EUnetHTA Joint Action 3 WP4

**Rapid assessment of other technologies using the HTA Core Model®
for Rapid Relative Effectiveness Assessment**

The 24-hour blood pressure measurement device Mobil-O-Graph® with the built-in algorithm ARCSolver® to measure arterial stiffness for the optimization of hypertension treatment and assessment of cardiovascular disease risk

Project ID: OTCA-24

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Disclaimer

The content of this assessment represents a consolidated view based on the consensus within the Authoring Team, it cannot be considered to reflect the views of the European Network for Health Technology Assessment (EUnetHTA), EUnetHTA's participating institutions, the European Commission and/or the Consumers, Health, Agriculture and Food Executive Agency or any other body of the European Union. The European Commission and the Agency do not accept any responsibility for use that may be made of the information it contains.

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Conflict of interest

All authors, co-authors, dedicated reviewers, external experts and patients or patient representatives involved in the production of this assessment have declared they have no conflicts of interest in relation to the technology and comparator assessed according to the EUnetHTA declaration of interest and confidentiality undertaking (DOICU) statement form.

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LIST OF ABBREVIATIONS

AAMI	American Association for the Advancement of Medical Instrumentation
AB(I)	Ankle-brachial index
ABPM	Ambulatory blood pressure measurement
ACC/AHA	American College of Cardiology/American Heart Association
ACS	Acute coronary syndrome
A/D	Analog to digital
AIx	Augmentation index
AIx(75)	Augmentation index at 75 bpm
AMI	Acute myocardial infarction
a(o)SBP	Aortic systolic blood pressure
ASCVD	Atherosclerotic cardiovascular disease
AZ	Arizona
ba-PWV	Brachial-ankle pulse wave velocity
BHS	British Hypertension Society
BMI	Body mass index
bn	Billion
BP	Blood pressure
bPP	Brachial pulse pressure
br-BP	Brachial blood pressure
CAI	Central augmentation index
CAVI	Cardio-ankle vascular index
C-BP	Central blood pressure
cDBP	Central diastolic blood pressure
CE mark	Certification mark
cf-PWV	Carotid-femoral pulse wave velocity
CHD	Coronary heart disease
CI	Confidence interval
CM	Calculated mean
cBP	Central blood pressure
cSBP	Central systolic blood pressure
CT	Computer tomography
CUR	EUnetHTA domain for health problem and current use
CVD	Cardiovascular disease
DBP	Diastolic blood pressure
DM	Diabetes mellitus
ECG	Electrocardiogram
ECHI	European Care Health indicators

EEC	European Economic Community
EFF	EUnetHTA clinical effectiveness domain
EN	European Norm
ESC	European Society of Cardiology
ESH	European Society of Hypertension
EU	European Union
EUnetHTA	European Network for Health Technology Assessment
g	Gram(s)
GDP	Gross domestic product
GRADE	Grading of Recommendations, Assessment, Development and Evaluation
h	Hour
HBPM	Home blood pressure measurement
HDL	High-density lipoprotein
HMS	Hypertension management system
HR	Hazard ratio
HRQoL	Health-related quality of life
HTA	Health technology assessment
Hz	Unit Hertz
ICC	Intraclass correlation coefficient
ICD	International Classification of Diseases
ID	Identity
I.E.M	Industrielle Entwicklung Medizintechnik
MAP	Mean arterial pressure
MeSH	Medical Subject Headings
MI	Myocardial infarction
mmHg	Unit millimetre of mercury
kHz	Unit kilohertz
MOGARC	Mobil-O-Graph® with the ARCSolver® algorithm
MRI	Magnetic resonance imaging
NA	Not available
NG	New generation
OECD	Organisation for Economic Co-operation and Development
OscM	Oscillometric mean
PAD	Peripheral arterial disease
PICOS	Population, Intervention, Comparison, Outcomes, Study design
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PRESS	Peer Review of Electronic Search Strategies
pSBP	Peripheral systolic blood pressure

PWA	Pulse wave analysis
PWV	Pulse wave velocity
r	Pearson coefficient
R&TTE Directive	Radio and Telecommunication Terminal Equipment Directive
RCT	Randomised Controlled Trial
REA	Relative Effectiveness Assessment
S	Seconds
SAF	EUnetHTA safety domain
SBP	Systolic blood pressure
SD	Standard deviation
SF-12	12-Item Short Form Health Survey
SW	Software
TEC	EUnetHTA domain for description and technical characteristics
TOD	Target organ damage
UK	United Kingdom
USA	United States of America
YLD	Years lived with disability

SUMMARY OF RELATIVE EFFECTIVENESS OF MOBIL-O-GRAPH® WITH ARCSOLVER®

The scope of the project is described by the PICOS process (Population, Intervention, Comparison, Outcomes, and Study design). In this assessment the population is broad - it includes all those at risk of hypertension or cardiovascular disease. The intervention is ARCSolver®, an algorithm used primarily in Mobil-O-Graph® NG [as a package it is called Mobil-O-Graph® Pulse Wave Analysis (PWA)]. Mobil-O-Graph® NG is a blood pressure measuring device that measures peripheral blood pressure. ARCSolver® uses pulse wave analysis (PWA) to calculate central aortic blood pressure, cardiac output, peripheral resistance, augmentation index (AIx), augmentation pressure, reflection coefficient, and pulse wave velocity (PWV). These parameters are considered measures of arterial stiffness and are based on peripheral blood pressure, which is calculated by Mobil-O-Graph® NG and other devices. Arterial stiffness parameters can be used to get a more accurate measure of hypertension and to assess the risk of cardiovascular disease. Thus, in terms of comparison, this Rapid Assessment primarily compares: 1) Mobil-O-Graph® PWA to Mobil-O-Graph® NG only, 2) Mobil-O-Graph® PWA or ARCSolver® algorithm to any other devices that measure arterial stiffness, 3) Mobil-O-Graph® PWA or ARCSolver® algorithm to cardiovascular disease risk scores. Any outcomes being compared will be included in the review, but especially critical are those related to treatment change or mortality.

The research questions of the REA are as follows:

1) Is the ARCSolver® algorithm, as part of Mobil-O-Graph® PWA, or coupled with any other device more effective and/or safer than currently approved blood pressure monitoring devices in the diagnosis and monitoring of hypertension?
2) Is the ARCSolver® algorithm, as part of Mobil-O-Graph® PWA, or coupled with any other device more effective and/or safer than other commercially available non-invasive, non-hospital based, pulse wave analysis measurement methods in the diagnosis and monitoring of hypertension?
3) Is the ARCSolver® algorithm, as part of Mobil-O-Graph® PWA or coupled with any other device more effective and/or safer than cardiovascular risk equations and measures currently used in routine practice for primary and secondary prevention of CVD?

Introduction

The Austrian Social Insurance (Dachverband der Sozialversicherungsträger) has been tasked by the Austrian Ministry of Health to evaluate ARCSolver®, an Austrian born algorithm which is primarily used in a German device called Mobil-O-Graph®. The purpose of the assessment is to inform decision making about reimbursement and utilization of the algorithm and device coupled with the algorithm. The claimed benefit of the combination is that with its additional parameters it measures arterial stiffness to better inform clinical decisions on hypertension medication and on interventions to reduce cardiovascular risk.

Description of the technology and comparators

There are several devices for the noninvasive measurement of arterial stiffness developed and validated. The Mobil-O-Graph® (I.E.M, Stolberg, Germany) uses a cuff based method from single point pressure wave recording. Based on a transfer function, central pressure curves are obtained and processed using the ARCSolver® (Austrian Institute of Technology, Vienna, Austria) algorithm, which determines the aortic systolic blood pressure (aSBP) and Augmentation Index (AIx) in combination with the oscillometric blood pressure measurement. There are other devices which

use **cuff-based oscillometry** as well (Arteriograph, Vicorder® and BPLab®). In the scope of this report, MOGARC refers to the pulse wave analysis device Mobil-O-Graph® in combination with the ARCSolver® algorithm.

Currently the most common method to assess carotid-femoral pulse wave velocity (cf-PWV) is the **transcutaneous tonometry**. This method is based on pulse wave acquisition at common carotid and femoral artery site. Devices using this technology are SphygmoCor® and PulsPen®. Complior Analyse and Aortic are **piezoelectric mecanotransducer**. Other technologies are VaSera®, pOpmètre®.

Health problem

Within the scope of this assessment hypertension and cardiovascular disease are the two related health conditions. Mobil-O-Graph® with the ARCSolver® algorithm calculates arterial stiffness parameters from peripheral blood pressure values to identify people at risk of cardiovascular events or diagnosing hypertension. The global prevalence of hypertension was an estimated 1.13 billion of which over 150 million were in central and eastern Europe in 2015. In Europe in 2016, there were about 120 age-standardised deaths per 100,000 caused by cardiovascular events.

Methods

A systematic literature review was conducted to include studies in which Mobil-O-Graph® with ARCSolver® algorithm and the parameters therefrom were compared to other devices which elicit the same parameters, or which are used for the identification and monitoring of hypertension or cardiovascular risk but contain different parameters. The search was conducted using Embase.com platform, including Medline and Embase databases. Additionally, the Center for Research and Dissemination databases and clinicaltrials.gov were searched.

Results

Available evidence

A total of 14 studies were found that describe the efficacy of Mobil-O-Graph® with ARCSolver® either in identifying cardiovascular risk or in accurately measuring arterial stiffness compared to other devices that measure arterial stiffness. Several measures that are a result of ARCSolver® pulse wave analysis were studied, including pulse wave velocity.

Clinical effectiveness

The literature search identified 14 studies in total that evaluated the effectiveness of Mobil-O-Graph® and/or ARCSolver® for primary and secondary prevention of cardiovascular risk as well as for diagnosis and monitoring of hypertension. The considered studies varied in the number of observed patients from 27 to 502, with a mean age ranging from 29-68 years. The studies found a gap in the literature in terms of the effectiveness of these devices as tested to identify and monitor hypertension or as a cardiovascular risk assessment. The studies showed that the technical efficacy of ARCSolver® is comparable to other devices that measure central blood pressure and AIx. Some studies found that PWV was slightly underestimated by ARCSolver® coupled with Mobil-O-Graph®.

Safety

No evidence was found to address safety.

Upcoming evidence

No ongoing, non-published, relevant clinical trials were found on clinicaltrials.gov that would indicate future research on ARCSolver® alone or combined with any other device including Mobil-O-Graph®. A total of 10 relevant abstracts from the last 3 years were identified. These studies indicate a continuation of comparing technical efficacy of devices in various measures such as AIx. No study looked at the ability of the instrument to correctly diagnose, treat, or monitor hypertension or the use of the instrument as a cardiovascular risk assessment tool. In terms of technical efficacy, the results were variable, indicating that ARCSolver® coupled with Mobil-O-Graph® sometimes over, under, or accurately measured various PWA paramters compared to other devices. The implications of this on identification of hypertension or cardiovascular disease on a patient population are still lacking.

Reimbursement

No feedback was received from EuNETHTA partners. ARCSolver® as part of Mobil-O-Graph® is currently being reimbursed in Austria.

Discussion

It is unclear whether or not Mobil-O-Graph® with ARCSolver® is equal, more, or less effective than comparators in terms of patient outcome efficacy, therapeutic efficacy, or diagnostic thinking efficacy. There are challenges in defining the population as well as the medical device itself, as there are several variations of the algorithm and device that are currently available. Furthermore, technically, medical devices and algorithms advance over time. No evidence was found pertaining to therapeutic efficacy or patient outcome efficacy in this review and thus no GRADE assessment was done. Comparative evidence on diagnostic thinking efficacy was also not found in this review. Technical efficacy studies show evidence that Mobil-O-Graph® and/or ARCSolver® do have technical validity but no recommendation or quality of recommendation was made based on the protocol, as this was not the focus of the review.

Conclusion

The current literature on Mobil-O-Graph® with ARCSolver® still focuses on technical characteristics and technical efficacy compared to other devices that provide measures of arterial stiffness. There is a lack of evidence on whether or not the measurement of arterial stiffness using Mobil-O-Graph® and ARCSolver® pulse wave analysis leads to improvement in patient outcomes through better treatment pathways in the identification and management of hypertension and cardiovascular risk. In terms of technical efficiency, there is evidence of moderate quality that Mobil-O-Graph® is equivalent to other devices that provide measures of arterial stiffness, whether by algorithm or using carotid-femoral pulse wave velocity. There is a lack of evidence to determine if Mobil-O-Graph® with ARCSolver® is more effective and safer in triaging patients to better health care services and medicines to eventually improve outcomes in terms of hypertension control or cardiovascular events. Further research should focus on diagnostic accuracy compared to other cardiovascular risk assessment tools and equations, and diagnostic accuracy compared to regular blood pressure measurement in hypertension.

INTRODUCTION

Mortality and morbidity associated with hypertension and cardiovascular disease are increasing worldwide and pose a significant threat to public health.(1) The measurement of brachial blood pressure (br-BP) with a sphygmomanometer has become embedded in routine clinical assessment to help diagnose and monitor hypertension and is also part of cardiovascular risk equations.(2-5) Obtaining an accurate measure of blood pressure is important to diagnose and monitor hypertension, including the effectiveness of medications in controlling hypertension.(3) In the last decade, it has become common to take several blood pressure measurements throughout the day with mobile devices to obtrain an accurate measurement rather than only once at the doctor's office, because the measurement can be influenced by many factors that vary throughout the day such as coffee and exercise.(2) Additionally, some people experience "dips" in blood pressure during sleep, which can only be identified using a 24-h measurement device.(5)

Recent studies have emerged highlighting the importance of central (aortic or carotid) blood pressure (C-BP) beyond benefits of conventional brachial blood pressure.(2) Conventional blood pressure (BP) measurements taken in the peripheral arteries are not direct substitutes for central blood pressure because of differences in blood pressure waveforms and values between the central aorta and the peripheral arterial system. Central (aortic and carotid) blood pressure is pathophysiologically more relevant for the pathogenesis of cardiovascular disease (CVD). Using br-BP could thus lead to over- or under-treatment of hypertension or under-assessment of cardiovascular risk.(6, 7) Despite similar effects on brachial pressure, antihypertensives have differential effects on central pressure, which may explain the recent superiority of vasodilating drugs in trials.(8) Pulse wave analysis is a method which uses br-BP measurements taken over a 24-hour period to calculate pulse wave velocity of C-BP to evaluate arterial stiffness.(9) The incremental prognostic value of pulse wave analysis to evaluate arterial stiffness versus conventional blood pressure measures has not been consistently demonstrated in recent literature. (8)

In addition to the management and diagnosis of hypertension, measuring blood pressure is important for the prediction of cardiovascular events such as atrial fibrillation, stroke and myocardial infarction and thereby avoidance through timely treatment.(2, 7, 10) Studies have also explored if certain subgroups, for example elderly or those with diabetes, are particularly affected by the differential risk stratification from blood pressure measurement versus pulse wave velocity measurement of arterial stiffness.(11) However, there is no consensus on the role of pulse wave analysis in risk equations and due to inconclusive evidence, it has not been considered in guidelines. (8, 12)

Based on the conflicting nature of the available evidence, pulse wave velocity is currently recommended only as a 2b recommendation for the management of hypertension (5) and is not currently recommended to measure the risk of cardiovascular (CV) events.

Mobil-O-Graph® with ARCSolver® algorithm (MOGARC) uses br-BP measurements to calculate pulse wave velocity of c-BP over a 24-hour period.(9, 13) It is currently unclear if MOGARC is superior or non-inferior to current risk stratification tools for cardiovascular events and if it is more accurate than or just as accurate as standard practice in diagnosing hypertension and monitoring treatment success. Additionally, it is unclear how MOGARC compares to other pulse wave analysis devices.

Technical (TEC) and Current Use (CUR) domains

- Table 3-1 lists the known manufacturers of this technology.
- Input from clinical experts on the best available epidemiological data, current use of the technology and current standard care for the patient group will be sought.

- Guidelines will be searched and appropriate information on current recommendations as well as citations of epidemiological data will be extracted.

Clinical Effectiveness (EFF) and Safety (SAF) domains

The EFF and SAF domains will focus on identifying and monitoring hypertension (response to hypertension therapy) and primary and secondary prevention of cardiovascular events.

