

Early experiences using SDTM to organize clinical data collected using a physical activity tracker



PHUSE EU CONNECT 2019
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Introduction

- Real World Evidence provides improved insight
- Wearable technologies play a growing role in clinical trials
- We can pursue more readily useful endpoints
- One application is to investigate the physical activity level

- However, it is not clear how to incorporate device data in clinical trials

Select the device

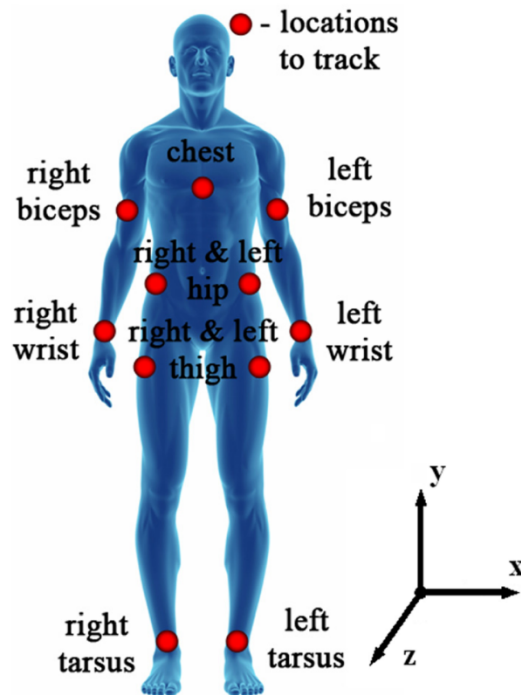
- Consumer grade devices
 - Apple Watch, Fitbit, Garmin etc.
 - Proprietary algorithms
 - Data transparency low
 - Data validity unknown
- Research grade devices
 - Digiwalker, Actigraph, Omron etc.
 - Publicly available algorithms
 - Data transparency high
 - Data validity can be documented

Other things to consider:

- FDA classified (Class I, II or III)
- Sufficient battery life
- Simple design, robust, waterproof
- Continuous data upload to cloud

The Anatomical Wear Location

- Wrist
- Hip
- Ankle
- Thigh
- Lower back
- Biceps



The Anatomical Wear Location



Wrist placement

- !! Current algorithms less mature
- ✓ Reported non-wear lower
- ✓ Enhances wear compliance
- ✓ Wear comfort is high

Hip placement

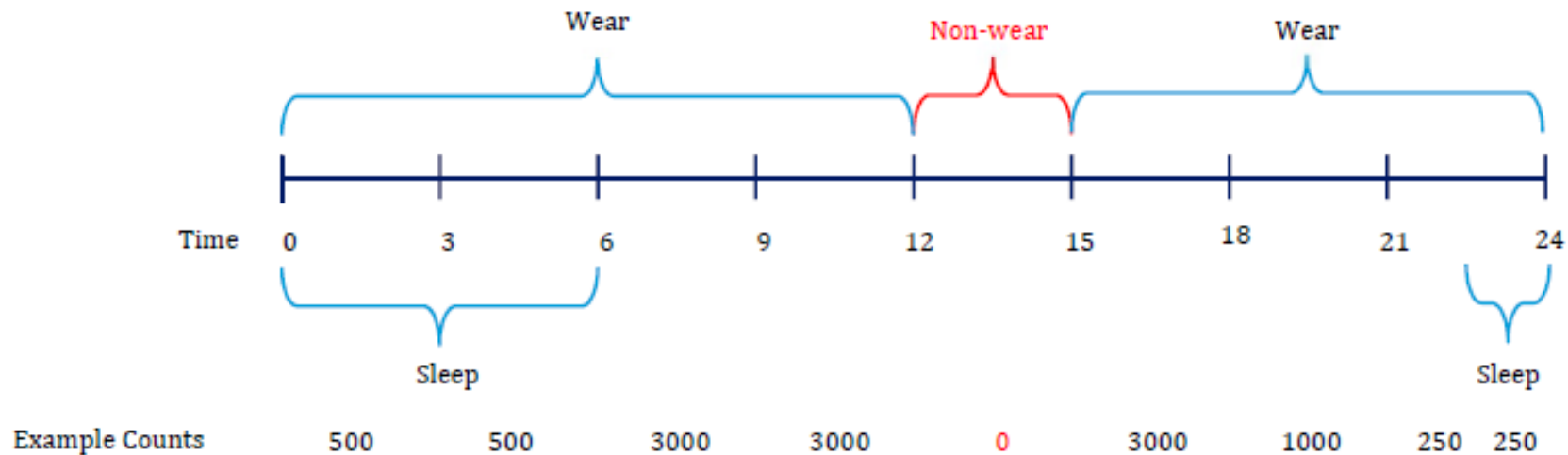
- ✓ Current algorithms more mature
- ✓ Near center of gravity
- !! Reported non-wear higher
- !! Patient burden higher



