Assessment of Physical Activity and relation to Diabetes traits

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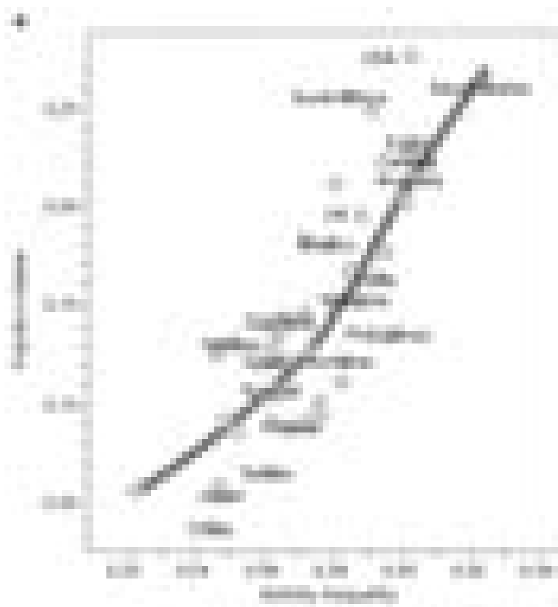
Smartphone-measures of physical activity

Large-scale physical activity data reveal worldwide activity inequality

N = 717,000 (68M person-days)
App counts steps (iPhone users)



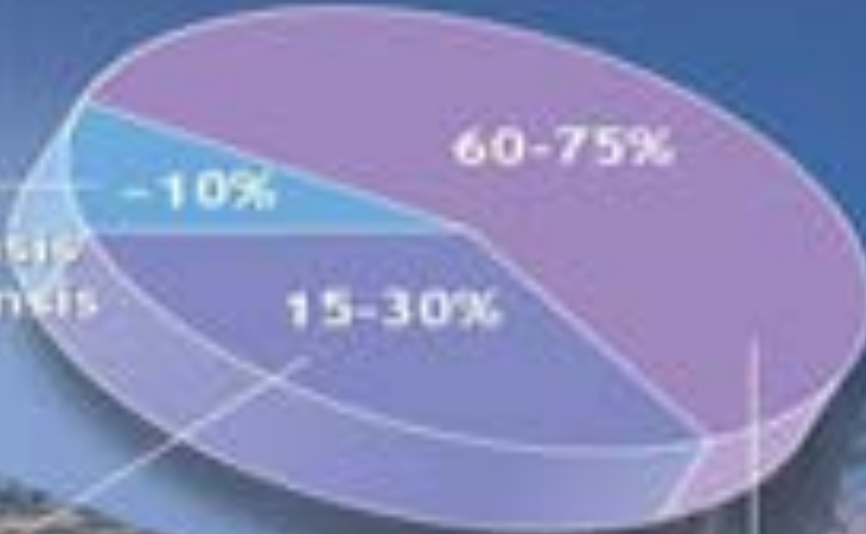
- Big Data = epi ?
- Reliability ?
- Validity ?
- Within-person selection bias ?
- Sample selection bias ?

Althoff et al, Nature 2017

Total Daily Energy Expenditure

Thermic effect of feeding
(Food intake; cold stress; thermogenic drugs)

- Obligatory thermogensis
- Facultative thermogenesis



Thermic effect of physical activity
(Duration and intensity)

- In occupation
- In home
- In sport and recreation

Resting metabolic rate
(Fat-free body mass; Gender; thyroid hormones; protein turnover)

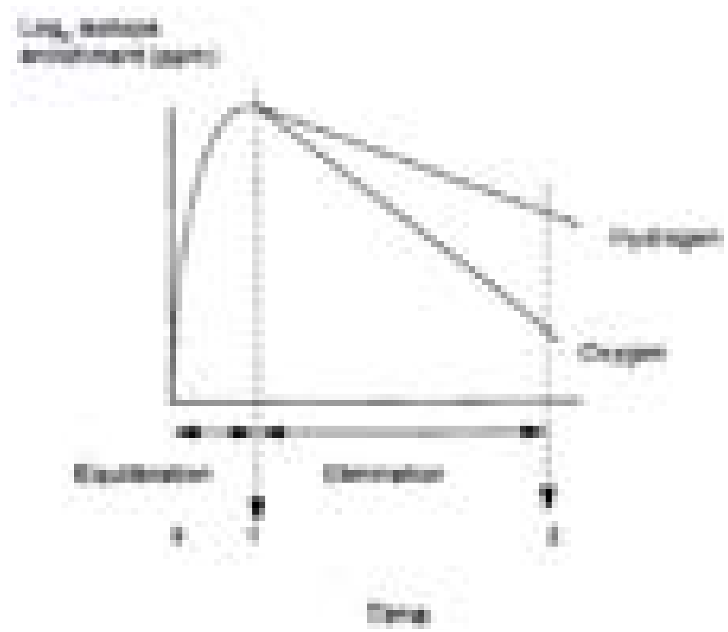
- Sleeping metabolism
- Basal metabolism
- Arousal metabolism

The Doubly Labelled Water (DLW) Method

Gold standard for assessment of TEE in real-life situations

Principle:

- Stable isotopes (^{2}H and ^{18}O) are drunk as water
- Equilibrate with body water (after several hours)
- ^{2}H is eliminated from the body as water
- ^{18}O is eliminated both as water and as CO_2
- The difference in elimination rates provides a **measure of CO_2 production** and therefore of TEE (over 10-14 days)
- No information on patterns, eg. intensity
- ~750 GBP per measurement (adults)



(Adopted from Speakman, 1998)

Dimensions of physical activity

- **Type**

  - The type or mode of activity refers to the different specific activities a person is engaged in (e.g. standing, walking, cycling, load bearing, etc)
- **Frequency**

  - Number of activity bouts during a specific time period
- **Duration**

  - Time (sec, min, hours) of participation in a single bout of activity
- **Intensity**

  - The physiological or biomechanical effort per unit time associated with participating in a specific type of activity
- **Volume**

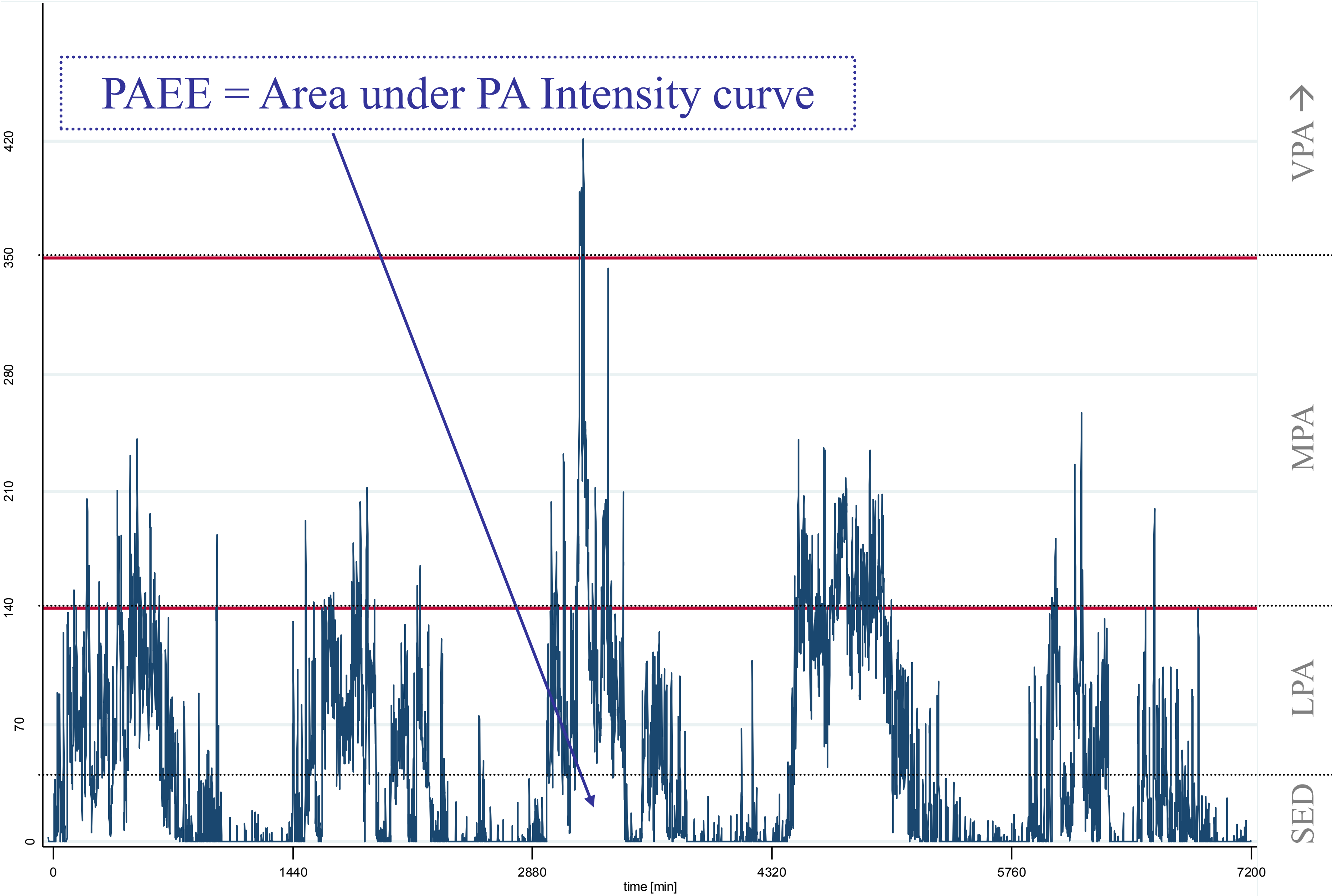
  - The integrated product of the above!
- **Domains / settings**

  - Leisure / occupational / transport

  - Social context (alone / with peers / with others)

  - Spatial (in-doors or out, green space, perceived safe, etc.)

Intensity time-series during free-living



Methodologies

Subjective (individual):

- Interviews
- Questionnaires
- Diaries / activity logs
- Proxy-reports
- And... _______________ ?

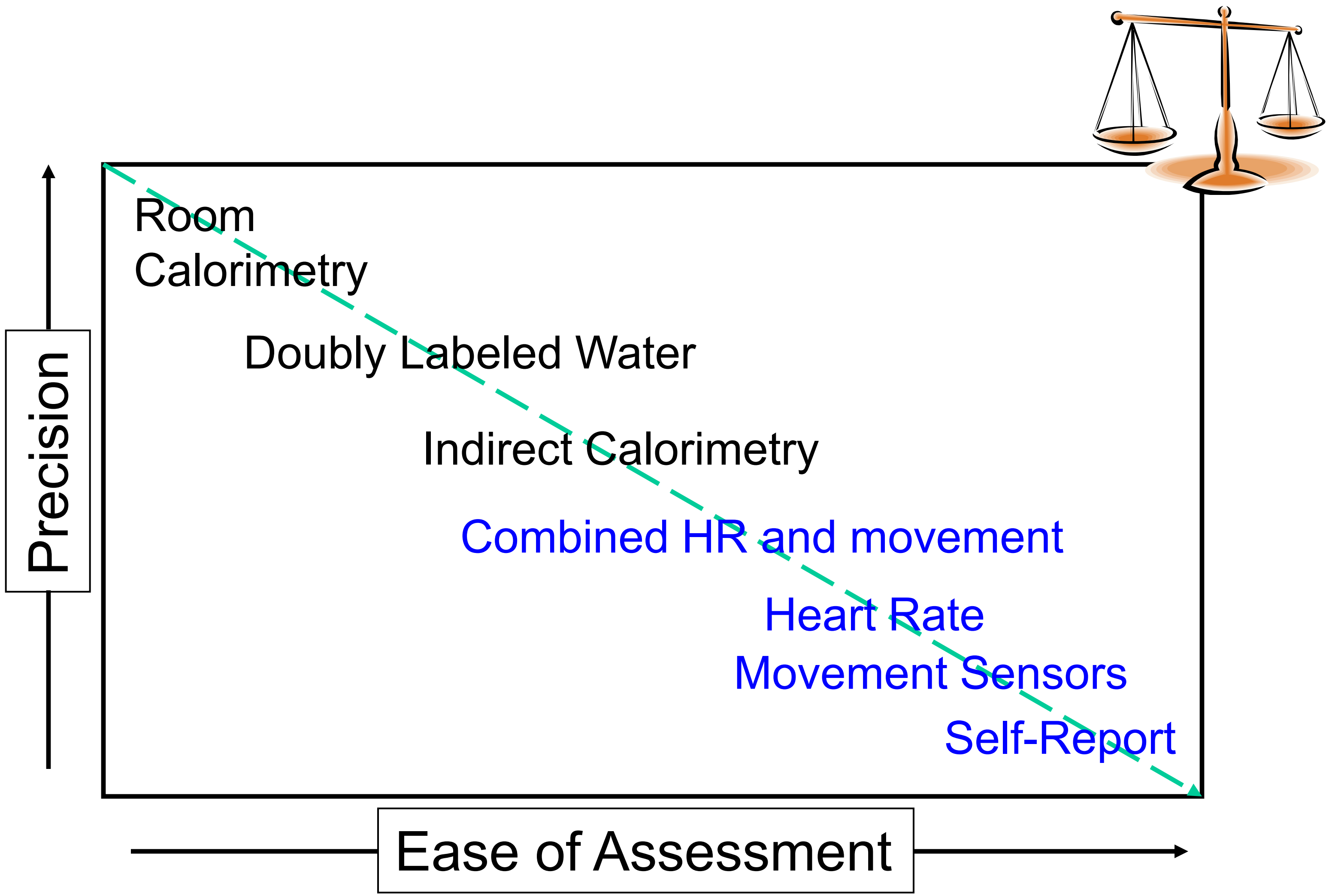
Non-individual:

- # cars / household
- # bikes / university
- ‘CCTV walk density’
- Google Street View
- Proximity sensors
- And...____________ ?

Objective (individual):

- Direct observation
- Pedometry
- Accelerometry
- Gyroscopy
- Heart rate monitoring
- GPS, other location systems
- Galvanic skin response
- Heat flux
- Doubly-labeled Water
- VO2 / VCO2
- Calorimetry
- “Smartphone apps”
- And...____________________ ?

Measuring Physical Activity: Validity vs feasibility



Methodological advances shifts the balance

A Volunteer Sitting with His Arms in Saline-Filled Tubs with Wires Connected to Einthoven's Electrocardiograph.

MRC | Medical Research Council

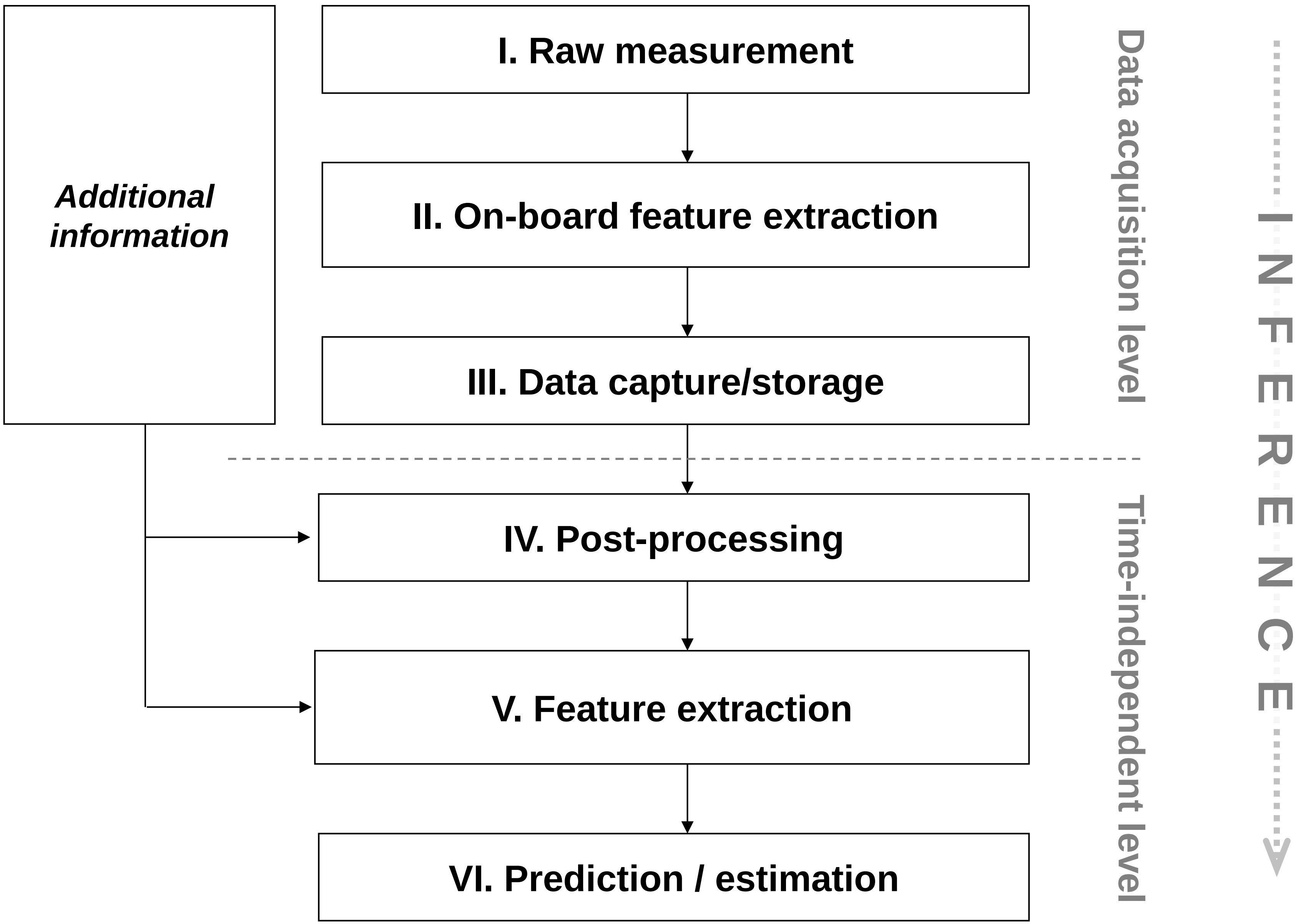
Method: Measurement + Inference = Estimate

Measurement method		Measured signal		Estimate
Room Calorimetry	→	Heat (or CO_2 and VO_2)	→	TEE → PAEE
Doubly Labeled Water	→	CO_2	→	TEE → PAEE
Indirect Calorimetry	→	CO_2 and VO_2	→	TEE → PAEE
Accelerometry	→	Acceleration	→	(counts) → PAEE
Heart Rate Monitoring	→	ECG, HR	→	PAEE
Self-Report	→	Memory! (time in behavior)	→	PAEE

Validity is determined by…

- *what is being measured*
- *what is being estimated and how*

"Inference is everything"

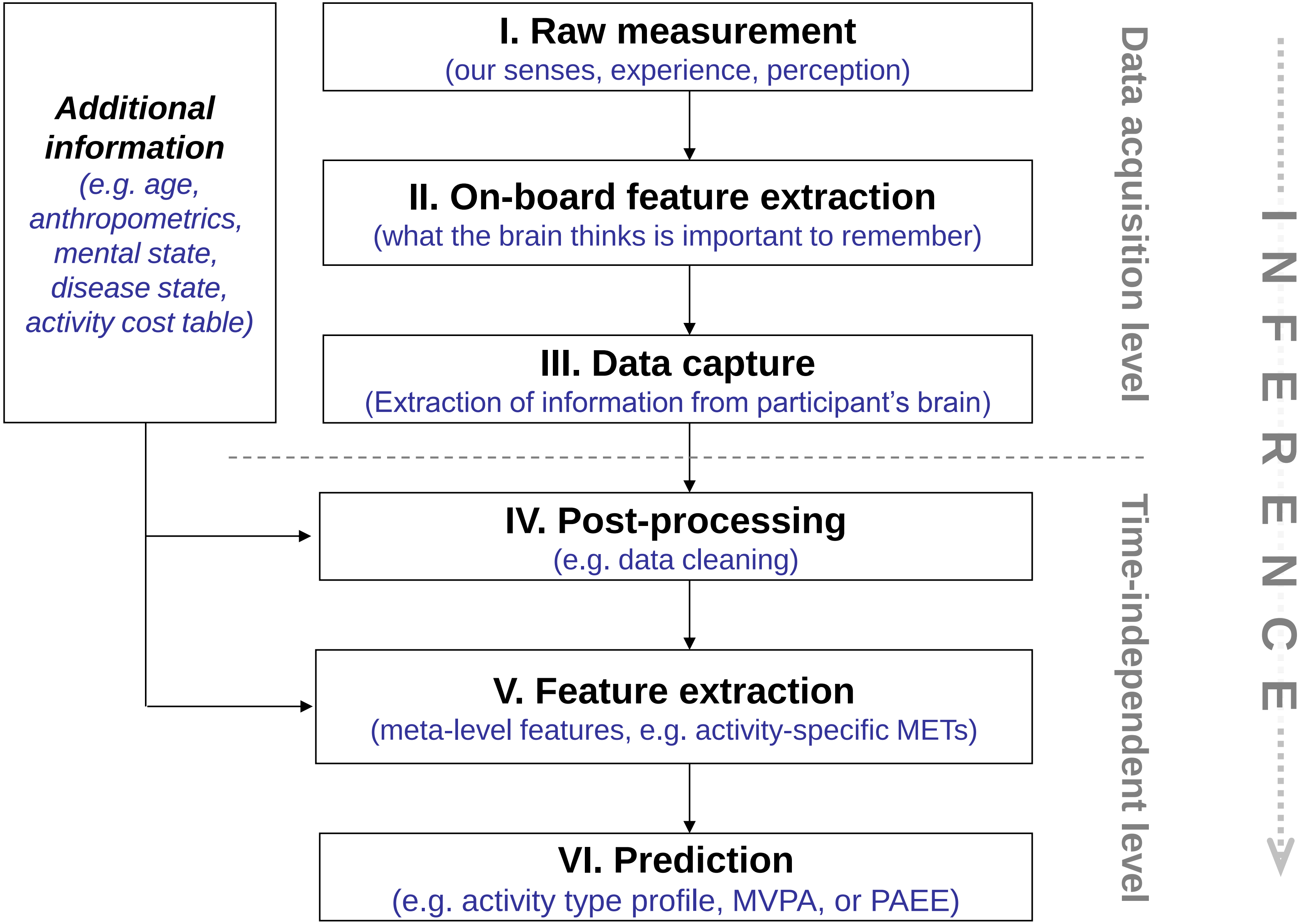


Adapted from: Corder et al, J Appl Phys 2008

Questionnaires

- Subjective measure of activity
- Relies on the *responses* from the person under investigation
- Time frame: 24-hr recall, week(s), 1 year, lifetime
- Self administered or interview based

- *Typical summary estimates:*
  - PAEE (total and by domain)
  - Time spent in intensity categories
  - Time spent in specific activities



Adapted from: Corder et al, J Appl Phys 2008

Computation of estimates of physical activity EE from questionnaires

Frequency x Duration x Intensity x Body weight

2 events/week x 1.5 hr/event x 6 METs x 70 kg

Time
3 hr/week

Energy expended
18 MET-hr/week (18 kcal/kg/week)

Energy expended
1260 kcal/week

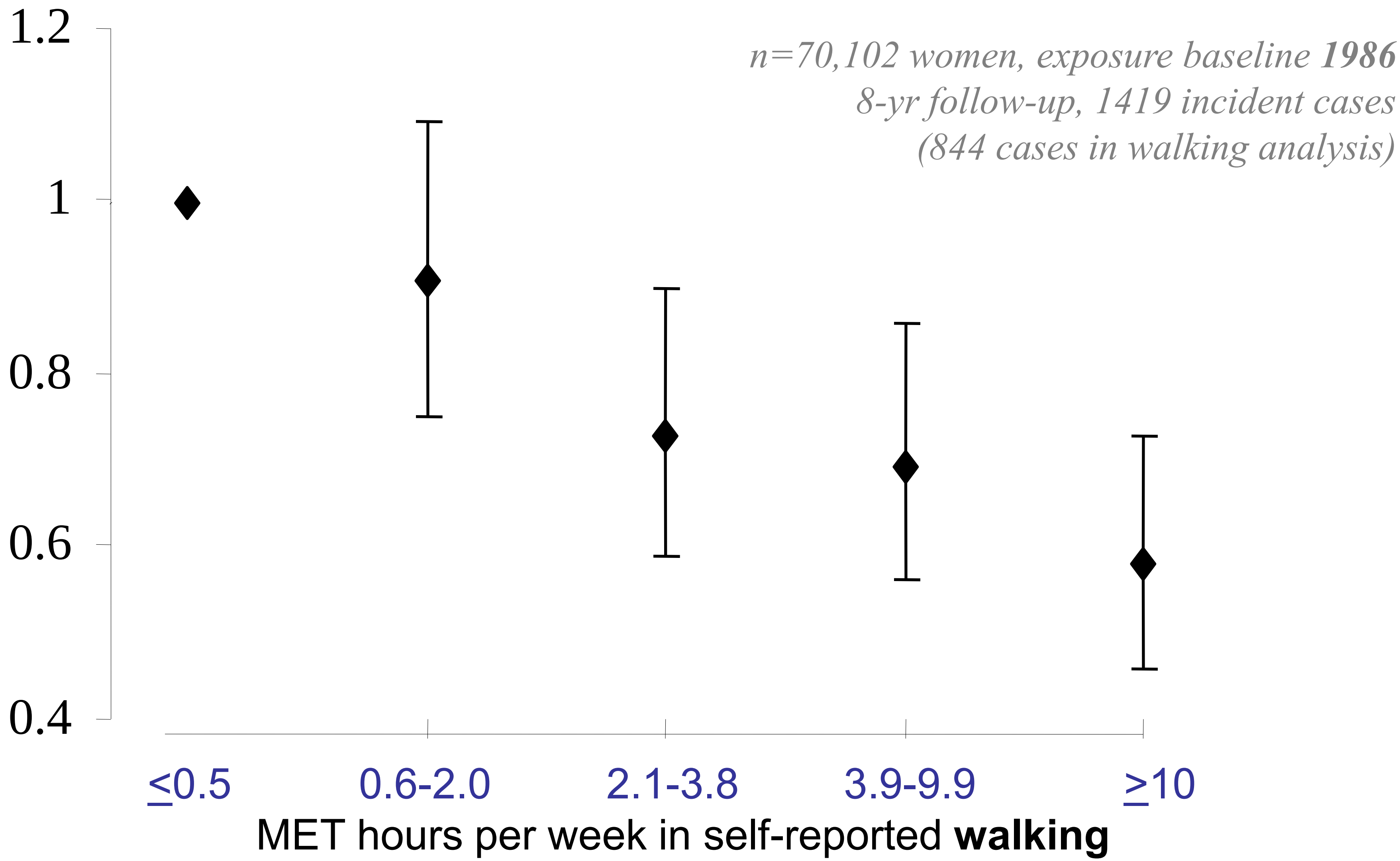
Physical activity and incidence of NIDDM
Nurses' Health Study