Systematic literature review will be conducted to answer the following questions:

1) Is the ARCSolver® algorithm, as part of Mobil-O-Graph® PWA, or coupled with any other device more effective and/or safer than currently approved blood pressure monitoring devices in the diagnosis and monitoring of hypertension?
2) Is the ARCSolver® algorithm, as part of Mobil-O-Graph® PWA, or coupled with any other device more effective and/or safer than other commercially available non-invasive, non-hospital based, pulse wave analysis measurement methods in the diagnosis and monitoring of hypertension?
3) Is the ARCSolver® algorithm, as part of Mobil-O-Graph® PWA or coupled with any other device more effective and/or safer than cardiovascular risk equations and measures currently used in routine practice for primary and secondary prevention of CVD?

Study and outcomes validity and level of evidence were assessed according to the EUnetHTA guidelines. The Cochrane Risk of bias tool will be used on study and outcome level. The quality of the body of evidence will be assessed using GRADE (Grading of Recommendations, Assessment, Development and Evaluation).

1.1 Objective

The rationale of this assessment is to collaboratively produce structured (rapid) core HTA information on other technologies. In addition, the aim is to apply this collaboratively produced assessment in the national or regional context.

Table 0-1: Project objectives

	List of project objectives	**Indicator (and target)**
1.	To jointly produce health technology assessments that are fit for purpose, of high quality, of timely availability, and cover the whole range of health technologies.	Production of 1 (rapid) relative effectiveness assessment.
2.	To apply this collaboratively produced assessment into the local (e.g. regional or national) context.	Production of ≥2 local (e.g. national or regional) reports based on the jointly produced assessment.

This rapid assessment addresses the research question whether the pulse wave analysis device Mobil-O-Graph® with the ARCSolver® algorithm (MOGARC) in the outpatient setting is more effective and/or safer in patients at risk of cardiovascular events or in diagnosing and monitoring hypertension, compared to current standard practice. For patients at risk of cardiovascular events, both primary and secondary prevention will be examined, comparing MOGARC to other pulse wave analysis devices, conventional blood pressure monitoring devices, and risk scores. For

diagnosis, treatment and monitoring of hypertension, MOGARC will be compared to other pulse wave devices, and conventional 24-hour blood pressure monitoring devices.

ARCSolver® is a patented algorithm invented in Austria. It uses 24-hour blood pressure values collected by a non-invasive oscillometric central blood pressure estimation device called Mobil-O-Graph® to calculate pulse wave velocity, central aortic blood pressure, cardiac output, peripheral resistance, augmentation index, augmentation pressure, reflection coefficient, and thereby indicate arterial stiffness.(9) Arterial stiffness has been shown to be related to future cardiovascular events and pulse wave velocity shown to be more sensitive to changes due to hypertensive medication.(1) Ischemic heart disease, stroke, hypertensive heart disease, and diabetes are among the top 10 causes of mortality in Austria and diabetes is the third biggest cause of disability.(14) Identifying and treating individuals at risk of cardiovascular events and managing hypertension medication is a priority to improve societal health.(14) This topic was chosen based on a request from the Ministry of Health in Austria who commissioned our agency (Austrian Social Insurance) to evaluate Mobil-O-Graph® and ARCSolver® algorithm, which measures pulse waves from blood pressure values (a measure of vascular aging, or vascular stiffness) (13) to identify people at risk of cardiovascular events or with hypertension. It is currently unclear if pulse wave analysis in the outpatient and primary care setting achieves better management of hypertension and/or leads to avoidance of cardiovascular events. It is also unclear to what extent the commercially available pulse wave analysis devices are interchangeable.

1 SCOPE

Table 1-1: Project Scope: PICO for use of MOGARC in diagnosing and monitoring of hypertension

Description	Project Scope
Population	Target population: adult population 18 and over. All patients eligible for diagnosis, treatment, or monitoring of hypertension will be included, and additionally, a subgroup with uncontrolled hypertension will be examined. Further subgroups identified in the literature will also be included. • Setting: outpatient setting, primary care • Intended use of the technology: diagnosis and monitoring • Condition intended to diagnose/monitor: hypertension • Relevant ICD-10 codes: I10-I16 Hypertensive disease • Relevant MeSH-terms: hypertension
Intervention	Pulse wave analysis through Mobil-O-Graph® device and ARCSolver® algorithm. ARCSolver® is a patented algorithm invented in Austria. It uses 24-h blood pressure values collected by a non-invasive oscillometric central blood pressure estimation device called Mobil-O-Graph® to calculate pulse wave velocity, central aortic blood pressure, cardiac output, peripheral resistance, augmentation index (AIx), augmentation pressure, reflection coefficient, and thereby indicate arterial stiffness.
Comparison	Conventional 24-h blood pressure measurement approved for use under "specialist" or "ambulatory blood pressure measurement (ABPM)" will be considered).(15) The rationale for choosing the comparators as such is that it is the current standard of practice in diagnosis of hypertension and monitoring of treatment success. Invasive Pulse wave analysis (PWA) will not be included as a comparator.
Outcomes	EFF: efficacy and effectiveness (reduction in uncontrolled hypertension, reduction in non-diagnosed hypertension, sensitivity and specificity, mortality, morbidity, reduction in cardiovascular risk, reduction of stroke and other cardiovascular events, all effectiveness outcomes measured in included studies) SAF: false positives and false negatives, mortality, morbidity, data safety and protection Compliance: compliance in using device, compliance in taking hypertension medication The outcomes have been chosen based on the hierarchical model of efficacy and effectiveness of medical devices. (16, 17)

Study design	Diagnostic accuracy studies, meta-analyses, prospective comparative observational studies, systematic literature reviews, and randomized controlled trials

Table 1-2: Project Scope: PICO for comparison of MOGARC to other PWA devices

Description	**Project Scope**
Population	Target population: adult population 18 and over
Intervention	Pulse wave analysis through Mobil-O-Graph® device and ARCSolver® algorithm. ARCSolver® is a patented algorithm invented in Austria. It uses 24-h ARCSolver® blood pressure values collected by a non-invasive oscillometric central blood pressure estimation device called Mobil-O-Graph® to calculate pulse wave velocity, and thereby indicate arterial stiffness.
Comparison	Non-invasive pulse wave analysis methods
Outcomes	EFF: efficacy and effectiveness (reduction in uncontrolled hypertension, reduction in non-diagnosed hypertension, sensitivity and specificity, mortality, morbidity, reduction in cardiovascular risk, reduction of stroke and other cardiovascular events, all effectiveness outcomes measured in included studies) SAF: false positives and false negatives, mortality, morbidity, data safety and protection Compliance: compliance in using device, compliance in taking hypertension medication The outcomes have been chosen based on the hierarchical model of efficacy and effectiveness of medical devices(16, 17). (17, 18
Study design	Diagnostic accuracy studies, meta-analyses, prospective comparative observational studies, systematic literature reviews, and randomized controlled trials

Table 1-3: Project Scope: PICO for use of MOGARC in assessment of cardiovascular disease risk

Description	Project Scope

Population	Target population: adult population 18 and over. Primary and secondary prevention of CVD will be examined.
	• Setting: outpatient setting, primary care
	• Intended use of the technology: risk stratification
	  • Condition to risk stratify: cardiovascular events
	  • Relevant ICD-10 codes: Cardiovascular and Ischaemic Disease
	  I25.10 Cardiovascular Disease, Unspecified (ASCVD) I48.91 Atrial Fibrillation I50.9 Congestive Heart Failure I63.9 CVA I63.9 Stroke I65.23 Carotid Artery Occlusion, Bilateral I65.23 Carotid Artery Stenosis, Bilateral I65.29 Carotid Artery Occlusion I65.29 Carotid Artery Stenosis I67.2 Cerebral Atherosclerosis I67.9 Ischaemic Cerebrovascular Disease I73.9 Peripheral Vascular Disease
	  • Relevant MeSH-terms: cardiovascular risk

Intervention	Pulse wave analysis through Mobil-O-Graph® device and ARCSolver® algorithm. ARCSolver® is a patented algorithm invented in Austria. It uses 24-h blood pressure values collected by a non-invasive oscillometric central blood pressure estimation device called Mobil-O-Graph® to calculate pulse wave velocity, and thereby indicate arterial stiffness.
Comparison	Cardiovascular risk equations listed in a recently published study comparing cardiovascular risk equations.(18) The rationale for choosing this comparator is that they are currently the standard practice and have been evaluated by various HTA organizations.
Outcomes	EFF: efficacy and effectiveness (identification of cardiovascular risk, reduction of cardiovascular risk, reduction/avoidance of cardiovascular events, avoidance of mortality due to cardiovascular events, avoidance of morbidity due to cardiovascular events, sensitivity and specificity, all other effectiveness outcomes measured in included studies) SAF: false positives and false negatives, mortality, morbidity, data safety and protection The outcomes have been chosen based on the hierarchical model of efficacy and effectiveness of medical devices.(16, 17)
Study design	Diagnostic accuracy studies, meta-analyses, prospective comparative observational studies, systematic literature reviews, and randomized controlled trials

2 METHODS AND EVIDENCE INCLUDED

2.1 Assessment Team

Austrian Social Insurance (Author)

- Developed the first draft of the EUnetHTA project plan
- Performed the literature search and study selection
- Undertook the assessment (data extraction, analysis, synthesis and interpretation of findings)
- Lead on writing of the draft report
- Circulated draft report to dedicated reviewers and external experts, compiled and responded to feedback and edited the draft report, as appropriate
- Sent final document to manufacturers for fact check
- Prepared final assessment and wrote the final summary of the assessment

Universita Cattolica del Sacro Cuore (Co-Author)

- Collaborated in the development of the EUnetHTA project plan
- Collaborated in undertaking the assessment (data extraction, analysis, synthesis and interpretation of findings)
- Collaborated in writing of the draft report (certain domains)
- Checked, provided input and endorsed content of all domains
- Collaborated on the writing of the discussion and conclusions and endorsed the same
- Reviewed drafts of the assessment, proposed amendments where necessary and provided written feedback

Health Information and Quality Authority and Galician Agency for HTA (Dedicated Reviewers)

- Reviewed draft project plan, proposed amendments where necessary and provided written feedback
- Rated the relevance of outcomes (GRADE method)
- Reviewed assessments, proposed amendments where necessary and provided written feedback

External experts

- Guaranteed quality assurance by thoroughly reviewing the project plan and the assessment drafts
- Reviewed methods, results and conclusions based on the original studies included

2.2 Source of assessment elements

Sources for CUR and TEC domain specific information: UptoDate, manufacturer documents, manufacturer websites, reviews, guidelines from European and US stakeholders, HTA reports, studies found in systematic review for EFF and SAF which contain relevant CUR and TEC information

Sources for locating EFF and SAF domain specific information: Embase and Medline databases using Embase.com platform, CRD database, clinicaltrials.gov

2.3 Search

Mobil-O-Graph® and ARCSolver® were the search terms used. No further restrictions were added for disease area or outcomes due to the dearth of studies. The exact search strategy is included in **Appendix 1**. The PRESS (Peer Review of Electronic Search Strategies) checklist was used for the quality check of search strategies in bibliographic databases.

2.4 Study selection

Studies were included based on Table 2-1. The PRISMA flow chart in Figure 2-1 describes the number of studies found and reasons for exclusion.

Table 2-1: Study Selection

Study Selection
Time span: The last 10 years of studies, the last 3 years of conference abstracts, and the last 3 years of ongoing randomized controlled trials on clinicaltrials.gov. Language: studies in English will be included. Study types: meta-analyses, diagnostic accuracy studies, comparative observational studies, systematic literature reviews, and randomized controlled trials Inclusion: primary and secondary prevention of cardiovascular events, management, treatment, and diagnosis of hypertension, identification of arterial stiffness. Exclusion: 1. Studies which use Mobil-O-Graph® but do not compare it to alternatives for the measurement of arterial stiffness, identification of hypertension or cardiovascular risk, or monitoring of hypertension. 2. Studies comparing to invasive methods or methods that are only available in a hospital (MRI, CT scan) will be excluded. 3. Studies in which the data was collected prior to 2008 will be excluded. 4. Comments or editorials that did not examine the use of Mobil-O-Graph® and ARCSolver® algorithm in patients. 5. Studies that only used Mobil-O-Graph® to assess brachial blood pressure and not assess any central measures. Gray literature will not be examined for the EFF and SAF domains except for conference abstracts indexed in Embase and Medline in the last 3 years and clinical trials registered on clinicaltrials.gov in the last 3 years.

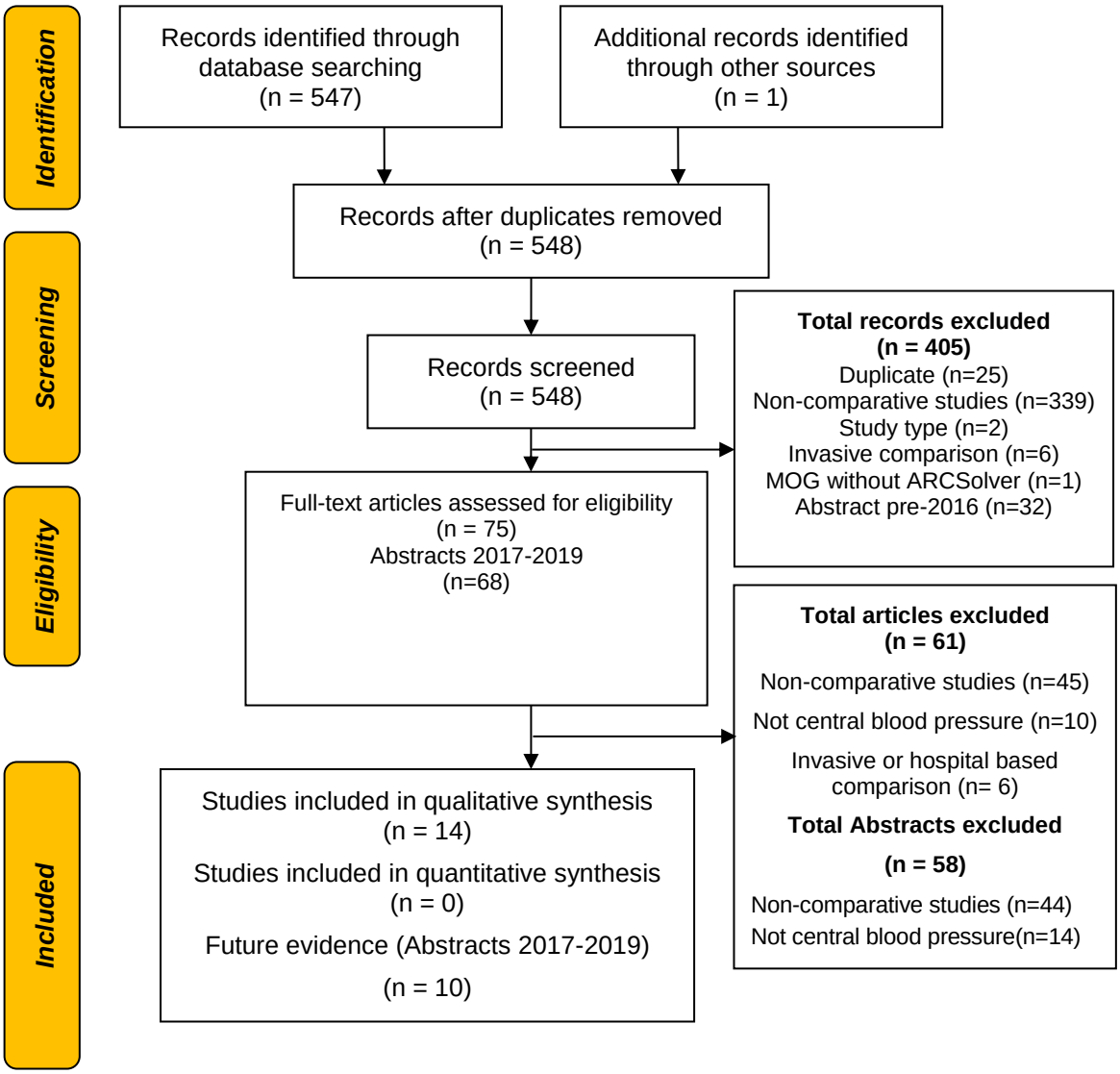

Figure 2-1: Flow chart

2.5 Data extraction and analyses

Table 2-2: Data extraction

Data Extracted
Data will be extracted for the EFF and SAF domain regarding: • Author • Title • Year • Setting • Study Design • Clinical Trial ID or study name • Funding source • Topic • Devices/algorithms/risk scores compared

- Measurement details/methods
- Duration of follow-up
- N patients
- N for each device
- Age
- Disease area
- Subgroups
- Hypertension:
  - Screening for hypertension or monitoring
  - Uncontrolled yes/no
- Cardiovascular risk
  - Compared to actual cardiovascular diagnosis/risk
  - Replace risk score or blood pressure within risk score
  - Primary or secondary prevention
- Outcomes
- Results
- Methods
- Loss to follow-up
- Relevant cut-off values
- Additional identified studies from reference list
- Conclusion
- Quality assessment (risk of bias)

2.6 Quality rating

Study and outcomes validity and level of evidence will be assessed according to the EUnetHTA guidelines. The Cochrane Risk of bias tool will be used on study level. The quality of the body of evidence will be assessed using GRADE (Grading of Recommendations, Assessment, Development and Evaluation).