Which anatomical location is considered valid in a submission?

Non-Wear and Sleep

A normal day...



Non-Wear

- Non-wear are periods during a day where the subject is not wearing the device
- In real life subjects will take the device off during a trial
- Zero activity is recorded during this period although the subject likely did some activity
- It follows that any non-wear during waking hours will underestimate the total daily activity level

Approaches to handle non-wear

- Ignore it
- Extrapolate the activity pattern from the other part of the day
- Extrapolate the activity pattern from other similar days (time-specific imputation)
 - Multiply with the same number of hours for all subjects
 - Multiply with the number of waking hours
- Only accept days having very high wear time
- Report the data as percentage of wear time

How is non-wear handled in the best way?

Sleep

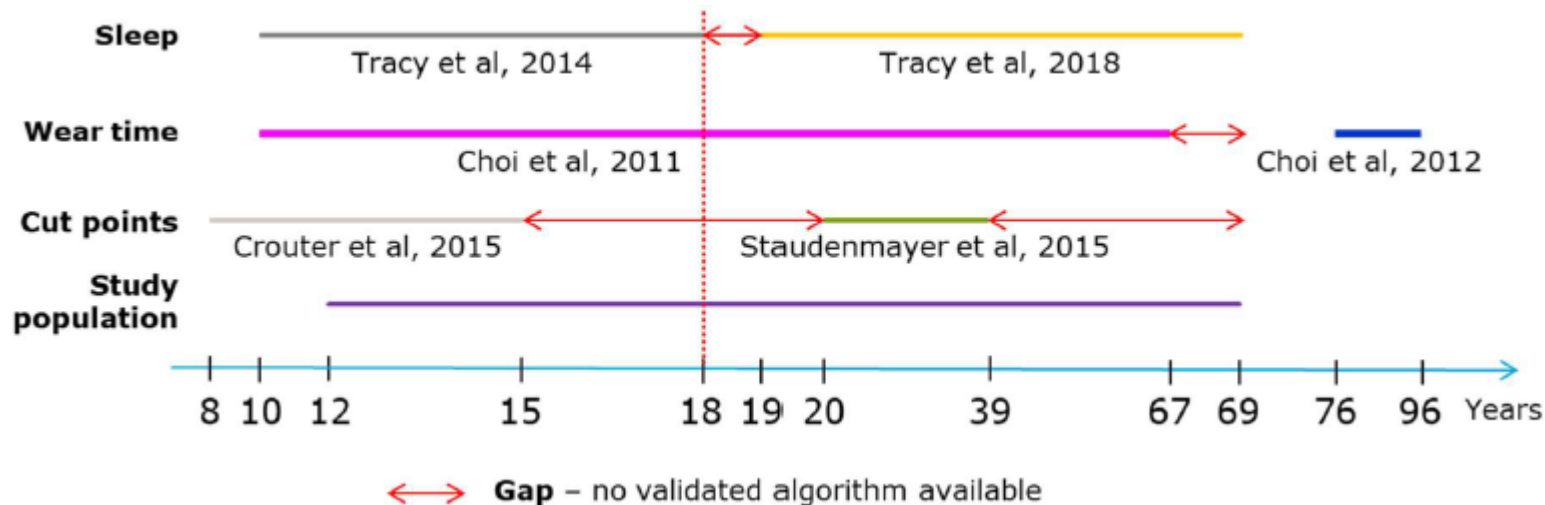
- If physical activity is the focus, sleep would usually be excluded
- Sleep can be excluded manually or automatically using:
 - Individualised time filters
 - Standard time filters