Vigorous activity *(episodes per week)*	RR *age adjusted*	RR *age & BMI adjusted*
0	1	1
1	0.74 (0.60-0.91)	0.89 (0.72-1.11)
2	0.55 (0.44-0.68)	0.71 (0.56-0.89)
3	0.73 (0.59-0.90)	0.93 (0.73-1.16)
4+	0.63 (0.53-0.75)	0.86 (0.71-1.04)
at least once weekly	0.67 (0.60-0.75)	0.84 (0.75-0.95)

*n=87,253 women, 34-53 yrs, exposure baseline **1980***
8-yr follow-up, 1303 incident cases

Manson et al, Lancet 1991

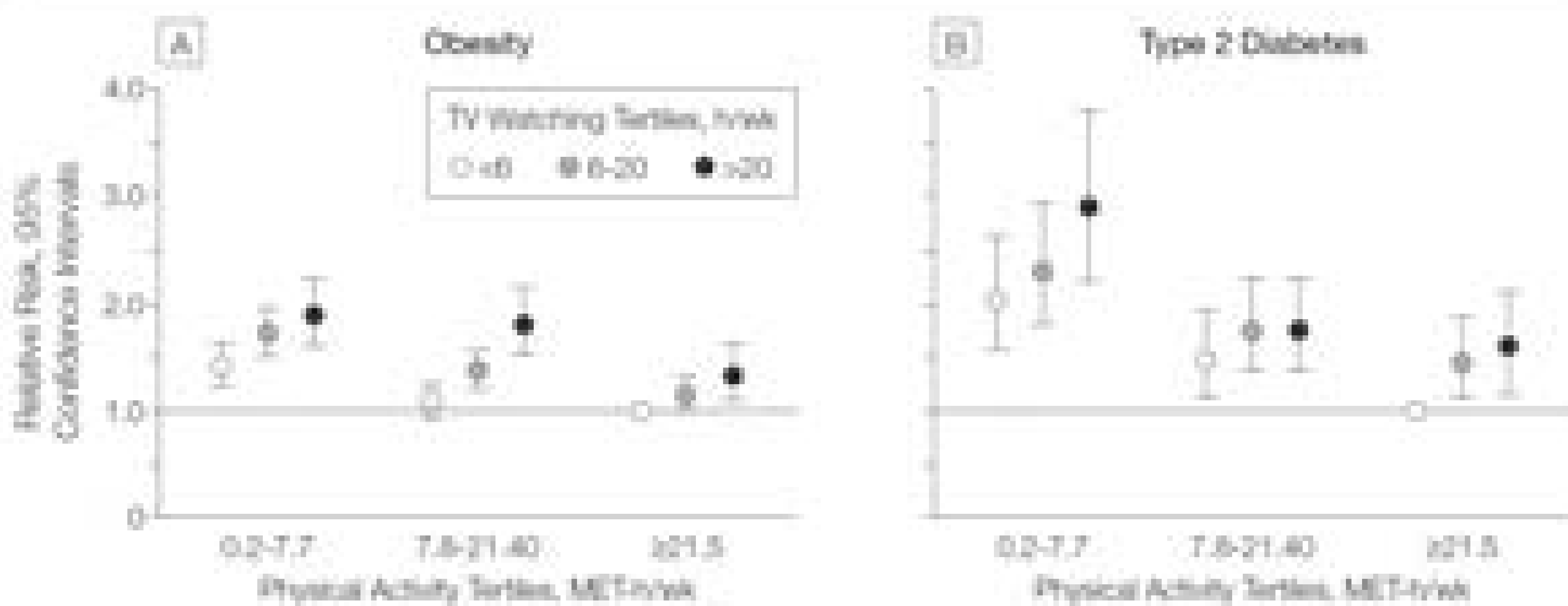
RR of T2DM among women who did **not report vigorous activity**



Hu et al, JAMA 1999

Combined effects of physical activity and sedentary behaviour

Figure 2. Relative Risks of Developing Obesity Among Nonobese Women and of Developing Type 2 Diabetes Among Nondiabetic Women According to Joint Classification of Physical Activity Levels (Metabolic Equivalent Hours/Wk [MET-h/wk]) and Time Spent Watching Television (TV)



T2DM analysis:
n=68,497 women, exposure baseline ***1992***
6-yr follow-up, 1515 incident cases

Hu et al, JAMA 2003

Critical appraisal: Metabolic Equivalent Task (MET)

	Activity A	Activity B	Ratio (B/A)
Intensity			
VO_2 (ml O_2/min/kg)	7.0	14.0	2.0
Standard MET	2	4	2.0
Marginal MET	1	3	3.0
PAEE (J/min/kg)	70	210	3.0

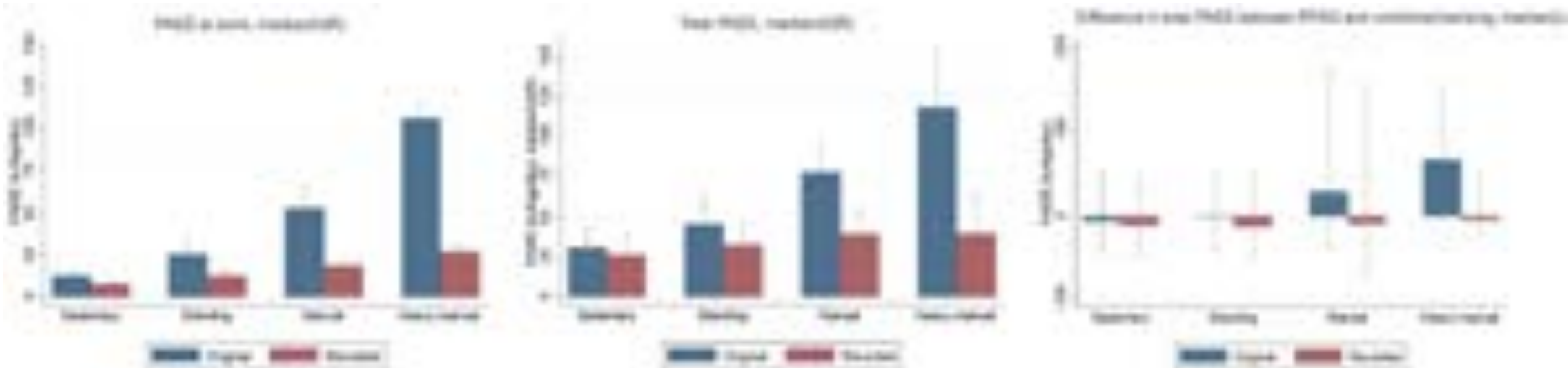
Q: How do activities A and B equate?

1 standard MET = 3.5 ml O_2/min/kg

1 ml O_2 ~ 20 J

Exposing our PAQ assumptions:

Intensity distribution of working hours



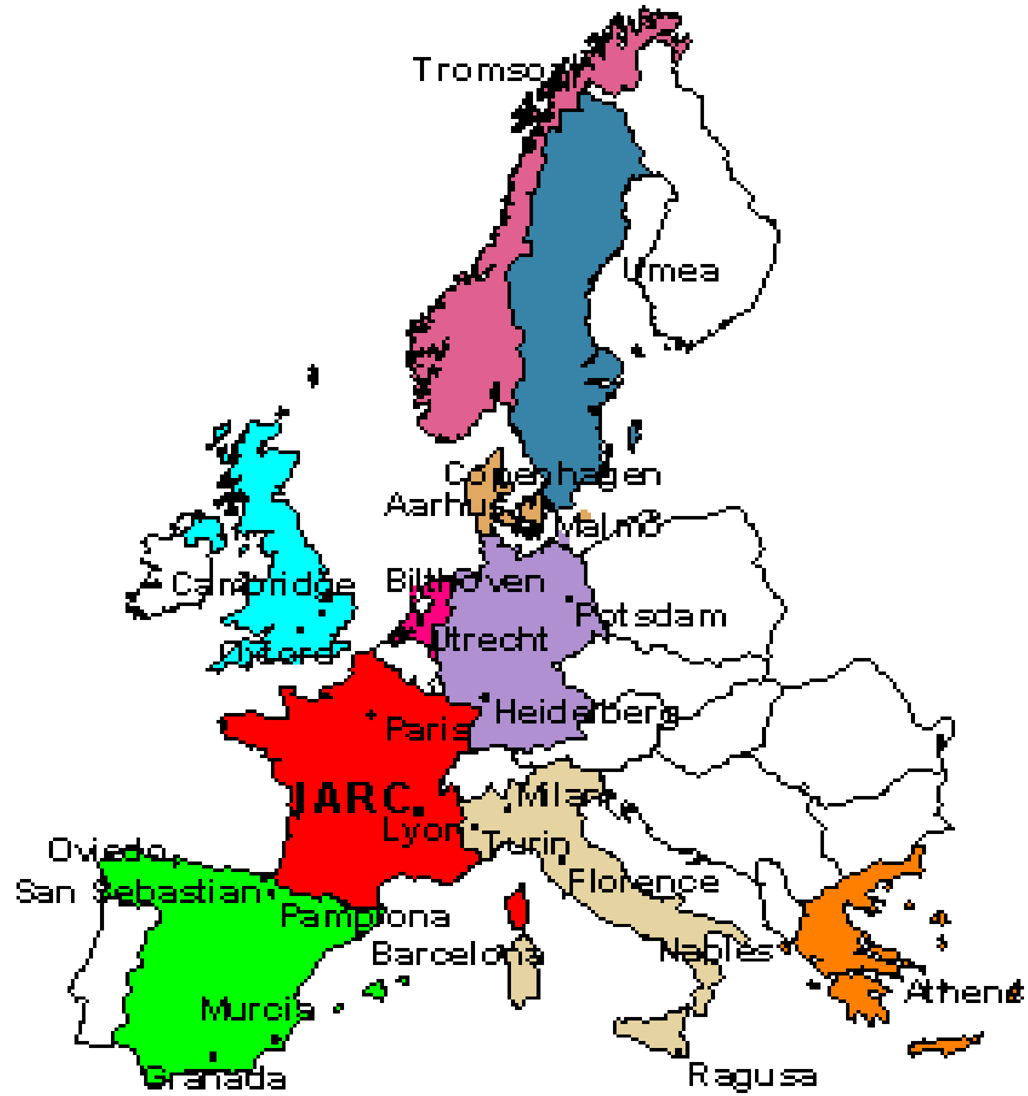
Golubic et al, PLoS ONE 2014

Physical activity in EPIC Europe

Time frame: Past year

- Work category
  Sedentary, Standing, Manual, Heavy manual

- Leisure time:
  Walking, Cycling, Gardening, DIY, Physical exercise, Housework

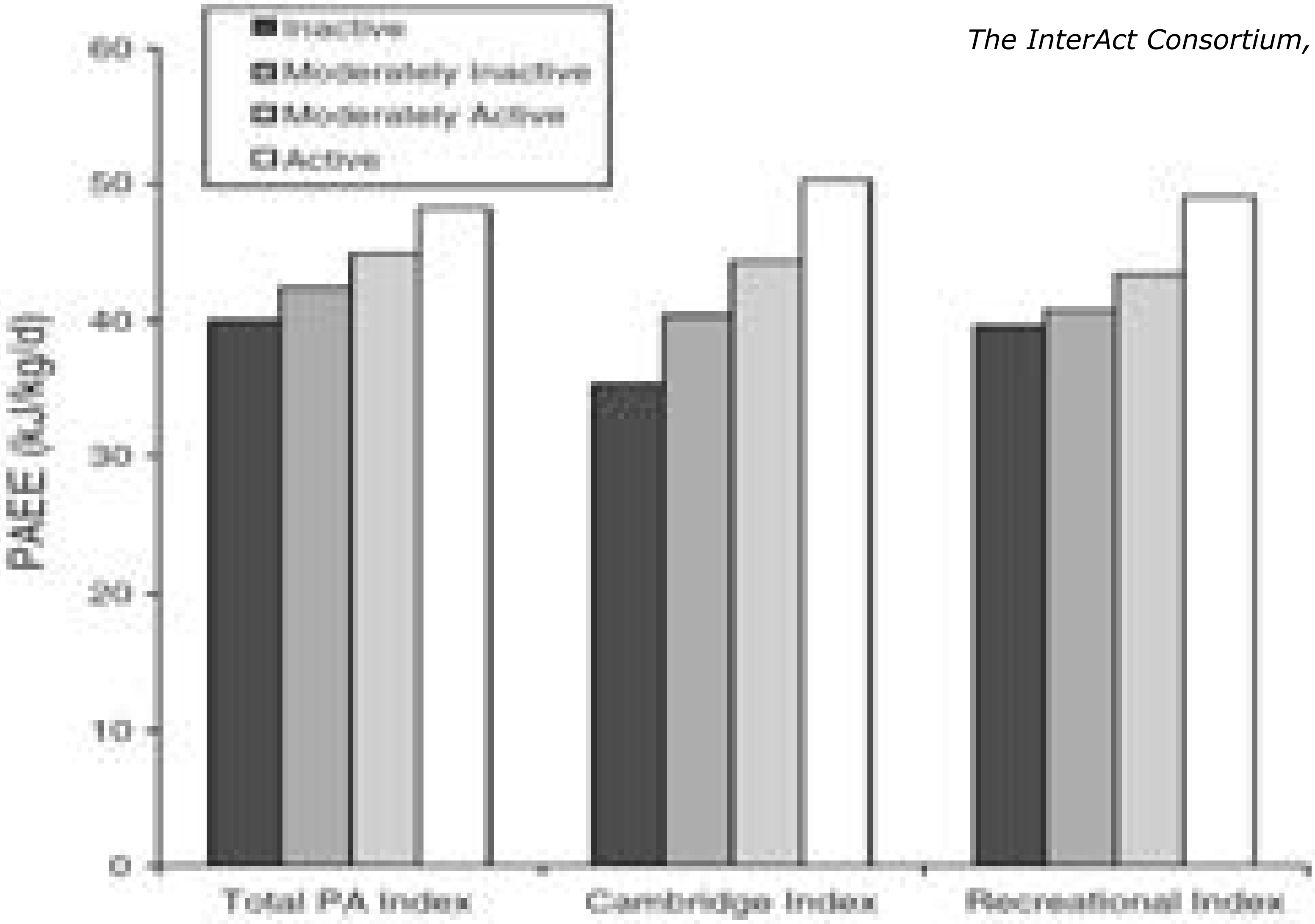


Derived PA index ("Cambridge index")

Work activity	Leisure time physical activity (Duration of sport and cycling in hrs/wk)			
	No	≤3.5	>3.5 and ≤7.0	> 7.0
Sedentary	Inactive	Moderately inactive	Moderately active	Active
Standing	Moderately inactive	Moderately active	Active	Active
Manual	Moderately active	Active	Active	Active
Heavy manual	Active	Active	Active	Active

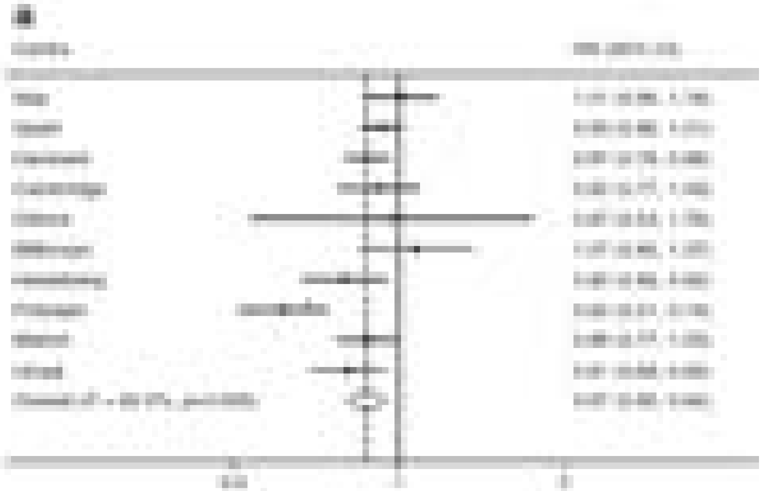
Country-specific validity of three indices of PA derived from short EPIC PAQ: *Acc+HR estimates of PAEE by category*

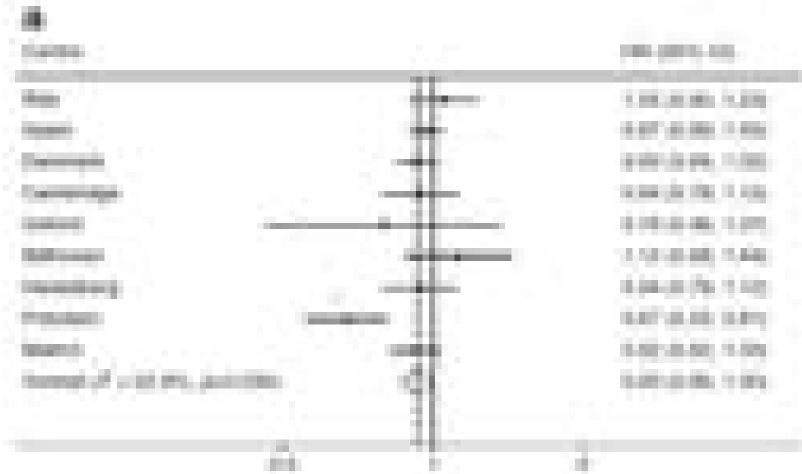
The InterAct Consortium, Eur J Epid 2012



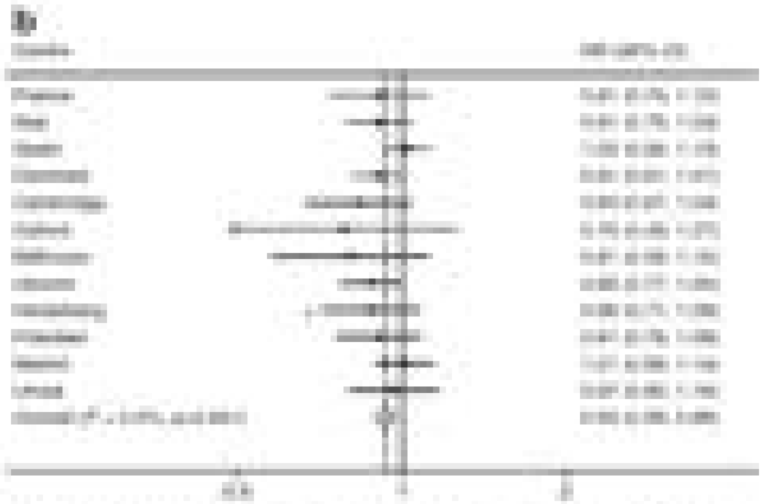
Physical Activity and incident Diabetes

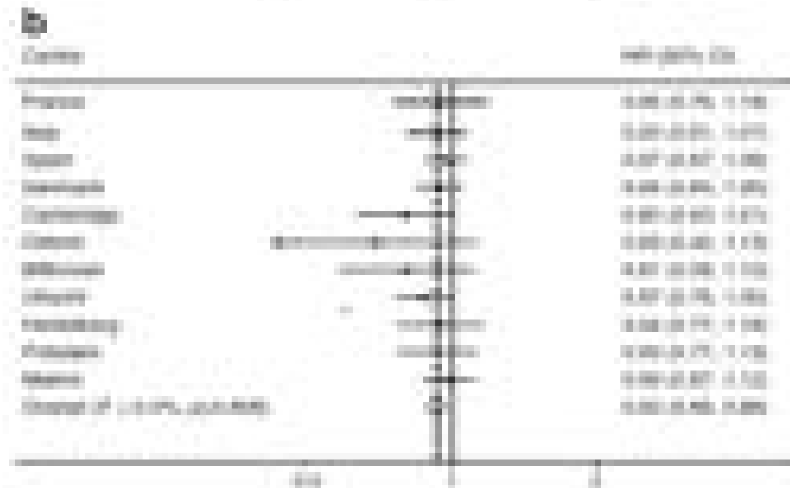
Men:





Women:





PA-T2DM: Effect modification by obesity?

Table 2 Combined effects (HR (95% CI)) of overall physical activity and BMI on incident diabetes in men (n=[illegible]) and women (n=[illegible])

Variable	Activity category			
	Active	Moderately active	Moderately inactive	Inactive
Men				
n	2,645	2,764	3,669	2,690
Normal weight (BMI <25 kg/m²)	1.00	0.93 (0.62, 1.10)	1.32 (1.01, 1.72)	1.81 (1.34, 2.45)
Overweight (BMI 25–30 kg/m²)	1.00	1.09 (0.93, 1.28)	1.15 (0.99, 1.34)	1.38 (1.14, 1.62)
Obese (BMI ≥30 kg/m²)	1.00	1.11 (0.87, 1.40)	1.36 (1.08, 1.71)	1.38 (1.08, 1.76)
Women				
n	2,438	3,134	5,428	4,473
Normal weight (BMI <25 kg/m²)	1.00	1.12 (0.88, 1.41)	1.22 (0.99, 1.40)	1.50 (1.17, 1.93)
Overweight (BMI 25–30 kg/m²)	1.00	1.17 (0.96, 1.43)	1.27 (0.97, 1.41)	1.45 (1.19, 1.72)
n.s. → Obese (BMI ≥30 kg/m²)	1.00	1.19 (0.91, 1.55)	1.17 (0.92, 1.48)	1.2 (0.94, 1.54)

Table 3 Combined effects of overall physical activity and central obesity (WC) on incident diabetes in men (n=[illegible]) and women (n=[illegible])

Variable	Activity category			
	Active	Moderately active	Moderately inactive	Inactive
Men				
n	2,511	2,524	3,449	2,261
WC (<94 cm)	1.00	1.11 (0.88, 1.40)	1.23 (0.98, 1.51)	1.44 (1.11, 1.87)
WC (≥94 cm)	1.00	1.05 (0.90, 1.22)	1.2 (1.00, 1.40)	1.38 (1.17, 1.62)
Women				
n	2,294	2,890	5,204	4,429
WC (<80 cm)	1.00	1.06 (0.82, 1.39)	1.22 (0.96, 1.56)	1.57 (1.19, 2.07)
WC (≥80 cm)	1.00	1.15 (0.98, 1.36)	1.08 (0.92, 1.25)	1.19 (1.01, 1.39)

Values are HR (95% CI), unless specified otherwise

Models are adjusted for study location, education (none, primary, technical/other secondary, professional), smoking status (never, former, current), alcohol consumption (grams/day), energy intake (kilojoules/day) and BMI

PA, obesity, and diabetes in Korea

675,496 men

PA: Minutes of exercise “causing sweating”

52,995 incident cases

[illegible]

[illegible]	[illegible]			[illegible]			[illegible]			[illegible]		
	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
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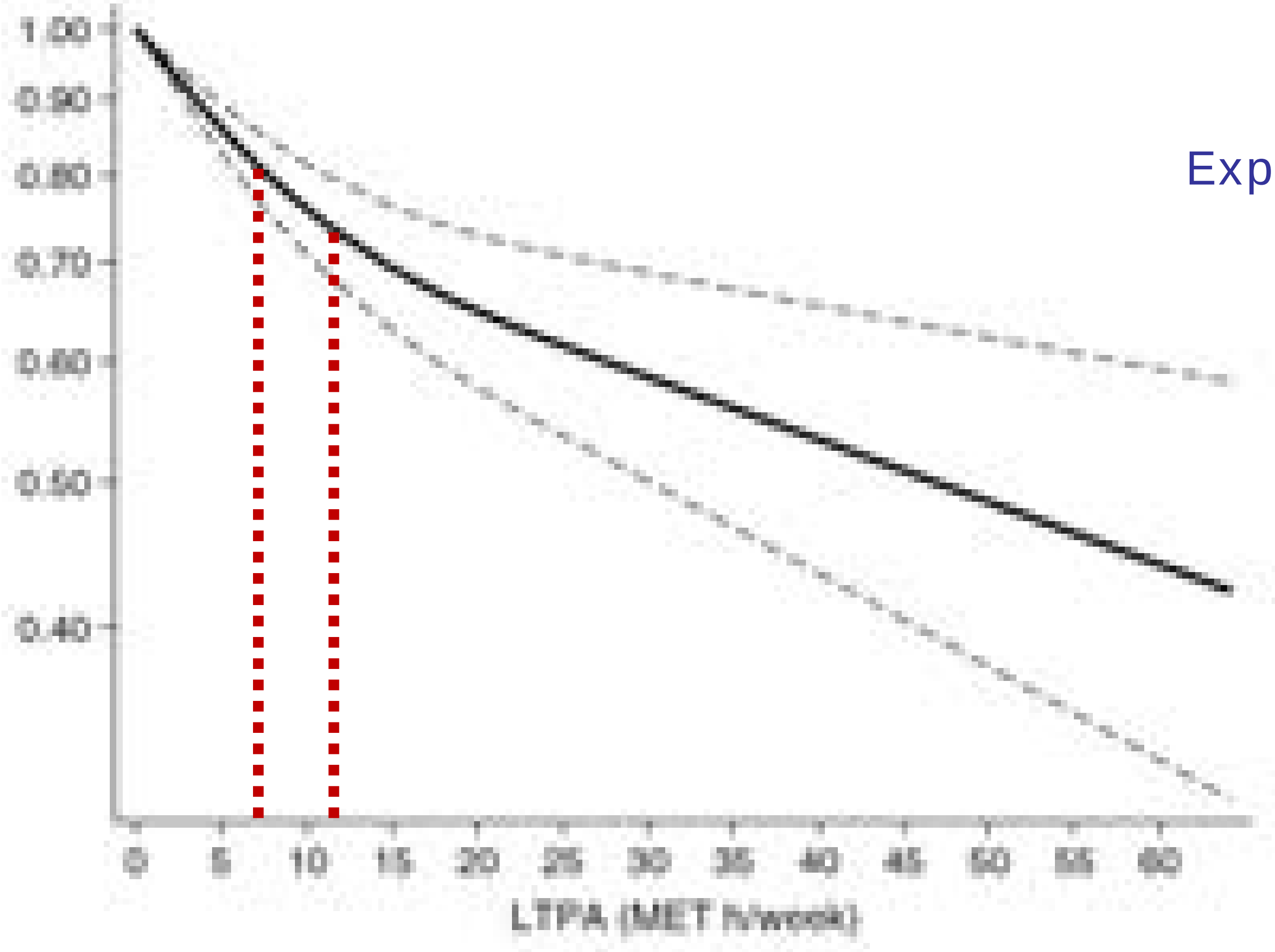
[illegible]