2.7 Description of the evidence used

Table 2-3: Main characteristics of studies included

Author and year	Study type	N	Intervention (s)	Main endpoints	Included in EFF or SAF
Benas et al. (2019)	Cross-sectional	316	• MOGARC • Arteriograph • Complior	Intraclass correlation coefficient (ICC) PWV Intraclass correlation coefficent (ICC) cSBP correlation of PWV and cSBP values	EFF
De La Sierra et al. (2017)	Consecutive cross-sectional	208	• MOGARC	Odds ratio for each mmHg increase of the association of each blood pressure value with the presence of target organ damage	EFF

Díaz et al. (2019)	Part of population study	269	• MOGARC • Arteriograph • ultrasound	Association between blood pressure levels (peripheral-, brachial- or central-, aortic-) Agreement (Bland-Altman mean error) among aoSBP and/or pSBP Association between blood pressure (peripheral-, brachial or central- aortic-) level and cardiac and structural on functional parameters	EFF
Endes et al. (2015)	Convenience sample	68	• ARCSolver® with VaSera® • SphygmoCor®	reproducibility/variation mean cSBP difference mean PWV difference	EFF
Gotzmann et al. (2019)	Cross-sectional	502	• MOGARC • SphygmoCor® XCEL • Invasively measured aortic BP	Correlations between invasively and noninvasively measured values (cSBP & cDBP)	EFF
Grillo et al. (2018)	Cross-sectional	102	• MOGARC • Complior Analyse • PulsePen®-ET • SphygmoCor® • BPLab®	Coefficient of repeatability (differences observed between 2 measurements of PWV according to the mean values)	EFF
Luzardo et al. (2012)	Cross-sectional	25/83	• MOGARC • SphygmoCor®	absolute difference between tonometry vs. oscillometry relative difference between tonometry vs. oscillometry	EFF
Salvi et al. (2019)	Consecutive cross-sectional	102	• MOGARC • Complior Analyse • PulsePen® - ET • PulsePen® - ETT • SphygmoCor® • Proprietary Algorithms • BPLab® v.5.03 • BPLab® v.6.02	r (pearson correlation coefficient) and mean differences (SD) between devices r (pearson correlation coefficient) and mean differences (SD) with invasive for each device trend association with coronary damage	EFF
Salvi et al. (2019)	Cross-sectional	90	• MOGARC • PulsePen®	Correlation analysis PWV Distribution of PWV related to age Distribution of PWV related to systolic blood pressure	EFF
Sarafidis et al. (2014)	Cross-sectional	73	• MOGARC • SphygmoCor®	Correlation analysis aSBP Correlation analysis AIx75 Correlation analysis PWV	EFF

Sarafidis et al. (2017)	Cohort study	170	• MOGARC	combination of all-cause death, nonfatal MI and nonfatal stroke all-cause mortality cardiovascular mechanism within 30 days after an MI or fatal stroke a combined outcome of cardiovascular death, nonfatal MI, nonfatal stroke	EFF
Vaios et al. (2018)	Cross-sectional	27	• MOGARC • SphygmoCor®	Correlation analysis of the agreement between the Mobil-O-Graph and SphygmoCor® devices in the estimation of heart-rate-adjusted AIx75, aSBP and PWV	EFF
Wassertheurer et al. (2010)	Cross-sectional	302	• oscillometric method using ARCSolver® algorithm • SphygmoCor®	mean difference AIx mean difference aSBP	EFF
Weber et al. (2011)	Prospective cross-sectional	131	• MOGARC • SphygmoCor® • Invasively measured aortic BP	aSBP r2 compared to invasive	EFF

Abbreviations: aoSBP=aortic systolic blood pressure, AIx=augmentation Index, AIx(75)=augmentation index at 75 bpm, cSBP=central systolic blood pressure, cDBP=central diastolic blood pressure, ICC=Intraclass correlation coefficient, MI=Myocardial Infarction, mmHg=millimeter of mercury, pSBP=peripheral systolic blood pressure, SD=standard deviation, PWV=pulse wave velocity

2.8 Deviations from project plan

There were deviations from the project plan due to the stance of the evidence on the hierarchical model of efficacy (Figure 2-2) being at a Level 1, rather than the questions of interest, which would require evidence from higher levels of efficacy (effectiveness) as illustrated conceptually by the Fryback and Thornberry model which was originally developed to understand the body of evidence around diagnostic imaging.(16) This meant that the inclusion of studies in the search was expanded further than intended and therefore did not include limiting terms such as pulse wave velocity. Almost all studies dealt with the technical comparison of devices in predicting pulse wave analysis. Nevertheless, it was important to assess MOGARC at the highest point on the hierarchy for which literature exists. This information, while it does not sufficiently help answer the questions originally relevant, does help pinpoint relevant comparators and issues, which are necessary for conducting future studies to answer the original questions.

Due to the studies being included not being of patient efficacy, or clinical efficacy as of original interest and not allowing for any assessment of the research questions at hand, the GRADE assessment was not used on an outcome level. Despite the level of evidence not being that of the target level, information on what was available was extracted to highlight the gaps and potential next steps in this topic.

Another deviation from the project plan was to include devices other than Mobil-O-Graph which contain the ARCSolver® algorithm or where the ARCSolver® algorithm is retrospectively applied. As the intent was to specifically understand the ARCSolver® coupled with a device, studies that coupled ARCSolver® with devices other than Mobil-O-Graph were also included. Mobil-O-Graph is identified in this review as it is the main and first relevant device coupled with ARCSolver®.

Searches specifically for the other device (VaSera®) were conducted subsequently to assure no additional evidence was missed. No studies were found in this additional search.

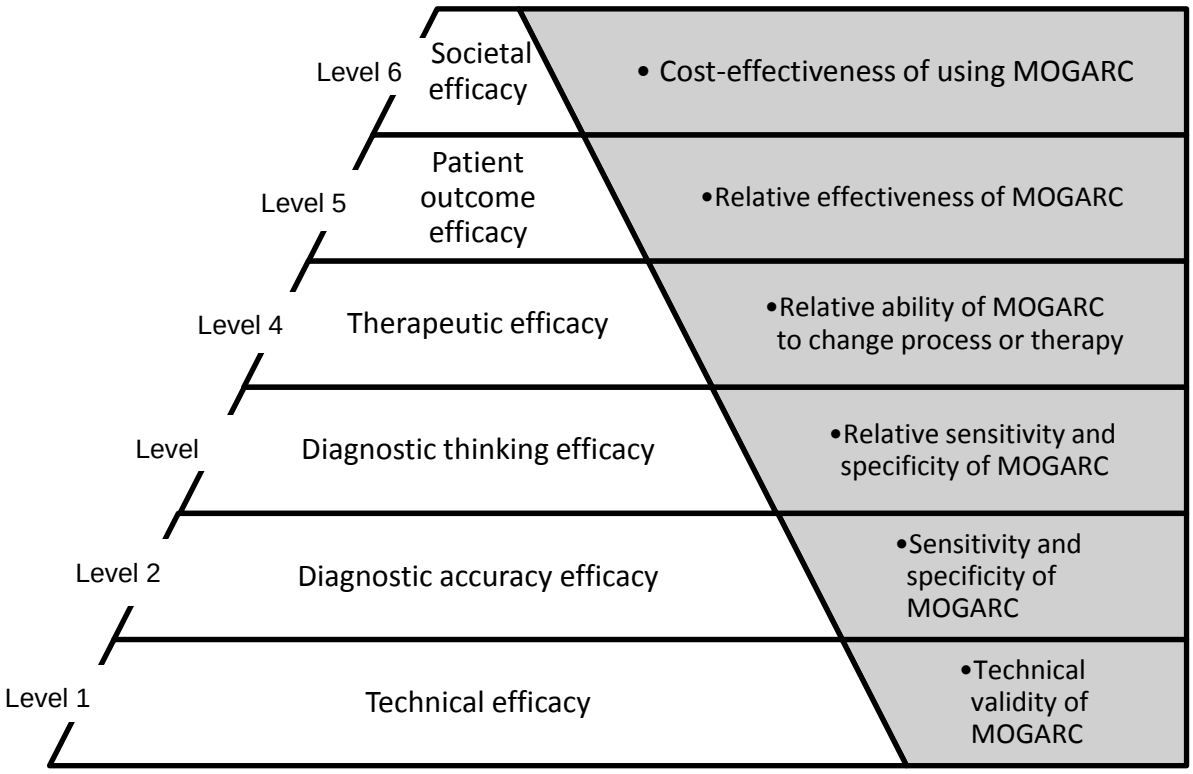

Figure 2-2: Hierarchical Model of Efficacy adapted from Fryback and Thornberry 1991

3 DESCRIPTION AND TECHNICAL CHARACTERISTICS OF TECHNOLOGY (TEC)

3.1 Research questions

Element ID	Research question
B0001	What is pulse wave analysis through Mobil-O-Graph® device and ARCSolver® algorithm? What are the conventional 24-h blood pressure measurement devices approved for use under "specialist" or "ambulatory blood pressure measurement (ABPM)" ? What are cardiovascular risk equations? What are other non-invasive pulse wave analysis devices?
B0002	What is the claimed benefit of pulse wave analysis through Mobil-O-Graph® device and ARCSolver®algorithm in relation to conventional 24-h blood pressure measurement devices approved for use under "specialist" or "ambulatory blood pressure measurement (ABPM)"? What is the claimed benefit in relation to cardiovascular risk equations? What is the claimed benefit in relation to non-invasive pulse wave analysis methods?
B0003	In what phase of development and implementation is the Mobil-O-Graph® device and ARCSolver® algorithm, conventional 24-h blood pressure measurement approved for use under "specialist" or "ambulatory blood pressure measurement (ABPM)", cardiovascular risk equations, and other non-invasive pulse wave analysis methods?
B0004	In what setting and context, and by which medical professionals is the Mobil-O-Graph® device and ARCSolver® algorithm, conventional 24-h blood pressure measurement approved for use under "specialist" or "ambulatory blood pressure measurement (ABPM)" , cardiovascular risk equations and other non-invasive pulse wave analysis devices used?
B0008	What kind of special premises are needed for the use of Mobil-O-Graph® device and ARCSolver® algorithm, conventional 24-h blood pressure measurement approved for use under "specialist" or "ambulatory blood pressure measurement (ABPM)" , cardiovascular risk equations and other non-invasive pulse wave analysis methods?
B0009	What equipment and supplies are needed to use the Mobil-O-Graph® device and ARCSolver® algorithm, conventional 24-h blood pressure measurement approved for use under "specialist" or "ambulatory blood pressure measurement (ABPM)" , cardiovascular risk equations, and other non-invasive pulse wave analysis methods?
A0020	For which indications has the Mobil-O-Graph®device and ARCSolver® algorithm received marketing authorisation or CE marking?
A0021	What is the reimbursement status of the Mobil-O-Graph® device and ARCSolver® algorithm?

3.2 Results

In this assessment the TEC section is very important due to the multifaceted nature of this topic. The components important for this assessment include not only the devices themselves, but how they are coupled with algorithms, and the different measures that the devices and algorithms entail. Due to the technical characteristics of Mobil-O-Graph®, comparisons are relevant not only on a device level, but also on an algorithm level, a calibration level, and a parameter level as different devices measure different parameters. The method of obtaining the base data (peripheral blood pressure) is also relevant before the algorithm is applied. This interplay makes the comparison of a device coupled with an algorithm complex. The following TEC domain questions describe the nuances of these devices, algorithms, and the parameters they measure in detail.

Features of the technology and comparators

[B0001] – What is pulse wave analysis through Mobil-O-Graph® device and ARCSolver® algorithm?

What are the conventional 24-h blood pressure measurement devices approved for use?

What are cardiovascular risk equations?

What are other non-invasive pulse wave analysis devices?

Arterial stiffness has gained recognition as a risk factor in patients with arterial hypertension and other cardiovascular diseases. As a gold standard for arterial stiffness in clinical practice, the carotid-femoral pulse wave velocity (cf-PWV) is considered.(19) There are several devices for the noninvasive measurement of arterial stiffness developed and validated. They are illustrated below, grouped by the different methods on which the devices are based and shown in Figure 3-1.

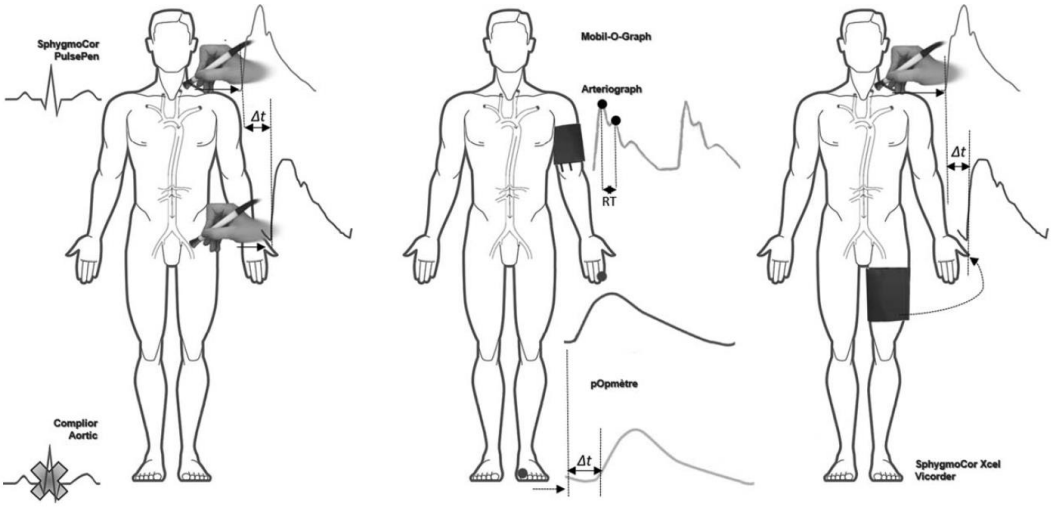

Figure 3-1: Graphic representation of currently available devices for pulse wave velocity measurement

Source: Milan A, Zocaro G, Leone D, Tosello F, Buraioli I, Schiavone D, et al. Current assessment of pulse wave velocity: Comprehensive review of validation studies. Journal of Hypertension. 2019;37(8):1547-57

Currently the most common method to assess cf-PWV is the transcutaneous tonometry. This method is based on pulse wave acquisition at common carotid and femoral artery site.(19) The observed technology (MOGARC) uses a cuff-based oscillometric method.