Challenge:

- Sleep, sedentary activity and non-wear looks similar
- Classification of awake sedentary time and movement during sleep is difficult

How is sleep handled in the analysis?

Availability of Fit-For-Purpose Algorithms



These algorithms have not been validated in the full age range. Is the data output considered valid in a submission?

When is an algorithm validated, and when is it good quality?

A step...

Easy and intuitive to understand, and often used...

...or is it:



step [step]

noun



- 1 a movement made by lifting the foot and setting it down again in a new position, accompanied by a shifting of the weight of the body in the direction of the new position, as in walking, running, or dancing.

Some challenges with steps

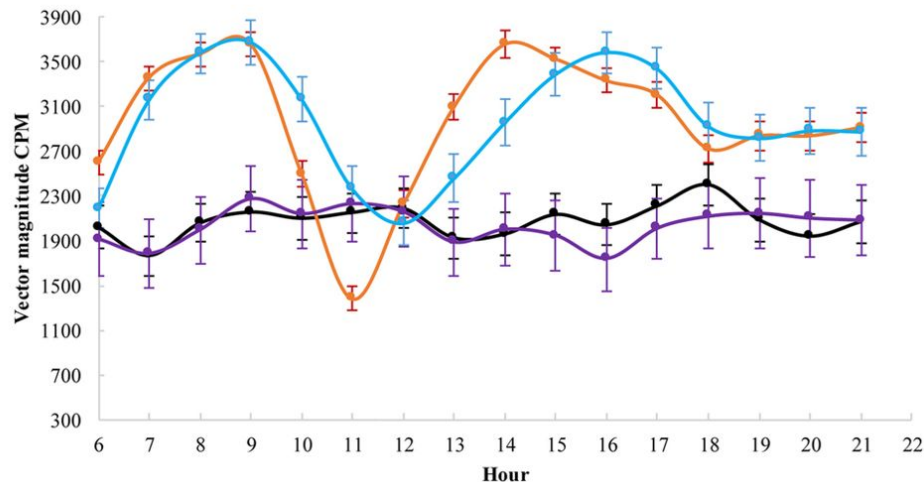
- What is a step exactly?
- Difficult to measure on the wrist
- Prone to type 1 error
- Activity and gait pattern different between children and adults
- Very few validations done in free-living conditions
- An algorithm validated on all criteria (age, anatomical location, population and the endpoint steps) can still be inaccurate

Several “validated” step algorithms exist. Arguably none of them are accurate in a free-living environment

Data granularity

- The collection of minute level data is challenging on many aspects

- Data volume
- Processing time
- Submission
- ...



Johansson, E. *et al.* Physical activity in young children and their parents—An Early STOPP Sweden—China comparison study. *Sci. Rep.* **6**, 29595; doi: 10.1038/srep29595 (2016)

- But scaling up the data granularity, could potentially mask interesting patterns hidden in the data

- All collected data must be tabulated in SDTM format
 - About 300 subjects enrolled
 - 12 Weeks (>120.000 Minutes)
 - 25 Derived parameters
- } >800.000.000 records
>200 gb



