Nieuwe ontwikkelingen bij het meten van bloeddruk: van SPRINT tot cuffloze devices

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PRESENTATIOIN OUTLINE

- Brief history
- Challenges
- Insights of cuffless blood pressure measurement
  - What we know
  - And what we don’t

Disclosures

Declaration of financial interest, potentially relevant relationships for this meeting	
Sponsorship or research funding:	Léman Micro Devices, Biospectal, Aktiia
Fee or other (financial) compensation:	No
Shareholder:	No
Other relationship, namely ...	No

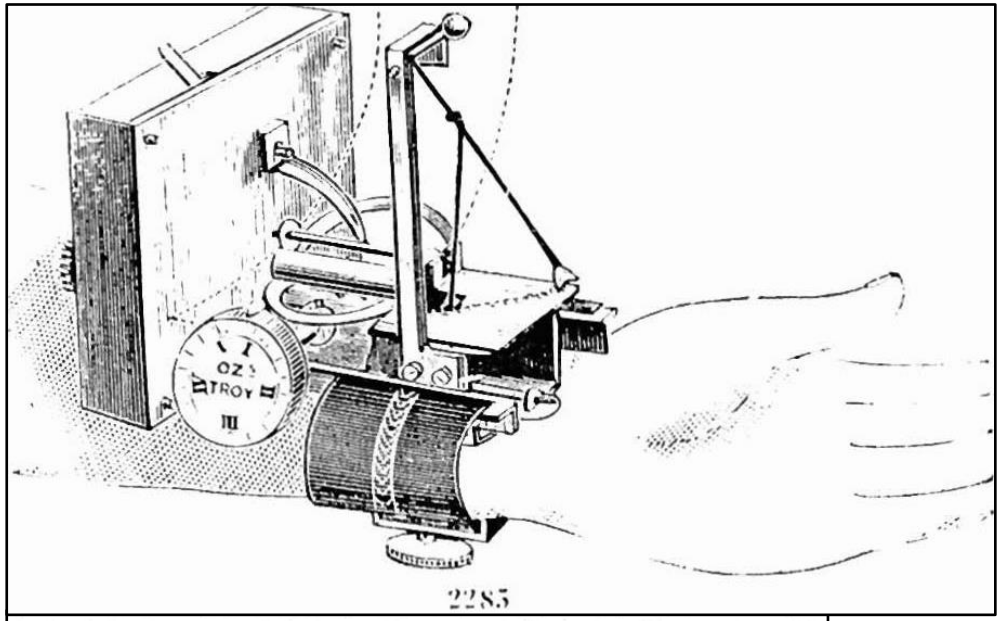
THE QUEST OF HOLY GRAIL OF BLOOD PRESSURE MEASUREMENT

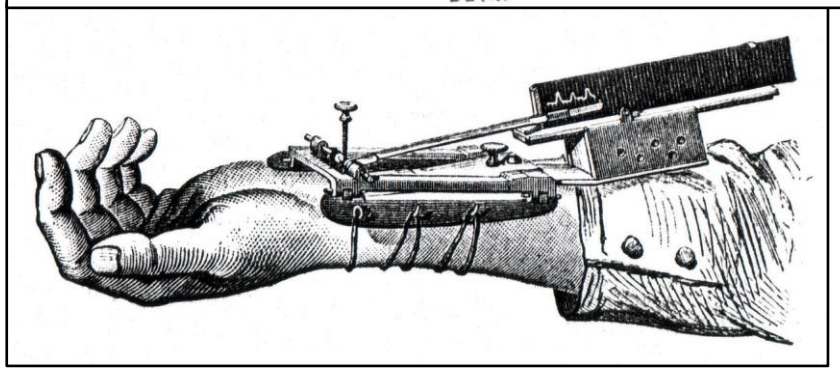
HISTORY OF BLOOD PRESSURE MEASURMENT

- 1733: First measured by Reverend Stephen Hales
- Can you imagine unattended field BP measurement?

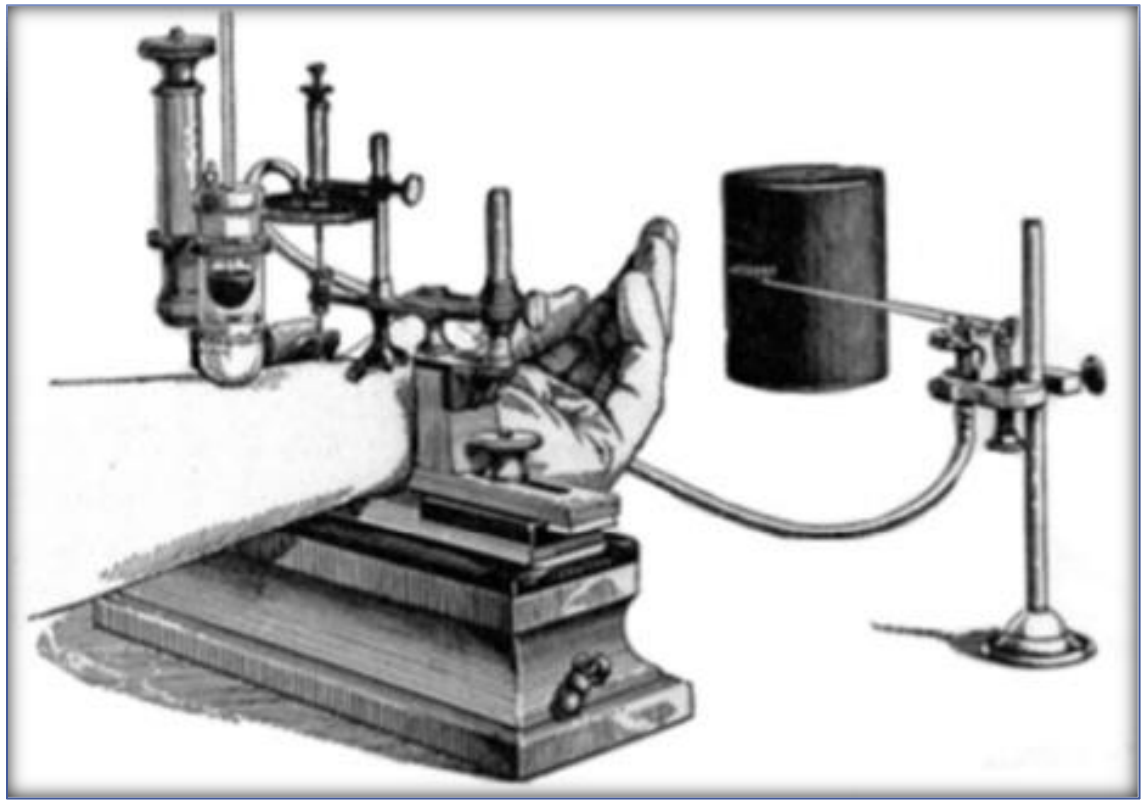
THE SPHYGMOGRAPH: 1860, DR ETIENNE JULES MAREY

- Precise measure of pulse
- Lack of accuracy to measure BP
- First device to be used clinically
- Simplification, 1882, by Robert Ellis
  - portable et easy use
- Standard equipment for the US Navy