Cuff-based oscillometry

Mobil-O-Graph® NG is a blood pressure monitor and Mobil-O-Graph® PWA provides additional pulse wave monitoring for central hemodynamic assessment and risk stratification of arterial hypertension. The **Mobil-O-Graph®** (IEM, Stolberg, Germany) uses a cuff-based method to estimate cf-PWV from single point pressure wave recording. After obtaining systolic blood pressure (SBP) and diastolic blood pressure (DBP) the brachial cuff is inflated to the DBP level and held for 10 seconds to record pulse waves. Using a transfer function, central pressure curves are obtained and processed using the ARCSolver® algorithm (Austrian Institute of Technology, Vienna, Austria).(19) This algorithm aims to be a novel method for the determination of the aSBP and AIx in combination with the oscillometric blood pressure measurement. The method uses the pulse

waves assessed at brachial artery. The recordings are carried out at diastolic pressure level for approximately 10 seconds using a conventional blood pressure cuff and a high fidelity pressure sensor (MPX5050, Freescale Inc., Tempe, AZ, USA). The sensor is connected to a 12 bit A/D converter by means of an active analogue band bass filter (0<>25 Hz). After digitalization, the signal processing is performed using a three level algorithm. First of all, the single pressure waves are verified by testing the position of minima and the corresponding wavelengths. After this, all single pressure waves are compared with each other to recognize artifacts. An aortic pulse wave is then generated by the means of a generalized transfer function. This is because of the modification of a certain frequency range within the acquired pulse signal to get the aortic pressure wave (Figure 3-2a).(20) Figure 3-2b shows that the first positive zero crossing of the fourth-order time derivative of the generated aortic pulse wave represents the desired inflection point. After this, the inflection point of each single pulse wave is compared with the mean inflection point. The determination of aSBP and AIx is carried out in the same way as in SphygmoCor®. According to the statements by the producers, the ARCSolver® alogirthm inbuilt in Mobil-O-Graph® is based on age, systolic BP and pulse waveform characteristics. (21)

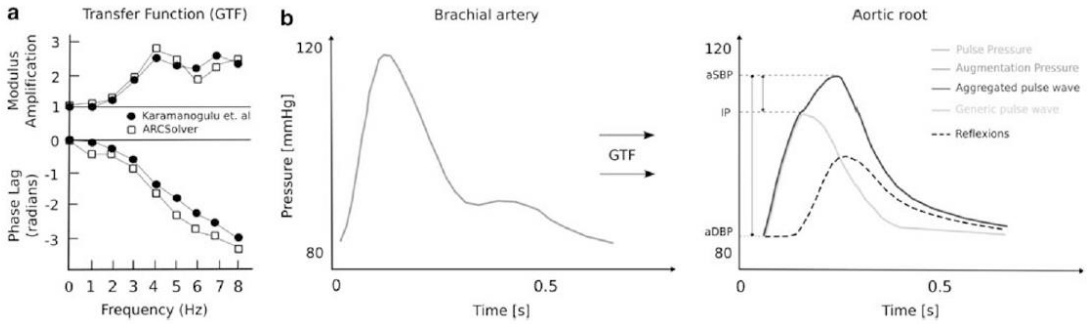

Figure 3-2: (a) Characteristic modulus amplifications and phase shifts of pressure wave harmonics between aortic root and brachial artery used for the ARCSolver® (b) Principles to derive aSBP and Aix from brachial waveform.

Source: Wassertheurer S, Kropf J, Weber T, van der Giet M, Baulmann J, Ammer M, et al. A new oscillometric method for pulse wave analysis: comparison with a common tonometric method. Journal of Human Hypertension. 2010.

The Mobil-O-Graph® PWA uses the ARCSolver® algorithm to calculate the following measures:

- central aortic blood pressure
- cardiac output
- peripheral resistance
- augmentation index (AIx) and augmentation pressure
- reflection coefficient and
- pulse wave velocity.

Both Mobil-O-Graph® NG and Mobil-O-Graph® PWA have the ability to capture office blood pressure, or can be used as ambulatory blood pressure monitors (ABPM), which are taken home over a period of 24-h to measure blood pressure and other outputs several times during the day.(13)

Arteriograph (TensioMed, Budapest, Hungary) is another cuff-based oscillometric device which is an operator-independent device.(22) It is equipped with an inflatable cuff, which is placed on the patient's upper arm and inflated 35 mmHg above the individuals SBP. Pressure variations are detected by a pressure receptor and a signal is transferred to a computer. PWV acquirement is based on the generation of two systolic peaks: the first one results from systolic volume ejection in

the aorta, the second one and lower peak P2 is given by wave pressure reflection from peripheral arteries. Return time is the difference between the first and the reflected systolic peak.(19)

Vicorder® (Skidmore Medical, Bristol, UK) is a system which is fitted with proximal and distal inflatable cuffs, that are placed respectively at the carotid site and around the upper part of the right thigh. Distance is measured superficially. (19)

The **BPLab®** (Petr Telegin, Russia) device is also an automated oscillometric arm cuff-based ambulatory BP monitoring device, estimating aortic PWV by proprietary algorithm. The algorithm Vasotens Office 6.02 version used by BPLab® is based on age, systolic BP, length of aorta (as derived from the distance between the suprasternal notch and pubic symphysis), and the transition time between forward and reflected components of pulse wave. (21)

Applanation tonometry

SphygmoCor® (AtCor Medical, Sydney, Australia) uses a tonometric sensor placed on a pen-like support acquiring pressure waves first at the carotid site and then at the femoral site and recorded on a personal computer. Registration is not simultaneous, thus an ECG recording is needed to synchronize the R peak with the two different pulse waves. Transit time is determined using the intersecting tangent method. **SphygmoCor® Xcel** (Actor Medical, Sydney, Australia) is the newest version which allows femoral and carotid signals to be acquired simultaneously. SphygmoCor® registers the carotid pulse waves, whereas the femoral pulse wave is recorded using a partially inflated oscillometric cuff. (19)

The **PulsePen®** (DiaTecne, Milano, Italy) is another tonometric device and composed of a high-definition tonometry, an ECG unit and a wireless receiver. Since 2014 a two tonometer version, the so called PulsePen®-ETT is available, which allows an ECG-free PWV assessment. In both devices wave foot is determined using the intersecting interpolating algorithm. It is based on the intersection of the horizontal line crossing the lowest point of the pressure waveform with the interpolant line of the early protosystolic phase. (19)

Piezoelectric mecanotransducer

The **Complior Analyse** (AlamMedical, Paris, France) is equipped with two piezoelectric mechanotransducers and PWVs are acquired simoultanesly. Sensors are placed at the common carotid artery and at the femoral site. Path length is assessed by direct superficial measurement of the distance between the two sites. Additional probes are provided, radial and distal, allowing PWV measurements on three different segments one. (19)

Aortic (Exxer, Berazategui, Argentina) is also a device that uses two piezoelectric transducers and registers cf-PWV simoultanesly. (19)

Other techniques

VaSera® (Fukuda Denshi, Tokyo, Japan) acquires cardiacankle pulse wave velocity by placing cuffs on all four limbs and a microphone at the sternal notch for phonocardiography. PWV is estimated by dividing the distance from the aortic valve to the ankle cuff by the sum of the difference between the time the pulse waves are transmitted to the brachial and the ankle cuffs, and the time difference between the second heart sound on the phonocardiogram and the notch of the brachial waves. (19)

In **pOpmètre®** device (Axelife SAS, Nicolas-de-Redon, France), photodiode sensors are placed on the finger and on the toe, allowing pulpar arteries detection. Finger and toe pulse transit time (ft-PTT) is assessed and finger-toe PWV (ft-PWV) is obtained. (19)

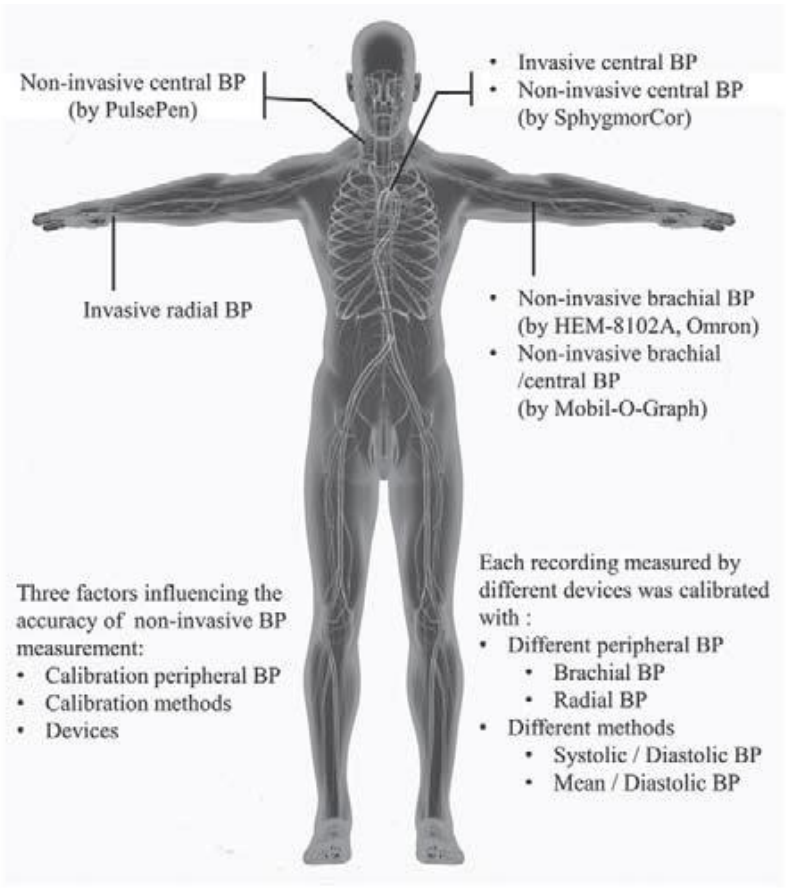

Figure 3-3: Schematic diagram of BP measurements and calibration strategies

Source: Chi C, Zhou Y, Lu Y, Tang Y, Li Y, Zhang Y, et al. Three influencing factors for the accurate measurement of non-invasive central blood pressure as compared to invasive measurement: The matchy study. Journal of Hypertension. 2019;37:e43-e4.

Table 3-1: Features of the intervention and PWA comparators

	Technology	Comparator 1	Comparator 2	Comparator 3	Comparator 4	Comparator 5	Comparator 6	Comparator 7	Comparator 8	Comparator 9
Name	Mobil-O-Graph® PWA	SphygmoCor®	SphygmoCo®r Xcel	Complior Analyse	PulsePen®-ETT	PulsePen®-ET	pOpmetre®	BPLab®	Arteriograph	Vicorder®
Manufacturer	I.E.M	AtCor Medical	AtCor Medical	Alam Medical	DiaTecne	DiaTecne	Axelife	Petr Telegin	Tensiomed	Skidomore Medical
Country of Origin	Germany	Australia	Australia	France	Italy	Italy	France	Russia	Hungary	UK
Reference codes										
Class/GMDN code										
Aortic PWV Assessment	Cuff-based method	Carotid-femoral PWV	Carotid-femoral PWV	Carotid-femoral PWV	Carotid-femoral PWV	Carotid-femoral PWV	Finger-toe PWV	Cuff-based method	Cuff-based method	Cuff-based Carotid femoral
Probes	Upper arm cuff oscillometric system	1 tonometer +ECG	1 tonometer	2 piezoelectric sensors	2 tonometers	1 tonometer +ECG	2 photodiode sensors	Upper arm cuff oscillometric system	Upper arm cuff oscillometric system	Upper arm cuff oscillometric system
Recording time	10 s	NA	NA	10 cardiac cycles	10 cardiac cycles	10 cardiac cycles	10 cardiac cycles	4-8 cardiac cycles	NA	NA
Method	Algorithm primarily based on age and systolic blood pressure	Sequential ECG-gated pulse wave recording at carotid and femoral artery	Femoral and carotid signals are acquired simultaneous	Simultaneous pulse wave recording at carotid and femoral artery	Simultaneous pulse wave recording at carotid and femoral artery	Sequential ECG-gated pulse wave recording at carotid and femoral artery	Simultaneous pulse wave recording at finger and toe	5.03 SW: analysis of reflected wave transit time. 6.02 SW: algorithm primary based on age and systolic blood pressure	PWV acquirement is based two systolic peak	Transit time is computed using the maximum of the second derivate, based on the maximum of the second derivative algorithm
Transit time	-	Foot-to-foot method: intersecting tangent algorithm	NA	Foot-to-foot method: intersecting tangent algorithm	Foot-to-foot method: intersecting interpolating algorithm	Foot-to-foot method: intersecting interpolating algorithm	Maximum of the second derivative algorithm	-	NA	NA
Sampling rate	100 Hz	128 Hz	256 Hz	1 kHz	1 kHz	1 kHz	1 kHz	100 Hz	200 Hz	556 Hz
Central BP Assessment	Brachial oscillometric blood pressure cuff-based method	Transfer function from radial artery	NA	Direct method from carotid artery	Direct method from carotid artery	Direct method from carotid artery	From digital volume pulse by photodiode sensor on the finger	Brachial oscillometric blood pressure cuff-based method	NA	NA

	Technology	Comparator 1	Comparator 2	Comparator 3	Comparator 4	Comparator 5	Comparator 6	Comparator 7	Comparator 8	Comparator 9
24h monitoring	Ambulatory blood pressure monitoring (ABPM)	No	NA	No	LP software allows up to 24h track recording	LP software allows up to 24h track recording	No	Ambulatory blood pressure monitoring (ABPM)	Ambulatory blood pressure monitoring (ABPM)	NA
Weight, g	240	800		450	121	88	375	226	250	600
Other characteristics	Handheld system	-	-	-	Pocket-sized wireless system	Pocket-sized wireless system	-	Handheld system	Handheld system	-

Abbreviations: ABPM=ambulatory blood pressure monitoring, ECG=electrocardiographic, g=grams, Hz=Hertz, kHz=kilohertz, NA=not available, SW=software, PWV=pulse wave velocity, s=seconds, UK=United Kingdom

Sources: Milan A, Zocaro G, Leone D, Tosello F, Buraioli I, Schiavone D, et al. Current assessment of pulse wave velocity: Comprehensive review of validation studies. Journal of Hypertension. 2019;37(8):1547-57. Medical A. SphygmoCor® CPV. In: Medical A, editor. 2020. http://www.atcormedical.com.au/pdf/German/SphygmoCor%20CPV%20(German).pdf

Table 3-2: Features of the intervention and 24-h blood pressure (non-PWA) comparators

	Technology	Comparator 1
Name	Mobil-O-Graph® PWA	Mobil-O-Graph® NG
Manufacturer	I.E.M	I.E.M
Country of Origin	Germany	Germany
Reference codes		
Class/GMDN code		
Aortic PWV Assessment	Cuff-based method	No PWV Assessment, blood pressure assessed via Cuff-based method
Probes	Upper arm cuff oscillometric system	Upper arm cuff oscillometric system
Recording time	10 s	NA
Method	Algorithm primarily based on age and systolic blood pressure	NA
Transit time	-	-
Sampling rate	100 Hz	100 Hz
Central BP Assessment	Brachial oscillometric blood pressure cuff-based method	Brachial oscillometric blood pressure cuff-based method
24-h monitoring	Ambulatory blood pressure monitoring (ABPM)	Ambulatory blood pressure monitoring (ABPM)
Weight, g	240	240
Other characteristics	Handheld system	Handheld system

Abbreviations: ABPM=ambulatory blood pressure monitoring, BP=blood pressure, g=gram, GMDN=Global Medical Device Nomenclature, H=hours, Hz=Hertz, NG=new generation, s=seconds; PWA=pulse wave analysis, PWV=pulse wave velocity
Sources: Milan A, Zocaro G, Leone D, Tosello F, Buraioli I, Schiavone D, et al. Current assessment of pulse wave velocity: Comprehensive review of validation studies. Journal of Hypertension. IEM. Mobil-O-Graph® Operating Manual. In: (R) I, editor. 2018

[B0002] – What is the claimed benefit of pulse wave analysis through Mobil-O-Graph® device and ARCSolver® algorithm in relation to conventional 24-h blood pressure measurement devices approved for use under "specialist" or "ambulatory blood pressure measurement (ABPM)"? What is the claimed benefit in relation to cardiovascular risk equations? What is the claimed benefit in relation to non-invasive pulse wave analysis methods?

In relation to Mobil-O-Graph® NG without pulse wave analysis, and other blood pressure measurement devices without pulse wave analysis, the claimed benefit of Mobil-O-Graph® PWA (MOGARC) is the calculation of central blood pressure parameters such as central aortic blood pressure, cardiac output, peripheral resistance, augmentation index, augmentation pressure, reflection coefficient, and pulse wave velocity.(13) These additional measures are measures of arterial stiffness, which can be implemented to determine cardiovascular risk and improve measurement of hypertension and measurement of organ damage related to arterial stiffness.