Lee et al, Am J Epid 2012

Dose-response Meta-analysis: Leisure-time activity

28 studies
1.26 million people
84 k incident cases
Self-reported LTPA
Exposure harmonisation

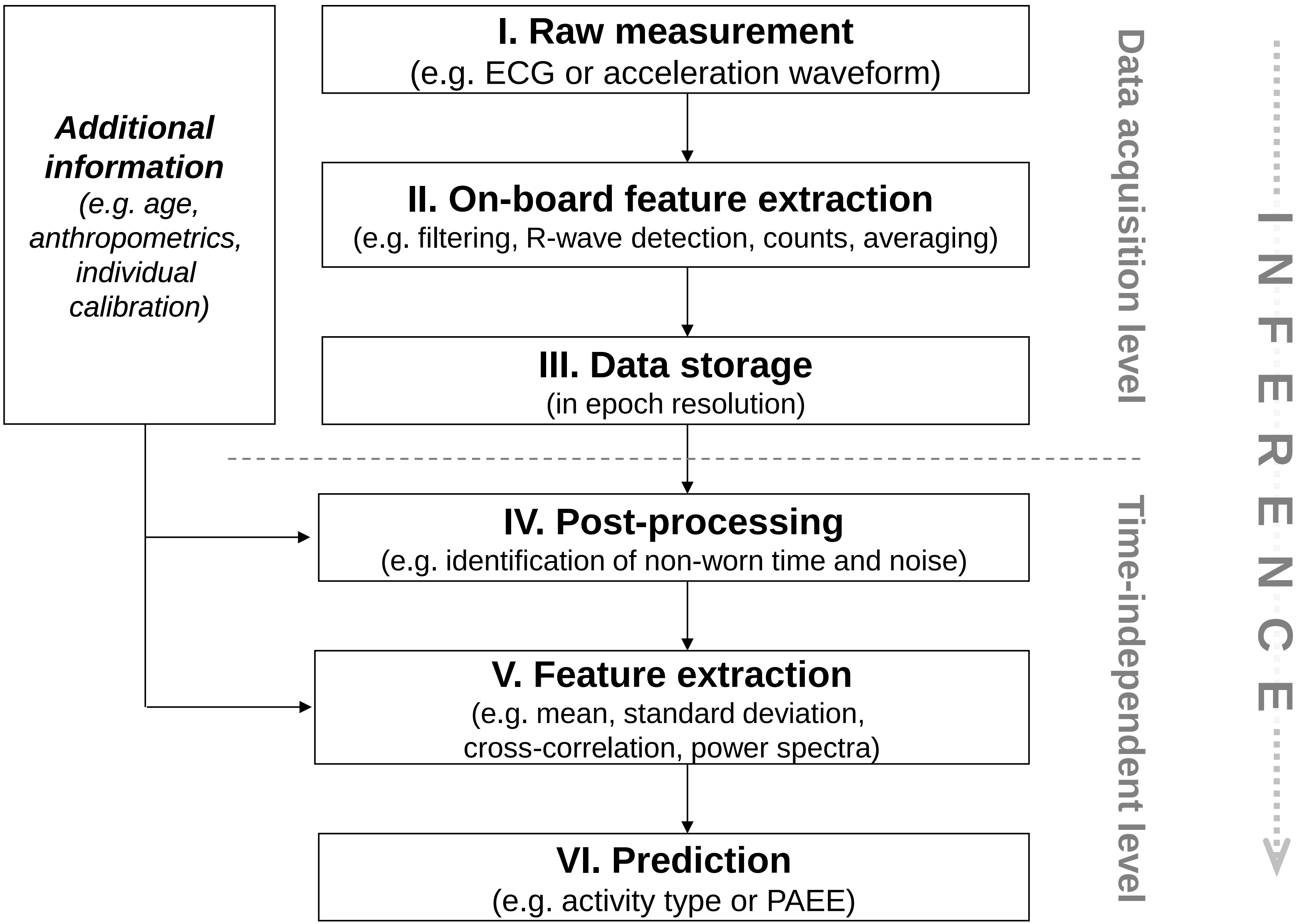


2.5 hrs/wk @ 3.0 METs = 7.50 MET-hrs/wk

2.5 hrs/wk @ 4.5 METs = 11.25 MET-hrs/wk

Smith et al, Diabetologia 2016

Biosensing



Corder et al, J Appl Phys 2008

Accelerometry

Principle:

Direct measure of body movement (acceleration)

When a person moves, the body segments are accelerated by muscular forces, which should in theory relate to EE.

Acceleration can be measured along one axis (e.g., longitudinal or vertical), two (e.g., longitudinal + medio-lateral) or three (longitudinal + medio-lateral+anterior-posterior) axes and it can be measured at one or more body sites.

Principles of accelerometry

The measured value of a raw acceleration signal contains **3 components**

1. Acceleration as a result of **movement**
   - The component we are most interested in when estimating activity energy expenditure

2. Acceleration as a result of **gravitational** force
   - In static situations this tells us the orientation of the accelerometer

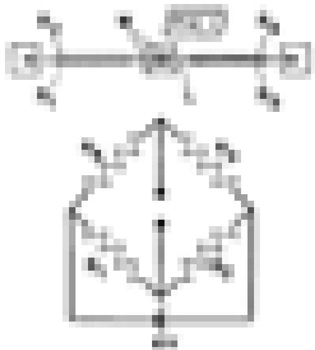
3. **Noise**

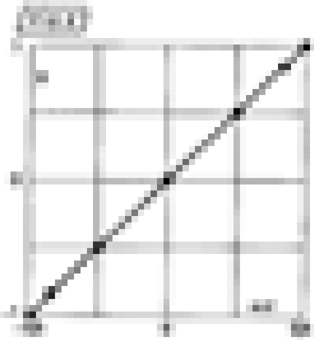
History of accelerometry

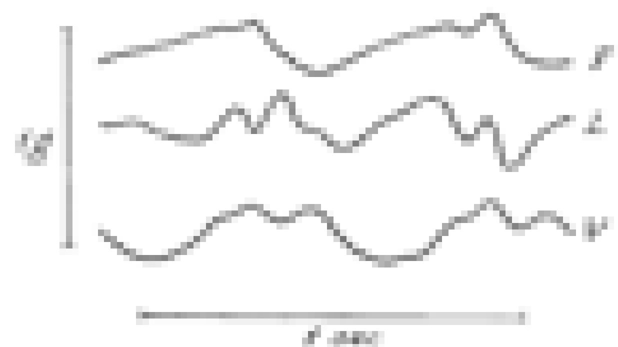
Journal of Biomechanics, 1961:

A three-directional accelerometer for analyzing body movements

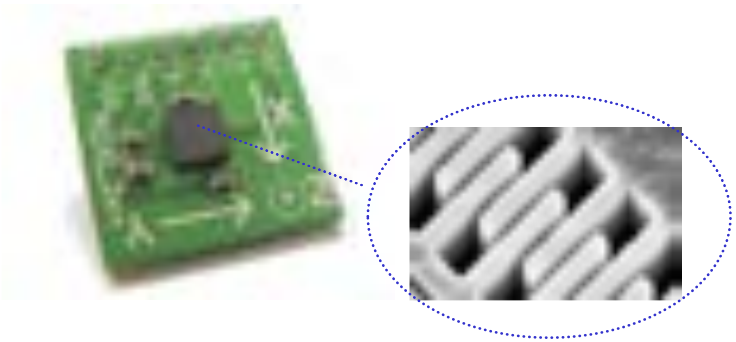
G. CAVAGNA, F. SAIBENE AND R. MARGARIA
Istituto di Fisiologia, Università di Milano, Milan, Italy







How does an accelerometer work?



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Transducer or Sensor

-**Energy converter**
(e.g., movement to electric signals)

Important characteristics:
Range, sensitivity, linearity, internal frequency, hysteresis, drifts (temperature, humidity, etc)

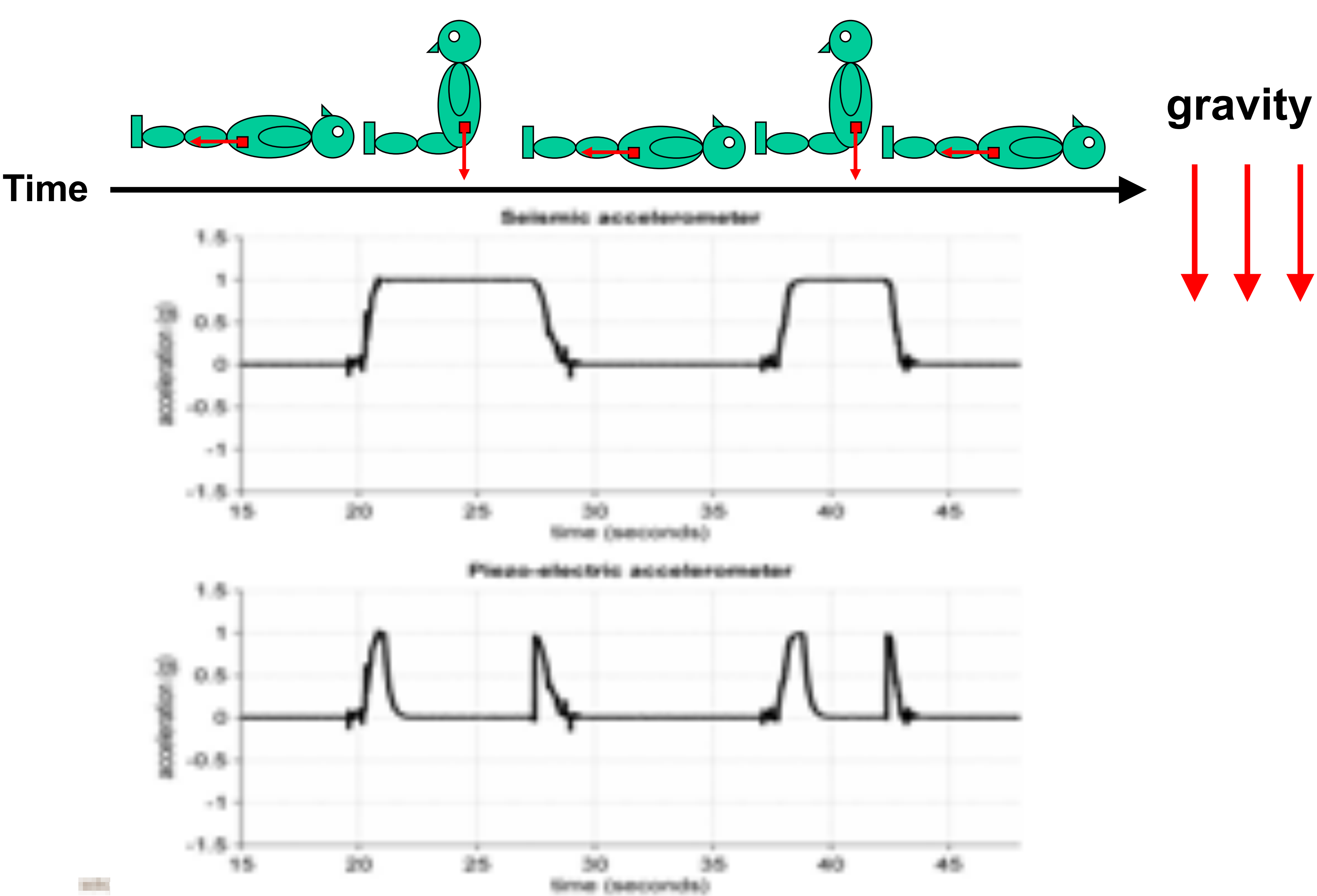
Data Acquisition System

-**Data sampler and pre-processor**
(e.g., raw signals to desirable parameters)

Important characteristics:
Sampling frequency, signal conditioning, digital signal processing, size, cost

Chen & Bassett, MSSE, 2005

Two types of accelerometers



Pop quiz!

A triaxial seismic accelerometer measures the following stable (>3 sec) acceleration values in its 3 axes:

X = 0.7g

Y = 0.7g

Z = 0.0g

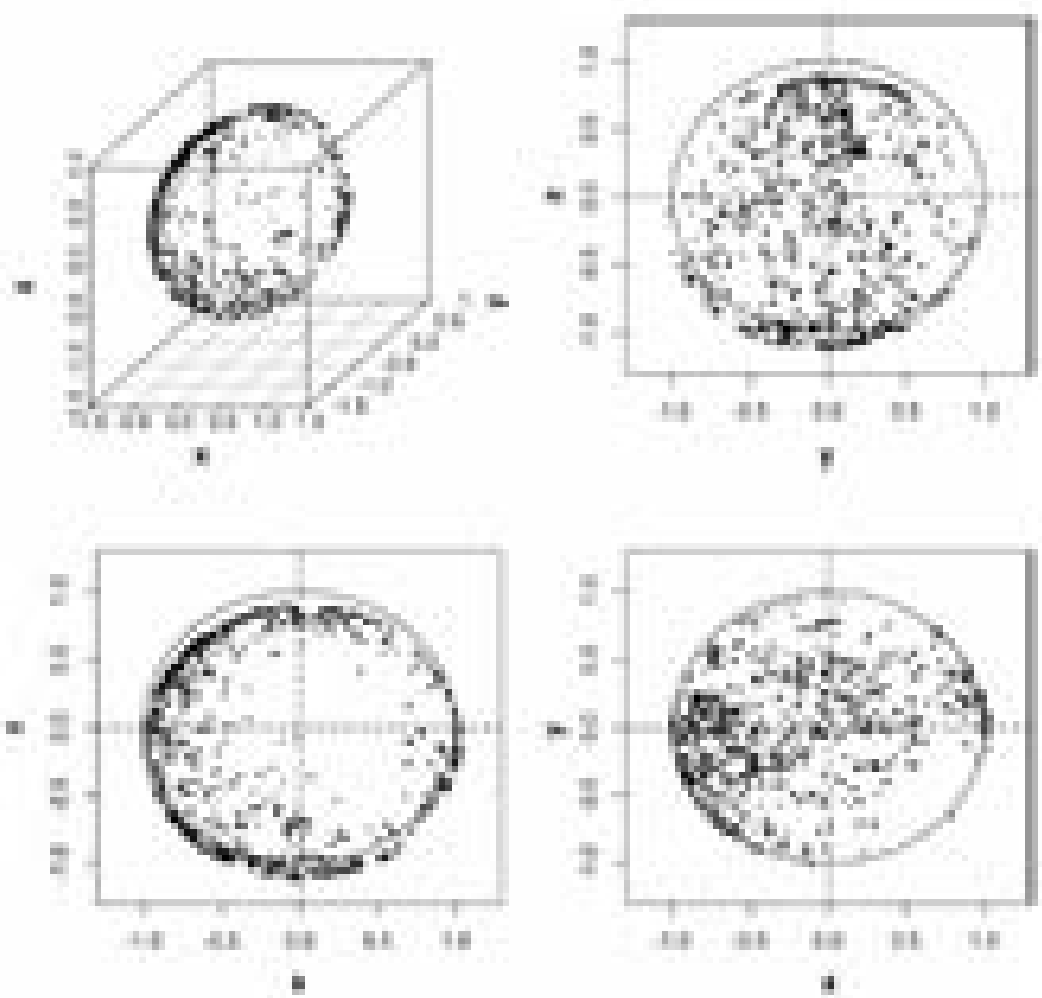
What is the orientation of the accelerometer?

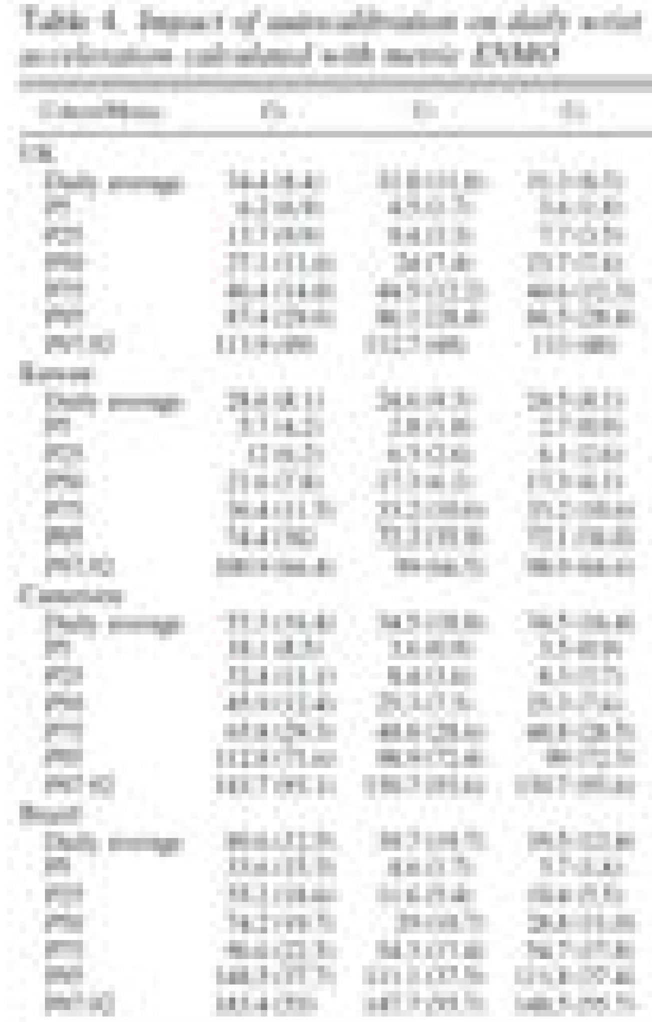
Hint: Vector magnitude = $\sqrt{X^2 + Y^2 + Z^2} = 1$ (when static)

… and you may find your trigonometric math useful too!

OR open a picture on your smartphone and note when it flips it to landscape viewing! Do the same when shaking it!

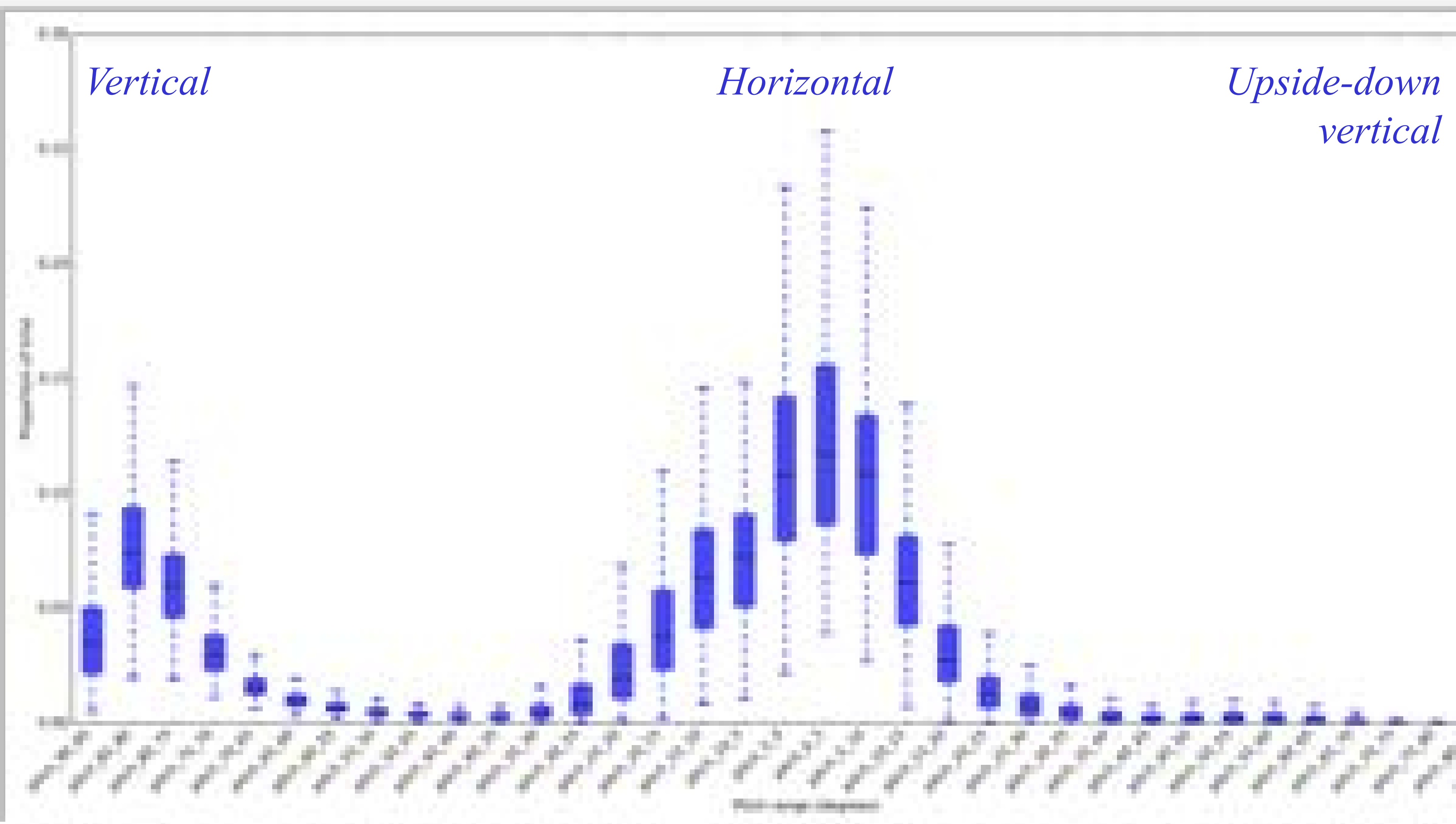
Accelerometer auto-calibration to local gravity

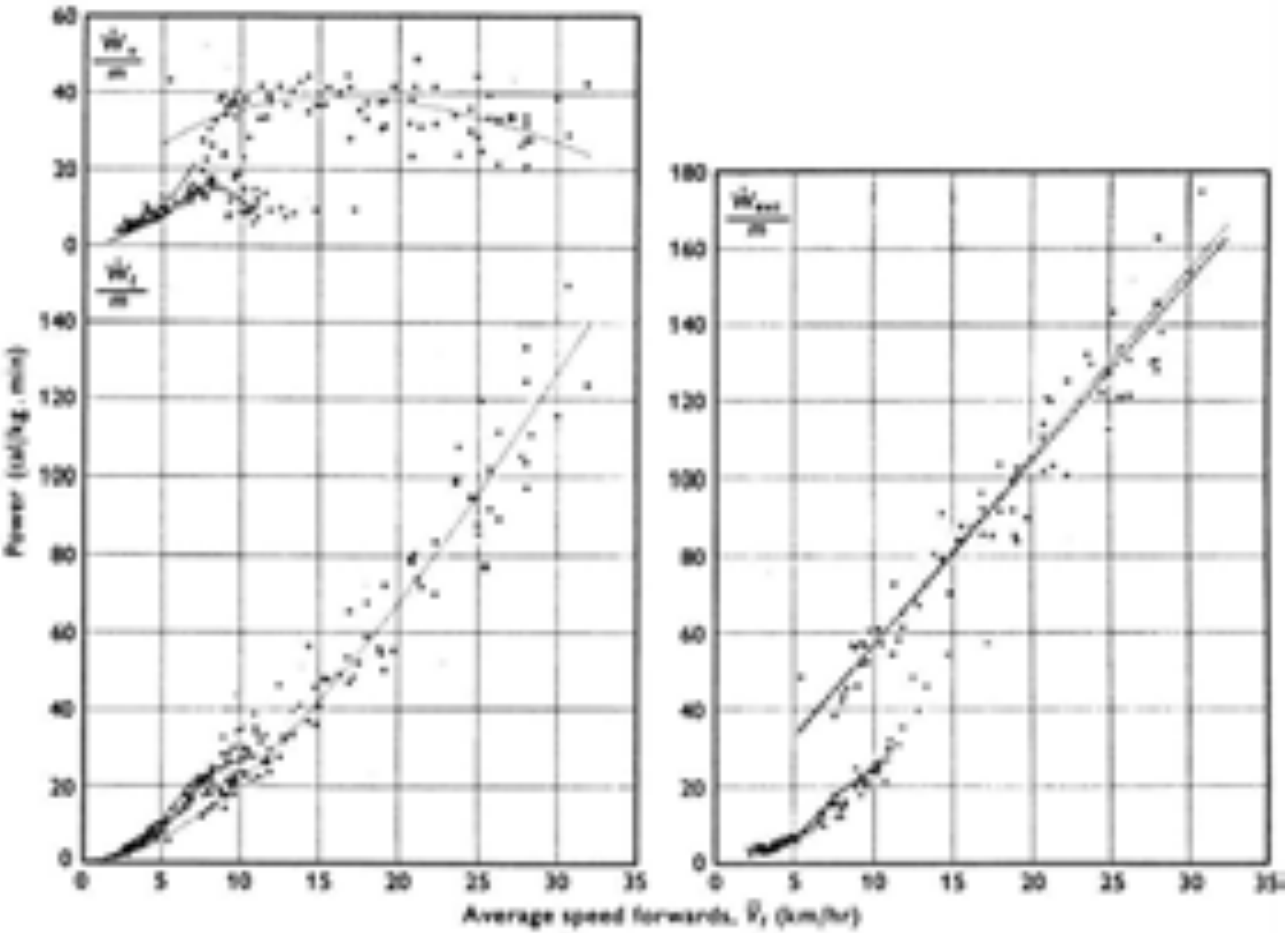




Van Hees et al, JAP 2014

Thigh acceleration:
Pitch angle distribution during static periods of free-living