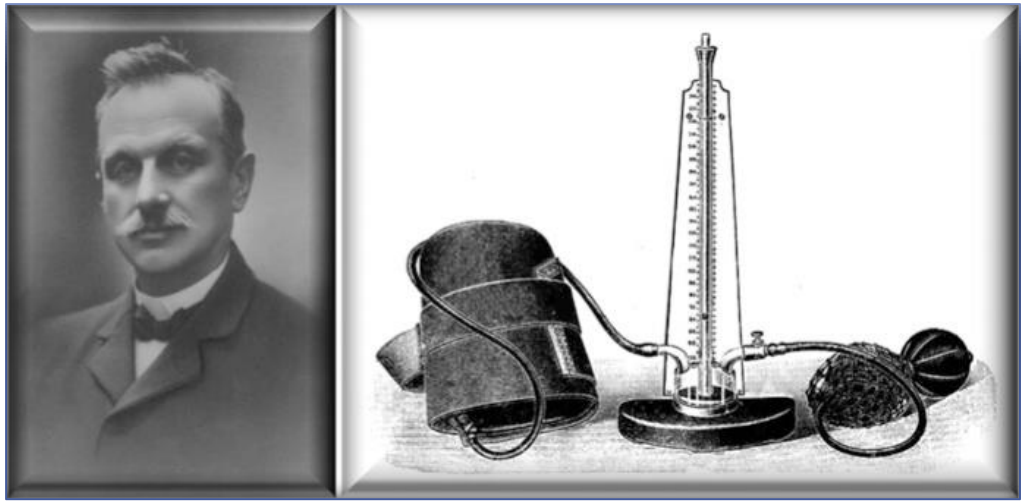
THE SPHYGMOMANOMETER:
1881, SAMUEL SIEGFRIED KARL RITTER VON BASCH



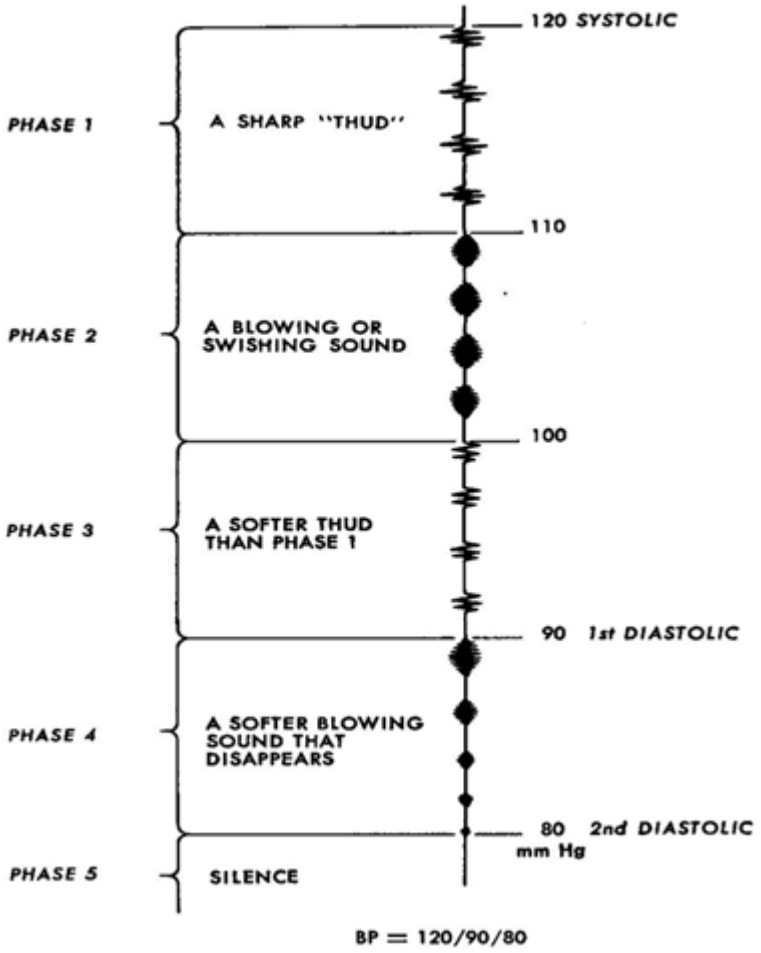
- Rubber ball, filled with water or mercury
- The ball was placed against the radial artery
- Use of a manometer and the disappearance of pulse unabled systolic blood pressure measurement
-

1896: DECISIVE YEAR FOR BP MEASUREMENT

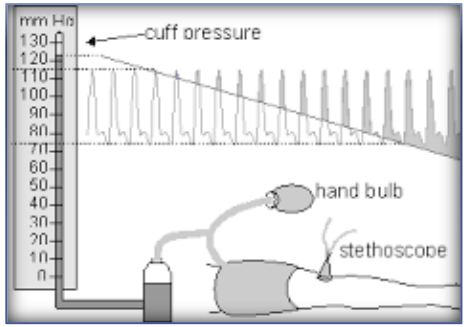
- Scipione Riva-Rocci developps the first mercury sphygmomanometer



1905: NICOLAI KOROTKOFF ADDS THE USE OF A STETHOSCOPE

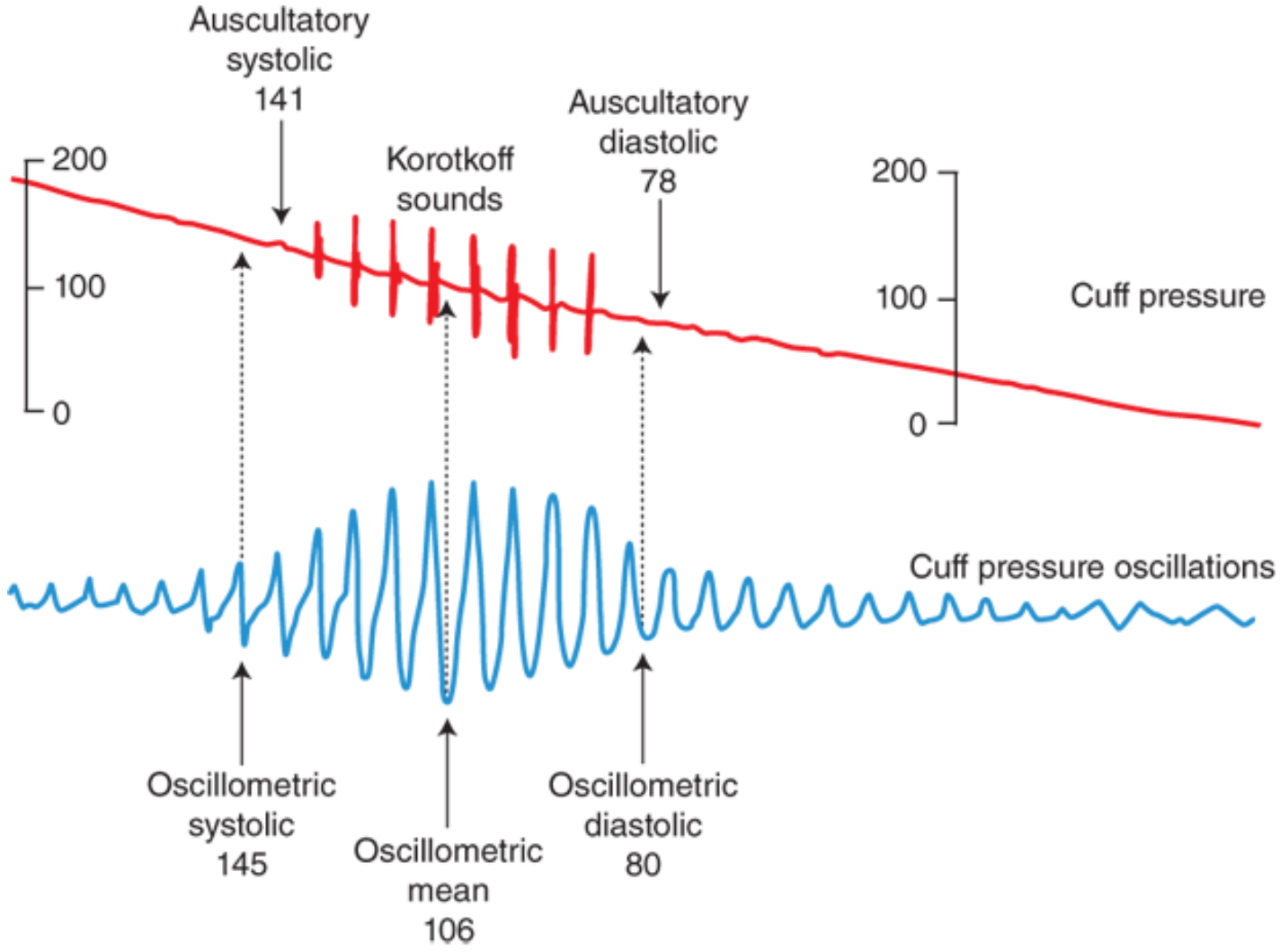


- More reliable than previous techniques



MODERN BLOOD PRESSURE MEASUREMENT

- Panasonic launches its first oscillometric device in 1974
- Sytolic and diastolic BP are calculated from the mean BP using algorythms



FIRST CHALLENGE OF OFFICE BP MEASUREMENT: 1940

- Ayman D et al.
- Blood pressure determinations by patients with essential hypertension: The difference between clinic and home readings before treatment.
- *Am J Med Sci*. 1940; 200: 465–474.