The assumed potential benefit in relation to other PWA measures could be a more accurate and/or more consistent measure of central blood pressure parameters.

In terms of benefit to the population, the claimed benefit of pulse wave analysis measures is to better stratify cardiovascular risk, which may lead to avoidance of cardiovascular events through timely and more appropriate interventions. The second claimed benefit of pulse wave analysis measures is that it is better at identifying hypertension and effectiveness of hypertension medica-

tion which may lead to better hypertension control. Other claimed benefits of pulse wave analysis measures are that they can help stratify organ damage as related to arterial stiffness. (12)

In terms of health related quality of life (HRQL) the observed devices do not influence it directly. However, García-Ortiz et al. (2016) investigated the relationship between cardiovascular outcomes and health-related quality of life by using VaSera® and Mobil-O-Graph® for the measurement. The authors analyzed the relationship of vascular structure and function as assessed by ABI (ankle/brachial index), CAVI (cardio ankle vascular Index), PWV (pulse wave velocity) and AIx (augmentation index) with HRQL as assessed by the Short Form-12 (SF-12) questionnaire in a population with intermediate cardiovascular risk in the context of the MARK study (n=303). In this sample of subjects with intermediate cardiovascular risk, the findings showed that there is a positive association between a normal ranged ABI and HRQL in the physical dimension. The higher this parameter the better the health-related quality of life is reported. Regarding the physical dimension there was no association with the PWV and only an inverse unadjusted relationship with the AIx. CAVI has also a positive relation to HRQL. (23)

[B0003] – In what phase of development and implementation is the Mobil-O-Graph® device and ARCSolver® algorithm, conventional 24-h blood pressure measurement approved for use under "specialist" or "ambulatory blood pressure measurement (ABPM)", cardiovascular risk equations, and other non-invasive pulse wave analysis methods?

All technologies assessed in this review are available for purchase by physicians or individuals.

[B0004] – In what setting and context, and by which medical professionals is the Mobil-O-Graph® device and ARCSolver® algorithm, conventional 24-h blood pressure measurement approved for use under "specialist" or "ambulatory blood pressure measurement (ABPM)", cardiovascular risk equations and other non-invasive pulse wave analysis devices used?

The technologies assessed in this review are provided in a hospital setting, outpatient setting, and primary care and specialist care setting. Mobil-O-Graph® with ARCSolver® can be administered during a doctor's visit or over a 24-h ambulatory blood pressure measurement, during which the patient takes the blood pressure device home.(13) The administration of the other technologies is similar and can be found in Table 3-1.

[B0008] – What kind of special premises are needed for the use of Mobil-O-Graph® device and ARCSolver® algorithm, conventional 24-h blood pressure measurement approved for use under "specialist" or "ambulatory blood pressure measurement (ABPM)" , cardiovascular risk equations and other non-invasive pulse wave analysis methods?

There are no special premises required to use the technology. (13)

[B0009] – What equipment and supplies are needed to use the Mobil-O-Graph® device and ARCSolver® algorithm, conventional 24-h blood pressure measurement approved for use under "specialist" or "ambulatory blood pressure measurement (ABPM)" , cardiovascular risk equations, and other non-invasive pulse wave analysis methods?

There is no special equipment or supplies needed to use the technology or the comparators besides technology and comparators themselves. The following supplies come with the MOGARC: 1. Mobil-O-Graph® (NG or PWA) 2. S-, M- and L-Cuff 3. Mobil-O-Graph® Universal Case 4. Recharger including 4 NiMH batteries 5. Operating instructions 6. Measuring tape 7. Event protocol.

Additionally, doctors can order analysis unit HMS Client-Server which links to Mobil-O-Graph® to download information: 1. HMS Client-Server on CD 2. Bluetooth-Dongle alternatively 3. IR-MED serial or USB alternatively 4. PC hybrid cable USB or serial. (13)

Traditional CVD risk assessments are based on history and physical examinination. Blood testing for lipid concentrations, typically low-density lipoprotein (LDL) cholesterol and/or high-density lipoprotein (HDL) cholesterol, is a requirement for risk assessment tools/scores. An alogorithm (several are available in published literature and clinical guidelines) then calculates the risk based on patient characteristics, lipid concentrations, and history. There are several risk calculators available for different types of patients based on their age, ethnic group, and geographic region to best model and predict the risk of individual patients. (24)

[A0020] – For which indications has the Mobil-O-Graph® device and ARCSolver® algorithm received marketing authorisation or CE marking?

The Mobil-O-Graph® NG and PWA fulfil the requirements of the:

- Medical Devices Directive 93/42/EEC
- RED Directive 1999/5/EU
- RoHS 2011/64/EU Directives
- In particular, it fulfils the applicable requirements of the following standards: 1. EN 1060-1 Noninvasive blood pressure measuring equipment - Part 1: General requirements 2. EN 1060-3 Noninvasive blood pressure measuring equipment - Part 3: Supplementary requirements for electromechanical blood pressure measuring systems. (13)

[A0021] – What is the reimbursement status of the Mobil-O-Graph® device and ARCSolver® algorithm?

This product is currently reimbursed in Austria.

4 HEALTH PROBLEM AND CURRENT USE OF THE TECHNOLOGY (CUR)

4.1 Research questions

Element ID	Research question
A0002	What is hypertension and what is cardiovascular disease?
A0003	What are the known risk factors for hypertension and cardiovascular disease?
A0004	What is the natural course of hypertension and cardiovascular disease?
A0005	What is the burden of hypertension and cardiovascular disease and what are their symptoms?
A0006	What are the societal consequences of hypertension and cardiovascular disease?
A0024	How are hypertension and cardiovascular disease currently diagnosed according to published guidelines and how does that translate in practice?
A0025	How should hypertension and cardiovascular disease be managed according to current published guidelines and how are they managed in practice?
A0007	What is the target population in this assessment?
A0023	How many people belong to the target population?
A0011	To what extent is Mobil-O-Graph® device and ARCSolver® utilized?

4.2 Results

Overview of the disease or health condition

[A0002] – What is hypertension and what is cardiovascular disease?

Hypertension

High blood pressure (also known as hypertension) is a condition in which the blood pressure, the force of blood pushing against the walls of blood vessels, is consistently too high. This long-term force of the blood against the artery walls is high enough that it may cause damage to blood vessels, heart and many other organs, and thus cause various health problems such as stroke. In most adults, hypertension develops gradually over many years without an identifiable cause. This is called primary or essential hypertension. However, some people have high blood pressure caused by a specific underlying condition, called secondary hypertension. In general, this type of hypertension tends to appear suddenly and manifests in higher blood pressure values than the primary hypertension. Some underlying conditions include obstructive sleep apnea, kidney problems, adrenal gland tumours, thyroid problems, congenital blood vessel defects, and medications. In terms of blood pressure measurement, the most recent European guidelines define hypertension using office-based blood pressure as a systolic pressure ≥140 mmHg or diastolic pressure ≥90. (25) Hypertension can damage the body in several ways: it can cause hardening and thickening of the arteries, further advancing the development of atherosclerosis which can cause a heart attack or stroke; weakening or bulging of blood vessels which can cause aneurysm; thickening of the heart's pumping chamber called left ventricular hypertrophy which can lead to heart failure, weakened and narrowed blood vessels in the kidneys which can cause kidney failure;

thickened, narrowed or torn blood vessels in the eyes which can result in vision loss; metabolic syndromes which increase the likelihood of developing diabetes, heart disease, or stroke; narrowed or blocked arteries that limit blood flow to the brain and lead to vascular dementia.(26)
Atherosclerosis is a type of arteriosclerosis, otherwise known as hardening of the arteries. It is the bridge between the two conditions that are being studied in this assessment. It is important to note that the terms atherosclerosis and arteriosclerosis are sometimes used interchangeably. Atherosclerosis is the build-up of fatty substances in the arteries, which can lead to heart disease and stroke. It's a slow, complex disease that typically starts in childhood and progresses with age. In this disease, the blood vessels that carry oxygen and nutrients from the heart to the rest of the body, called arteries, become thick and stiff, sometimes restricting blood flow to organs and tissue, and causing arterial stiffness. Atherosclerosis is typically a cardiovascular condition but can affect arteries anywhere in the body. One of the causes of atherosclerosis is damage to the inner layer of the artery caused by high blood pressure. The complications of atherosclerosis depend on which arteries are blocked. These include cardiovascular diseases such as coronary artery disease, carotid artery disease, peripheral artery disease. Additionally it can cause aneurysms anywhere in the body and chronic kidney disease.(27)

Cardiovascular disease
The second related condition being studied herein, is the cardiovascular disease. Cardiovascular disease includes a range of conditions that affect the heart and/or blood vessels that lead to heart attack, angina, or stroke and are most commonly caused by atherosclerosis.
Cardiovascular disease (CVD) includes coronary heart disease (CHD), cerebrovascular disease, peripheral artery disease, and aortic atherosclerosis. The entities which are usually a part of the CHD are myocardial infarction, angina pectoris and heart failure, whereas stroke and transient ischemic attack are major cerebrovascular diseases. Intermittent claudication and critical limb ischemia are manifestations of peripheral artery disease. Finally, thoracic or abdominal aortic aneurysm are associated with aortic atherosclerosis.
The most common symptoms are chest pain, chest tightness, shortness of breath, pain, numbness, weakness or coldness in legs or arms, depending on which blood vessels are narrowed. (28)

[A0003] – What are the known risk factors for hypertension and cardiovascular disease?

Risk factors for cardiovascular disease (CVD)
CVD is caused by multiple factors. Individual risk factors could be potentially modifiable (variable) or nonmodifiable (invariable). Invariable risk factors are age, gender, family history/genetic heritage, ethnicity. In particular, family history is a significant independent risk factor for CHD among younger individuals with a family history of premature disease. Leading modifiable risk factors are hypercholesterolemia, diabetes, hypertension, obesity, and smoking. In addition, according to the INTERHEART study, alcohol intake, inadequate physical activity and bad eating habits (low vegetable and fruit consumption) are among the nine risk factors and health behaviours that account for more than 90% of the population's attributable risk of acute myocardial infarction.(29) The relevance of risk factors varies with age and gender (ie. diabetes and a low HDL-cholesterol/total cholesterol ratio operate with greater power in women). Furthermore, psychosocial factors (depression, anger, stress, social integration/support) contribute to the early development of CVD.(30, 31) Oxidative stress is associated with many atherosclerotic risk factors (hypertension, dyslipidaemia, peripheral artery disease, metabolic syndrome, diabetes, obesity).(32) Inflammatory markers (C-reactive protein, Interleukin-6, myeloperoxidase) have been reported to be associated with increased risk of CVD.(33) Determination of critical value for specific risk factors has been subject of debates as in the case of dyslipidemia.

The association between measures of arterial stiffness and cardiovascular risk has been investigated. Aortic pulse wave velocity (PWV) emerged as predictor of cardiovascular events in selected high risk patients, with hypertension, end-stage renal disease and hospitalized elderly patients. The Rotterdam Study concluded that aortic pulse wave velocity is also a predictor of CHD and stroke in healthy subject.(34) An extension of the Framingham Heart Study considered aortic stiffness as a potential risk predictor when added to traditional risk factors in the investigated community-based sample of middle-aged and older people.(35) Additionally, the stratification of CVD risk is important because there are apparently healthy and asymptomatic individuals who do not yet have manifest atherosclerotic disease but can develop CVD.(36) Thus, risk models for CVD risk assessment have been developed (i.e. Framingham risk score, ACC/AHA pooled cohort hard CVD risk score) to estimate the risk of initial CVD events. These models are multivariate and individualized using patient-specific characteristics as age, gender, and ethnicity.

Risk factors for hypertension

Risk factors that can increase the risk of high blood pressure include health conditions, lifestyle, and family history. The risk factors that are strongly and independently associated with primary (essential) hypertension development include: age (advancing age is associated with increased blood pressure), obesity, race (black ethnicity), reduced nephron number, high-sodium diet, excessive alcohol consumption, physical inactivity. Major causes of secondary hypertension include: prescription or over-the-counter medications (oral contraceptives, nonsteroidal antiinflammatory agents, antidepressants, corticosteroids, decongestants, sodium-containing antacids, erythropoietin, cyclosporine or tacrolimus, stimulants, atypical antipsychotics, including clozapine and olanzapine, angiogenesis inhibitors, tyrosine kinase inhibitors), illicit drug use, primary renal disease, primary aldosteronism, renovascular hypertension, obstructive sleep apnea, pheochromocytoma, Cushing's syndrome, coarctation of the aorta.(37) Hypertension often occurs alongside diabetes mellitus, including type 1, type 2, and gestational diabetes. The factors that contribute to hypertension in diabetes are the development of diabetic nephropathy, the extracellular fluid volume expansion, and increased arterial stiffness.(38)

[A0004] – What is the natural course of hypertension and cardiovascular disease?

Atherosclerotic cardiovascular disease - natural course

Cardiovascular disease (CVD) includes coronary heart disease (CHD), cerebrovascular disease, peripheral artery disease, and aortic atherosclerosis. More in general the term ”cardiovascular disease” refers to a damage to heart or blood vessels caused by atherosclerosis. Atherosclerosis is a slow, chronic, progressive disease. It starts when the endothelium becomes damaged and plaque can build up, made of cholesterol, macrophages, cellular waste products, calcium and fibrin. Hypercholesterolaemia is considered one of the main triggers of atherosclerosis because it impacts on arterial endothelial permeability which is linked to the migration of lipids, leading to inflammation (atherosclerosis is considered as an inflammatory disease of the wall of large- and medium-sized arteries).

The evolution of atherosclerosis occurs in a sequence of vascular modifications - intimal thickening, fatty streak, pathologic intimal thickening, fibroatheromas, vulnerable plaque, ruptured plaque.(39) Buildup of plaque narrows the channel within the artery, causing the arteries to harden and reduce blood flow. That reduces the amount of oxygen and other nutrients reaching vital organs and increases the risk of blood clots. Untreated atherosclerosis can lead to partial or total block of blood flow in large- or medium-sized arteries in the heart, brain, pelvis, legs, arms or kidneys; causing manifestations of the atherosclerotic disease of the arteries:coronary heart disease (coronary arteries clogged with plaques), angina (chest pain from reduced blood flow to the heart muscle), carotid artery disease (plaque in carotid arteries), peripheral artery disease (plaque in

arteries of the extremities), chronic kidney disease. Other complications of atherosclerotic plaques are renal artery stenosis, thrombotic or embolic stroke and abdominal aortic aneurysm, among others.