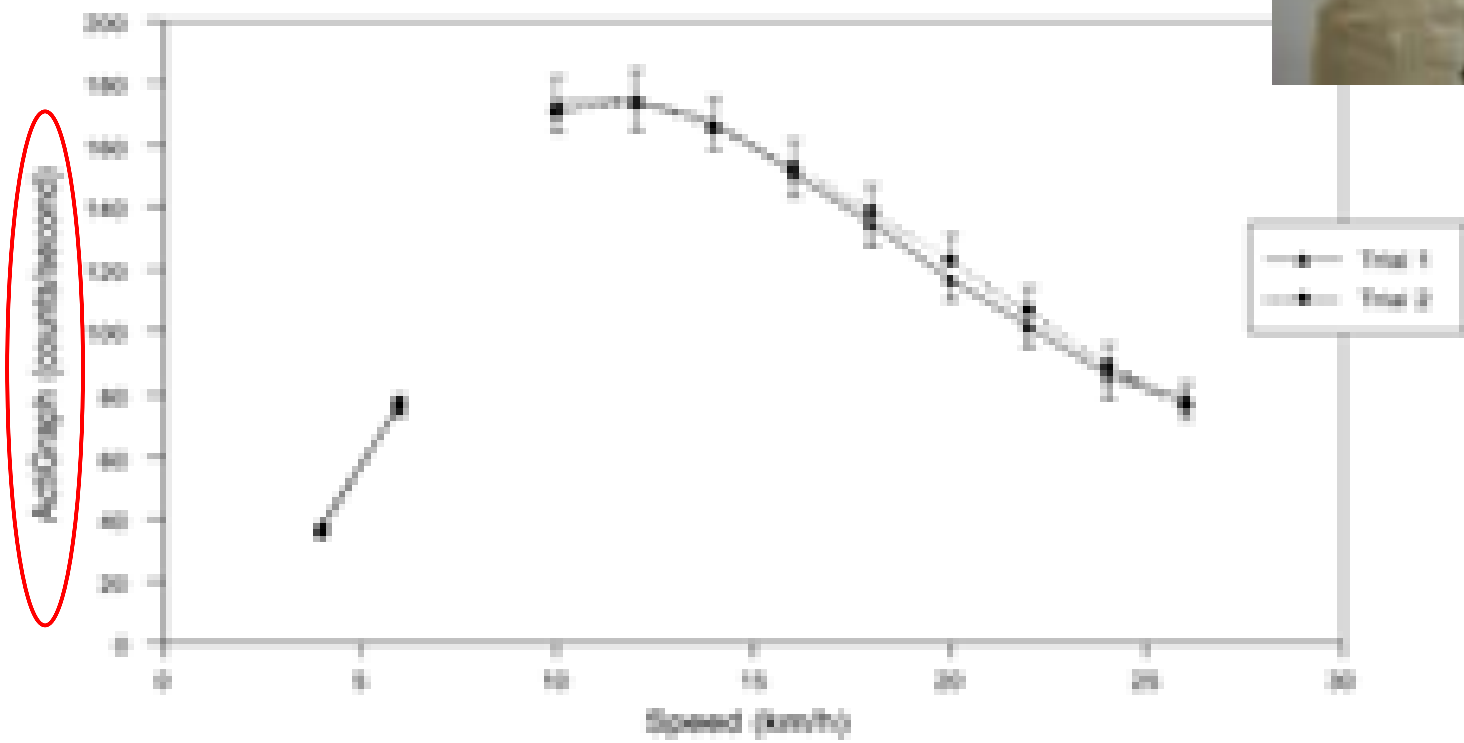




Power (cal/kg. min)
Average speed forwards, v̄x (km/hr)
0
5
10
15
20
25
30
35
20
40
60
80
100
120
140
160
180

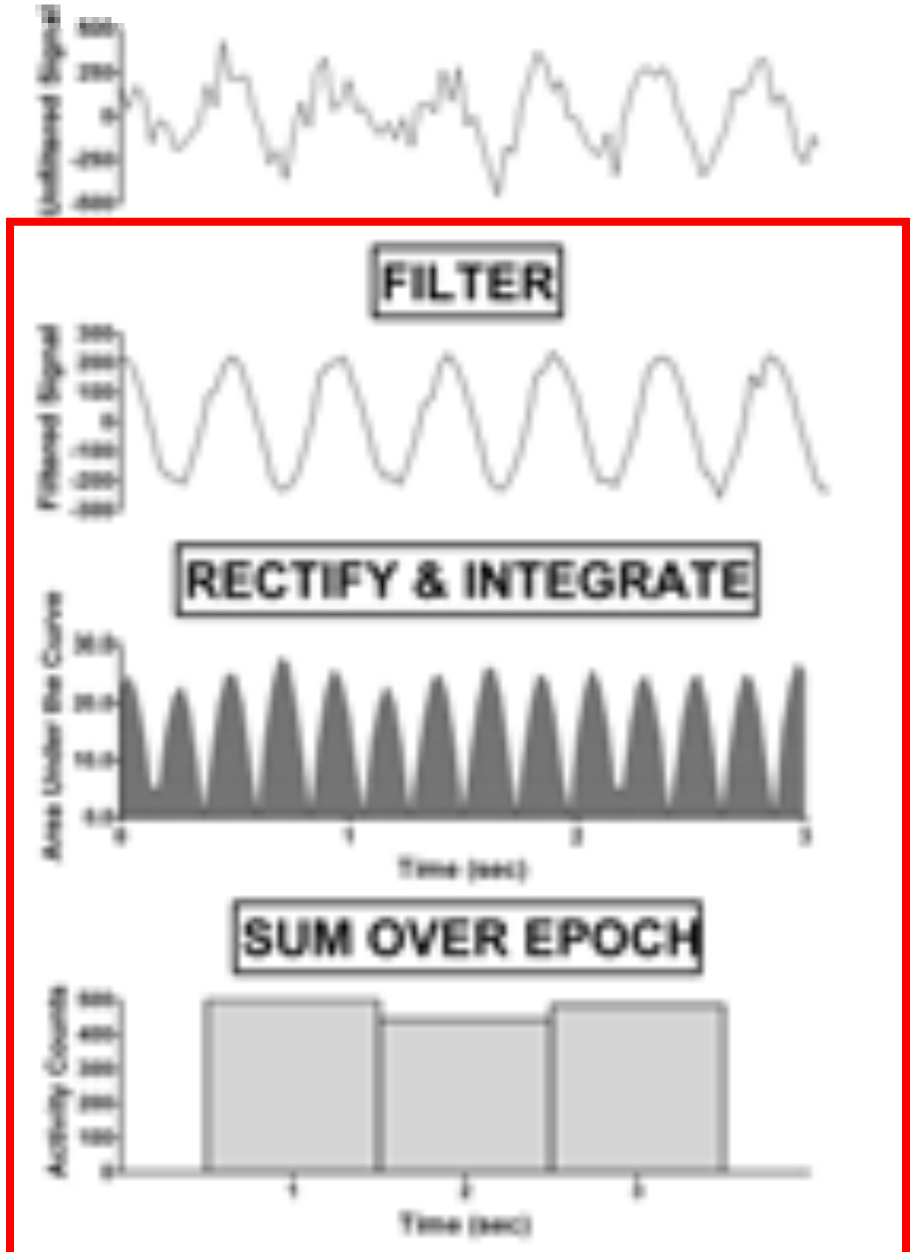
Influence of Speed and Step Frequency during Walking and Running on Motion Sensor Output

ANN V. ROWLANDS, MICHELLE R. STONE, and ROGER G. ESTON
School of Sport and Health Sciences, University of Exeter, UNITED KINGDOM



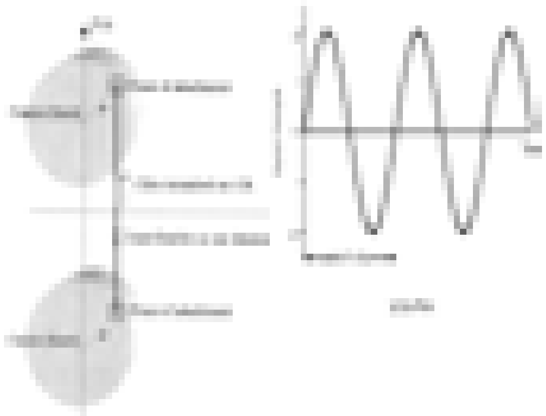
Rowlands et al, MSSE 2007

Data processing



Chen & Bassett, MSSE, 2005
Chen et al, MSSE 2012

Actigraph acceleration response



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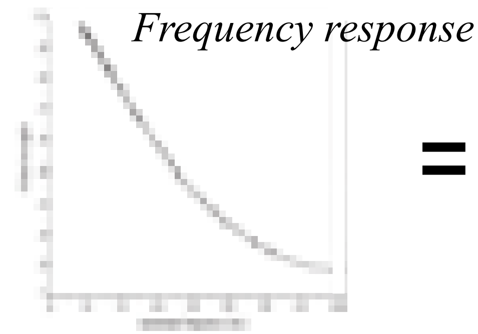

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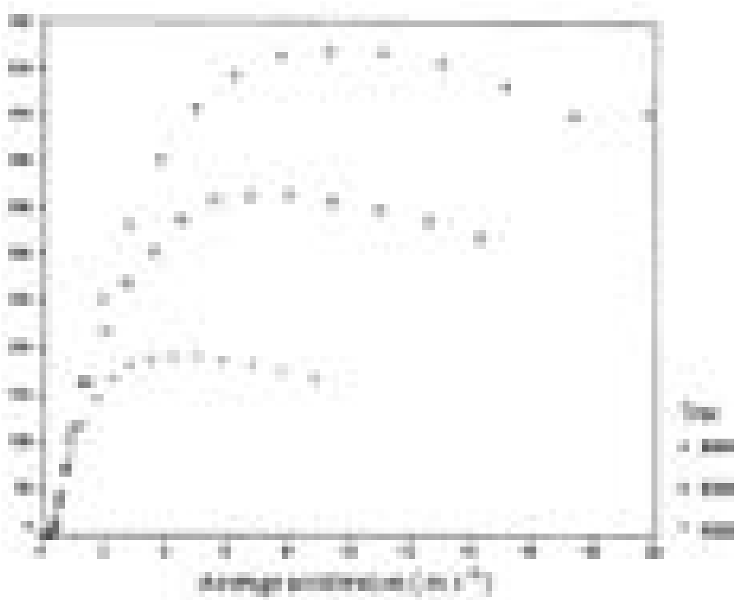
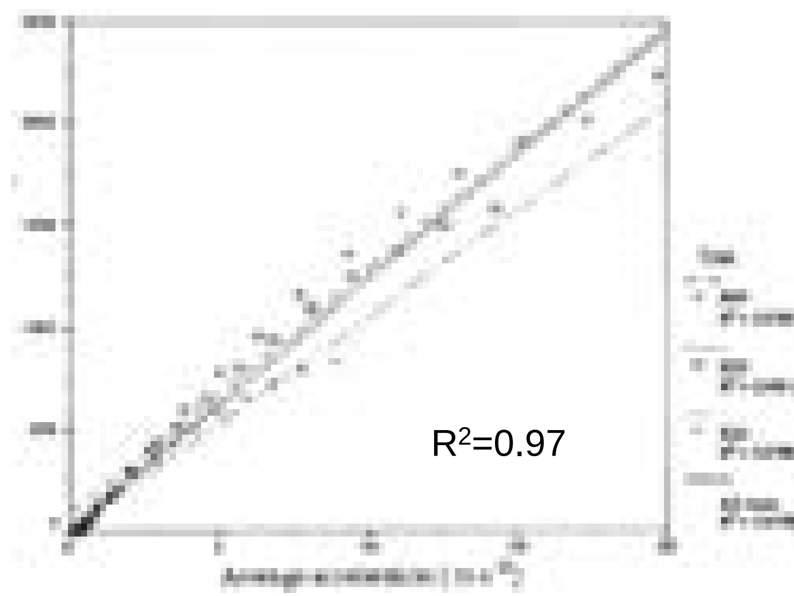
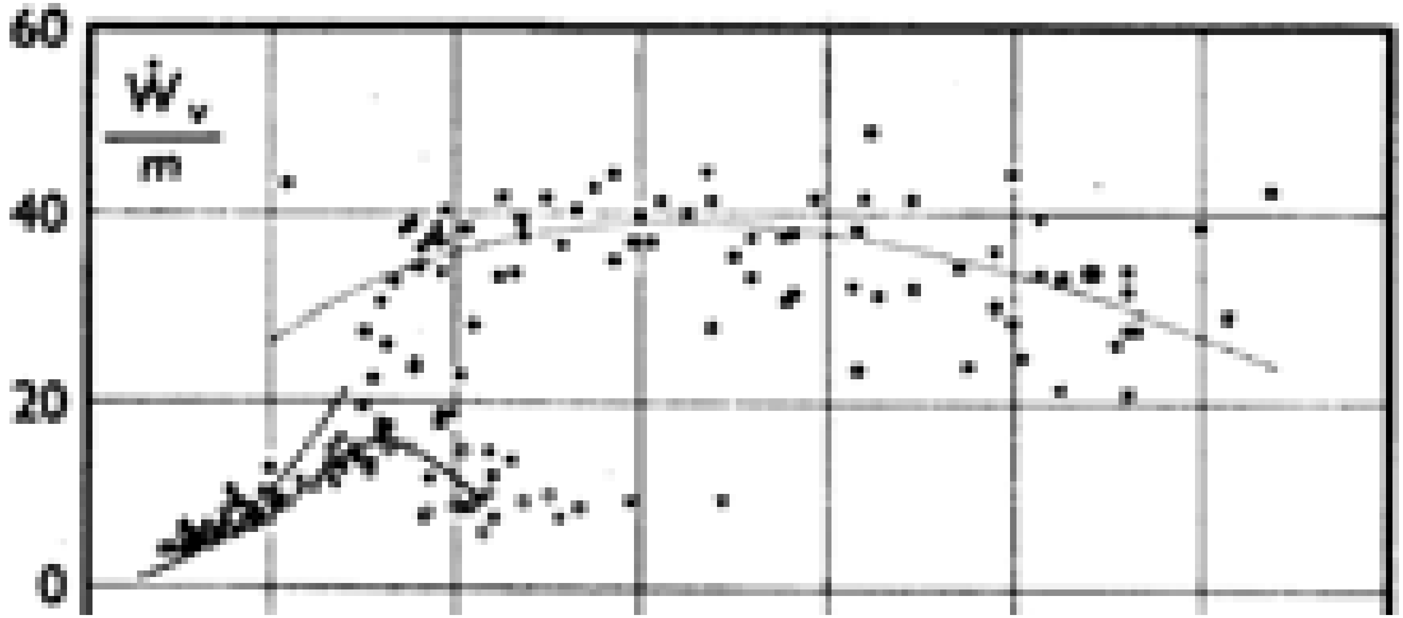
Actigraph counts vs 1/T ∫|acceleration| *dt*

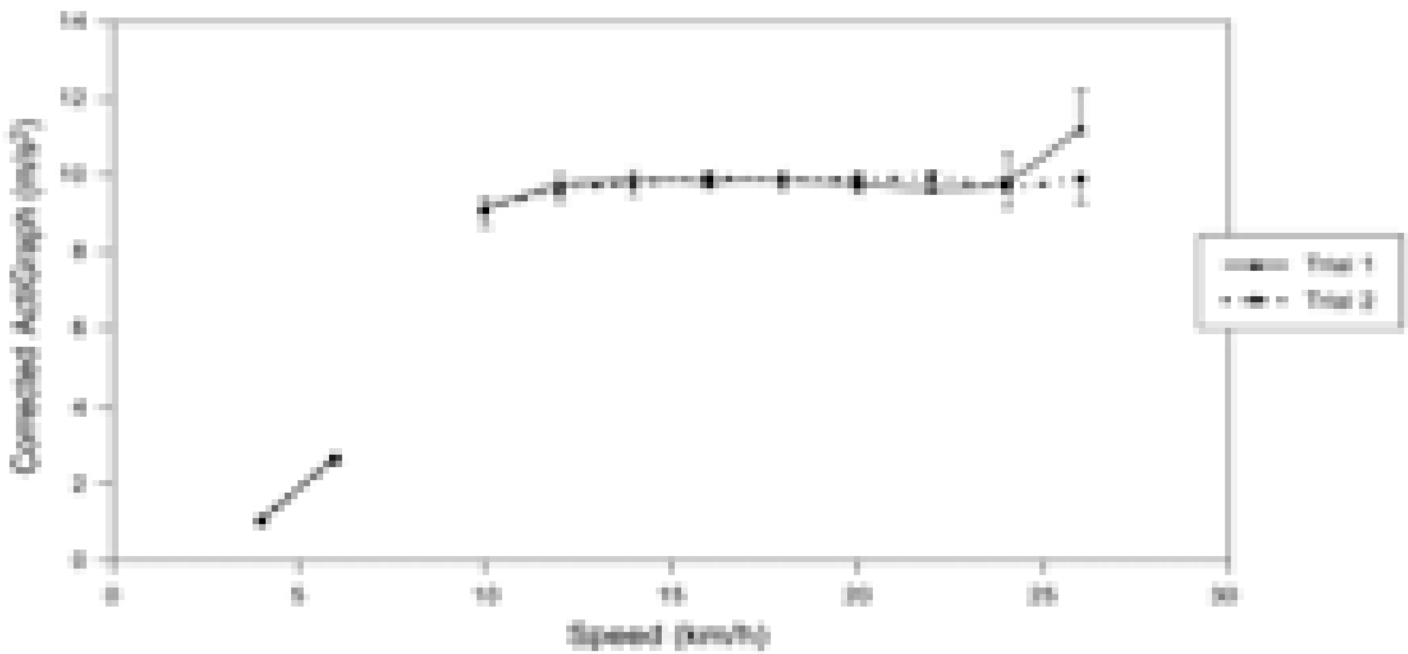


Filter-corrected counts



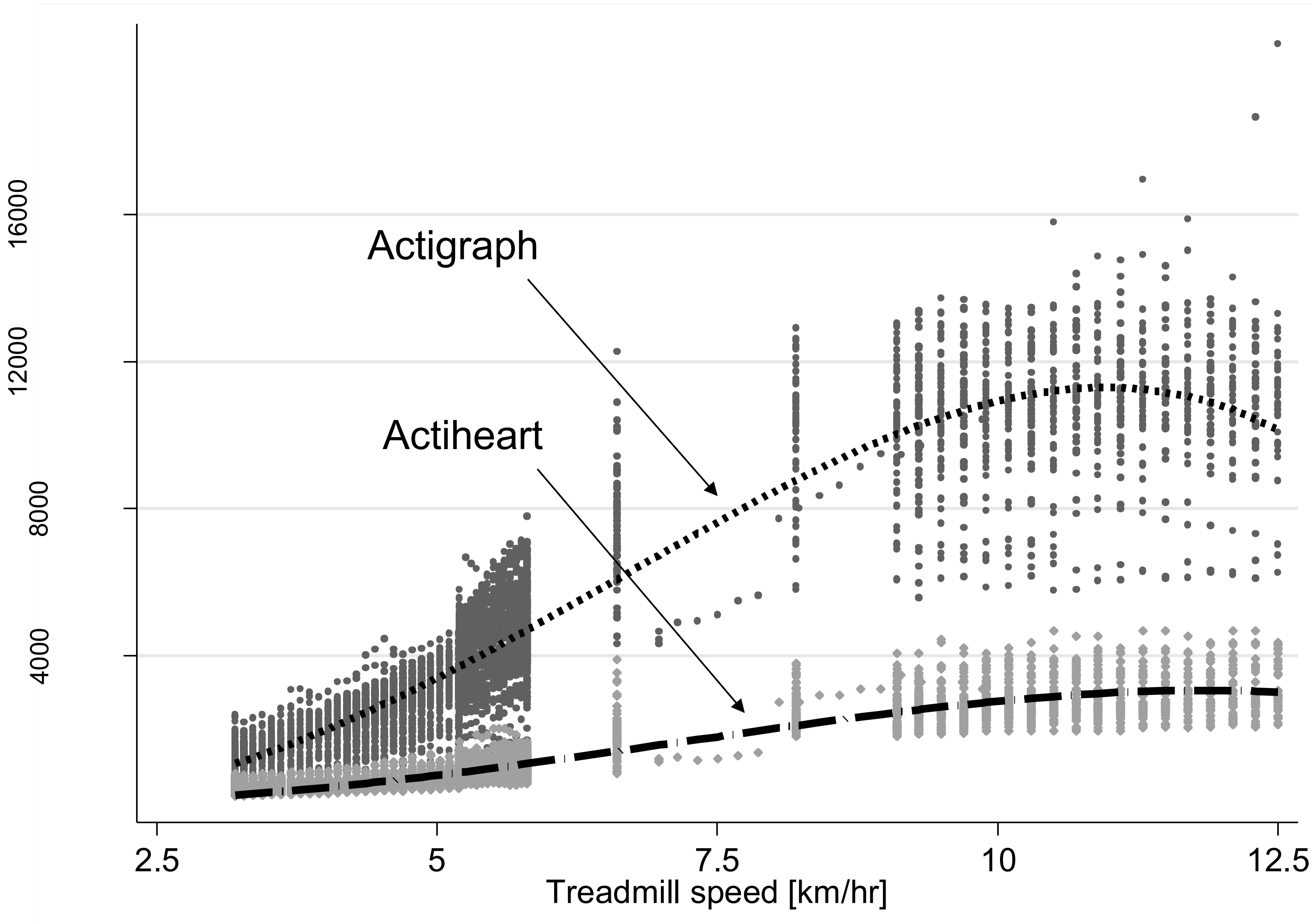


60
40
20
0
$\frac{\dot{W}_v}{m}$

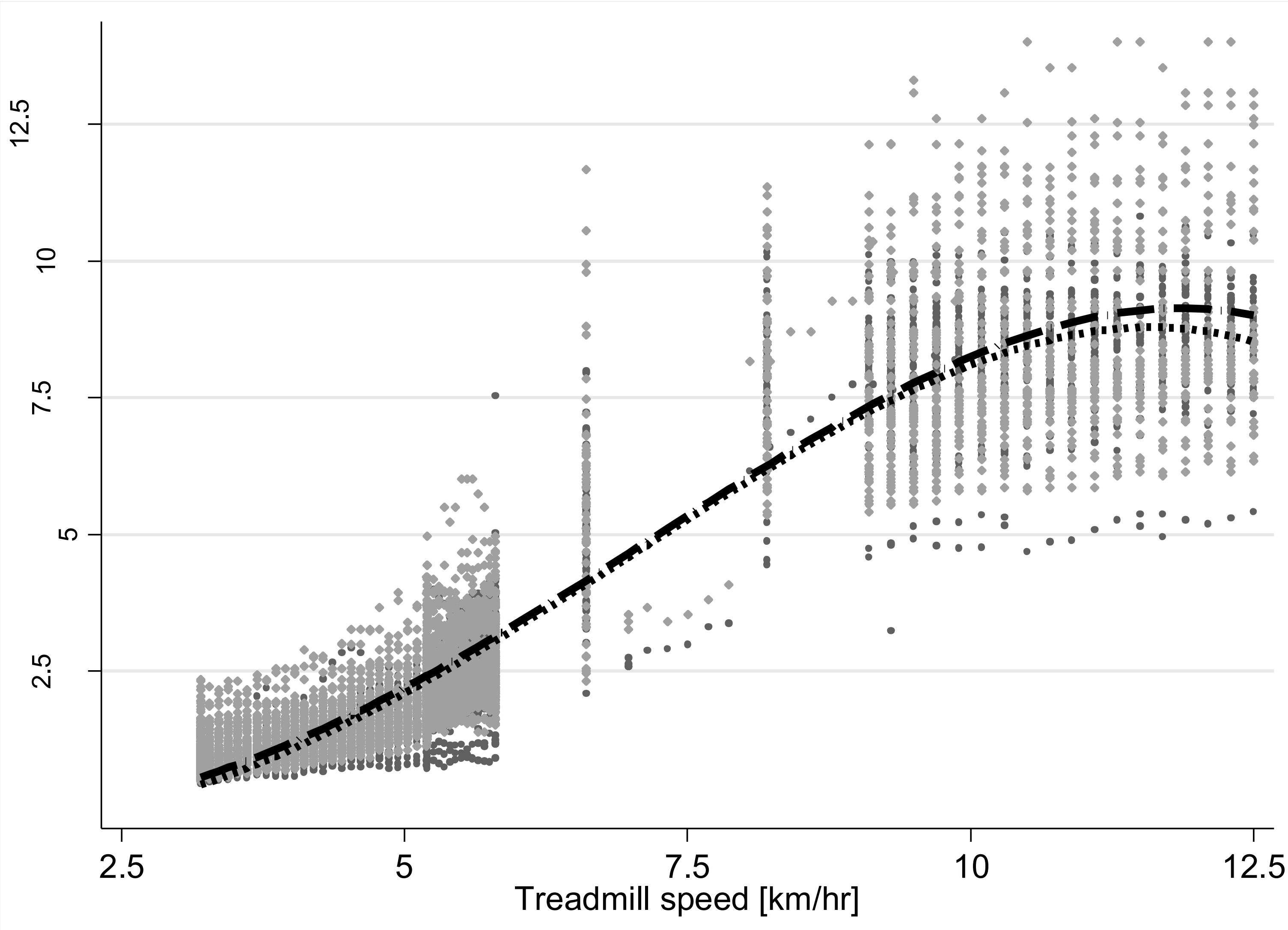


0
2
4
6
8
10
12
14
0
5
10
15
20
25
30
Speed (km/h)
Trip 1
Trip 2

Accelerometry output in "counts per min"