SITUATIONS IN WHICH BLOOD PRESSURE IS MEASURED

Attended

Unattended

UNIL | Université de Lausanne

Adapted from Paul Muntner et al. Journal of the American College of Cardiology, Volume 73, Issue 3, 2019,Pages 317-335.

COMPARISON OF 5 DIFFERENT BP MEASUREMENT METHODS

Methods

113 patients with hypertension

Multi-center:
3 hypertension clinics
2020-2022

Randomized
cross-over design

5 different BP measurement methods

E. H. Groenland, et al. Hypertension 2022 Vol. 79 Issue 10 Pages 2373-2382

RESULTS

Results	Mean 24-hour ambulatory BP: 126/73 mm Hg *(Reference standard)*			
	App-assisted home BP	30-min BP	Attended office BP	Unattended office BP
Mean BP (mm Hg)	**141/82**	**134/80**	**137/81**	**135/81**
Agreement hypertension* (κ-statistic (95% CI))	**0.33** (0.18 - 0.47)	**0.30** (0.13 - 0.47)	**0.48** (0.31 - 0.65)	**0.41** (0.22 - 0.59)

**Home BP monitoring (HBPM): ≥135/85 mm Hg, 30-min BP: ≥135/85 mm Hg, attended OBP: ≥140/90 mm Hg, unattended OBP: ≥140/90 mm Hg.*

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RESULTS

Diagnostic performance in detecting hypertension phenotypes by app-assisted HBPM:		
	Sensitivity (95% CI)	**Negative predictive value (95% CI)**
Sustained hypertension^	92% (78 – 98)	90% (74 - 98)
White-coat hypertension¶	32% (16 – 52)	81% (68 - 86)
Masked hypertension$	80% (44 - 97)	97% (91 - 100)

^ Consistently elevated BP on office and home or 24-hour ambulatory measurements. ¶ Elevated BP in the office and a normal home or 24-hour ambulatory BP. $ Elevated home or 24-hour ambulatory BP with normal office BP

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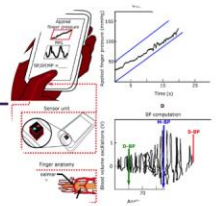
THE SETTING IS THUS IMPORTANT

WHAT IS NEXT?

Cuff-less or Cuff-free



Finger oscillommetry

Body sensors

Reflectance Pulse oximetry

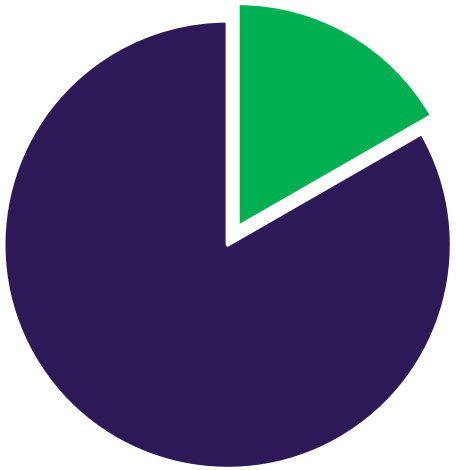
Optical sensors

A 90-SECOND SIT ON THE HEART SEAT COULD CAPTURE PATIENT VITAL SIGNS FOR MONITORING CHRONIC CONDITIONS

- “The Heart Seat” is a connected device that gathers heart rate, blood oxygen level (SpO2), ECG, cardiac output, and blood pressure while the patient is sitting on the toilet seat

CUFFLESS DEVICES FACILITATE REGULAR MEASUREMENT OF BLOOD PRESSURE

Adherence to HBPM monitoring



- Uses HBPM monthly or weekly
- Never uses HBPM or uses HBPM less than once a month

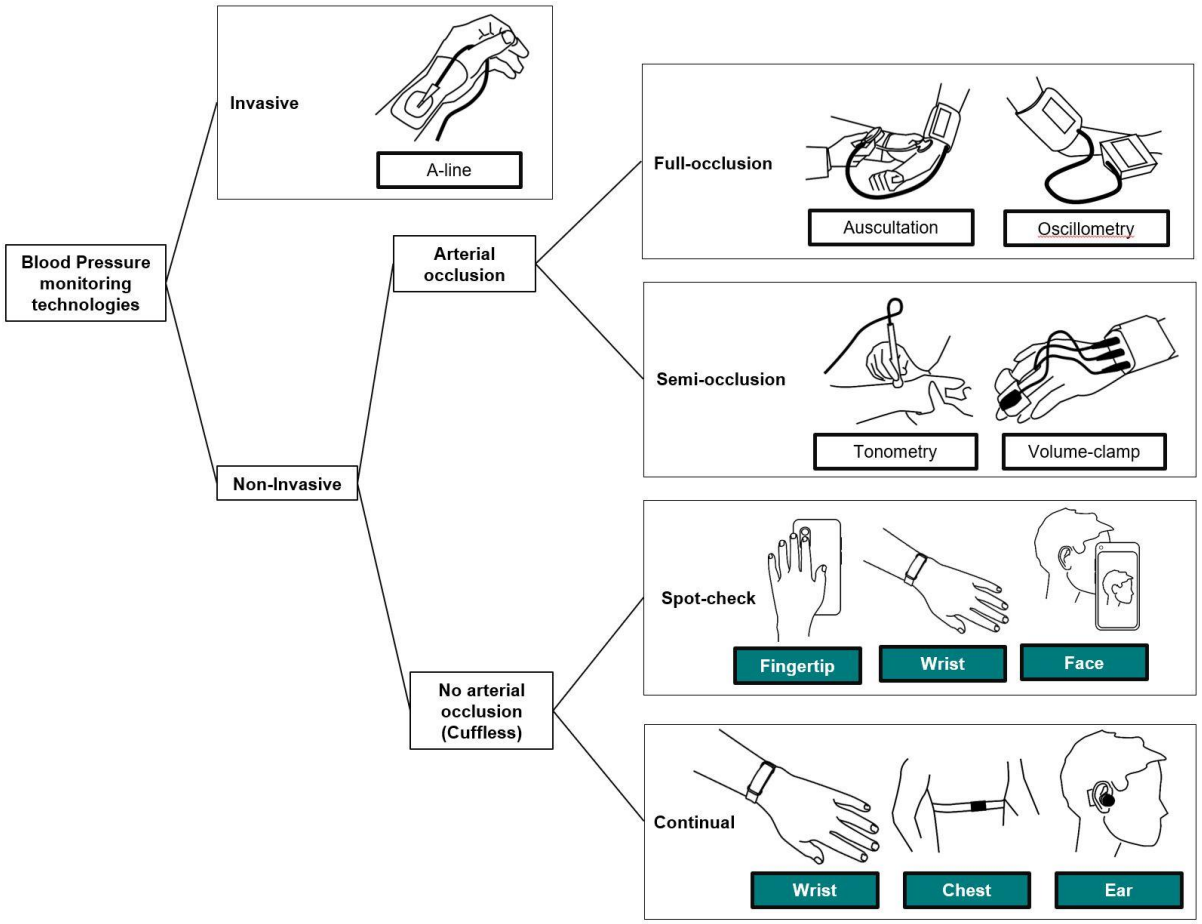
N = 10’958 US citizens from the NHANES survey between 2011 and 2014. Data from Am J Hypertens. 2017 Nov 1; 30(11): 1126–1132.

Adherence to cuffless monitoring

N = 8’471 EU citizens that started using a wearable device between January and July 2022. Internal Aktiia data.