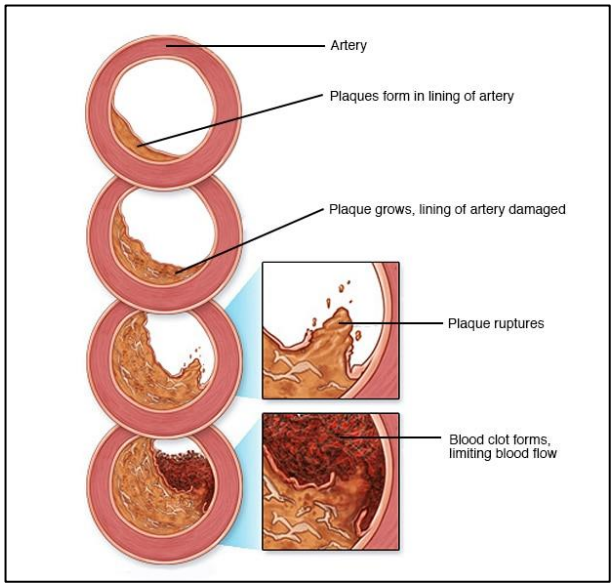

Figure 4-1: Development of atherosclerosis

Source: https://www.mayoclinic.org/diseases-conditions/heart-disease/symptoms-causes/syc-20353118

Arterial stiffness - natural course

The elastic property of the aortic wall is important for the pulsatile cardiac blood flow - as it acts as elastic buffering chamber for the blood once it is ejected from the heart (Windkessel function). The loss of elasticity therefore determines alterations in central hemodynamics. Furthermore, biologically, arterial rigidity is based on the delicate balance between production and degradation of elastin and collagen. Blood pressure, vascular structure and function are the major components involved in arterial stiffness. With low blood pressure, vessel wall is relatively extensible. Higher level of blood pressure potentiates the stiffer property of collagen and vessel becomes inextensible. Other relevant vascular functionalities are endothelial dysfunction and smooth muscle tone, which also has an impact on artery elasticity.(40) Many mechanisms contribute to the development of arterial stiffness (vascular calcification, vascular inflammation, insulin resistance, uric acid, adipose tissue, aging).(41) Changes resulting in artery stiffening are similar to those of other common diseases as hypertension, diabetes mellitus, and aging. Also, the association between aging and arterial stiffening is strong. An increase of arterial stiffening is one of the main manifestations of arterial aging and, at the same time, aging is the main factor leading to arterial stiffening.(42)

Hypertension

Patients with hypertension have special problems related to the nature of their disease. Hypertension is associated with a significant increase in risk of adverse cardiovascular and renal outcomes. Quantitatively, hypertension is the most important modifiable risk factor for premature cardiovascular disease, being more common than cigarette smoking, dyslipidemia, or diabetes, which are the other major risk factors. Hypertension often coexists with these other risk factors as well as with overweight/obesity, an unhealthy diet, and physical inactivity. The presence of more than one risk factor increases the risk of adverse cardiovascular events. The likelihood of having a cardiovascular event increases as blood pressure increases. Interventions to prevent hyperten-

sion include nonpharmacologic methods, such as weight reduction; increased consumption of fresh fruits, vegetables, and low-fat dairy products; exercise; salt restriction, and avoidance of smoking and excess alcohol ingestion. Treatment of hypertension should involve nonpharmacologic therapy (also called lifestyle modification) alone or in concert with antihypertensive drug therapy. The decision to initiate drug therapy should be individualized and involve shared decision-making between patient and provider.(37) Pharmacologic agents should be initiated in patients whose blood pressure is ≥140/≥90 mmHg or ≥130/≥80 mmHg, depending upon risk for cardiovascular disease. Early treatment of hypertension is particularly important in diabetic patients both to prevent cardiovascular disease and to minimize progression of renal disease and diabetic retinopathy. Due to high risk for cardiovascular complications, all diabetic patients with persistent blood pressures above 140/90 mmHg should be started on antihypertensive drug therapy.(38)

Effects of the disease or health condition

[A0005] – What is the burden of hypertension and cardiovascular disease and what are their symptoms?

Cardiovascular disease - symptoms

Atherosclerosis does not tend to have any symptoms at first. When it becomes evident, warning signs and symptoms differ according to the type cardiovascular disease and may be different for men and women. Common symptoms are: irregular heartbeat, chest pain, chest pressure/discomfort; shortness of breath during regular activities and rest; nausea; pain and weakness or coldness in legs or arms; pain in the neck, throat, upper abdomen or back. Those symptoms are more diffuse in women and manifest themselves often as: nausea, vomiting, extreme fatigue, feeling of systemic illness without chest pain. (43)

Cardiovascular disease - burden of disease

A significant impact on the quality of life of patients with non-fatal cardiovascular events has been demonstrated due to associated physical and mental well-being impairments, impact on ability to work and presence of other comorbidities. In adults of working age, CVD may be associated with productivity losses from absences from work, premature exits from workforce, long-term absence from work during hospitalisation, temporary or permanent reduction of working time, and impaired performance at work (presenteeism). Long term therapies, acute treatments, hospital in-patient care, need of informal care in case of worsening of clinical conditions are elements of the perceived burden of care by patients. (43)

Hypertension

Most people with hypertension are unaware of the problem because it may have no warning signs or symptoms. For this reason, it is essential that blood pressure is measured regularly.

When symptoms do occur, they can include early morning headaches, nosebleeds, irregular heart rhythms, vision changes, and buzzing in the ears. Severe hypertension can cause fatigue, nausea, vomiting, confusion, anxiety, chest pain, and muscle tremors.(44)

In 2010, 31.1% (95% confidence interval, 30.0%–32.2%) of the world's adults had hypertension; 28.5% (27.3%–29.7%) in high-income countries and 31.5% (30.2%–32.9%) in low- and middle-income countries. An estimated 1.39 (1.34–1.44) billion people had hypertension in 2010: 349 (337–361) million in high-income countries and 1.04 (0.99–1.09) billion in low- and middle-income countries.(43)

[A0006] – What are the societal consequences of hypertension and cardiovascular disease?

Cardiovascular disease

Cardiovascular disease is still the most common cause of death in Europe accounting for nearly half of all deaths (47% and 39% of all deaths in females and males, respectively), and over 4 million deaths each year (2.2 million deaths in females and 1.9 million deaths in males).(29) The World Health Organisation (WHO) estimated that CVD accounts for 812,093 (CI 95% 581,858 to 1,068,991) unstandardized YLD (years lived with disability) in Central Europe and 1,309,704 (CI 95% 936,467 to 1,711,540) in Eastern Europe in 2015.(45) According to available estimates, combined productivity losses of patients and caregivers during the first year after an acute coronary syndrome (ACS) amounted to 70 and after a stroke to 68 working days lost, equal to 25% of annual workdays for the patient and about 5% for the caregivers.(46)

Healthcare budget dedicated to CVD exceeds 10% of Gross Domestic Product (GDP) in Western countries due to both disease prevention and treatment strategies (invasive and not).(29) The total cost of CVD in the European Union has reached €210 billion a year. Direct healthcare costs account for 53%, work productivity losses for 26% and informal care for 21% of the total cost.(47) The high and increasing worldwide burden of hypertension is a major global health challenge because it increases morbidity and mortality from cardiovascular and kidney diseases and financial costs to society.

Hypertension

Suboptimal adherence with prescribed antihypertensive medication and lifestyle changes contributes to the burden of hypertension. Suboptimal adherence is a major barrier to realizing the benefits of evidence-based pharmacologic therapies for many conditions, and nonadherence remains a key barrier to better patient outcomes.(48) Hypertension is recognized as a tremendous threat to medical and financial health. The increasing prevalence of hypertension and BP-related mortality may continue to drive the cost of cardiovascular disease upwards even in the setting of improving BP control and treatment. Kirkland and colleagues calculated that in US individuals with hypertension are estimated to face nearly $2000 higher annual healthcare expenditure compared with their non-hypertensive peers. This trend has been relatively stable over 12 years. National medical costs associated with hypertension account for about $131 billion, or over 3% of the $3 trillion US national healthcare expenditure.(49)

Current clinical management of the disease or health condition

[A0024] – How are hypertension and cardiovascular disease currently diagnosed according to published guidelines and how does that translate in practice?

In 2007, the European Society of Cardiology (ESC) and European Society of Hypertension (ESH) acknowledged the role of arterial stiffness on cardiovascular mortality. At the same time, the combined societies noted the lack of devices and methods that provide easily and widely available measures of arterial stiffness. Some surrogates of arterial stiffness are the augmentation index (AIx) and aortic systolic blood pressure (aSBP).

Cardiovascular disease is “diagnosed” via assessment of the risk of a cardiovascular event, for example, myocardial infarction or stroke, over a given period of time. (50) This risk assessment essentially helps assess individuals with asymptomatic atherosclerosis, and depends on their particular risk profile.(24, 51, 52) In most estimators the variables of age, gender, total cholesterol, HDL cholesterol, systolic blood pressure, diabetes mellitus (DM), and current smoking are used. As additional information in risk models family history and individual history of comorbidities

and medical tests, body mass index – BMI – and other measures related to obesity as well as socio economic characteristics are used.(24) The WHO recommends these diagnostic risk assessment tools be used in asymptomatic patients. Patients who already have symptoms of atherosclerosis, such as angina or intermittent claudication, or who have had a myocardial infarction, transient ischaemic attack, or stroke are at very high risk of coronary, cerebral, and peripheral vascular events which can lead to death. For these patients, treatment decisions are not based on risk stratification charts, but clearly delineated by guidelines as an immediate combination of lifestyle and pharmacological interventions. Due to the high level of risk in most populations, the WHO suggests population-wide public health strategies to prevent CVD in the general asymptomatic population as well as high risk strategies to prevent CVD in those with the highest risk. (50)

One of the risk factors of CVD is hypertension. Hypertension is diagnosed by using repeated office BP measurements or out-of-office BP measurement with ABPM (ambulatory BP measurement) and/or HBPM (home BP measurement) if logistically and economically feasible. According to guidelines this is the recommended gold standard.(25)

[A0025] – How should hypertension and cardiovascular disease be managed according to current published guidelines and how are they managed in practice?

In both hypertension and CVD, management begins with prevention. A key factor in the management of CVD is the prevention of cardiovascular events in those with no history of CVD and prevention of subsequent events in patients with established CVD. Clinical guidelines recommend the use of risk assessment tools, including risk equations to assist in clinical disease management. (18) Hypertension is managed through monitoring of peripheral blood pressure, either in the doctor's office or through ambulatory blood pressure measurement at home.(24) The World Health Organization (WHO) suggests targeting high risk groups, based on age and sex and identifying those who have a high chance of accelerating the natural processes of atherosclerosis through risk factors such as smoking.

Once hypertension or risk of CVD is confirmed, guidelines and recommendations are to start with life style changes including

- Dietary changes
    - Reduction of sodium intake
    - Reduction of alcohol consumption
    - "healthy diet" (e.g. "Mediterranean diet", vegetables, fruits and unsaturated fatty acids)
- Weight reduction
- Increased physical activity
- Smoking cessation

If treatment targets are not achieved, pharmacological treatment based on individual characteristics and with informed consent respecting personal preferences is necessary.(25) Long term pharmacological treatment should be reserved for individuals with high risk. The threshold for pharmacological treatment is difficult to set and varies between countries. The National Service Framework for coronary heart disease in the UK defined a 30% risk of developing coronary heart disease over a 10-year period to be high risk, warrenting pharmacological treatment. The WHO recommends 20% risk in a high-resource health setting (developed country with ample available health resources), 30% in a medium-resource setting, and 40% in a low-resource setting. Pharmacological treatment is then based on management of risk factors, including lipid lowering medications and aspirin.

Target population

[A0007] – What is the target population in this assessment?

The target population of this assessment are those at risk of hypertension or cardiovascular disease, or for whom organ damage related to arterial stiffness should be assessed. Mobil-O-Graph® and ARCSolver® algorithm measure pulse waves from blood pressure values to identify people at risk of cardiovascular events or of hypertension. The target population of this review is: adult population 18 and over, all patients eligible for diagnosis, treatment, or monitoring of hypertension, and for prevention of cardiovascular and ischaemic disease.

The relevant ICD-10 codes are:

- I10-I16 Hypertensive disease
- I24 Other acute ischemic heart diseases
- 125 Chronic ischemic heart disease
- I25.10 Cardiovascular Disease, Unspecified (ASCVD)
- I48.91 Atrial Fibrillation
- I50.9 Congestive Heart Failure
- I63.9 CVA
- I63.9 Stroke
- I65.23 Carotid Artery Occlusion, Bilateral
- I65.23 Carotid Artery Stenosis, Bilateral
- I65.29 Carotid Artery Occlusion
- I65.29 Carotid Artery Stenosis
- I67.2 Cerebral Atherosclerosis
- I67.9 Ischaemic Cerebrovascular Disease
- I73.9 Peripheral Vascular Disease

[A0023] – How many people belong to the target population?

Data from international and national databases were combined with epidemiological studies to accertain the relevant population for use of ARCSolver®. To get an impression of hypertension epidemiology, the use of pharmaceuticals was obtained. No database was found to report pharmacoepidemiology (use of antihypertensive drugs) on a European level.

The global prevalence of hypertension was estimated to be 1.13 billion and of over 150 million in central and eastern Europe in 2015. Hypertension affects 30 - 45% of adults, with a prevalence increasing with age to over 60% in people over 60 years old. The high prevalence of hypertension is consistent across the world, irrespective of income status. It was estimated that the prevalence of hypertension worldwide will increase by 15–20% by 2025, reaching close to 1.5 billion. (25)

Elevated blood pressure was reported to be the leading global contributor to premature death in 2015, accounting for almost 10 million deaths and over 200 million disability-adjusted life years. Despite advances in diagnosis and treatment over the past 30 years, the number of disability-adjusted life years attributable to hypertension has increased by 40% since 1990. A systolic blood pressure (SBP) of ≥140 mmHg accounts for 70% of the mortality and disability. The number of SBP-related deaths per year due to ischaemic heart disease is 4.9 million, due to haemorrhagic stroke 2.0 million, and due to ischaemic stroke 1.5 million. (25)

Atherosclerotic cardiovascular disease (ASCVD) outcomes remain the leading cause of morbidity and mortality globally. In the United States, it is also the leading cause of death, with an estimated cost of >200 billion dollars annually in healthcare services, medications, and lost productivity. (53)

Statistical data mainly show death rates and hospital discharges by collective diagnoses of „cardiovascular diseases“. International data from OECD, show a decreasing trend in death rates caused by cardiovascular events in European countries.(54) Figure 4-2**Error! Reference source not found.** shows the decreasing trend from more than 90 to less than 84 age-standardised deaths per 100.000 caused by cerebrovascular events, and a decrease from 140 to about 120 age-standardised deaths per 100.000 caused by cardiovascular events from 2011 to 2016 in the EU.(55)

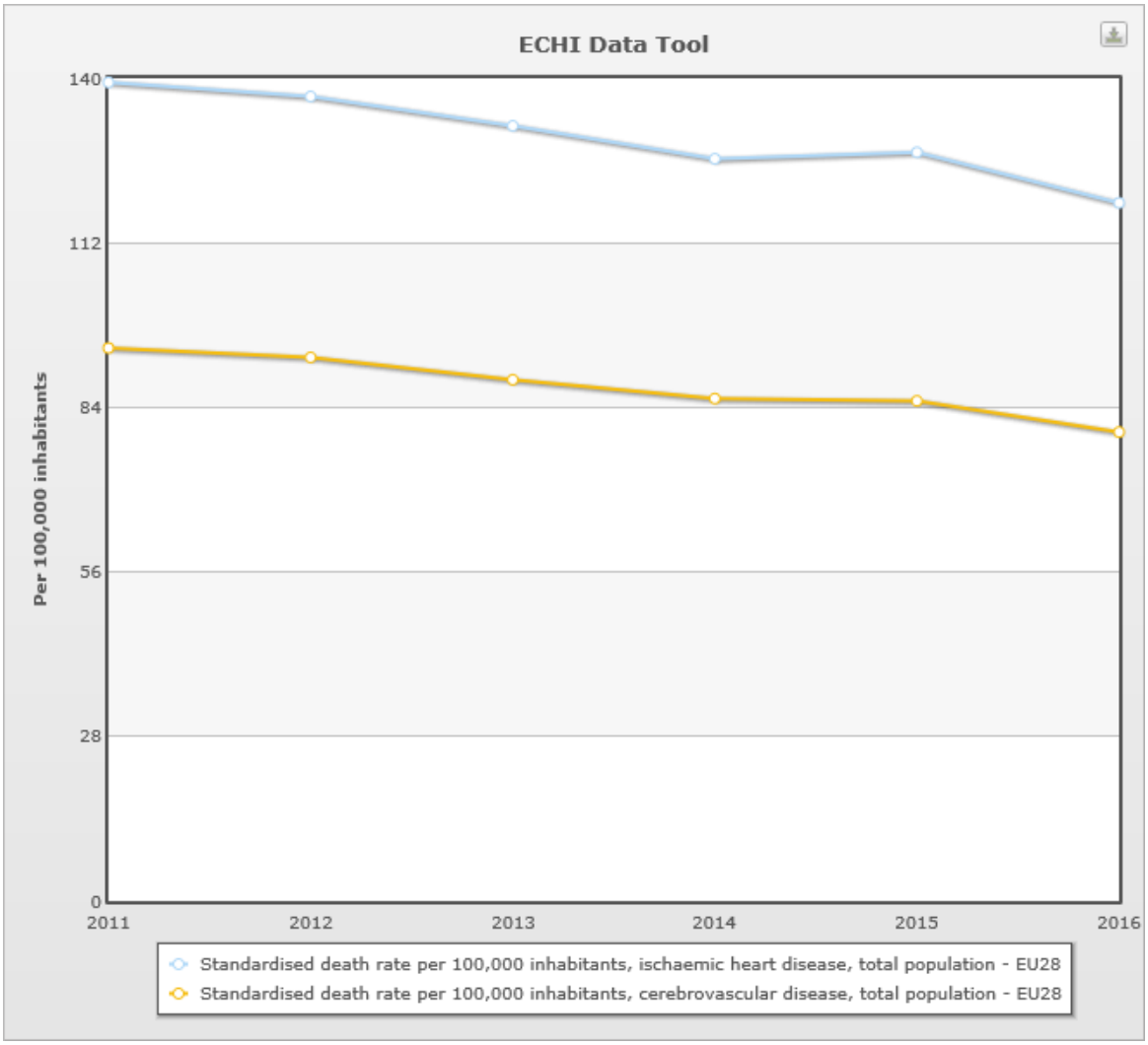

Figure 4-2: EU28 standardised death rate per 100.000 for ischaemic heart disease and cerebrovascular disease