SDTM domains selection

USUBJID	XAGRPID	XATESTCD	XAORRES	XAORRESU	XADTC
NNXXXX-YYYYY/123456	86	AC11WEAR	Y		2019-07-25T14:12
NNXXXX-YYYYY/123456	86	AT14SLA	N		2019-07-25T14:12
NNXXXX-YYYYY/123456	86	AT18SLAD	N		2019-07-25T14:12
NNXXXX-YYYYY/123456	86	S15ADLI	30	sec	2019-07-25T14:12
NNXXXX-YYYYY/123456	86	S15ADMO	30	sec	2019-07-25T14:12

XA

USUBJID	SPEVID	DXLAT	DXSTDTC	DXENDTC
NNXXXX-YYYYY/123456	XYZ1A37180280	RIGHT	2019-05-28T16:22	2019-09-24T10:11

DX

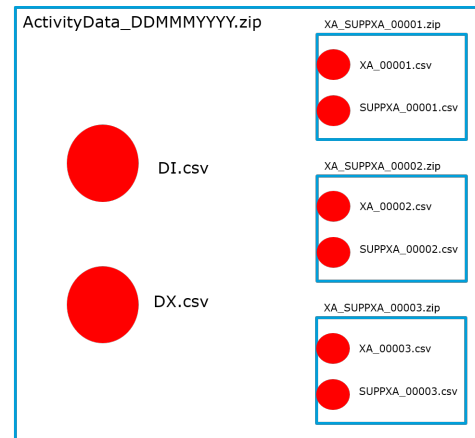
SUPPXA

USUBJID	IDVARVAL	QNAM	QVAL
NNXXXX-YYYYY/123456	86	UTCDATTM	2019-02-28T21:22Z
NNXXXX-YYYYY/123456	86	TIMEZONE	America/New_York

DI

SPDEVID	DIPARMCD	DIVAL
XYZ1A37180280	TYPE	Kinesiology Ambulatory Recorder
XYZ1A37180280	MANUF	Provider Name
XYZ1A37180280	MODEL	XYZ01
XYZ1A37180280	SERIAL	XYZ1A37180280
XYZ1A37180280	FDAUDI	FDAUDI Number

- XA – DX
- XA – SUPPXA (UTC Datetime)
- DX – DI (SPDEVID)



Parameters categorisation

Number of TESTCD's	ALGORITHM	ENDPOINT	ADOLESCENTS	ADULTS	SEDENTARY	LIGHT	MODERATE	VIGOROUS
1	CHOI 2011	WEAR						
4	AXIS COUNTS	ACTIVITY						
2	TRACY 2014/2018	SLEEP						
2	UWF STEPS	ACTIVITY						
6	STAUDENMAYER 2015	ACTIVITY						
5	VA CROUTER 2015	ACTIVITY						
5	VM CROUTER 2015	ACTIVITY						

XATEST

XACAT

XASCAT

Relevance of SDTM variables

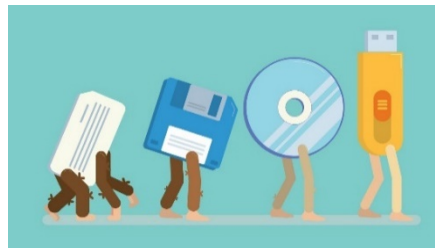
- Preset variables
- Duplicated variables
- Probably unnecessary variables



STUDYID	USUBJID		XASTAT
DOMAIN	XAGRPID		XAREASND
	XATESTCD	XATEST XACAT XASCAT	XABLFL
	XAORRES	XASTRESN XASTRESC	ELEMENT
	XAORRESU	XASTRESU	ETCD
	XADTC		EPOCH
			XADY

Questions

- Which anatomical location is considered valid in a submission?
- How is non-wear and sleep handled in the best way?
- When is an algorithm validated, and when is it good quality?
- Are all expected variables in SDTM necessary in activity data?
- Will alternative naming conventions for split domains be considered valid in a submission?
- Is SDTM following the evolution of the data?



Conclusions

- Wearable medical devices have a great potential
- Work still needs to be done to solve challenges on data collection
- Uncertainty on submission
- Building awareness, kickstarting discussion



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Thank you for the attention