- Engages with BP data monthly or weekly
- Stops engaging with wearable or engages less than once a month

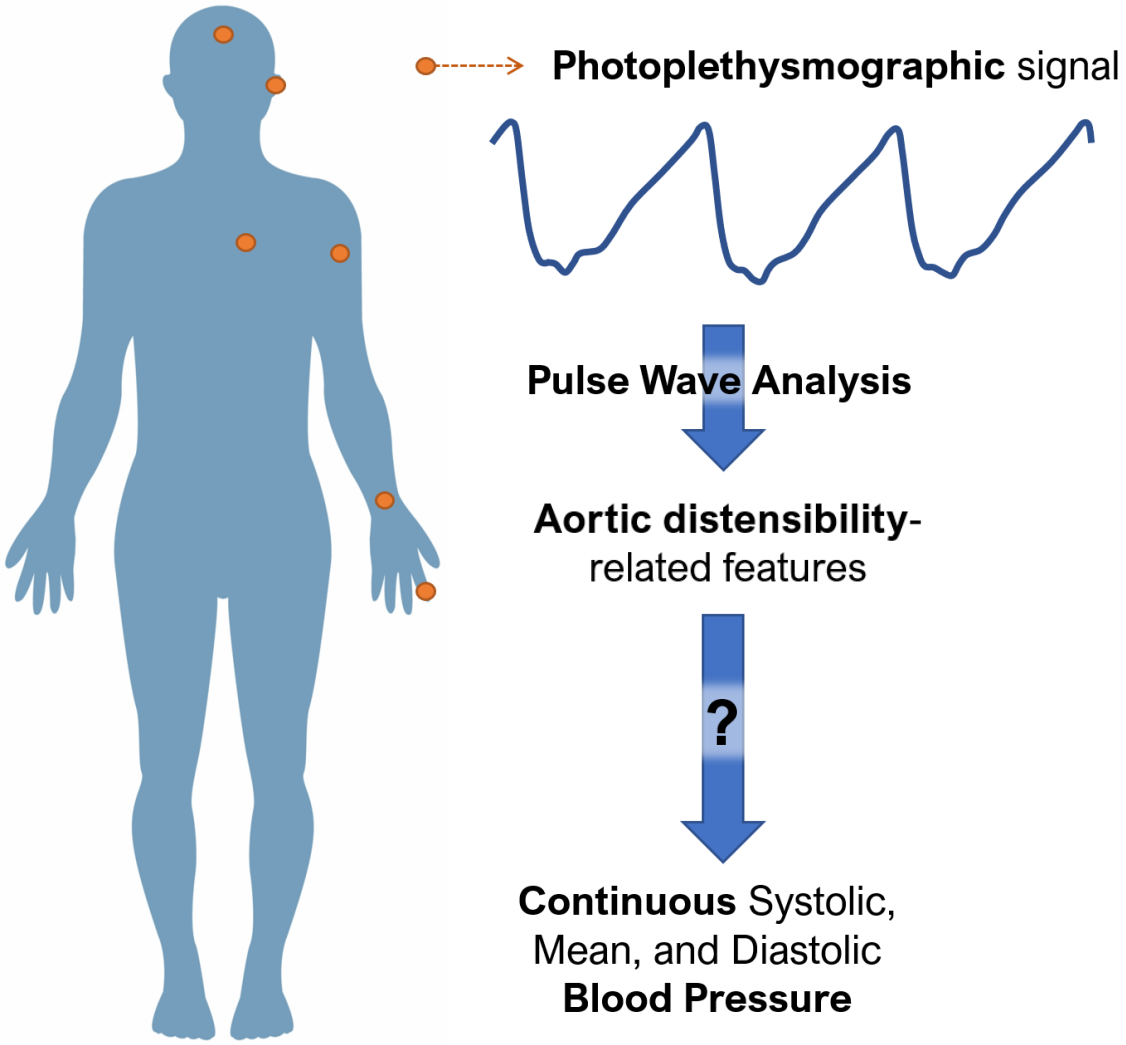
BLOOD MONITORING TECHNOLOGIES



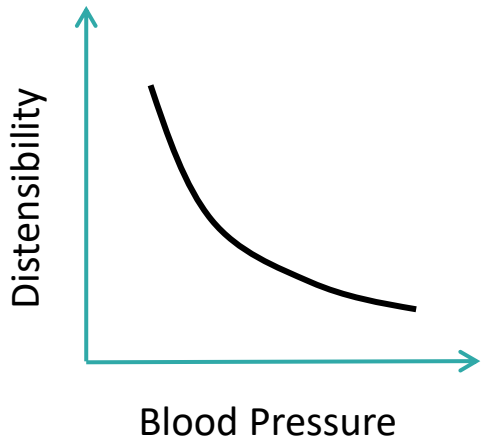
- **PWV algorithms** or on **PWA algorithms**
- **Require an initialization/calibration**

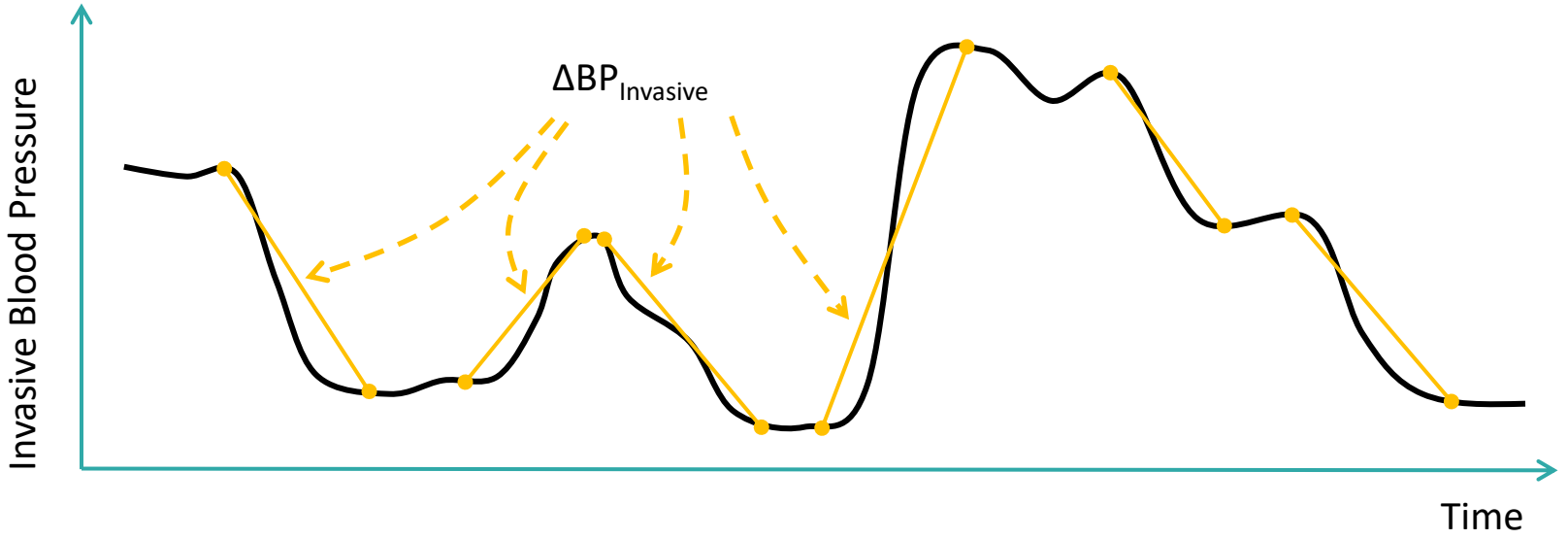
Sola J. et al. Front. Med. Technol. 4:899143.doi: 10.3389/fmedt.2022.899143

OBPM®: PHYSIOLOGICAL BACKGROUND & ALGORITHM PIPELINE

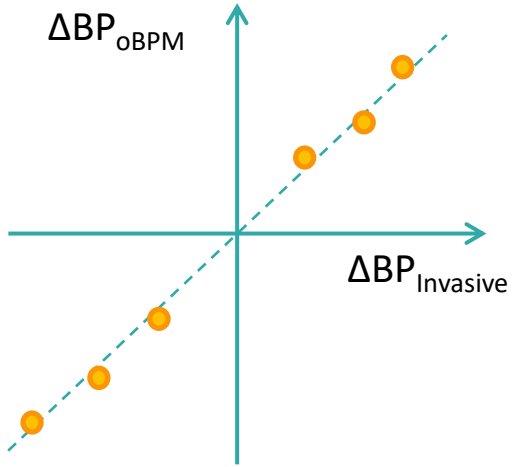


OBPM®: PHYSIOLOGICAL BACKGROUND & ALGORITHM PIPELINE





Model parameters trained on significant BP changes (ΔBP)



swissmedic

Identification de l'essai clinique

- Titre : Optical Blood Pressure Monitoring (OptiBPTM) Mobile App, an accurate blood pressure measurement compared to invasive blood pressure measurement

TODAY'S CHALLENGES FOR CUFFLESS VALIDATION STUDIES

- Intended use should be clear
  - screening? diagnosis? follow-up?
- Obtain a recognized and accepted standard for validation
- Must include sufficient intra- and inter-patient blood pressure variation.
- Impact of the mathematical model should be transparent
  - age, gender, ...