Source: https://ec.europa.eu/health/indicators_data/indicators_en (Last Accessed: 21.1.2020)

According to the European Core Health Indicators[1] (ECHI), the last reported deaths per 100.000 in EU countries vary between 157,3 and 646,9 for diseases of the circulatory system, between 38,3 and 382,5 for ischaemic heart diseases, between 17,1 and 49,3 for acute myocardial infarction and between 32,9 and 203,1 for cerebrovascular diseases.(55) OECD data is shown in detail

[1] The European Core Health Indicators (ECHI) are health indicators that were defined in several projects on European level and finally joined to the European Community Health Indicators Monitoring. The indicators aim to provide comparable health information and knowledge system to monitor health at EU level. Source: https://ec.europa.eu/health/indicators_data/echi_en (27.03.2020)

in Table 4-1 for deaths from diseases of the cardiovascular system, fromf ischaemic heart diseases, fromf acute myocardial infarction and from cerebrovascular diseases.(54)

Table 4-1: Deaths per 100.000 population (standardised rates) in EU from OECD

Deaths per 100 000 population (standardised rates)	Diseases of the circulatory system	Ischaemic heart diseases	Acute myocardial infarction	Cerebrovascular diseases	most recent year
Austria	286.5	121.9	42.2	41.2	2017
Belgium	197.9	50.1	28.4	44.8	2016
Czech Republic	419.4	207.3	39.1	72.6	2017
Denmark	191.7	57.6	22.6	52.1	2015
Estonia	469.3	181.9	28.1	55.5	2016
Finland	268.1	137.6	42.5	59.5	2016
France	157.3	38.3	17.1	34.8	2015
Germany	280.4	101.6	41.3	46.1	2016
Greece	268.3	76.8	40.9	81.5	2016
Hungary	574.9	286.1	49.3	99.2	2017
Iceland	212.4	95.9	35.8	39	2017
Ireland	244.5	116	51	50.6	2015
Italy	243.7	75.6	28.1	62.2	2015
Latvia	646.9	320.9	46.7	203.1	2015
Lithuania	596.9	382.5	30.8	141.1	2017
Luxembourg	209.3	61.4	29.6	36.7	2016
Netherlands	195.2	43.4	25.4	48.1	2016
Norway	186	65.6	39.5	41.4	2016
Poland	410.5	94.8	30	71	2016
Portugal	220.6	51	30.6	78.2	2016
Slovak Republic	493.5	290.8	43.4	110.8	2014
Slovenia	317.1	82.3	46.7	77.8	2015
Spain	181.7	50.6	24.1	41	2016
Sweden	239.9	89.1	39.9	46.4	2016
Switzerland	195.2	66.4	21	32.9	2016
United Kingdom	192.6	84.2	32.6	47.2	2016

[A0011] – To what extent is Mobil-O-Graph® device and ARCSolver® utilized?

Mobil-O-Graph® and ARCSolver® are being sold in Europe. The market share is unclear. Country level reimbursement information is planned for analysis in a country adaptation for Austria.

5 CLINICAL EFFECTIVENESS (EFF)

5.1 Research questions

Element ID	Research question
D0001	What is the expected benefit of using the Mobil-O-Graph® device and ARCSolver® algorithm on mortality?
D0005	How does Mobil-O-Graph® and ARCSolver® affect symptoms and findings (severity, frequency) of hypertension and cardiovascular disease?
D0006	How does Mobil-O-Graph® and ARCSolver® affect progression (or recurrence) of hypertension and cardiovascular disease?
D0011	How does Mobil-O-Graph® device and ARCSolver® affect the patients' body functions?
D0016	How does the use of technology affect activities of daily living?
D0012	How does Mobil-O-Graph® and ARCSolver® affect generic health-related quality of life?
D0013	How does Mobil-O-Graph® and ARCSolver® affect disease specific quality of life?

5.2 Results

Included studies

The literature search identified three studies that evaluated the effectiveness of MOGARC or ARCSolver® coupled with another device for primary and secondary prevention of cardiovascular disease (Table 5-1) and twelve studies that evaluated the effectiveness of MOGARC or ARCSolver® for diagnosis and monitoring of hypertension (Table 5-2). All in all 14 studies were considered, one of them was considered for cardiovascular risk and hypertension.(56)

The considered studies for cardiovascular risk included 170-269 patients with a mean age ranging from 29-64 years. The disease areas observed were endstage renal diseases, target organ damage but also healthy individuals. The considered studies for hypertension were very heterogeneous considering the included number of patients (27 to 502), mean age (38.2 to 67.9) and also the disease area varied from patients with several cardiovascular risks to Marfan Syndrome, endstage renal disease.

Diaz et al. (2019) used different methodological and calibration approaches to analyze the association and agreement between peripheral and/or aortic systolic blood pressure, and the association with left ventricle and atrium structural-functional characteristics in 269 healty subjects with a subgroup of younger people (n=147 age<24 years). They used Mobil-O-Graph®, Arteriograph and RCD (ultrasonography) using systo-diastolic (SD) and calculated mean (CM) and oscillometric mean (OscM) as calibration scheme. Aortic systolic blood pressure obtained with Mobil-O-Graph® and calibrated to CM or OscM schowed lower association with other forms of aortcl and peripheral systolic blood pressure determination and higher levels of association with left ventricle and atrium structural-functional characteristics. Nevertheless the differences in aortic systolic blood pressure were more sensitive to the calibration method than to the device used.(22)

Sarafidis et al. (2017) examined the prognostic significance of ambulatory brachial blood pressure (BP), central BP, pulse wave velocity (PWV) and heart rate-adjusted augmentation index (AIx75) in the population of hemodialysis patients. A total of 170 hemodialysis patients underwent 48-hour

ambulatory monitoring with MOGARC during a standard interdialytic interval and were followed-up for 28.1 (SD 11.2) months. Ambulatory pulse wave velocity, AIx (75) and central pulse pressure were significantly associated with cardiovascular events and mortality in the population studied, in contrast to office and ambulatory blood pressure.(57)

The literature search identified twelve studies that evaluated the effectiveness of Mobil-O-Graph® with ARCSolver® for diagnosis and monitoring of hypertension (Table 5-2). The considered studies were very heterogenous considering the included number of patients (27 to 502), mean age (38.2 to 67.9) and also the disease area varied from patients with several cardiovascular risk to Marfan Syndrome, to end stage renal disease.

The studies that compared MOGARC or ARCSolver® coupled with a different device with SphygmoCor® found the following:

Endes et al. (2015) tested the ARCSolver® algorithm to provide estimates of aortic pressure and aortic pulse wave velocity using the VaSera® VS-1500 oscillometric device compared to the tonometric SphygmoCor® device. The study measured variation estimates, correlation coefficients, and the reproducibility and agreement between the two methods. cSBP reproducibility expressed as variability was 14.9% for ARCSolver® and 11.6% for SyphygmoCor. PWV reproducibility was better for ARCSolver® with a variation estimate of 6.5% compared with 20.9% using SphygmoCor®. The mean cSBP difference was 0.5 mmHg (SD 6.9 mmHg) and 0.32 m/s (SD 1.20 m/s) for PWV. Bland-Altman plots showed considerable agreement between the two methods without signs of systemic bias. (58)

Luzardo et al (2012) assessed the feasibility of ambulatory pulse wave analysis gained with Mobil-O-Graph® PWA compared to SphygmoCor®. Central blood pressure, Augmentation index and pulse wave velocity were compared. This study looked at the office setting as well as the ambulatory monitoring, and reported the mean absolute difference between the tonometric SphygmoCor® and oscillometric MOGARC. It found that brachial oscillometry compared with an established tonometric method provided similar estimates for cSP and systolic augmentation but slightly underestimated PWV. (59)

Sarafidis et al. (2014) evaluated the use of MOGARC compared to SphygmoCor® in 73 hemodialysis patients with endstage renal disease. The Aortic SBP, heart rate adjusted AIx and PWV were compared. The results show that there is evident agreement between Mobil-O-Graph® and Sphygmocor® for aSBP and AIx. PWV was slightly underestimated by Mobil-O-Graph® in hemodialysis patients. (57)

Vaios et al. (2018) compared the measurement of aSBP, AIx and PWV using Mobil-O-Graph® and SphygmoCor® in 27 patients receiving peritoneal dialysis. The parameters derived with Mobil-O-Graph® did not differ from the one derived with SphygmoCor®. The results show acceptable agreement between MOGARC and SphygmoCor® in the estimation of arterial stiffness indices in peritoneal dialysis patients.(60)

The study of Wassertheurer et al (2010) validated ARCSolver® oscillometric method for AIx and aSBP against the accepted tonometric method SphygmoCor® in different age gorups. For aSBP the mean difference was 0.1mmHg with an SD of 3.1mmHg. The mean difference for AIx was 1.2% with an SD of 7.9%. There was no significant difference in reproducibility of AIx for both methods. The variation estimate of inter- and intraobserver measurements was 6.3% for ARCSolver® and 7.5% for SphygmoCor®. In all parameters and different age groups, ARCSolver® was comparable to SphygmoCor® except for the youngest age group (16-24 years). For this age a moderate overestimation of AIx for negative values by ARCSolver® was observed. This effect

seems to result from a different AIx calculation method used by SphygmoCor® for negative values but may be of minor clinical relevance. (9)

Studies that compared MOGARC with SphygmoCor® and other devices had the following results:

Gotzmann et al. (2019) compared cBP measured noninvasively by two devices with invasively measured aortic BP in patients undergoing coronary angiography. The noninvasive assessment of cBP was performed by the SphygmoCor® XCEL device as well as MOGARC, simultaneously to invasive measurement. Correlations were highly significant for both sBP and DBP with both devices. The correlation coefficients in systolic and diastolic cBP were significantly higher for the SphygmoCor® device compared with the MOGARC. The study included 502 patients with an indication for an elective coronary angiography. The present study shows that the cBP values obtained by automated oscillometric cuff-based pulse contour analysis highly correlate to invasive measurements. The noninvasive devices thereby slightly underestimate systolic and slightly overestimate diastolic cBP. This inaccuracy (systematic underestimation of SBP but overestimation of DBP) has been described before and may be the consequence of the calibration method: In the present study, both devices made use of a traditional calibration based on SBP and DBP. This method, however may underestimate true systolic brachial and thereby true systolic cBP. Mean biases in systolic and diastolic cBP were sligthly but significantly lower for SphygmoCor® XCEL compared with MOGARC. In the meantime an alternative calibration using mean instead of SBP has become available for the MOGARC. Nevertheless, the results show that the two devices assess cBP with acceptable accuracy. (61)

To determine which devices are reliable approaches for the estimation of aortic stiffness, Salvi et al. (2019a) compared seven noninvasive devices with invasive aortic pulse wave velocity. All patients undergoing angiography at a cardiology unit of an Italian hospital were recruited over a 2 month period. PWV was estimated first noninvasively and then invasively. Devices evaluating carotid-femoral pulse wave velocity (Complior Analyse, PulsePen®-ET, PulsePen®-ETT, and SphygmoCor®) showed strong agreement between each other and with invasive aortic pulse wave velocity. The finger-toe pulse wave velocity, evaluated by pOpmetre showed only a weak relationship with invasive aortic recording and with noninvasive carotid-femoral pulse wave velocity measurements. Pulse wave velocity through BPLab® (v.5.03 and v.6.02) and Mobil-O-Graph® showed a weaker agreement with invasive pulse wave velocity compared with carotid femoral pulse wave velocity. Thus only the carotid-femoral pulse wave velocity (Complior Analyse, PulsePen®-ETT, PulsePen®-ET, and SphygmoCor®) appears to be a reliable approach for estimation of aortic stiffness. (21)

Weber et al. (2011) compared MOGARC to invasive and non-invasive methods (SphygmoCor®) of cSBP in patients undergoing elective coronary angiography for suspected coronary artery disease. They found that it is a valid measure compared to both invasive and non-invasive methods used. (62)

Studies that compared MOGARC to Arteriograph, Complior and PulsPen® are:

Benas et al. (2019) compared the readings for PWV and cSBP between the validated devices for the measurement of pulse wave velocity (Arteriograph and Complior) and MOGARC in 316 consecutive patients. The study shows acceptable agreement among the three devices regarding pulse wave analysis markers, though MOGARC appears to underestimate the values of these markers. (63)

Salvi et al. (2019b) compared the estimated algorithm-based PWV values, provided by the Mobil-O-Graph® system, with the standard noninvasive assessment of aortic PWV using PulsPen® in 103 patients with Marfan syndrom. Aortic PWV, estimated by the MOGARC was significantly lower than carotid-femoral PWV provided by arterial tonometry. The PWV resulting from the MOGARC can fit well with the real aortic PWV in the general population and can provide a relevant estimate of cardiovascular risk, relying on classic risk factors (age and blood pressure). On the other hand, this approach may not be able to provide additional prognostic information beyond that already supplied by these risk factors. According to the authors the PWV values provided by the MOGARC are related to an ideal subject for a given age and systolic BP, but may not be able to evaluate subclinical vascular damage expressed by high aortic stiffness in the individual patient, as shown in this population of patients with Marfan syndrome.(64)

De La Sierra et al. (2017) conducted a validation study for MOGARC compared to Mobil-O-Graph®. They compared 24-hr central blood pressure to 24-h peripheral blood pressure in terms of its association with hypertensive target organ damage. The findings showed that both peripheral and central BP are associated with target organ damage (TOD) in hypertension. ABPM-derived estimates exhibit stronger associations than office BP, especially for 24-h and night-time SBP and PP. However, central BP was superior to peripheral BP regardless of whether or not it was obtained at home or in office. Moreover, after simultaneous adjustment, only peripheral BP (24-h and night-time SBP and PP) maintained their significance. These results do not support the routine use of central BP monitoring for a better assessment of hypertensive patients with suspected target organ damage. Moreover, central BP is not more associated with hypertensive organ damage than 24-h peripheral BP. (56)

Cardiovascular risk

Table 5-1: Overview of main study characteristics of the studies found for cardiovascular risk assessment

Author	Year	Title	Patients *n* (mean age) disease area	Study type	Intervention	Comparator(s)	Main endpoints
De La Sierra et. al	2017	Twenty-four-hour central blood pressure is not better associated with hypertensive target organ damage than 24-h peripheral blood pressure	*208* (57 years) target organ damage in heart, brain and kidneys	Consecutive cross-sectional	- MOGARC	Mobil-O-Graph® NG without ARCSolver®	odds ratio for each mmHg increase of the association of each blood pressure value with the presence of target organ damage
Díaz et al.	2019	Impact of Methodological and Calibration Approach on the Association of Central and Peripheral Systolic Blood Pressure with Cardiac Structure and Function in Children, Adolescents and Adults	*269* (29 years) None – healthy individuals	Part of a population study	- MOGARC	- Arteriograph - ultrasound	- association between blood pressure levels (peripheral-, brachial- or central-, aortic-) - agreement (Bland-Altman mean error) among aoSBP and/or pSBP obtained with different devices and calibration schemes - association between blood pressure (peripheral-, brachial or central- aortic-) level and cardiac and structural on functional parameters
Sarafidis et al.	2017	Ambulatory pulse wave velocity and augmentation index predict cardiovascular events and all-cause mortality better than office and ambulatory blood pressure in hemodialysis patient	*170* (63.76 years) Hemodialysis patients with endstage renal disease	Cohort study	- MOGARC	Mobil-O-Graph® NG without ARCSolver®	- combination of all-cause death, nonfatal MI and nonfatal stroke - all-cause mortality - cardiovascular mechanism within 30 days after an MI or fatal stroke - a combined outcome of cardiovascular death, nonfatal MI, nonfatal stroke