Accelerometry output expressed in m/s^2

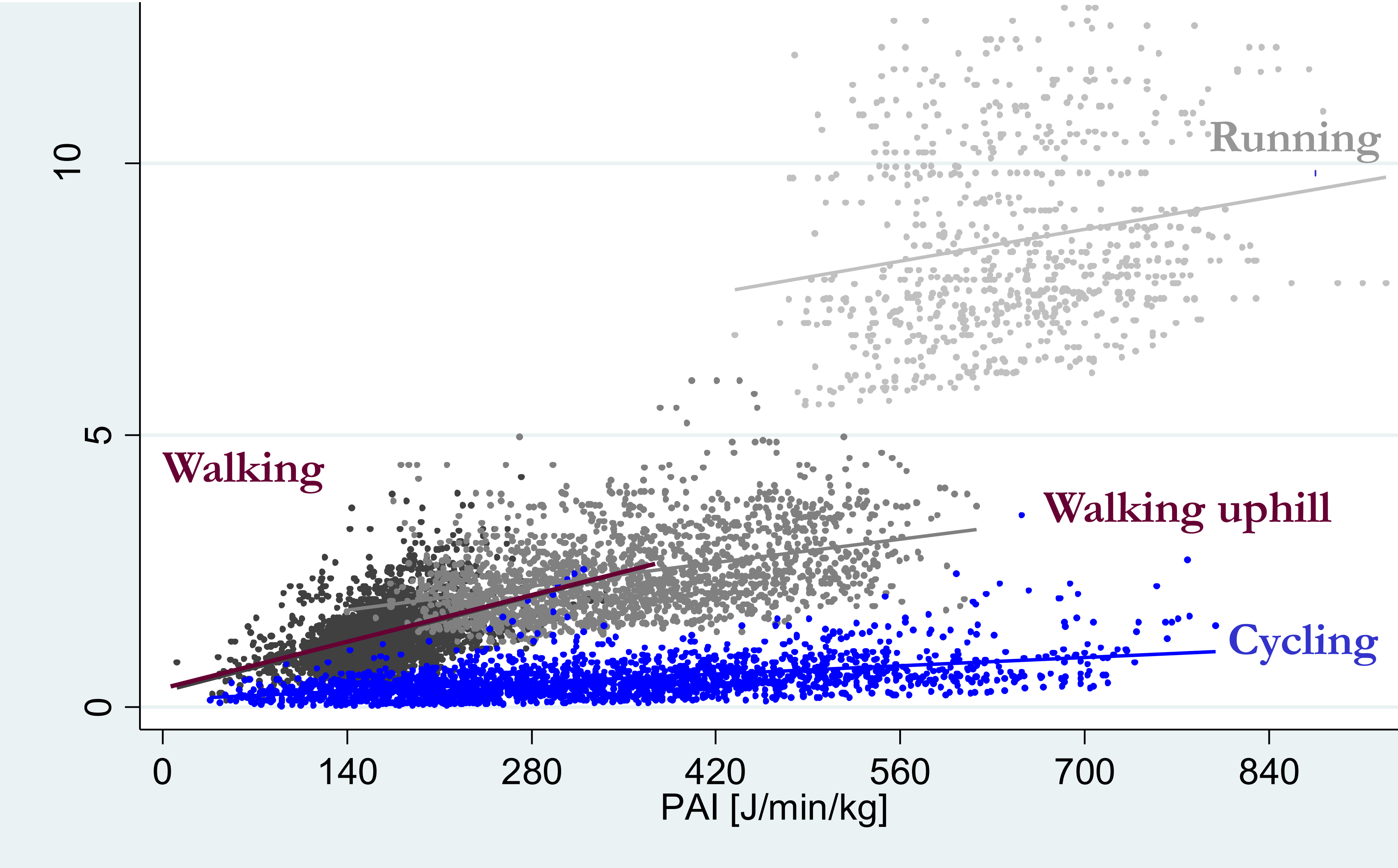


Modeling energy expenditure

(making bolder inferences!)

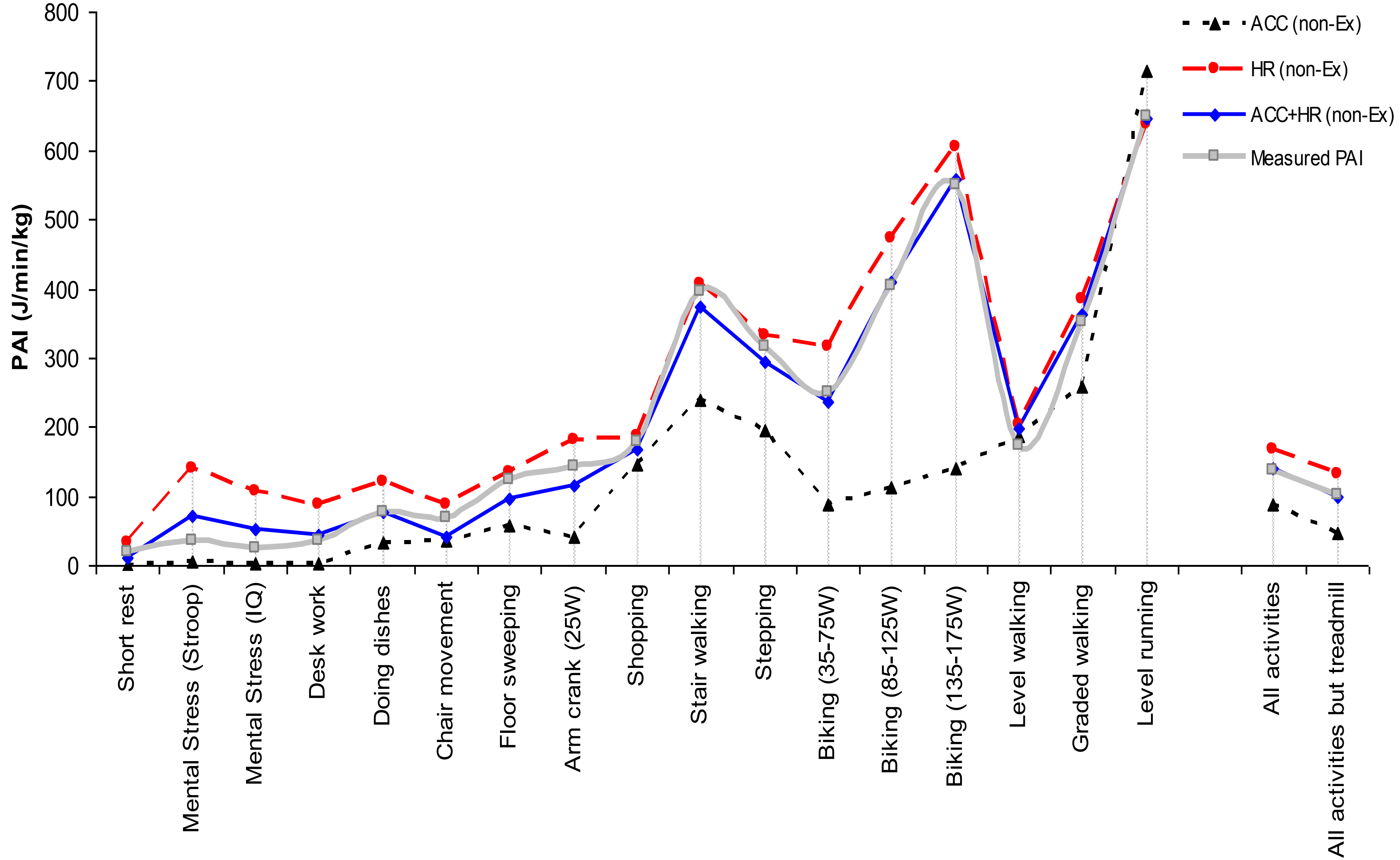
Accelerometry (magnitude):

Variability in the Acc-PAI relationship by mode of activity

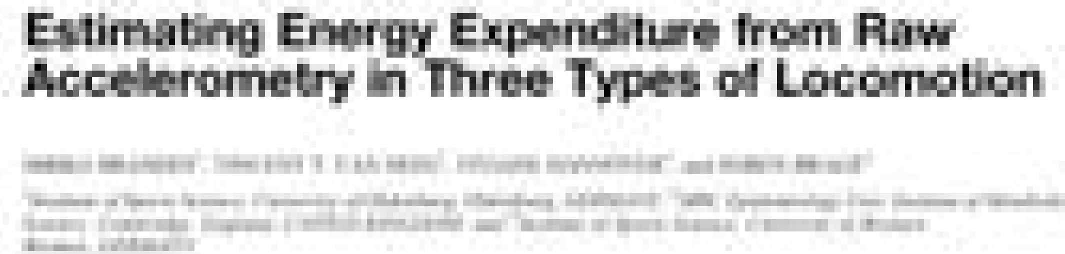


ACC (BLACK), HR, and ACC+HR during different activities

PAI reference**: breath² VO2+VCO2 **(GREY)

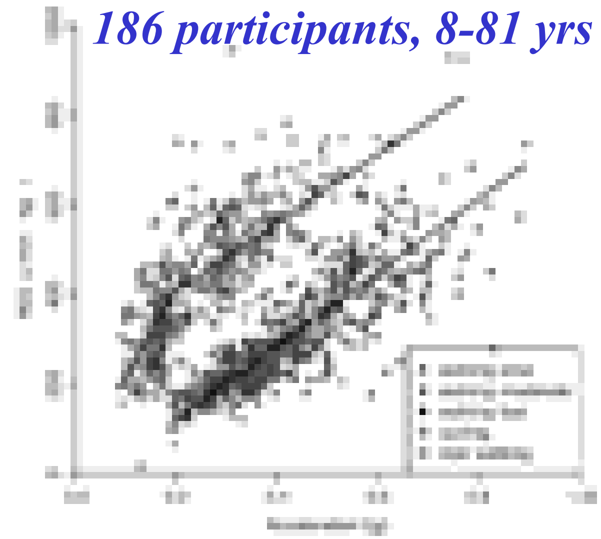


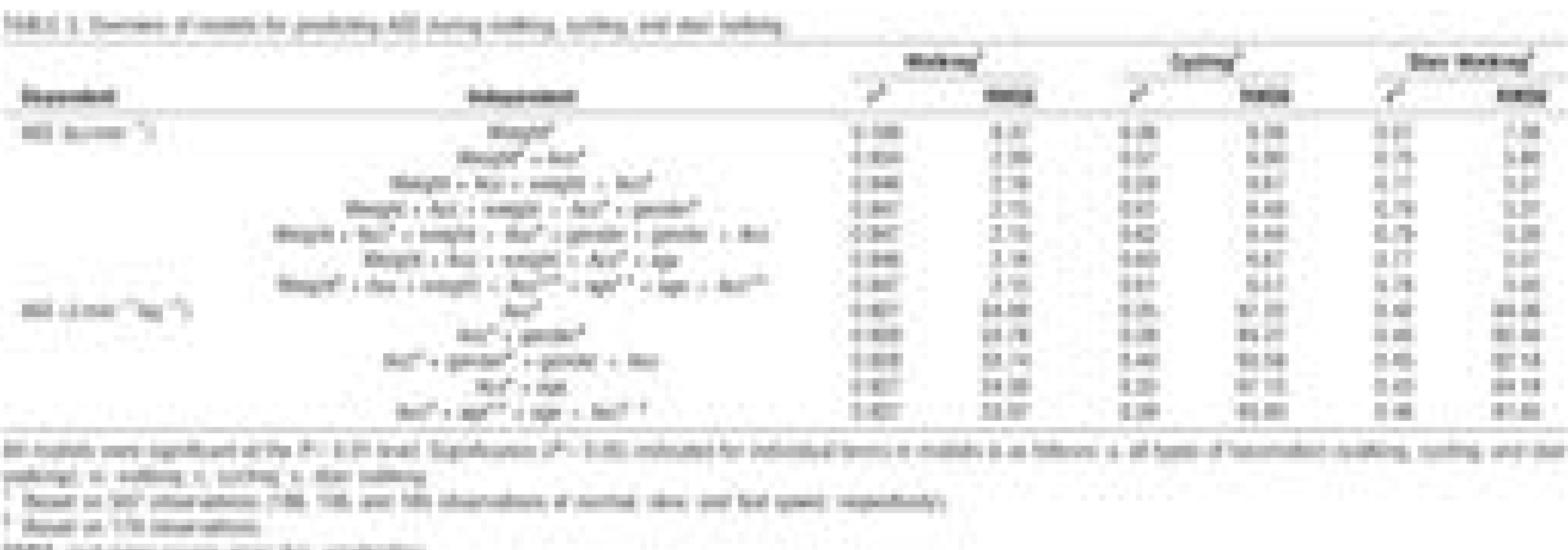
AEE estimated by waist-worn triaxial accelerometer


Estimating Energy Expenditure from Raw Accelerometry in Three Types of Locomotion

"Acceleration was summarised by applying a ***4th order Butterworth filter (ω$_0$ 0.1 – 15 Hz)*** *to each axis…"*

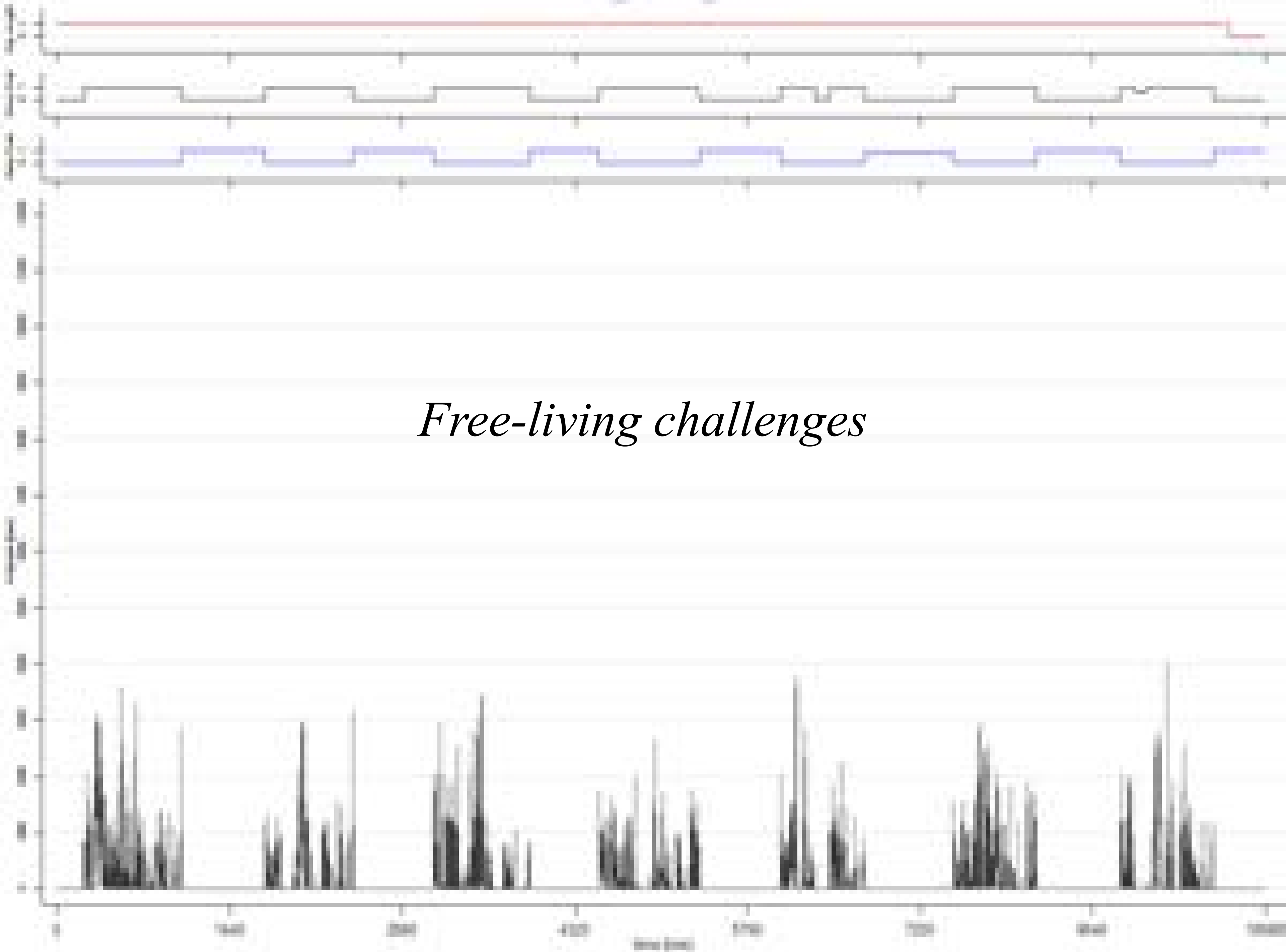
186 participants, 8-81 yrs



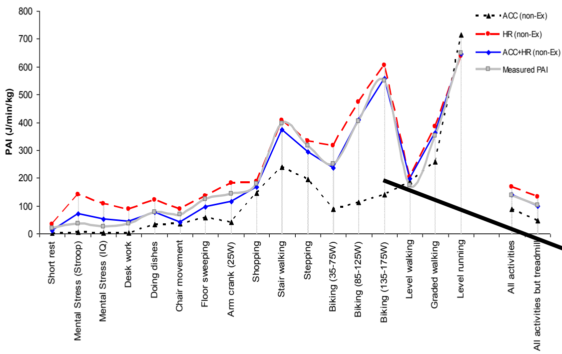


MSSE 2012

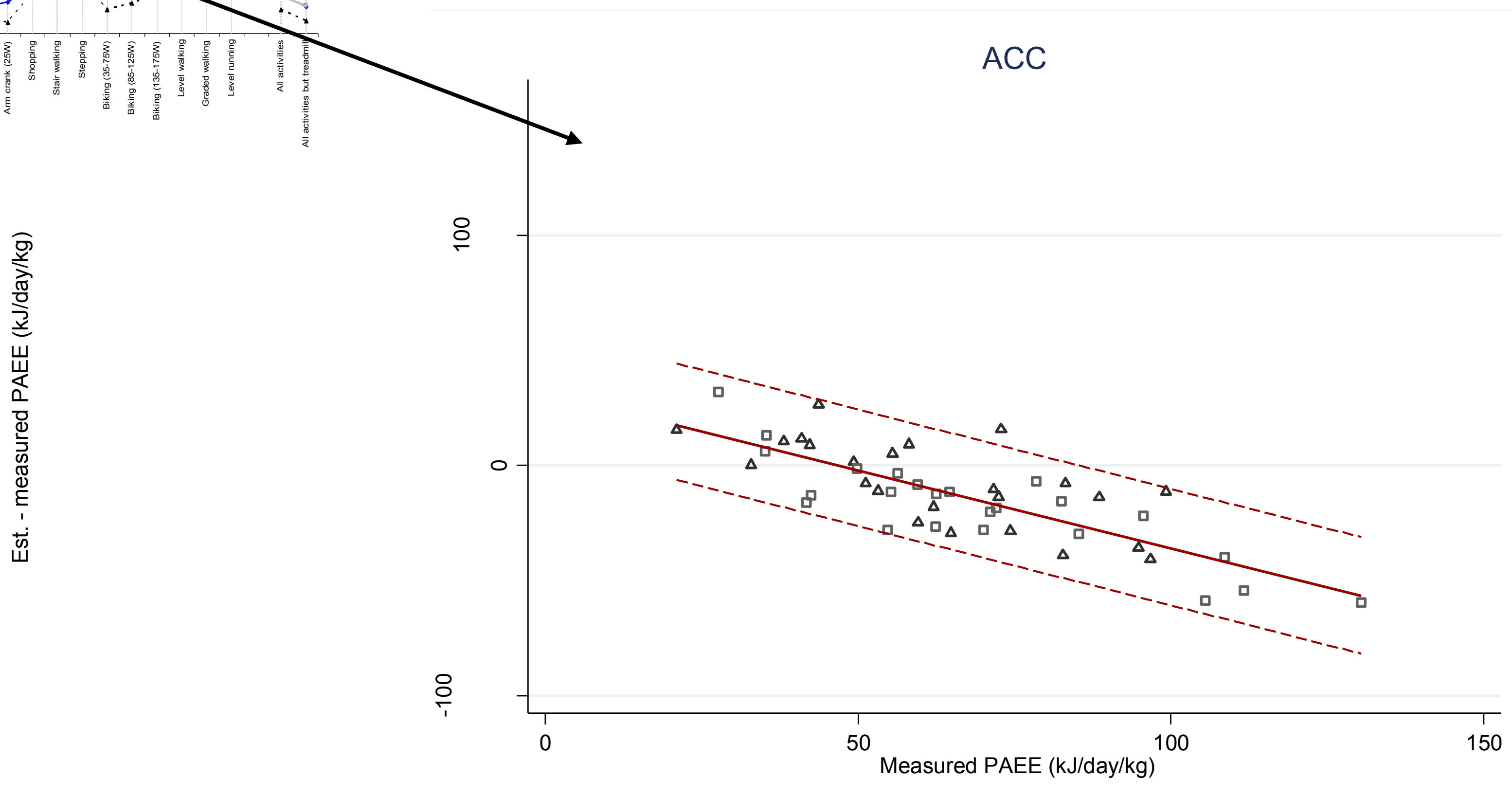
Free-living challenges



Estimation of free-living PAEE from uniaxial magnitude-based chest accelerometry model