MAIN FEATURES OF STANDARDS SPECIFICALLY DEVELOPED FOR THE VALIDATION OF CUFFLESS BLOOD PRESSURE MEASURING DEVICES

	Institute of Electrical and Electronic Engineers **IEEE** **1708-2014 & 1708a-2019**	International Organization for Standardization **ISO 81060-3** **(*Under development*)**
Intended use	Cuffless wearable BP devices	Cuffless continuous BP devices
Number of subjects	≥85	30-120 depending on intraclass correlation for each BP parameter
Reference method	Manual auscultatory	Intra-arterial
Validation phases		
A. Test immediately post calibration	Yes	Yes
B. Test after BP change	Specific requirements for BP change	Specific requirements for BP change
C. Test before re- calibration	Yes	Yes
Procedure for inducing BP changes	Not specified	Not specified (subjects may already be hemodynamically unstable)
BP measurement sequence	Simultaneous or sequential	Simultaneous
Pass requirements (mean error limit)	≤6 mmHg (for BP changes ≤7 mmHg)	≤6 mmHg (SD ≤10 mmHg)

Stergiou G. Journal of Hypertension: August 2022 - Volume 40 - Issue 8 - p 1449-1460

UNIQUE ASPECTS FOR CLINICAL VALIDATION OF CUFFLESS DEVICES

Ability to track BP changes

Impact of different device positions relative to the heart

Stability of cuff calibration accuracy over time

Impact of body movement and physical activity

Stergiou, George S et al. Journal of Hypertension DOI: 10.1097/HJH.0000000000003483

THE AKTIIA BRACELET

01
PPG Sensor

The Aktiia bracelet shines a green light to analyse how the arteries below the skin surface pulsate. This is the same sensing principle as most other optical heart rate monitors at the wrist.

02
Optical Signal

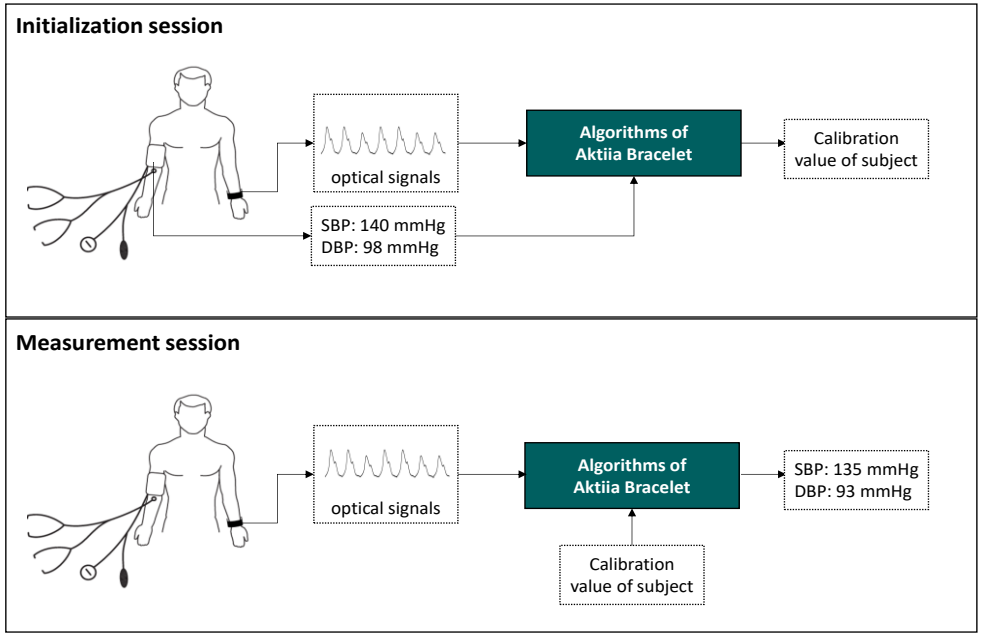
Aktiia goes beyond a heart rate monitor: instead of counting pulses, we examine their shape

03
OBPM Algorithm

The pulse shape of your skin arteries contains information on your actual blood pressure.

04
Blood Pressure

Unfortunately, this information is obscured by noise.
After 15 years of research and validation, Aktiia is able to extract this information to provide you with accurate blood pressure values around the clock.

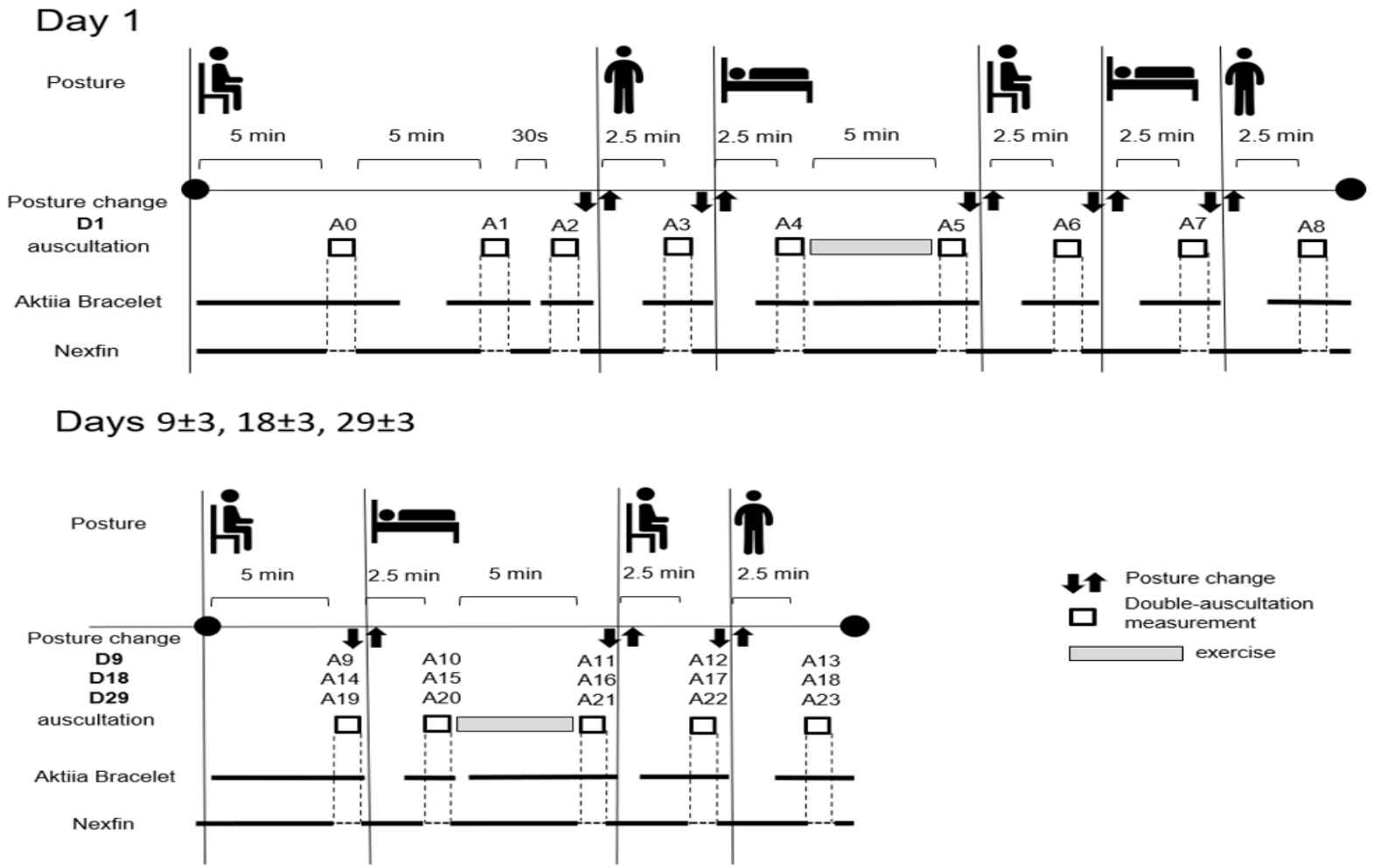


Vybornova, A et al. Blood Pressure Monitoring. 26(4):305-311, August 2021

DESIGN OF THE VALIDATION PROTOCOL (CE)

