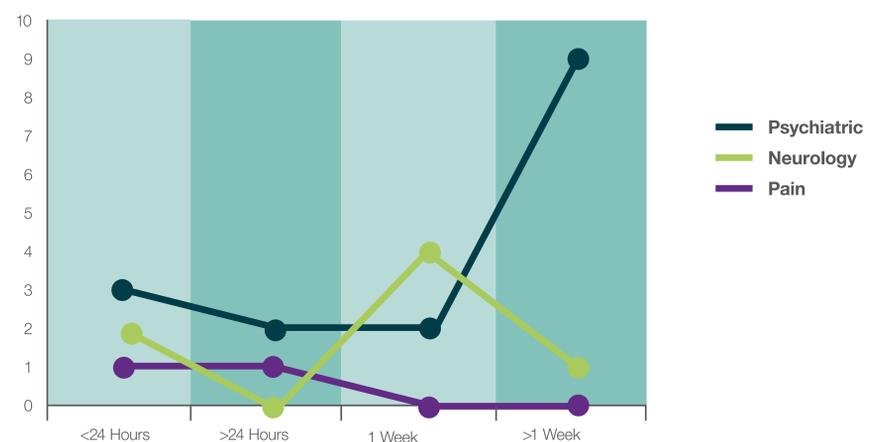
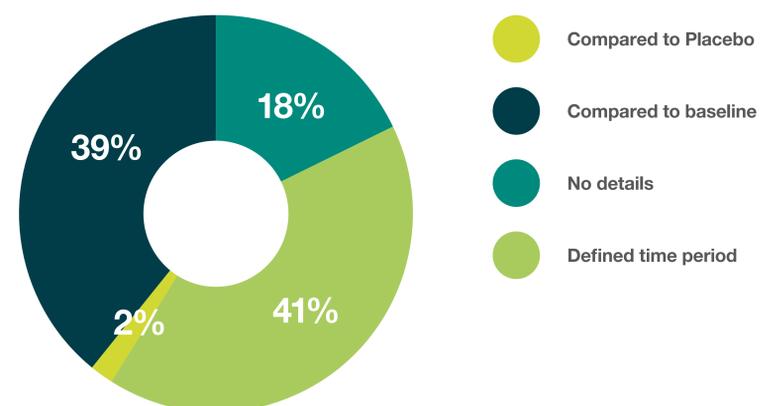


Figure 4: Recording Timeframe



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