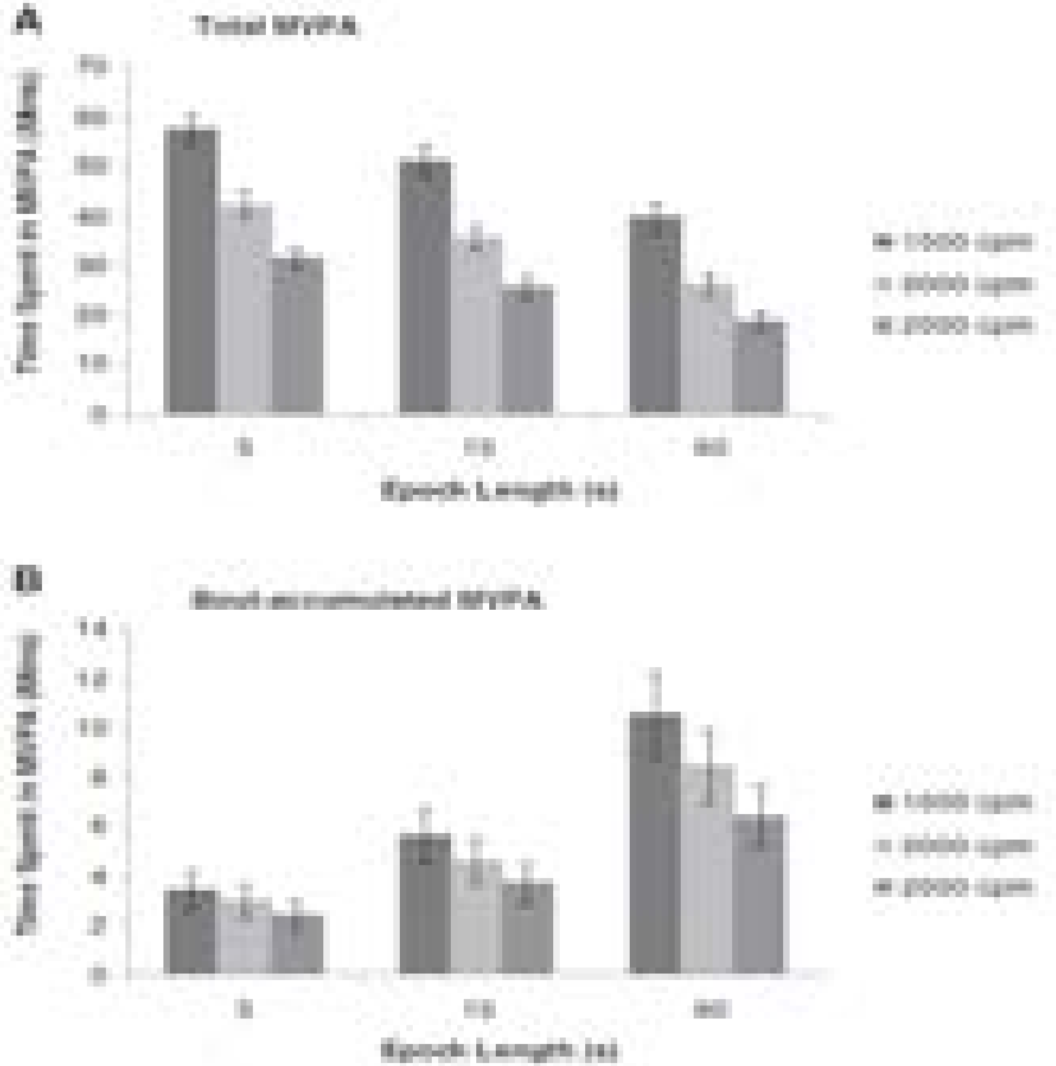
N=46 UK adults, 20-55 yrs



Brage et al, PLoS ONE 2015

Cutpoints, epochs, bouts …

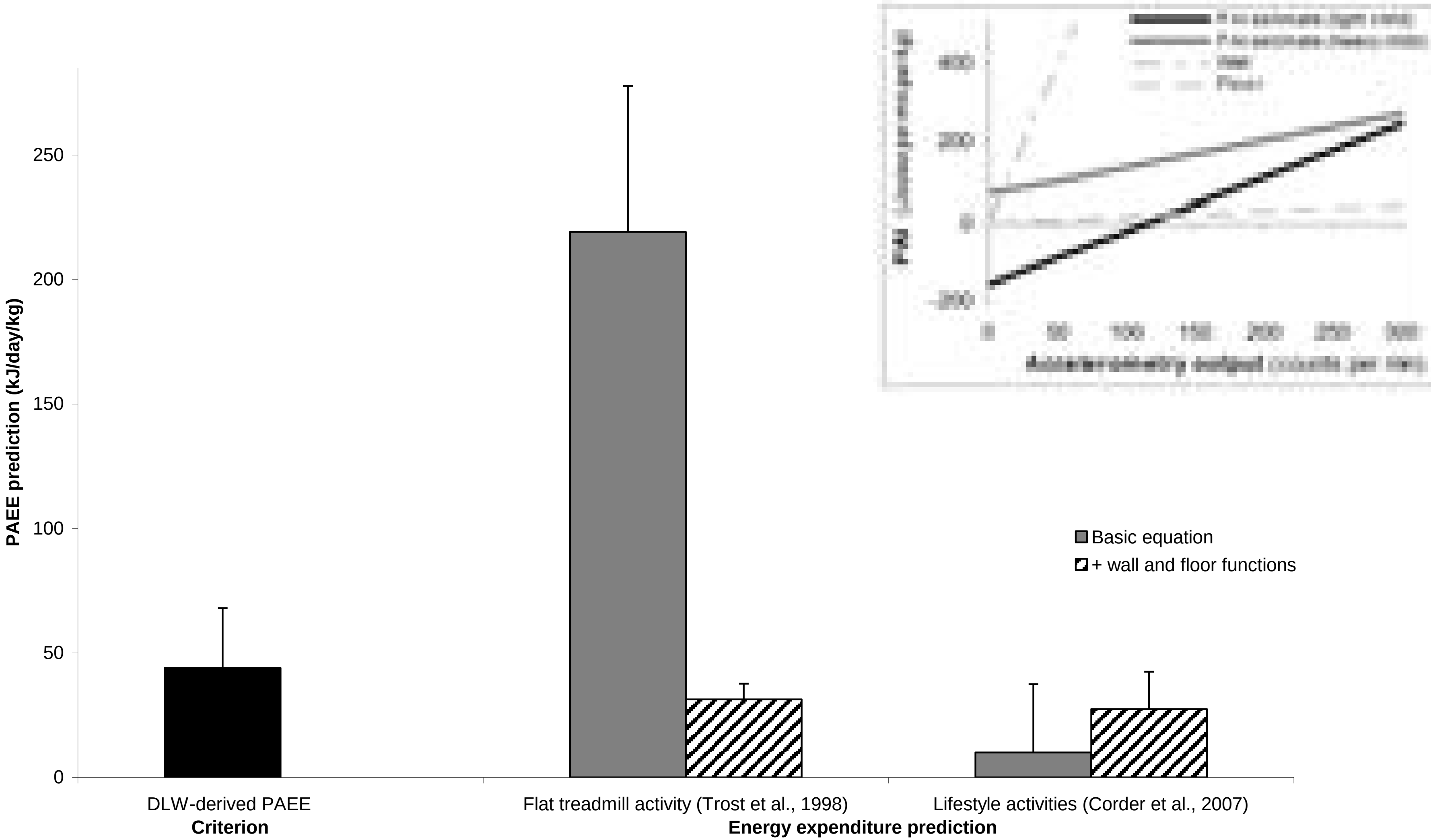
Same raw data



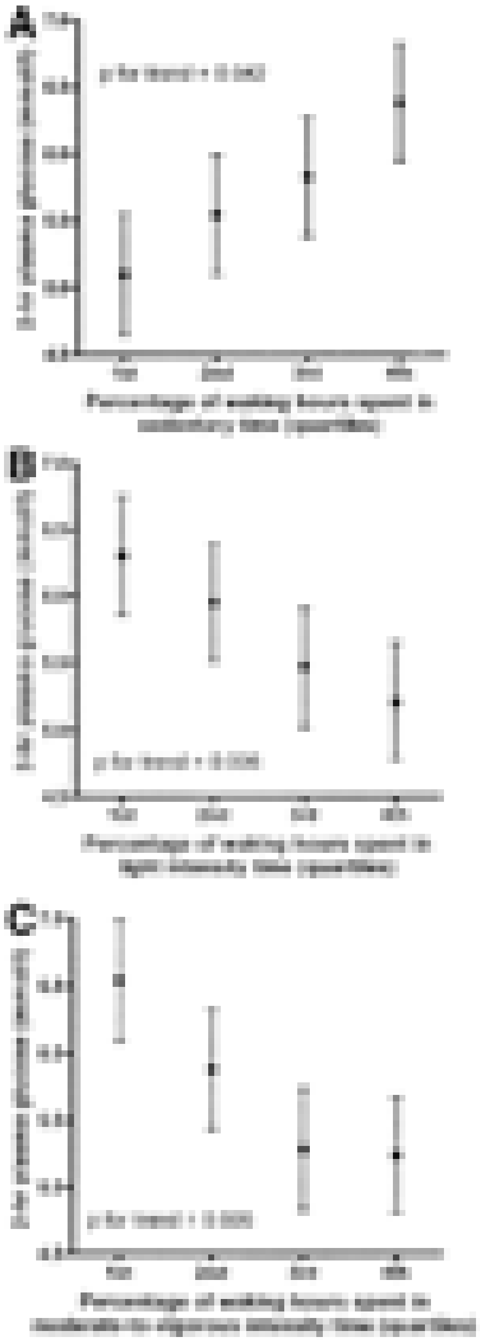
Orme et al, IJBNPA 2014

Modifying published prediction equations for activity intensity

Effect of censoring implausible estimates



Corder et al, 2008

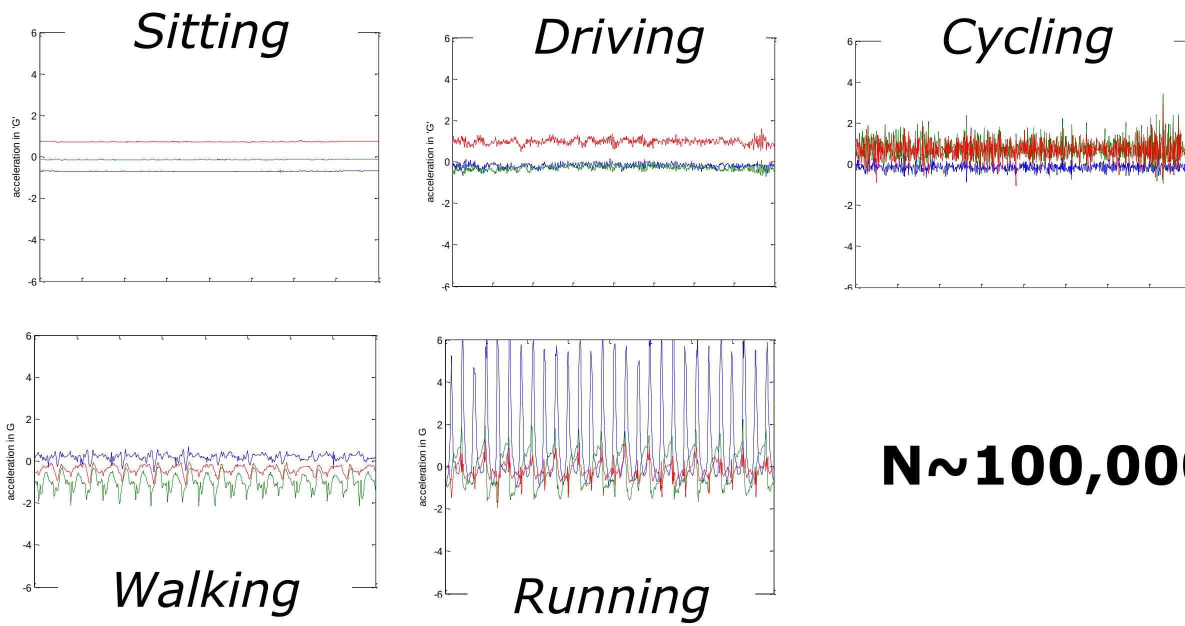


AusDiab:

Objectively (accelerometer) measured **sedentary** behaviour, **light-intensity** physical activity, and **moderate intensity** associated with 2-hr plasma glucose.

Source: Healy et al. Diabetes Care 2007

Waveform accelerometry in large cohorts



N~100,000

Validity

Vector magnitude ~ AEE_{DLW} : r=0.61

Vector magnitude ~ AEE_{Acc+Hr}: r=0.66

Van Hees et al 2013, 2014; White et al 2017; Doherty et al 2017

General activity classification: Machine-learning using camera criterion

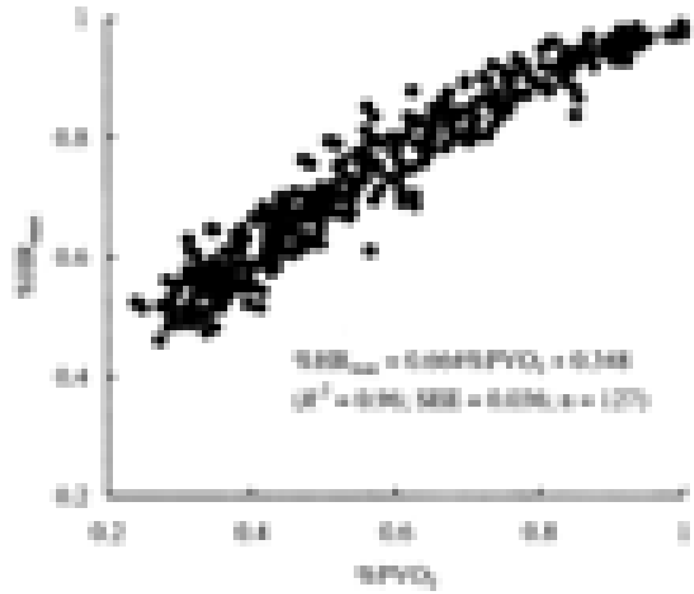
- **Photo every 20 sec**, then manually (researcher) coded activity type
- **126** signal **features -> Random Forest** (collection of decision trees) classifier

Table 1. Percentage of machine-learned behaviours automatically classified from wrist-worn accelerometer data. Confusion matrix after leave-one-out validation on 84,816 labelled minutes of human activity in free-living environments: the CAPTURE-24 study 2014-2015 (n = 57).

Prediction → Ground truth↓	Sleep	Sit/stand	Vehicle	Walking	Mixed-activity	Bicycling
Sleep	**95%**	4%	<1%	<1%	1%	<1%
Sit/stand	4%	**85%**	1%	2%	9%	0%
Vehicle	<1%	8%	**81%**	4%	7%	0%
Walking	<1%	13%	1%	**51%**	33%	2%
Mixed-activity	<1%	11%	3%	11%	**75%**	1%
Bicycling	<1%	<1%	3%	15%	7%	**75%**

Willetts et al, 2018

Heart Rate Monitoring



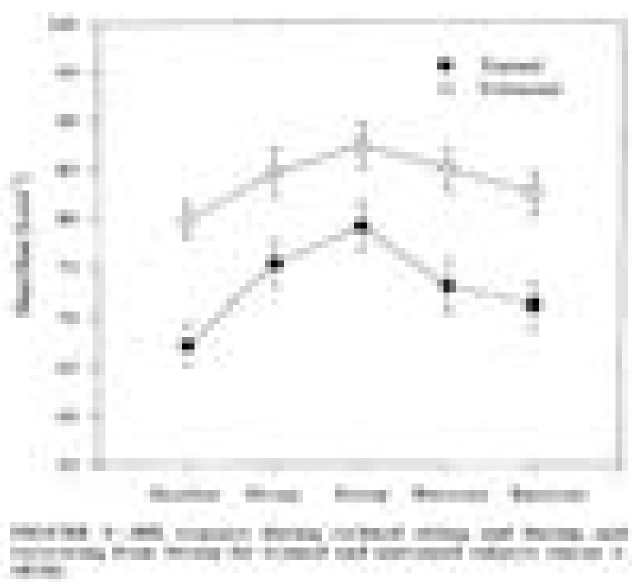
(Eur J Appl Physiol, 2001)

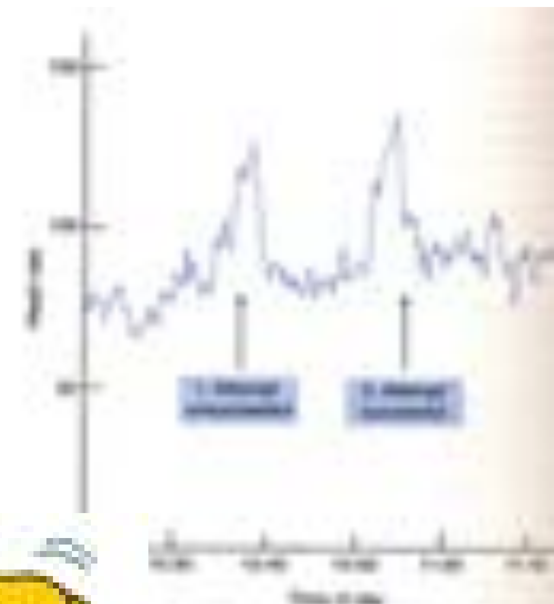
Principle:

There is a linear relationship between heart rate and energy expenditure during steady state work loads with large muscle groups (e.g., walking, cycling, running)

Minute-by-Minute Heart Rate Monitoring

- HR is a physiological response and therefore an indirect measure of physical activity
- HR may be affected by other factors than PA (e.g. stress, climate, dehydration)

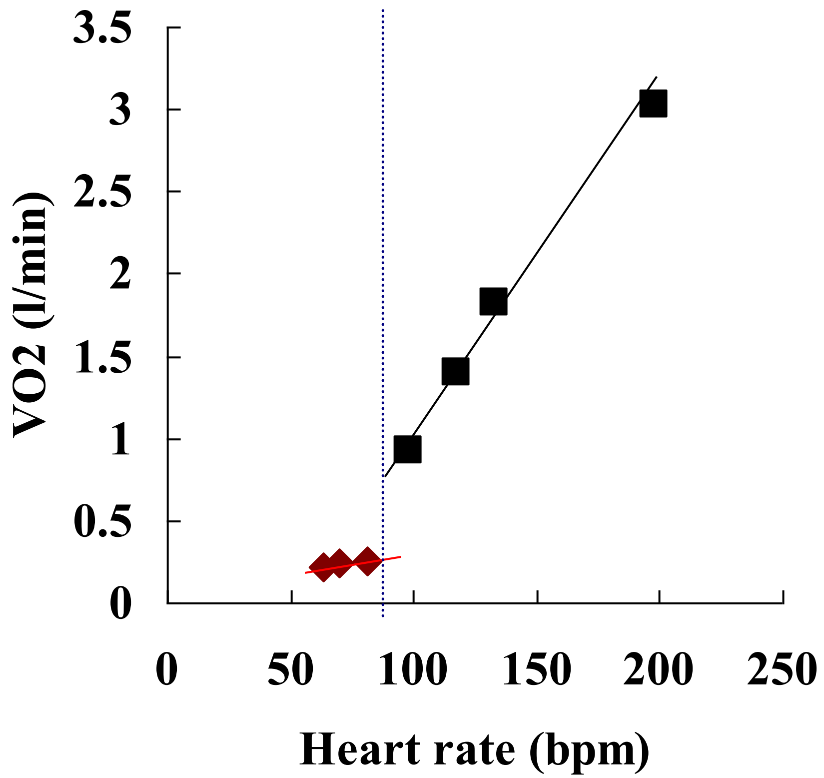




Individual calibration test

(CR fitness assessment)

The FLEX HR Method
(Spurr *et al*. 1988)



- **<u>CALIBRATION TEST</u>**: Assessment of energy expenditure and HR (supine rest, sitting, standing, exercising)
- **<u>DERIVE</u>**: Individually determined FLEX HR and HR-EE relationship
- **<u>MONITOR</u>**: Min-by-min HR during free-living and apply derived calibration factors to estimate intensity (EE)

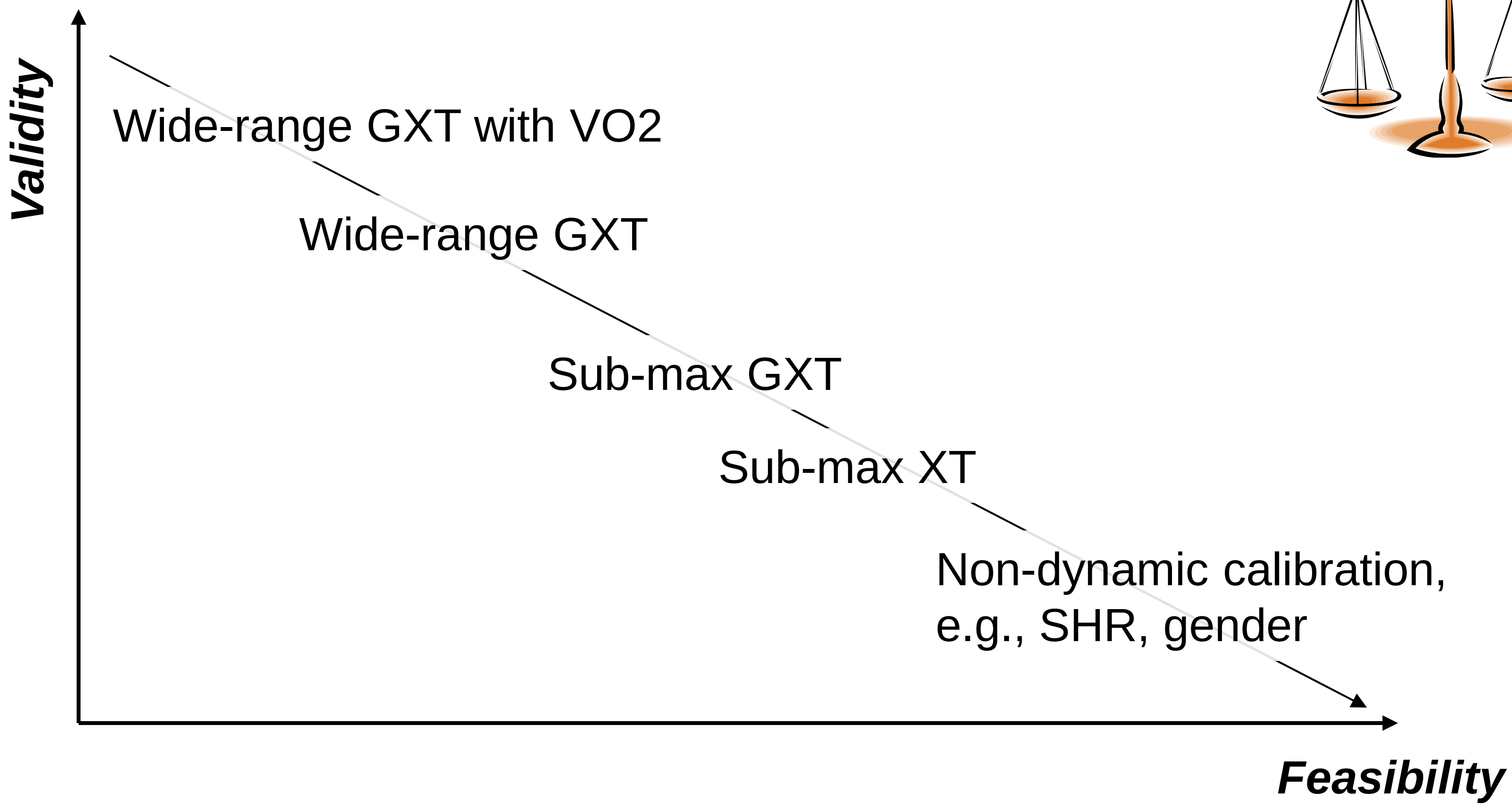
HR calibration models

	Calibration level	R^2 within	R^2 between	R^2 overall
I.	TM + VO2	.975	**.999**	.977
II.	TM	.963	**.808**	.947
III.	Step + VO2	.947	**.676**	.913
IV.	Step	.948	**.675**	.919
V.	Walk + VO2	.928	**.614**	.888
VI.	Walk	.928	**.590**	.892
VII.	Non-exercise (static)	.924	**.302**	.812

Brage et al, JAP 2007

Individual calibration hierarchy

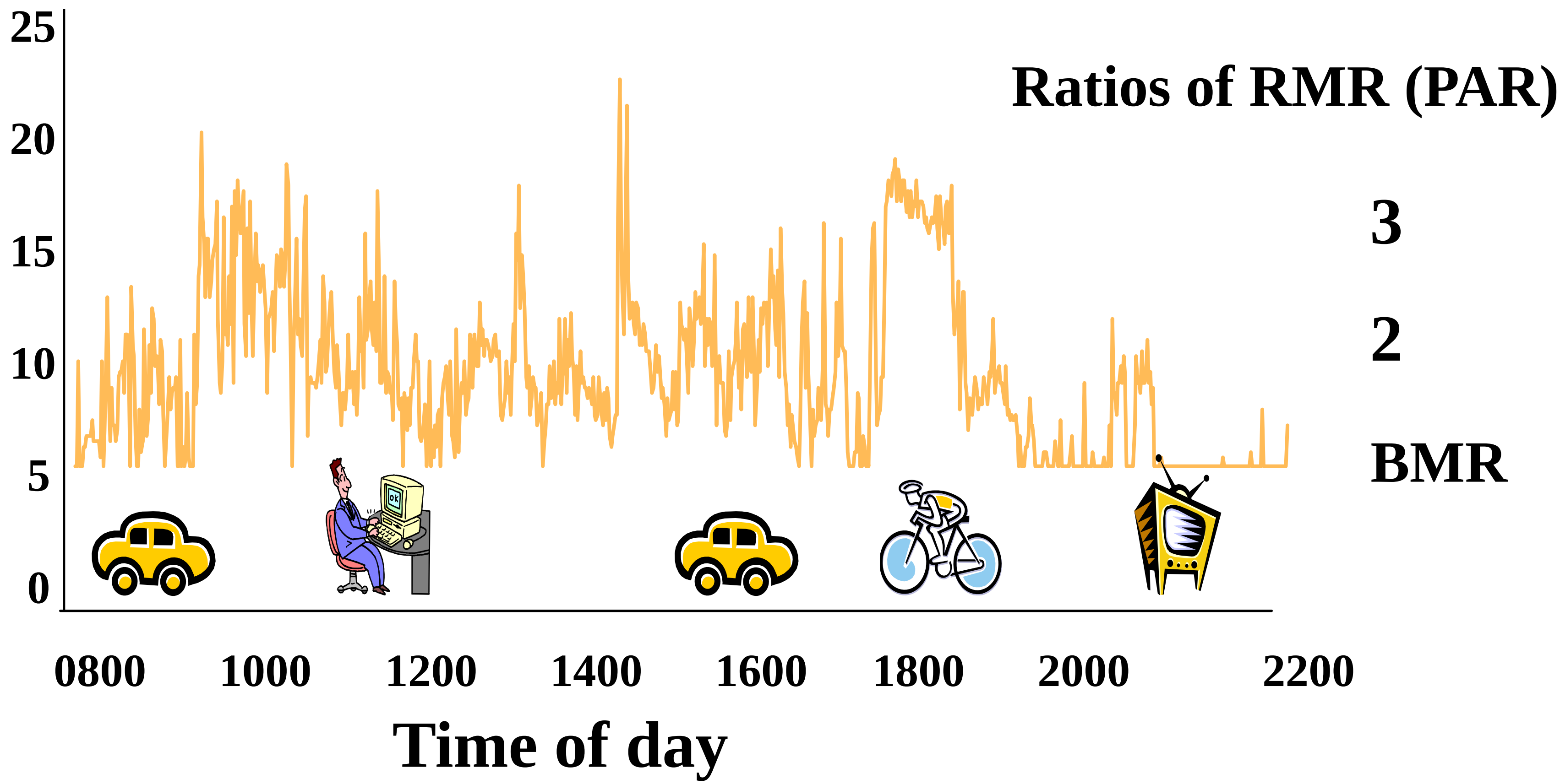
Balancing validity and feasibility



(applicable to HR monitoring)