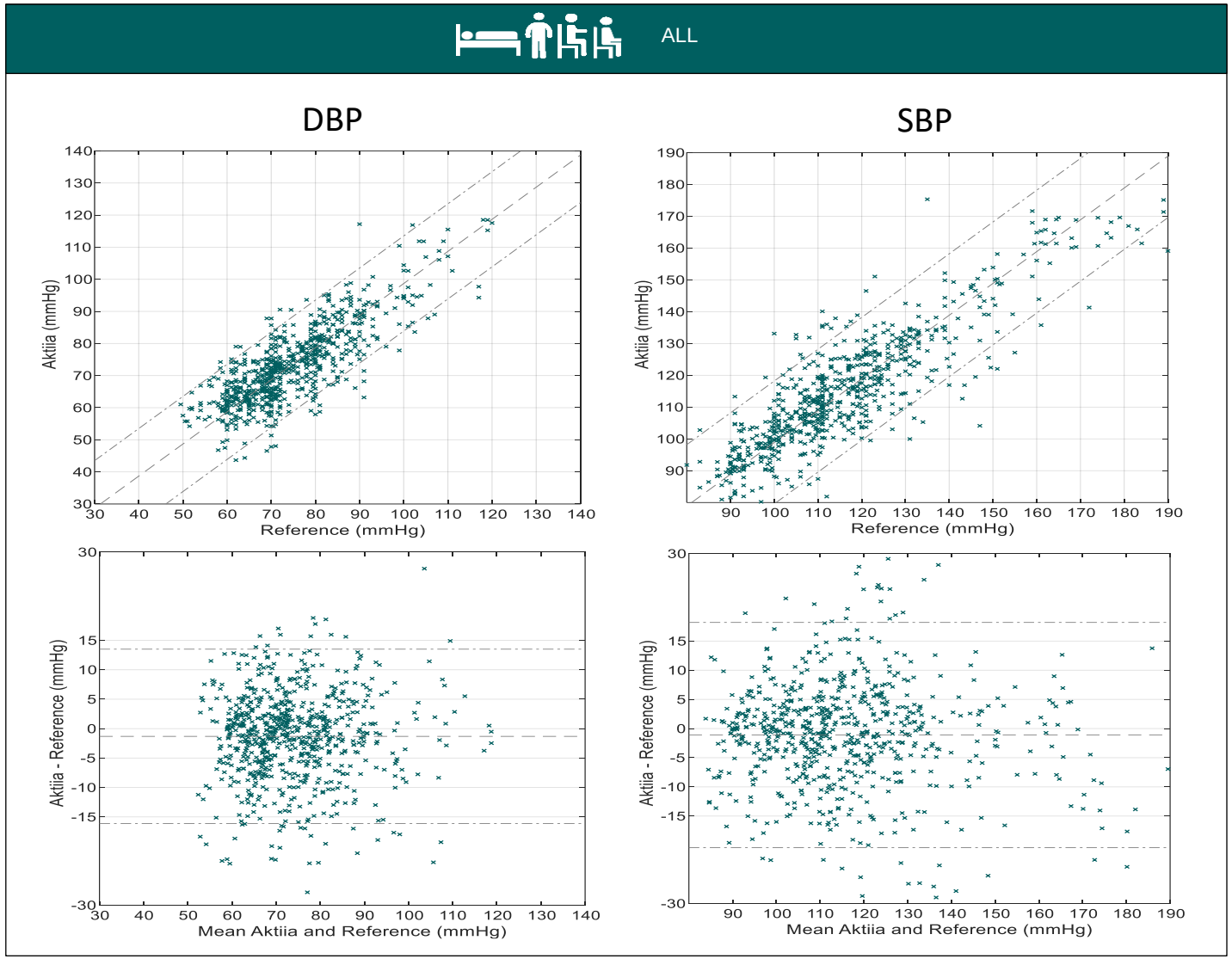
Day 1
- Immediate post qualibration accuracy
- Tracking of BP changes with position

Day 9 to 29
- Stability of accuracy with time



Sola J et al. Sci Rep. 2021 Oct 19;11(1):20644

PERFORMANCE IN DIFFERENT BODY POSITIONS



Sola J et al. Sci Rep. 2021 Oct 19;11(1):20644

PERFORMANCE IN DIFFERENT BODY POSITIONS

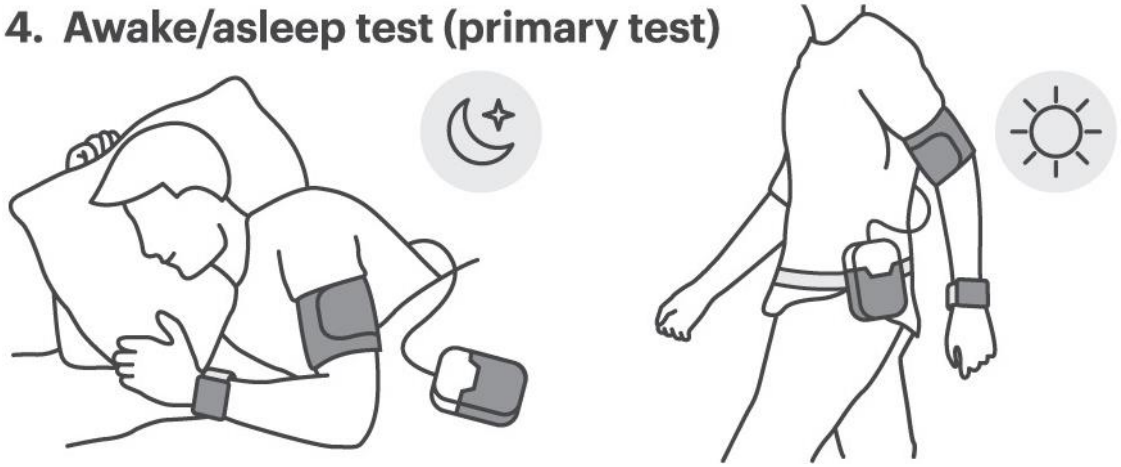
Mean ± Std (mmHg)	All positions	Lying	Sitting - wrist at heart level	Sitting - wrist at lap level	Standing
Systolic blood pressure	-1.11 ± 9.85	-2.44 ± 10.15	0.46 ± 7.75	-3.02 ± 6.10	-0.62 ± 12.51
Diastolic blood pressure	-1.32 ± 7.56	-1.93± 7.65	0.39 ± 6.86	-4.22 ± 6.56	-4.85 ± 9.11

Mean and SD of the differences between reference and the Aktiia

Sola J et al. Sci Rep. 2021 Oct 19;11(1):20644

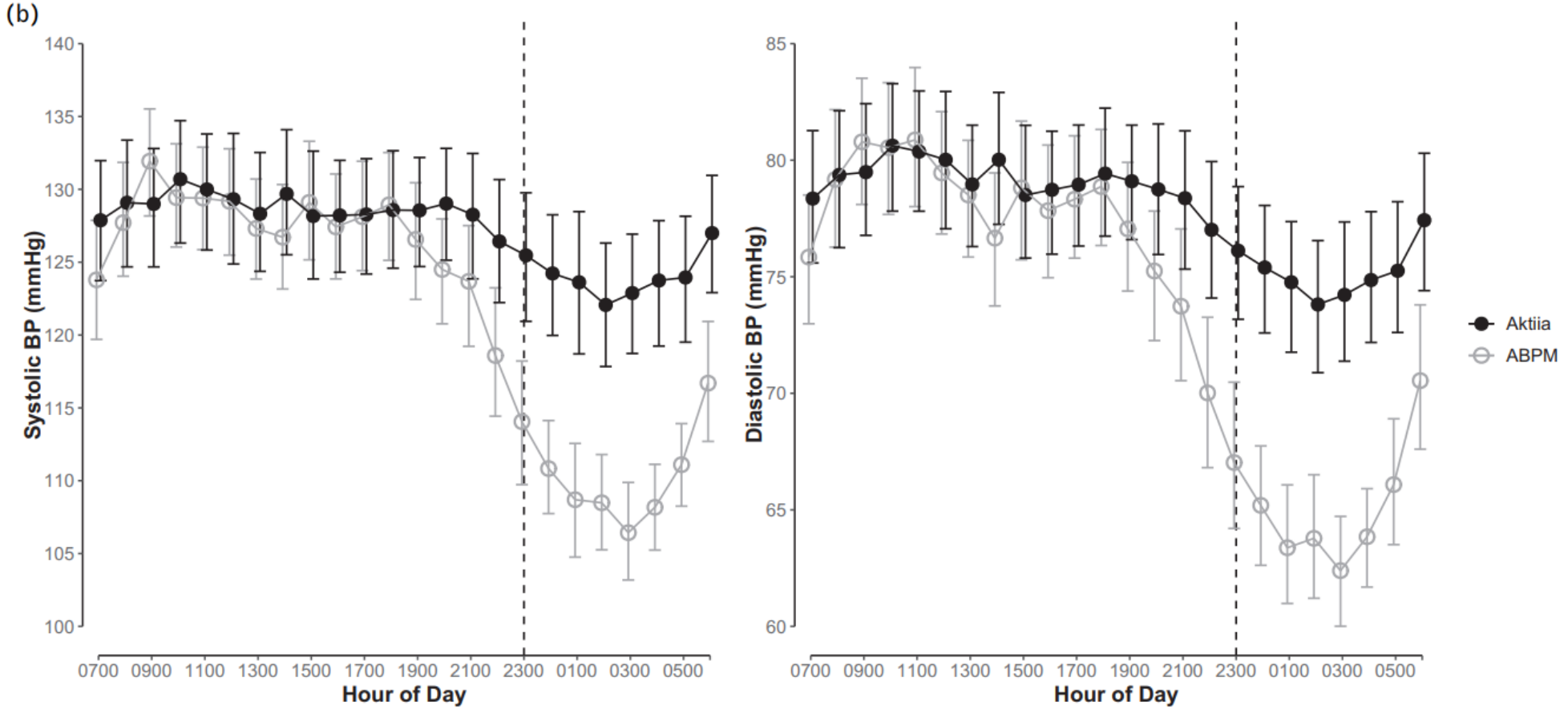
AWAKE ASLEEP TEST

4. Awake/asleep test (primary test)



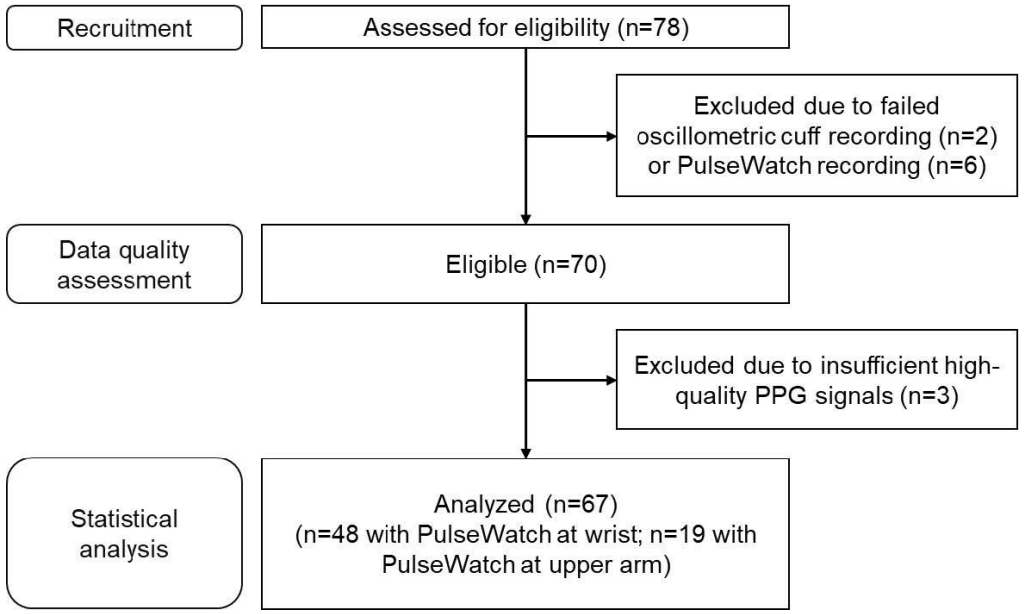
24-hour cuffless BP monitoring and upper-arm cuff oscillometric ambulatory monitoring to compare the awake/asleep BP change measured by the two devices	≥35	Error in awake/asleep BP change ≤5±8 (mean±SD) mmHg