Brage et al, JAP 2007

Energy Expenditure – Flex HR method



$$TEE = EE_{sleep} + EE_{rest} + EE_{act}$$

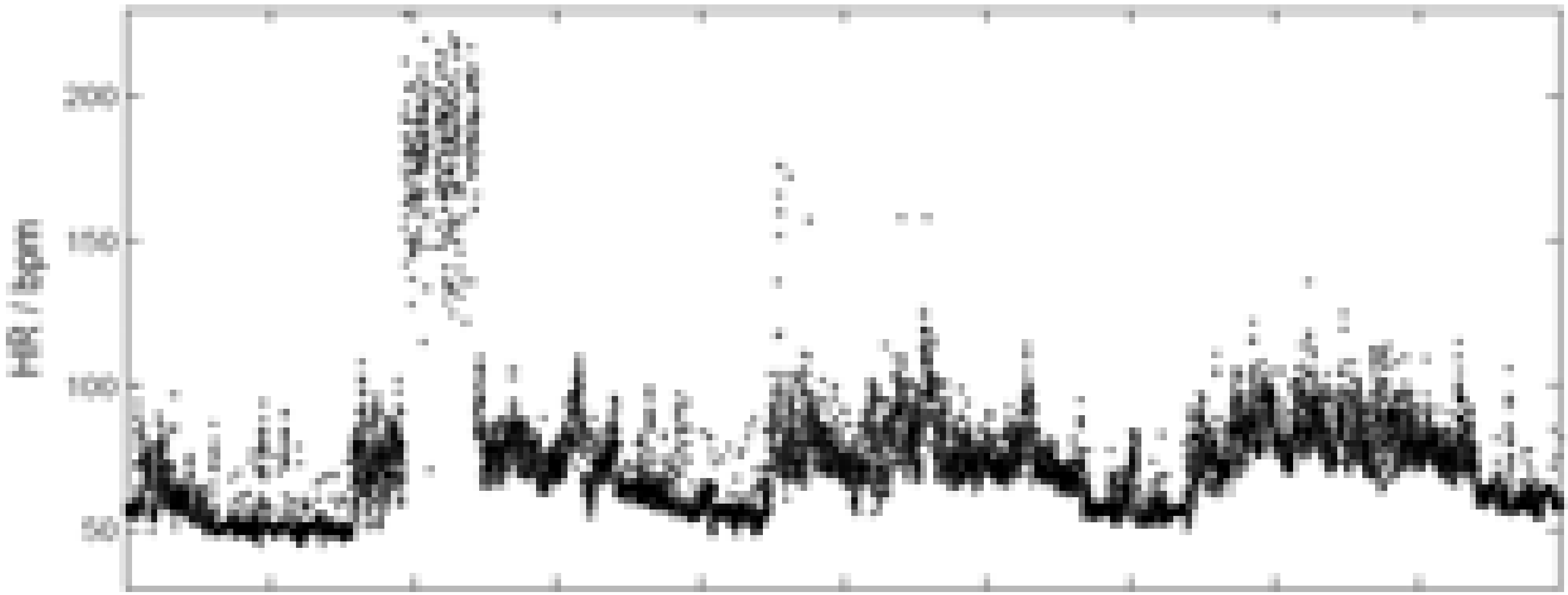
$$EE_{sleep} = 0.95 * REE$$

EE_{rest} = REE (for HR < FLEX HR)

EE_{act} = EE from regression equation (for HR $\geq$ FLEX HR)

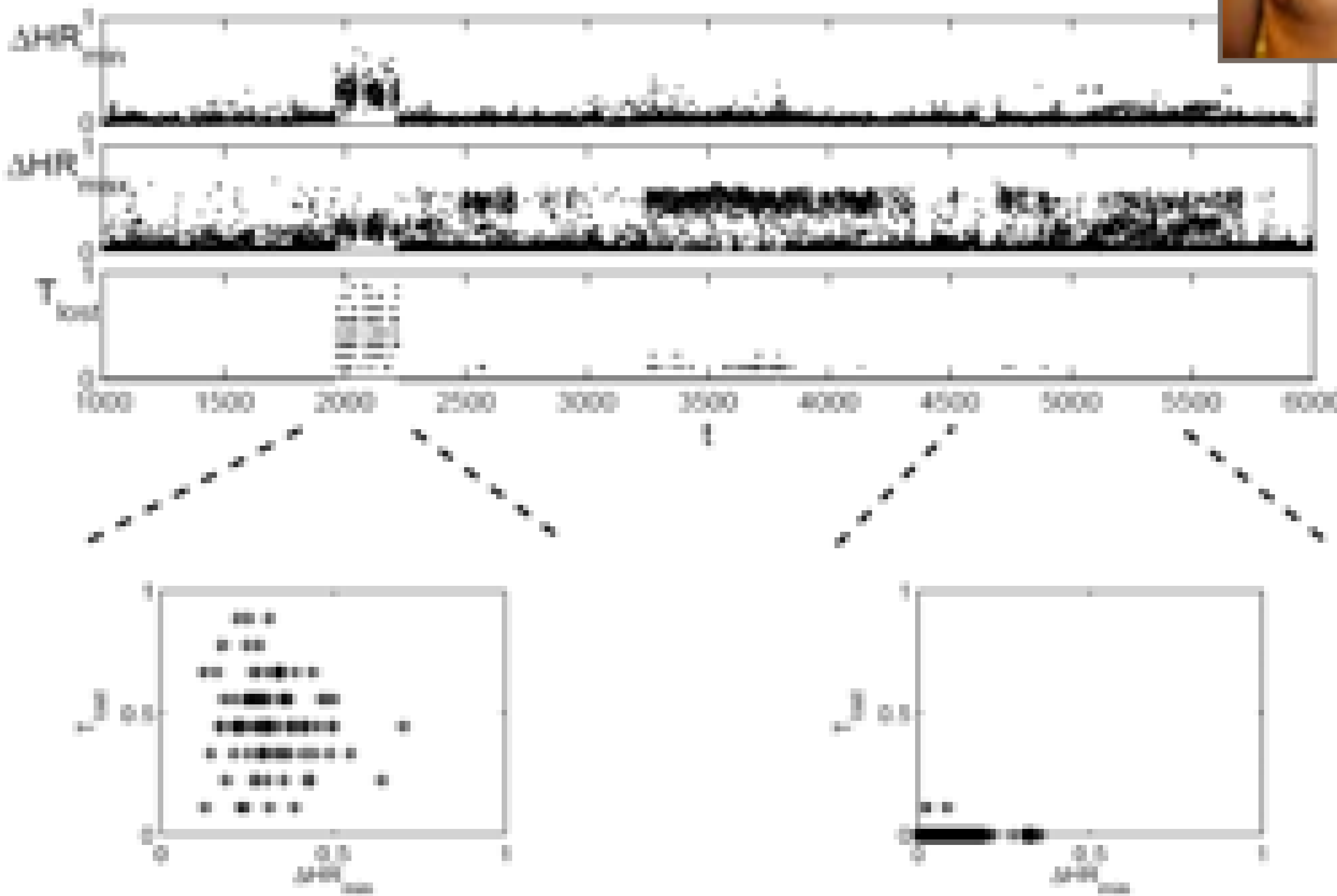
Free-living challenges: data are noisy and incomplete!

HR measurement noise



Standard average heart rate minute-by-minute

Noise detection



Stegle et al, IEEE Trans Biomed Eng 2008

HR inference model

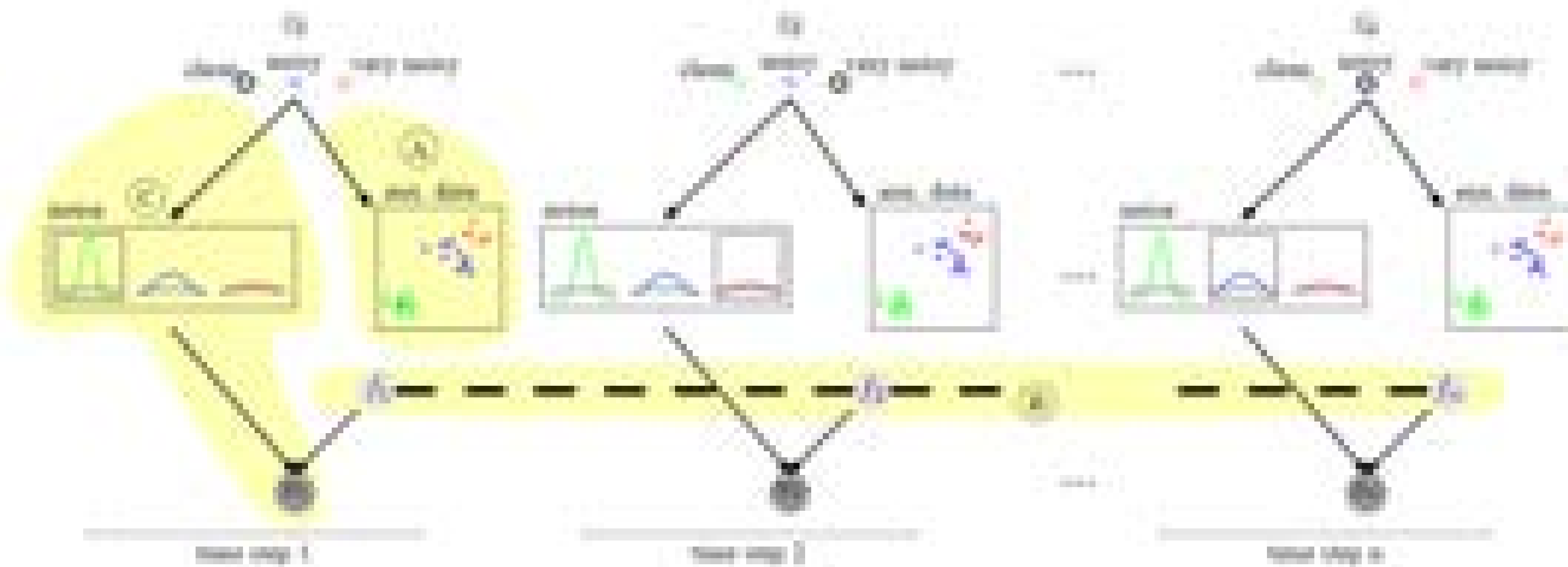


FIG. 2: Heart rate inference model comprised of clustering module (A), Gaussian Process prior (B), and noise model (C) with symbols as defined in the text. Variables y_n denote observed mean heart rate at time point n, f_n is the latent heart rate at this time, and z_n the status of this data point, i.e., its noise level.

Stegle et al, IEEE Trans Biomed Eng 2008

Physiological Priors

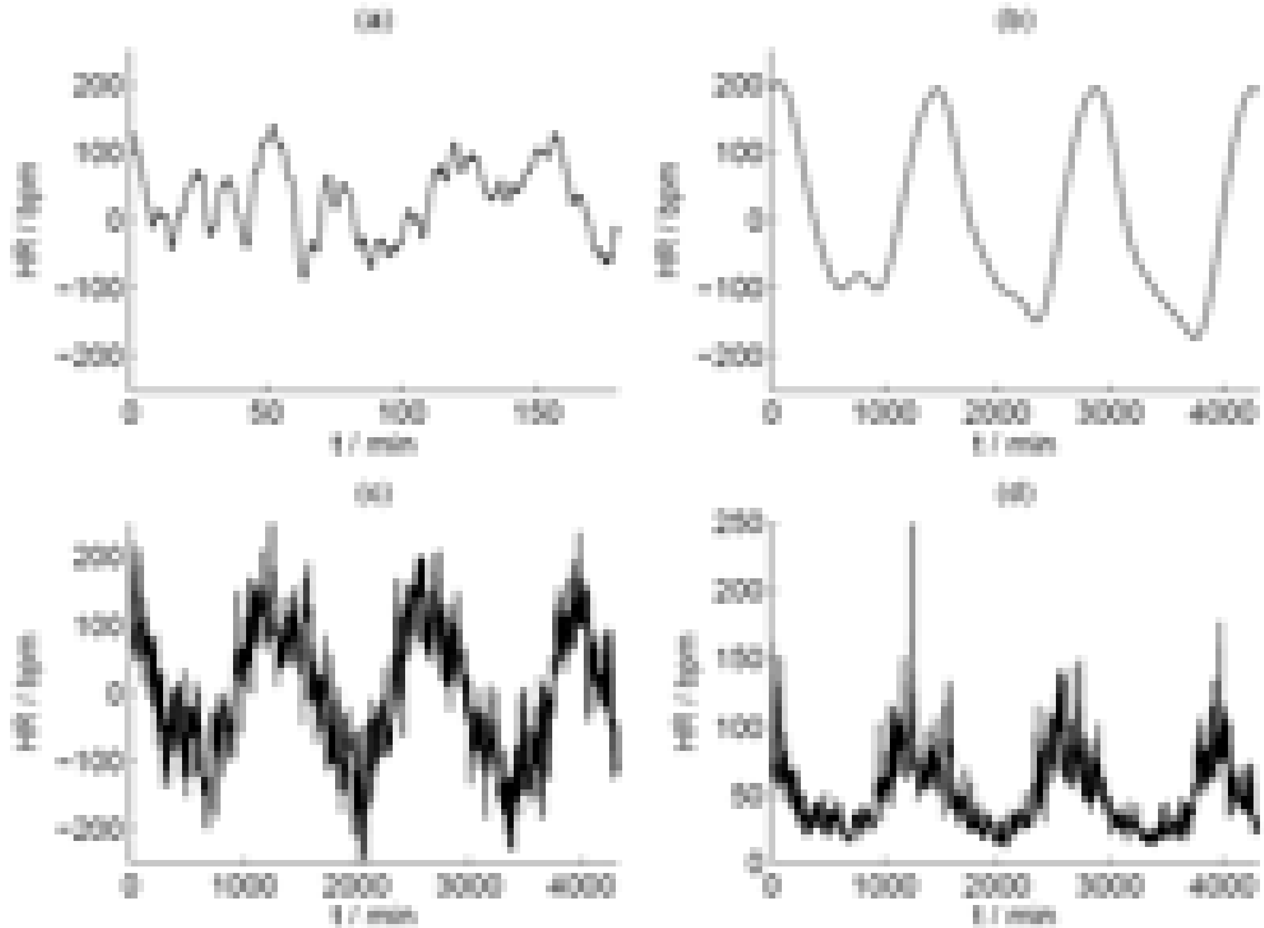
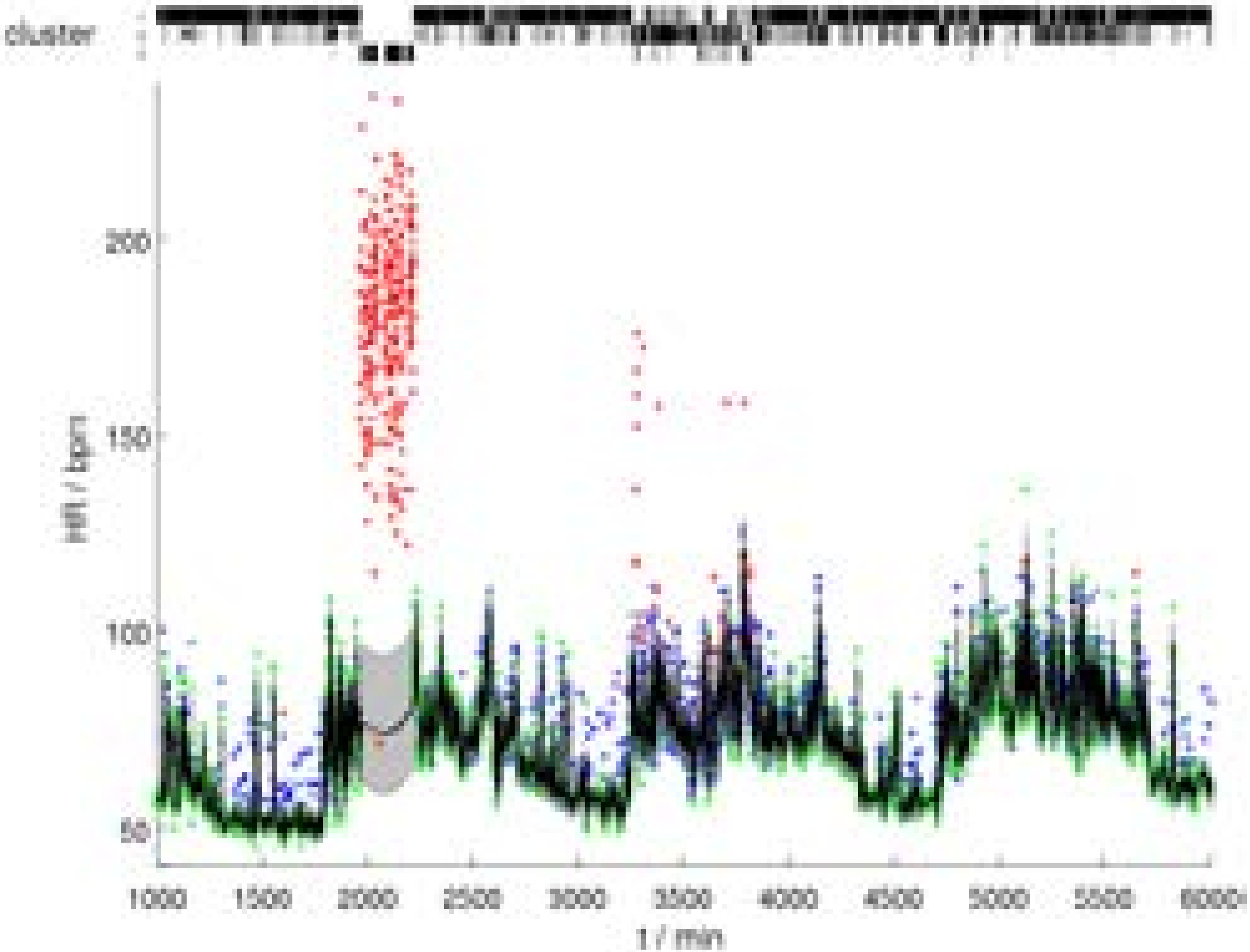


FIG. 4: Samples from the short lengthscale kernel K_2 (a), the long lengthscale kernel K_1 (b), their sum (c) and the log-transformed GP prior (d) with hyperparameters as defined in the text.



Stegle et al, IEEE Trans Biomed Eng 2008

Combined ACC + HR monitoring

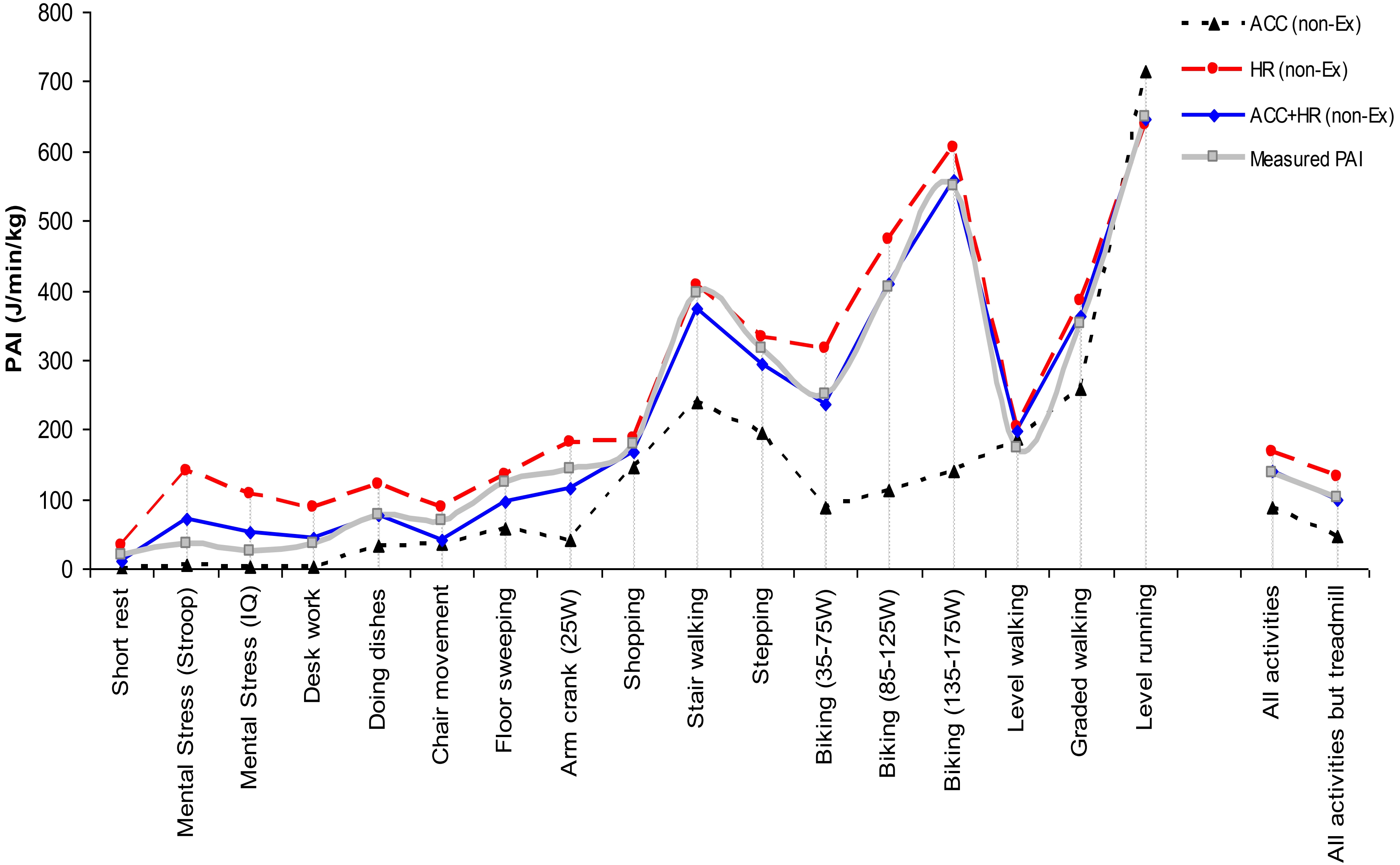
Eur J Clin Nutr 59, 561-70, 2005

ORIGINAL COMMUNICATION

Reliability and validity of the combined heart rate and movement sensor Actiheart

ACC, HR, and **ACC+HR** during different activities

PAI reference**: breath² VO2+VCO2 **(GREY)



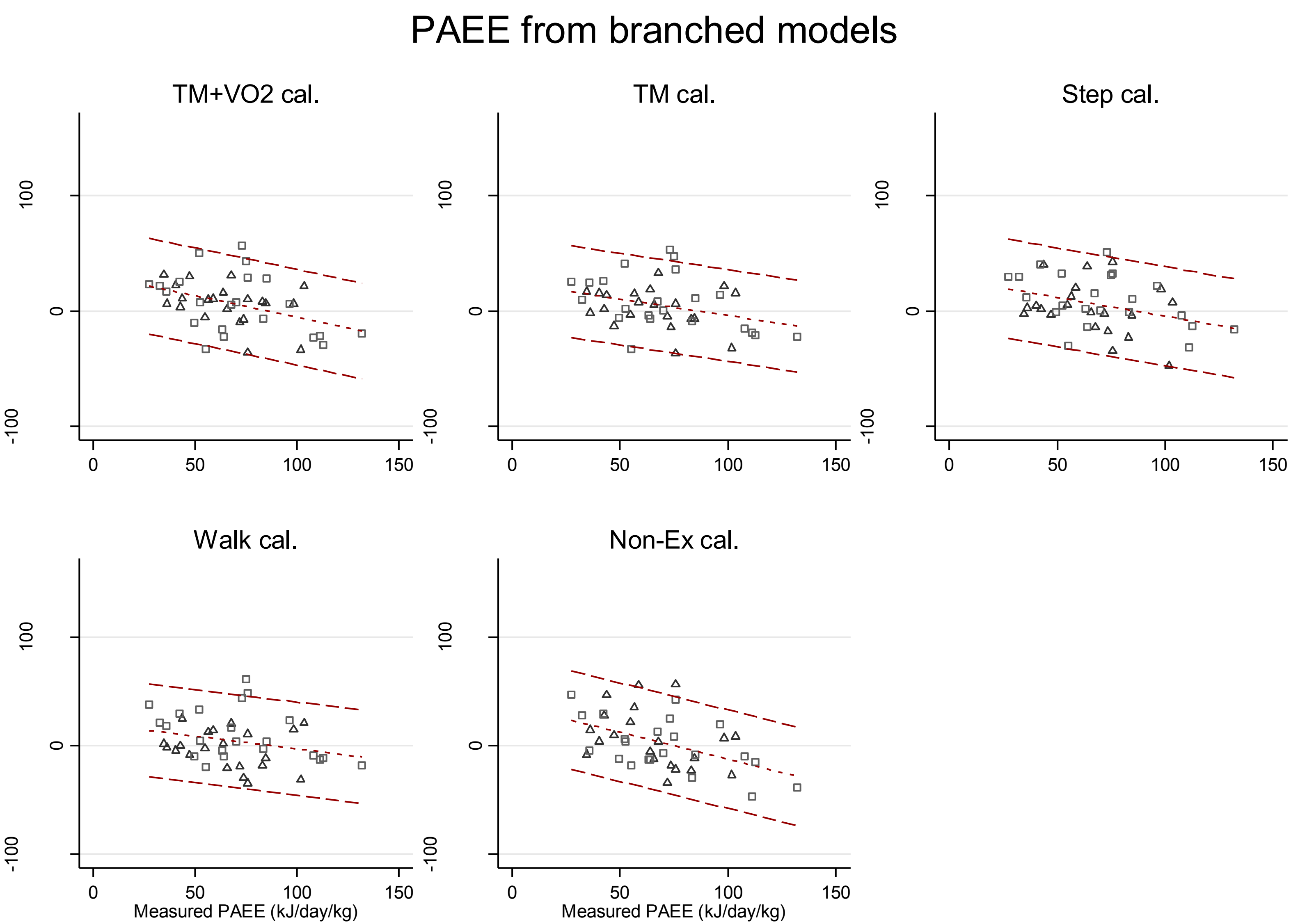
Simulated daily-living activities: **Error**

	Calibration level				
	TM+VO_2	TM	Step	Walk	Non-Ex
ACC	125 64%	127 65%	130 67%	128 66%	129 66%
Flex HR	56 29%	59 30%	72 37%	69 35%	93 48%
ACC+HR	55 28%	57 29%	58 30%	65 33%	71 36%

***Errors are J/min/kg** and also expressed relative to measured PAI*

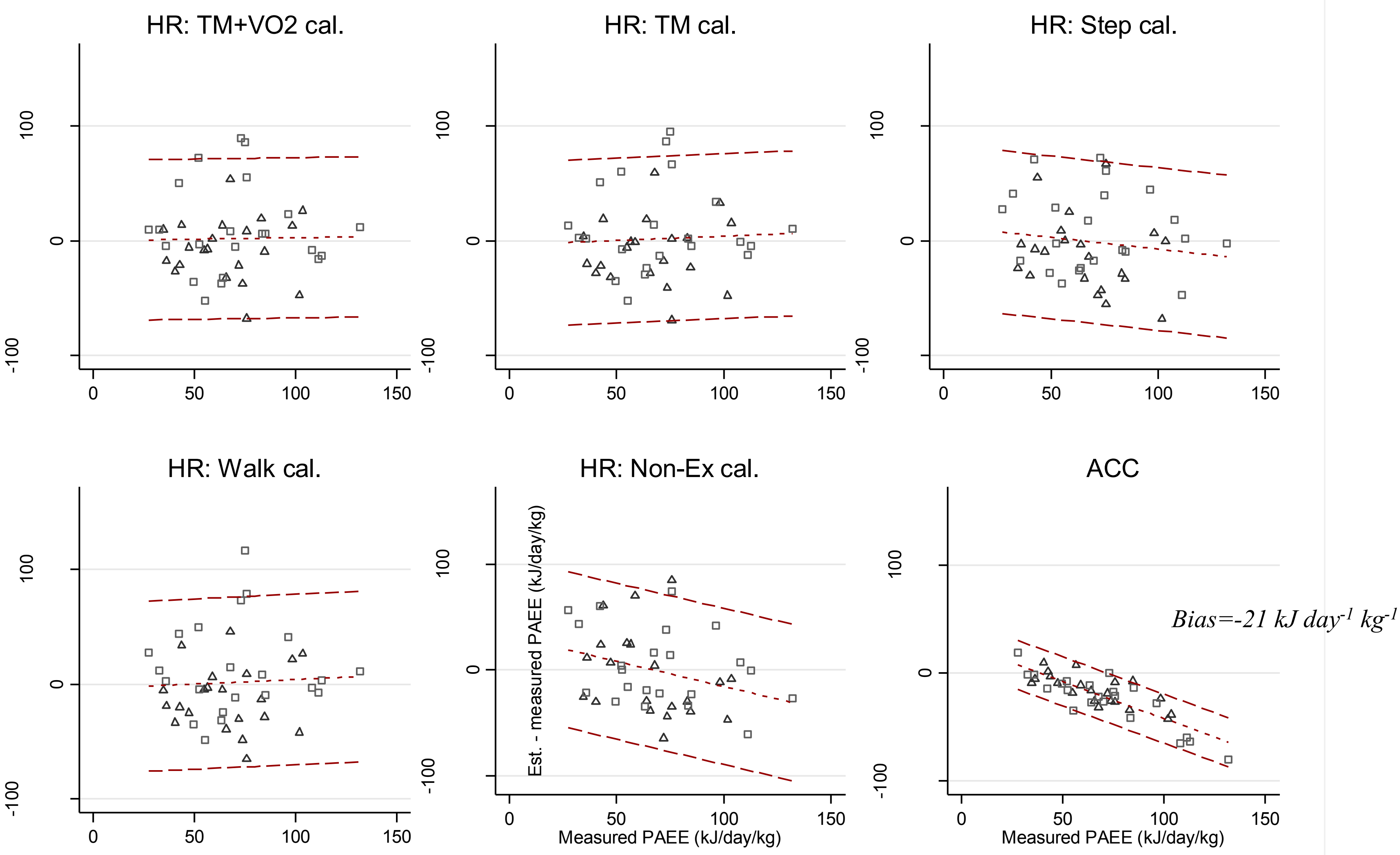
n=38, unpublished

Free-living validation (DLW)



Brage et al, PLoS ONE 2015

PAEE from singular models



Brage et al, PLoS ONE 2015

RMS Errors and correlations: Free-living PAEE

	Calibration level				
	$TM+VO_2$	TM	Step	Walk	Non-Ex
ACC	-	-	-	-	24 *(.52)*
Flex HR	33 *(.58)*	34 *(.58)*	32 *(.57)*	34 *(.57)*	37 *(.40)*
ACC+HR	21 *(.64)*	20 *(.67)*	21 *(.66)*	21 *(.66)*	24 *(.55)*

Data are RMSE in kJ/day/kg and correlations (brackets), based on DLW (Scholler method)

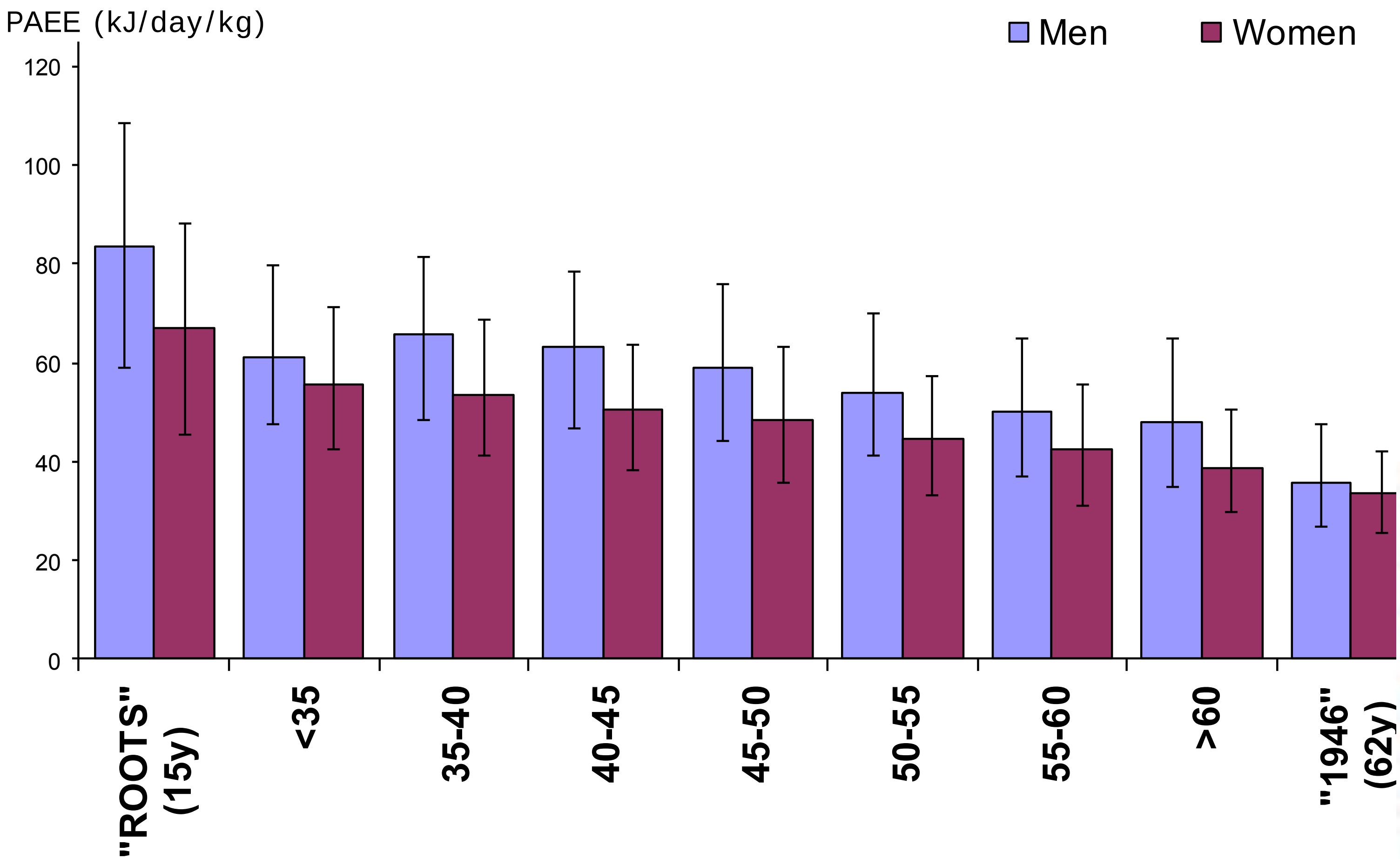
Brage et al, PLoS ONE 2015

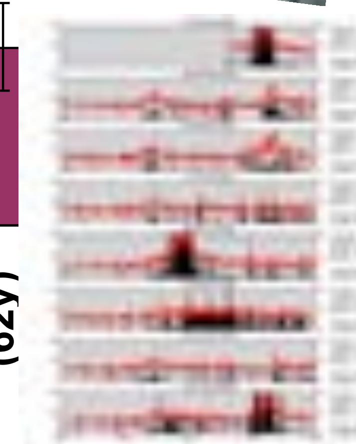
DLW-based PAEE validation: *UK, Cameroon, Alaska, France*

	UK (n=46)		Cameroon (n=33)		Alaska (n=28)		France (n=35 men)	
Calibration	***Step***	*Group**	***Step***	*Group**	***Step***	*Group**	***Bike***	*Group*
Mean bias	5 (8%)	5 (8%)	-5 (9%)	-9 (15%)	-2 (3%)	-6 (8%)	-5 (8%)	-8 (13%)
RMSE	**21**	**24**	**29**	**30**	**28**	**33**	**14**	**21**
Correlation, r	*.66*	*.55*	*.40*	*.39*	*.62*	*.43*	*.81*	*.62*

*Data are kJ/day/kg. DLW estimate based on Scholler method. *Population-specific group equations*

Physical activity energy expenditure



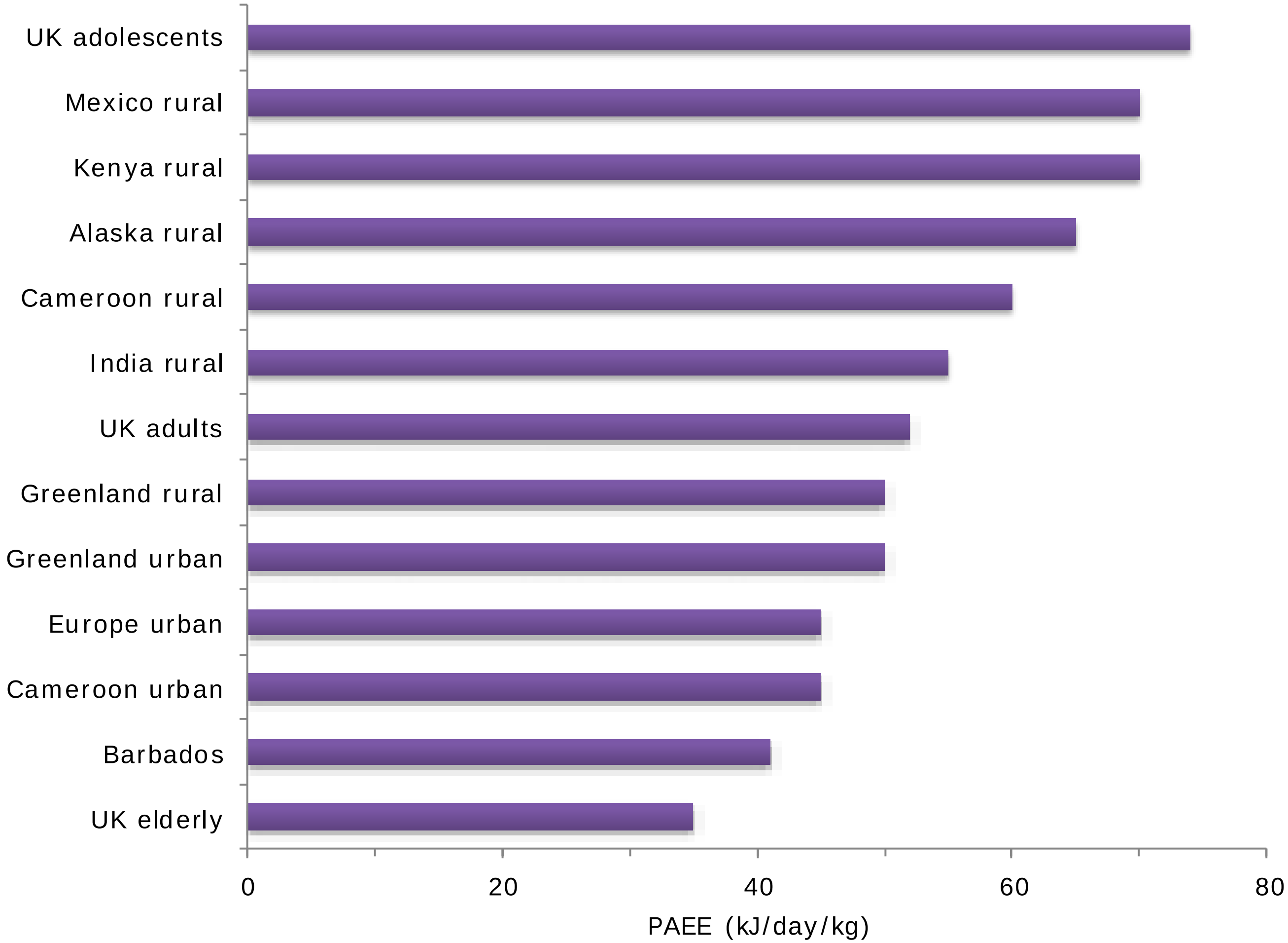


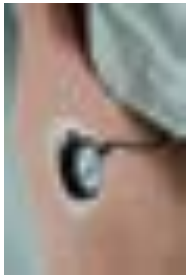
Collings et al, 2014

Lindsay et al (in prep)

Golubic et al, 2014

Global variation in activity energy expenditure





Assah et al, 2011+2015

InterAct Consortium, 2012

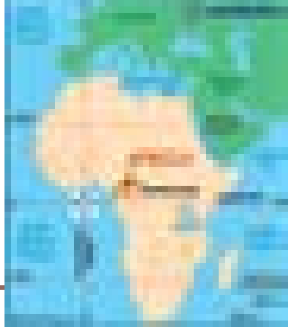
Christensen et al, 2012a+b

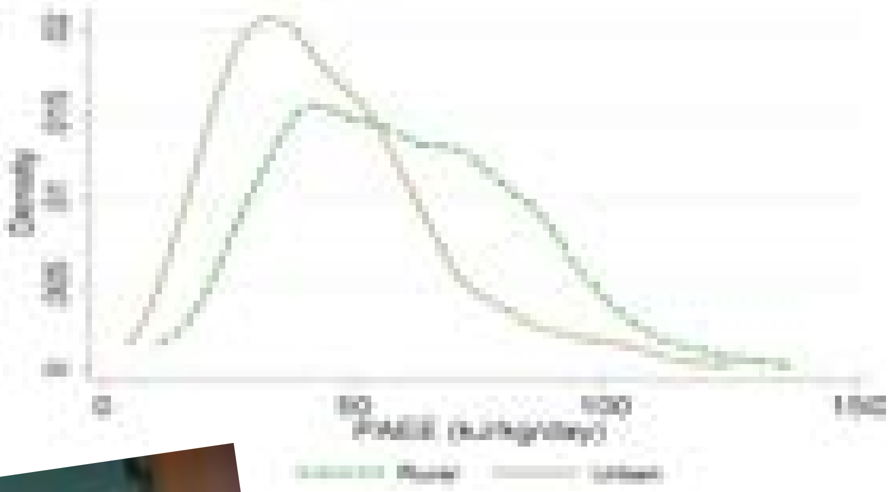
Dahl-Petersen et al, 2013+2014

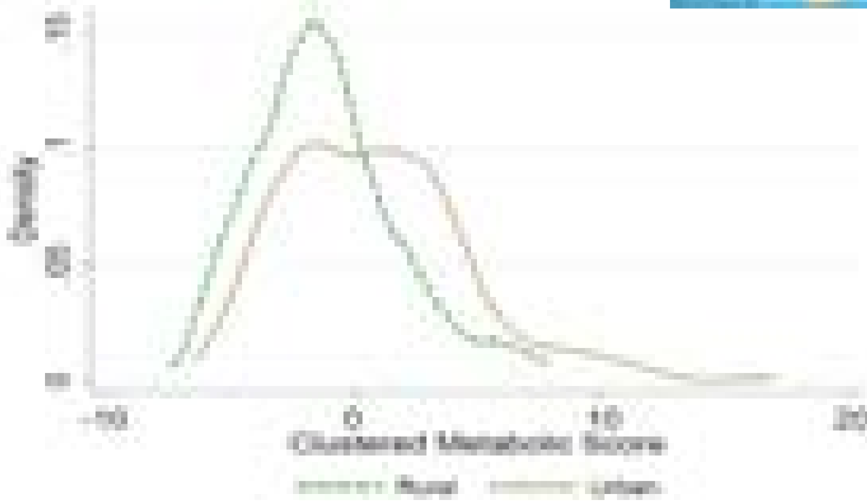
Collings et al, 2014

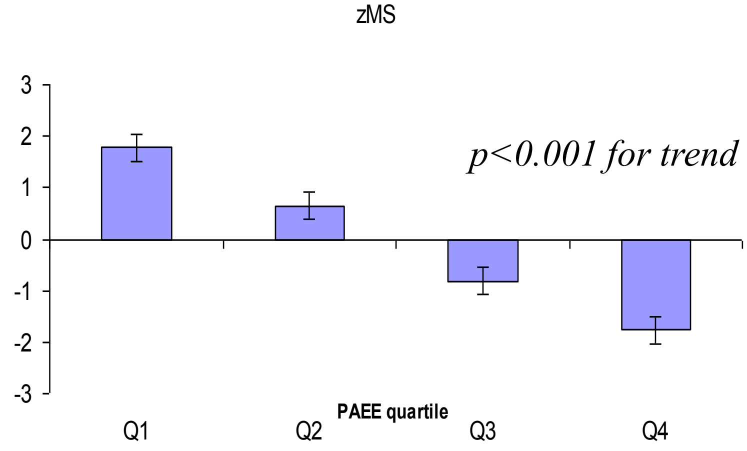
Golubic et al, 2014

Activity and Clustered Metabolic Risk in Cameroon
Rural - urban differences in 552 adults



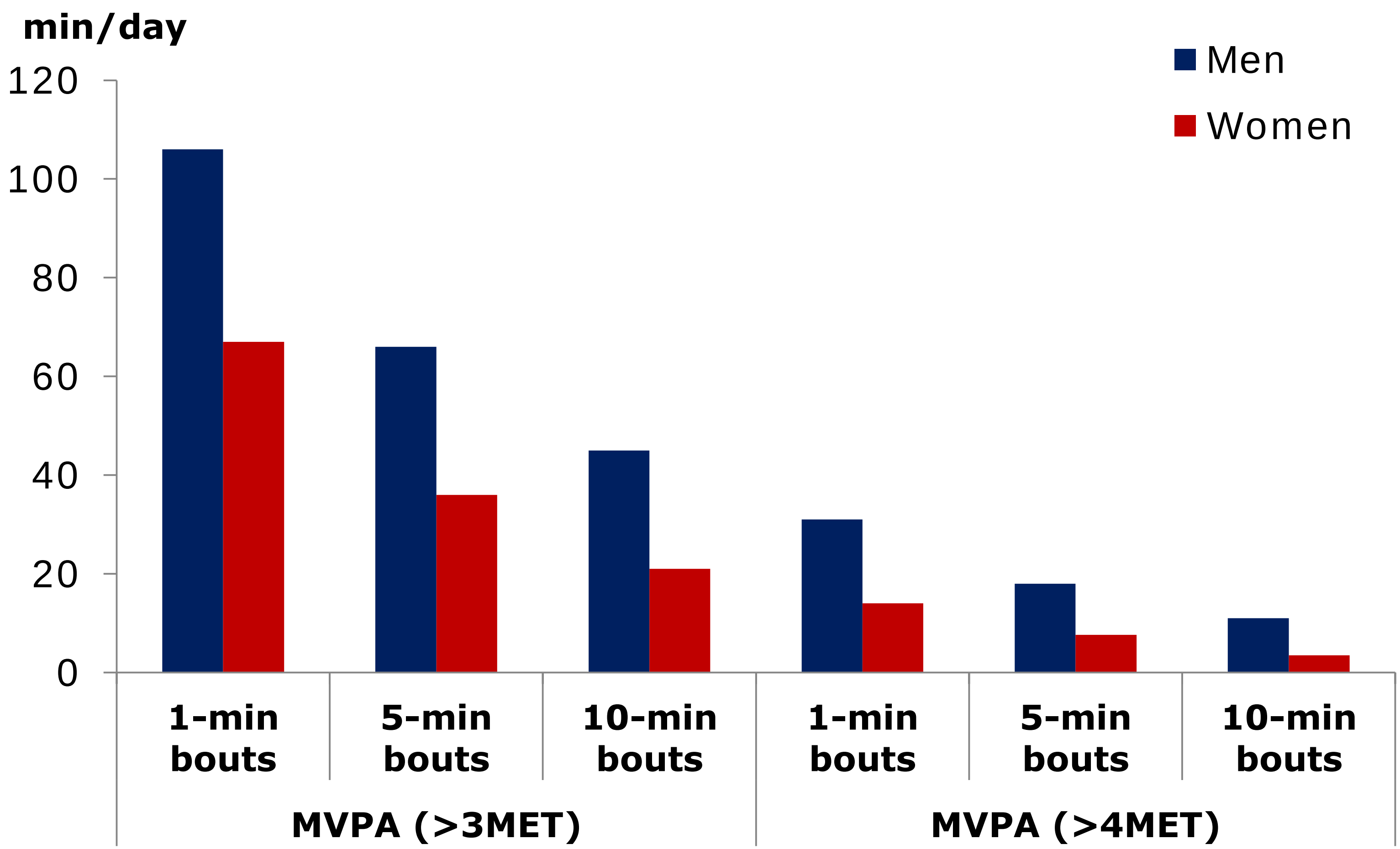






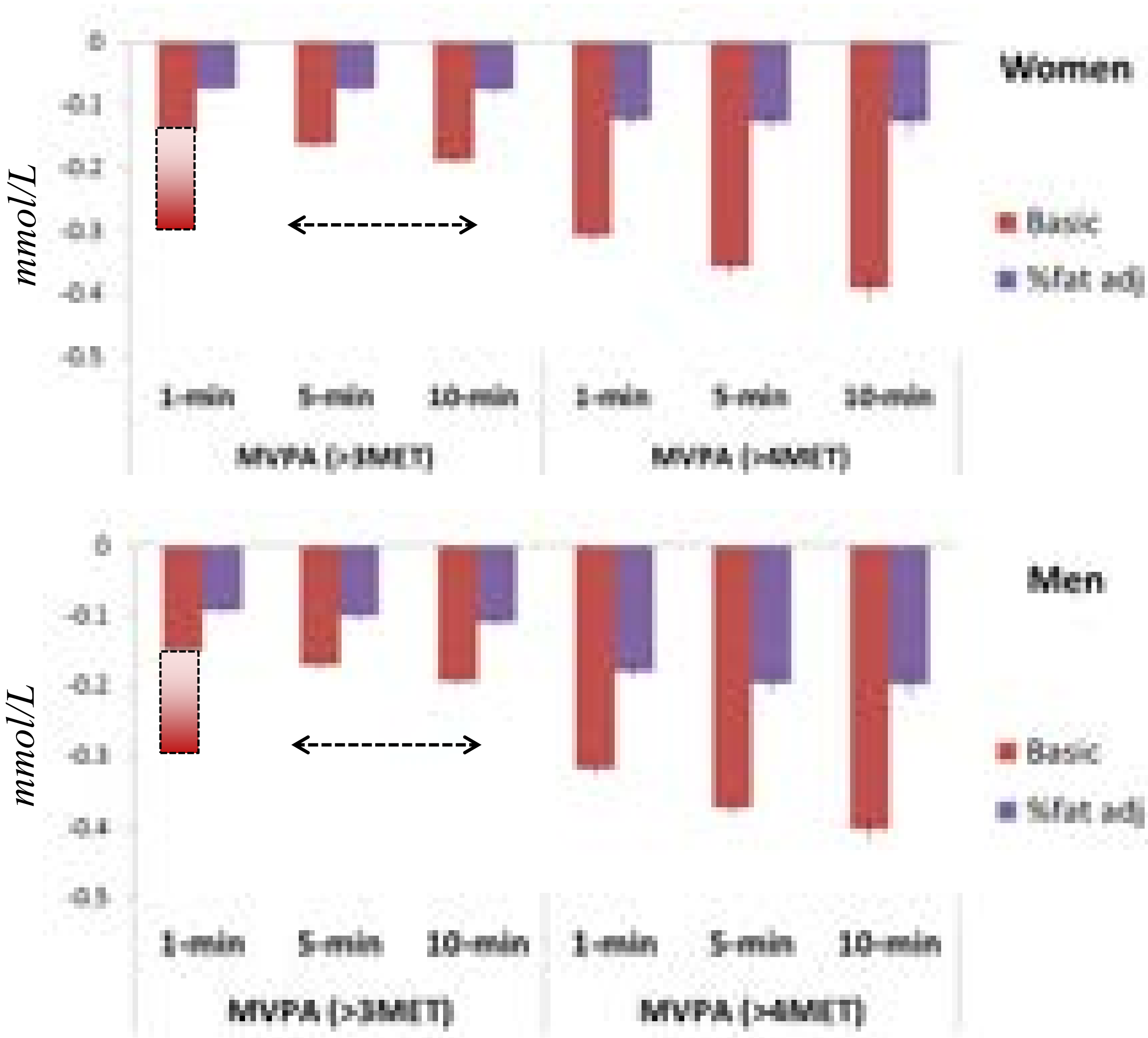
Assah et al, 2011

Physical activity levels by bout duration



Lindsay et al (in Review)

Associations with 2-hour glucose



For every
+30 min/day

Brage et al (in Review)