24H BP TRACKING:
ABPM VS COMMERCIALLY AVAILABLE CUFFLESS DEVICE



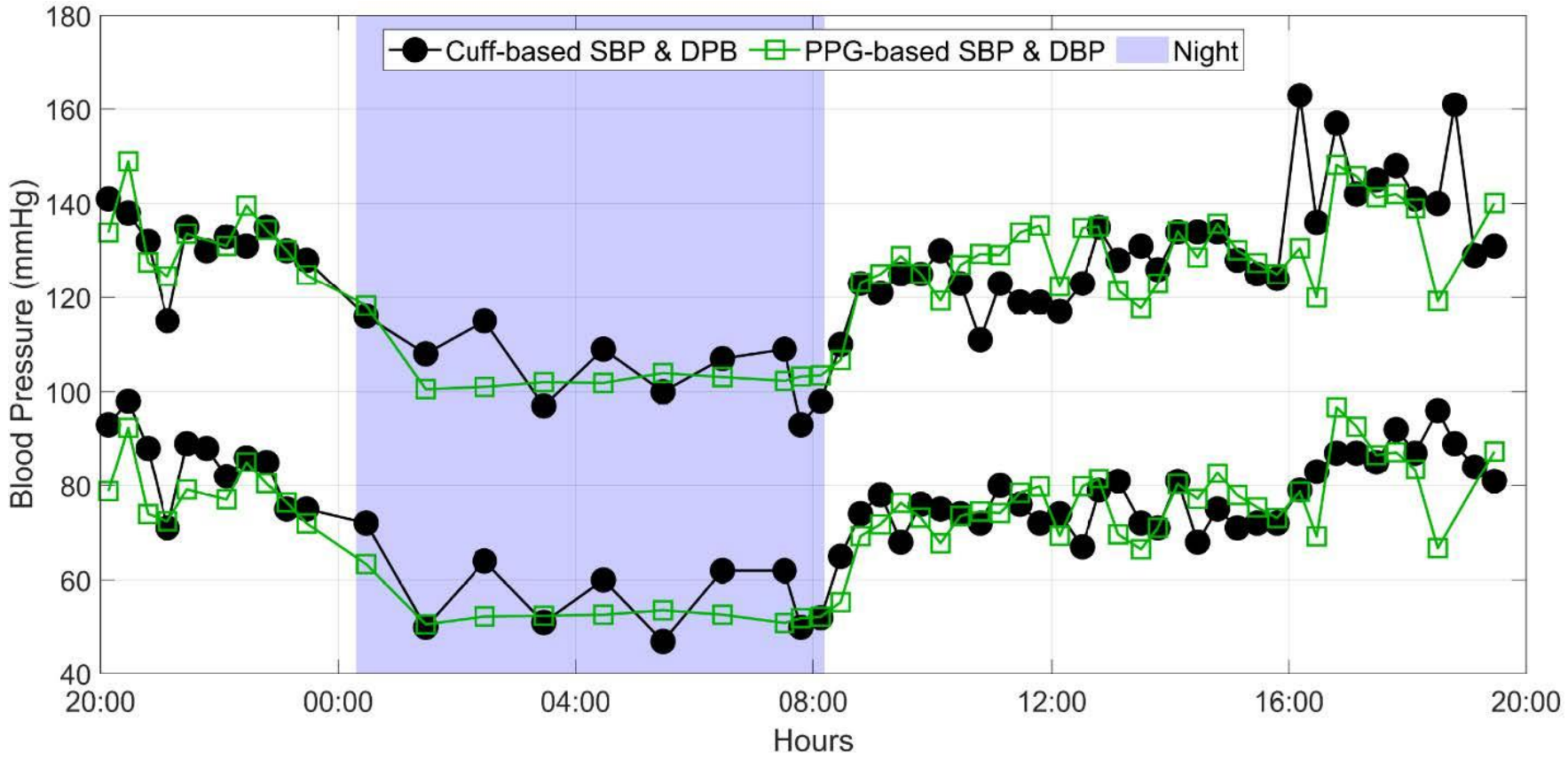
I. Tan et al. J Hypertens 2023

24H BP TRACKING:
ABPM VS NON-COMMERCIALLY AVAILABLE CUFFLESS DEVICE



M. Proença et al. Scientific Reports 2023 Vol. 13 Issue 1 Pages 6149

EXAMPLE OF A 24-HOUR PPG-BASED BP PROFILE COMPARED TO ITS CUFF-BASED COUNTERPART



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COMPARISON OF TWO OFFICE BP WITH IN BETWEEN CUFFLESS BP MEASURES

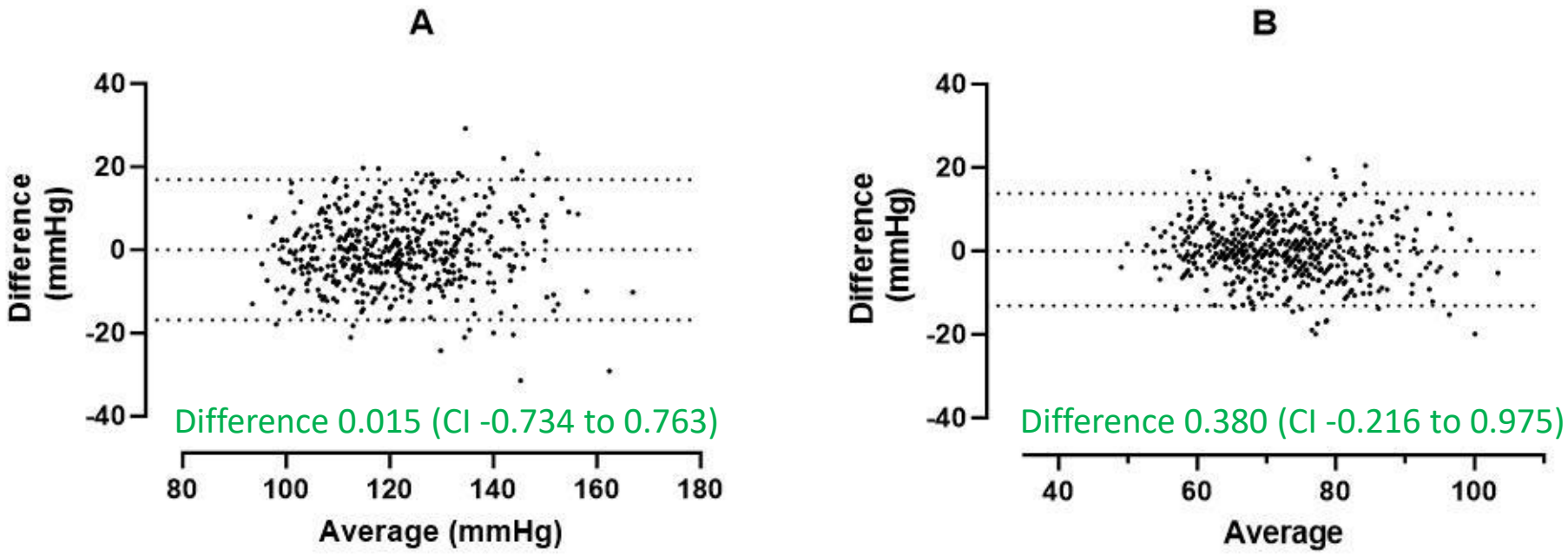


Figure 1. Bland-Altman plot of systolic (A) and diastolic (BP) blood pressure.

511 participants of the Swiss Salt Study 2 (46% women, age: 48.6±15.8 years)
Agreement for the diagnosis of hypertension was 92.4% with a kappa of 0.61±0.04 for systolic BP and 94.7% with a kappa of 0.50±0.04 for diastolic BP

Submitted abstract ESH

SCIENTIFIC EVIDENCE

	Diagnosis	TOD	Prognosis	Target BP
oBP	√	√	√	√
Unattended OB	√	√	√	√
Home BP	√	√	√	?
ABPM	√	√	√	?
Cuffless	?	?	?	?

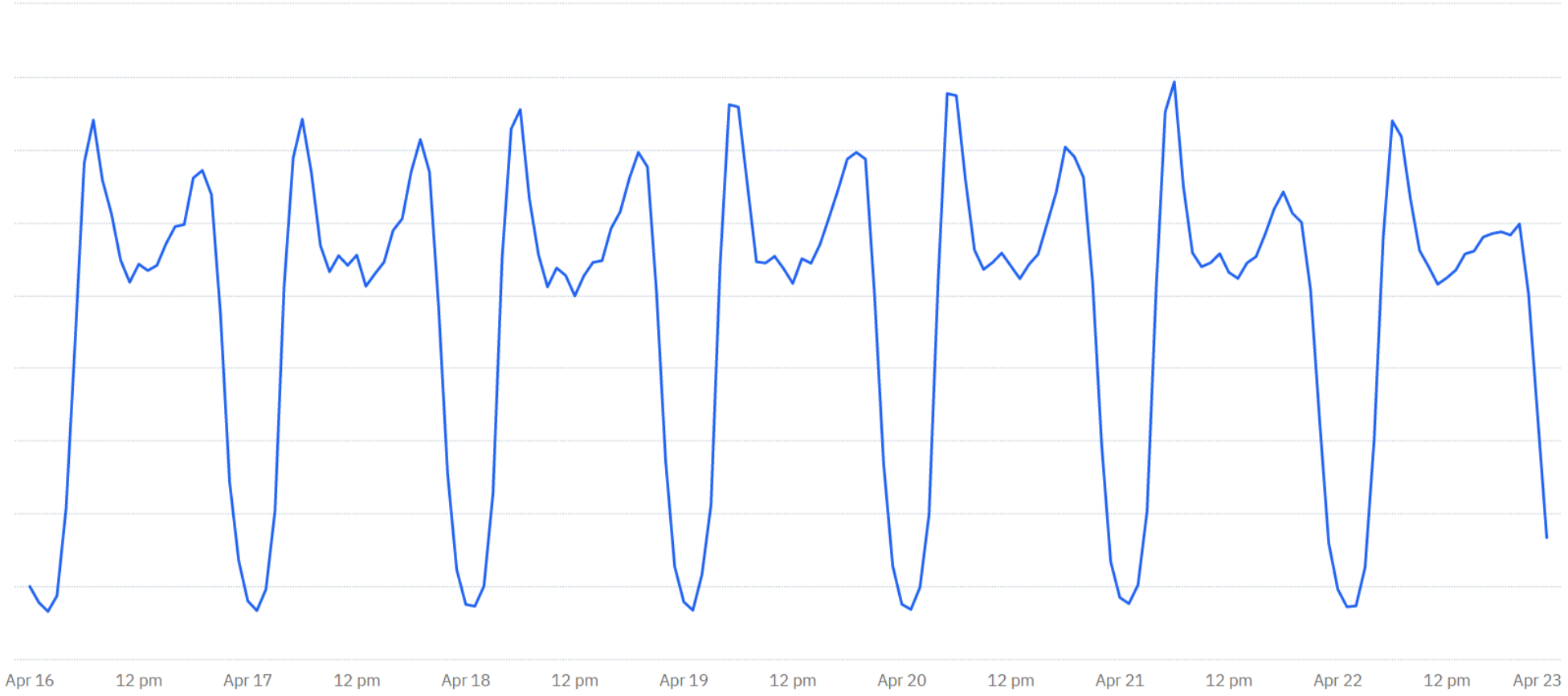
2023 ESH GUIDELINES: RECOMMENDATIONS AND STATEMENTS

Cuffless BP devices should not be used for the evaluation or management of hypertension in clinical practice.	III	C

"The world doesn't change in front of your eyes, it changes behind your back."
— Terry Hayes, I Am Pilgrim

2023 ESH Guidelines. Journal of Hypertension DOI: 10.1097/HJH.0000000000003480

DAILY PATTERN OF DEVICE SYNCHRONIZATION



Corthesy Aktiia SA. EU_Aktiia_Internal data

LE MOT DE LA FIN

*"…**complementary** rather than a **competitive** role in the evaluation of hypertension and provide similar but also different information about the BP profile and behavior of a patient"*

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