Abbreviations: aoSBP=aortic systolic blood pressure, mmHg=millimetre of mercury, pSBP=peripheral systolic blood pressure

Hypertension

Table 5-2: Overview of main study characteristics of the studies found for diagnosis and monitoring of hypertension

Author	Year	Title	Patients *n* (mean age) disease area	Study type	Intervention	Comparator(s)	Outputs measured	Main endpoints
Benas et al.	2019	Pulse wave analysis using the Mobil-O-Graph®, Arteriograph and Complior device: a comparative study	*316* (55 years) patients with several cardiovascular risks	Cross-sectional	- MOGARC	- Arteriograph - Complior	- cSBP - PWV	- intraclass correlation coefficient (ICC) PWV - intraclass correlation coefficent (ICC) cSBP - correlation of PWV and cSBP values measured by the 3 devices
De La Sierra et. al	2017	Twenty-four-hour central blood pressure is not better associated with hypertensive target organ damage than 24-h peripheral blood pressure	*208* (57 years) target organ damage in heart, brain and kidneys	Consecutive cross-sectional	- MOGARC	- Mobil-O-Graph®NG without ARCsolver®	- Target organ damage	- odds ratio for each mmHg increase of the association of each blood pressure value with the presence of target organ damage
Endes et al.	2015	Feasibility of oscillometric aortic pressure and stiffness assessment using the VaSera® VS-1500: Comparison with a common tonometric method	*68* (51 years) NA	Convenience sample	- ARCSolver® with VaSera®	- SphygmoCor ®	- cSBP - PWV	- reproducibility/variation - mean cSBP difference - mean PWV difference
Gotzmann et al.	2019	Accuracy of fully automated oscillometric central aortic blood pressure measurement techniques	*502* (67.9 years) Coronary artery disease (n=287) periperal occlusive disease (n=45) hypertension (n=454)	Cross-sectional	- MOGARC	- SphygmoCor ®XCEL - Invasively measured aortic BP	- cSBP - cDBP mmHg	- correlations between invasively and noninvasively measured values (cSBP & cDBP)
Grillo et al.	2018	Short-Term Repeatability of Noninvasive Aortic Pulse Wave Velocity Assessment: Comparison between Methods and Devices	*102* (65 years) High cardiovascular risk patients	Cross-sectional	- MOGARC	- Complior Analyse - PulsePen® - ET - SphygmoCor® - BPLab®	- PWV - MAP - HR	- coefficient of repeatability (differences observed between 2 measurements of PWV according to the mean values
Luzardo et al.	2012	24-h ambulatory recording of aortic pulse wave velocity and central systolic augmentation: A feasibility study	*35/83* (45.6 years) NA	Cross-sectional	- MOGARC	- SphygmoCor®	- cSBP - cDBP - PP - AIx - AIx (75) - PWV	- absolute difference between tonometry vs. oscillometry - relative difference between tonometry vs. oscillometry
Salvi et al.	2019	Noninvasive Estimation of Aortic Stiffness Through Different Approaches:	*102* (65 years) patients undergo-	Consecutive cross-	- MOGARC	- Complior Analyse	- PWV	- r (pearson correlation coefficient) and mean differences (SD) be-

Author	Year	Title	Patients *n* (mean age) disease area	Study type	Intervention	Comparator(s)	Outputs measured	Main endpoints
		Comparison with Intra-Aortic Recordings	ing angiography	sectional		- PulsePen® - ET - PulsePen® - ETT - SphygmoCor® - pOpmetre® - BPLab® v.5.03 - BPLab® v.6.02		tween devices - r (pearson correlation coefficient) and mean differences (SD) with invasive for each device - trend association with coronary damage of each device
Salvi et al.	2019	Unreliable Estimation of Aortic Pulse Wave Velocity Provided by the Mobil-O-Graph® Algorithm-Based System in Marfan Syndrome	*90* (38.2 years) Marfan Syndrome	Cross-sectional	- MOGARC	- PulsePen	- cSBP - cDBP - Heart rate	- Correlation analysis PWV - Distribution of PWV related to age - Distribution of PWV related to systolic blood pressure
Sarafidis et al.	2014	Evaluation of a novel brachial cuff-based oscillometric method for estimating central systolic pressure in hemodialysis patients	*73* (61.7 years) Endstage renal disease	Cross-sectional	- MOGARC	- SphygmoCor®	- bSBP - bDBP - bPP - aSBP - aDBP - aPP - AIx - AIx (75) - AP - PWV	- Correlation analysis aSBP - Correlation analysis AIx75 - Correlation analysis PWV
Vaios et al.	2018	Accuracy of a Newly-Introduced Oscillometric Device for the Estimation of Arterial Stiffness Indices in Patients on Peritoneal Dialysis: A Preliminary Validation Study	*27* (62.5 years) Endstage renal disease	Cross-sectional	- MOGARC	- SphygmoCor®	- bSBP - bDBP - bPP - aSBP - aDBP - aPP - AIx (75) - AP - PWV	- Correlation analysis of the agreement between the Mobil-O-Graph® and SphygmoCor devices in the estimation of heart-rate-adjusted AIx75, aSBP and PWV
Wassertheurer et al.	2010	A new oscillometric method for pulse wave analysis: comparison with a common tonometric method	*302* (56 years) NA	Cross-sectional	- oscillometric method using ARCSolver® algorithm	- SphygmoCor®	- AIx - aSBP	- mean difference AIx - mean difference aSBP
Weber et al.	2011	Validation of a brachial cuff-based method for estimating central systolic blood pressure	*131* (59 years) suspected coronary artery disease	Prospective cross-sectional	- MOGARC	- SphygmoCor ® - Invasively measured aortic BP	- aSBP	- aSBP r2 compared to invasive

Abbreviations: AIx=augmentation index, AIx(75)=Augmentation index at 75 bpm; aSBP=aortic systolic blood pressure, aDBP=aortic diastolic blood pressure, aPP=aortic pulse pressure, bSBP=brachial systolic blood pressure, bDBP=brachial diastolic blood pressure, bPP=brachial pulse pressure, cSBP=central systolic blood pressure, h=hours, ICC=intraclass correlation coefficient, HR=heart rate mmHg=millimetre of mercury, NA=not available, NG=new generation, SD=mean difference, PP= pulse pressure, PWV=pulse wave velocity

Upcoming Evidence

The systematic literature also identified studies which were not yet published in full text, but with preliminary results presented at conferences and available in abstract form. In total, there were ten relevant abstracts identified. Like in the published full text studies, the abstracts which were not yet published in full text were also about the technical accuracy of various parameters of arterial stiffness. All abstracts assessed MOGARC compared to other devices measuring arterial stiffness. The study results varied depending on parameter, with MOGARC sometimes being superior and sometimes inferior in terms of measurement.

Two of of the abstracts analysed the accuracy of MOGARC compared to other non-invasive devices in measuring the blood pressure in children and young adults. (65, 66) The results showed that the estimation of cSBP with the Mobil-O-Graph® is as effective as using the invasive catheter for measurement.(65) In one abstract the accuracy of SpyhgmoCor XCEL and Mobil-O-Graph® in 57 children were compared. Both devices overestimated the brachial and central systolic BP. Diastolic BP was acceptable.(66) In patients with long-term peritoneal dialysis, the aSBP, Aix75 and PWV measurements of the Mobil-O-Graph® are comparable with that one from Sphygmocor® in this cohort.(67) One abstract compared the influence of calibration of the device with different parameters on peripheral blood pressure, calibration method and device on the outcomes of the non-invasive central blood pressure. The results show that the use of radial BP rather than brachial BP might be better in non-invasive cSBP measurement and the use of Mobil-O-Graph® is not recommended when compared to two other non-invasive devices (SphygmoCor® and Pulse Pen).(68) Three abstracts analysed the effectiveness of Mobil-O-Graph® in detecting cardiovascular risk and arterial stiffness by measuring PWV and AIX75. In general, the Mobil-O-Graph® showed valid results when compared to other non-invasive devices, even in patients with peritoneal dialysis.(69-71) Nevertheless, the underestimations of high PWV values by non-invasive devices may lead to errors in the estimation of cardiovascular risk.(69) In comparison to other non-invasive devices, the Mobil-O-Graph® showed the highest evidence for wave reflection assessment, although the authors classified all of the observed devices as non-interchangeable.(72) Another study in patients with Marfan syndrome came to the result that the algorithm of Mobil-O-Graph® should not be used for the evaluation of PWV in this group of patients.(73) The advantage of the non-reactive PTT method, when using the Mobil-O-Graph® for measuring BP compared to cuff-based ABPM during night-time was the content of one abstract. It seems that the cuff inflation itself causes SBP increases.(74)

Mortality

[D0001] – What is the expected benefit of using the Mobil-O-Graph® device and ARCSolver® algorithm on mortality?

No study explicitly studied MOGARC to see if its use would lead to a reduction in mortality through timely and appropriate intervention as a result of risk stratification. However, one prospective cohort study examined hazard ratios for all-cause mortality and cardiovascular mortality compared between measurements that are only available in Mobil-O-Graph® NG and those central parameters additionally available through the ARCSolver® algorithm in Mobil-O-Graph® PWA. This study by Sarafidis et al. (2017) compared central blood pressure values measured over 48 hours with peripheral blood pressure values in 170 hemodialysis patients to evaluate the prognostic significance of ambulatory PWV and AIx(75). In multivariate Cox-regression analysis, 48h ambulatory PWV was the only vascular parameter independently associated with mortality. Hazard ratios for all-cause mortality, cardiovascular mortality, and the combined outcome of cardiovascular events were progressively increasing with higher quartiles of ambulatory PWV and ambulatory

AIx (75) compared to office BP and ambulatory central BP which were not prognostic for cardiovascular events or mortality. This study illustrates the value of the additional measurements provided by the ARCSolver® algorithm in Mobil-O-Graph® PWA compared to just Mobil-O-Graph® without the ARCSolver® algorithm. As a next step, the authors suggest that studies should be conducted to understand whether therapeutic measures to modify arterial stiffness and wave reflection parameters would result in beneficial long-term effects in haemodialysis populations.(75)

Morbidity

[D0005] – How does Mobil-O-Graph® and ARCSolver® affect symptoms and findings (severity, frequency) of hypertension and cardiovascular disease?

No evidence was found to answer this question. The severity and frequency of arterial stiffness or cardiovascular events was not an outcome in any of the studies found on MOGARC. To determine the frequency of cardiovascular events, or to determine if cardiovascular events could be avoided, the ability of MOGARC to triage patients to more appropriate and timely treatment options would be necessary.

[D0006] – How does Mobil-O-Graph® and ARCSolver® affect progression (or recurrence) of hypertension and cardiovascular disease?

No evidence was found to answer this question. The progression of hypertension or recurrence of cardiovascular disease would have to be studied in a context where an intervention follows the use of Mobil-O-Graph® and ARCSolver®, compared to existing comparators. Then, the effect of using such a device on instigating treatment to impede progression or prevent cardiovascular events would become clear.

[D0011] – How does Mobil-O-Graph® device and ARCSolver® affect the patients' body functions?

No evidence was found to answer this question. The measurement devices themselves do not have a direct effect on body functions. Indirectly, it would be possible that there is an impact on hypertension control or the occurance of cardiovascular risk, which then has an impact on patients' body functions, but this would have to be studied in a context in which an intervention follows the use of Mobil-O-Graph® and ARCSolver®, compared to existing comparators. Then, the effect of using such a device on instigating treatment to impede progression or prevent cardiovascular events would become clear.

[D0016] – How does the use of technology affect activities of daily living?

No evidence was found to answer this question. The measurement devices themselves do not have a direct effect on activities of daily living. Indirectly, it would be possible that there is an impact on hypertension control or the occurrence of cardiovascular risk, which in turn, impacts activities of daily living, but this would have to be studied in a context in which an intervention follows the use of Mobil-O-Graph® and ARCSolver®, compared to existing comparators.

Health-related quality of life

[D0012] – How does Mobil-O-Graph® and ARCSolver® affect generic health-related quality of life?

There was no specific evidence found to answer this question. One study analysed the health related quality of life by using the Mobil-O-Graph®. [71] The results are mentioned in the claimed benefits section.

[D0013] – How does Mobil-O-Graph® and ARCSolver® affect disease specific quality of life?

No evidence was found to answer this question. As mentioned in the answer before, the measurement devices also do not directly influence the disease specific quality of life.

6 SAFETY (SAF)

6.1 Research questions

Element ID	Research question
C0008	How safe is Mobil-O-Graph® and ARCSolver® in relation to the comparators?
C0004	How does the frequency or severity of harms change over time or in different settings?
C0005	What are the patient groups that are more likely to be harmed through the use of the technology?
B0010	What kind of data/records and/or registry is needed to monitor the use of Mobil-O-Graph® device and ARCSolver®, conventional 24-h blood pressure measurement approved for use under “specialist” or “ambulatory blood pressure measurement (ABPM)”, cardiovascular risk equations, and other non-invasive pulse wave analysis methods?

6.2 Results

No evidence was identified that contained safety outcomes.

Included studies

No studies were included for safety.

Patient safety

[C0008] – How safe is Mobil-O-Graph® and ARCSolver® in relation to the comparators?

The device is non-invasive and there are no reported harms to non-invasive blood pressure measurement. No evidence was found on the safety of the device.

[C0004] – How does the frequency or severity of harms change over time or in different settings?

There are no reported harms to non-invasive blood pressure measurement.

[C0005] – What are the patient groups that are more likely to be harmed through the use of the technology?

There was no evidence of susceptible patient groups that are more likely to be harmed through the use of the technology.

[B0010] – What kind of data/records and/or registry is needed to monitor the use of Mobil-O-Graph® device and ARCSolver®, conventional 24-h blood pressure measurement approved for use under “specialist” or “ambulatory blood pressure measurement (ABPM)”, cardiovascular risk equations, and other non-invasive pulse wave analysis methods?

No need to monitor the use of the technology or its comparators was identified in this assessment.

7 DISCUSSION

Mobil-O-Graph® PWA is a precision medicine tool under two categories: tests for prognostic biomarkers, and a risk prediction tool.(76) In terms of test for prognostic biomarkers, MOGARC is used to identify hypertension and inform the patient treatment pathway. In terms of a risk prediction tool, it is a static algorithm that determines risk for cardiovascular disease. Both of these are via the quantification of arterial stiffness called pulse wave analysis via several central blood pressure parameters including pulse wave velocity. Whether Mobil-O-Graph® PWA informs treatment is unclear after this analysis. Although a diagnostic device, Mobil-O-Graph® PWA was not assessed in terms of diagnostic accuracy yielding information on sensivity and specificity. The evidence remained on the level of technical accuracy- trying to mimic results from invasive tests or a selected gold standard test (usually Sphymocore) without specification of cut-off points for diagnosis or patient stratification.

In this case, where the device exists also on its own, without the algorithm, the first obvious comparison to be made would be that of Mobil-O-Graph® NG vs. Mobil-O-Graph® PWA. This comparison, however, is more complex as it is essentially assessing 2 things: the accuracy and value of the algorithm in measuring the parameters it claims to measure; and the value of measuring these parameters in the first place beyond existing measures. Therefore, studies using Mobil-O-Graph® and ARCSolver® comparing central parameters to simple peripheral blood pressure measures are also included as a relevant comparator, in a way, making the output of the device and algorithm also subject to evaluation. What has not been included in this review, but is also relevant, is comparison of the ABPM with office blood pressure measurements. Another relevant point of comparison in this instance, is the comparison between central and peripheral hemodynamic parameters. In this sense, the efficacy of ARCSolver® in calculating the parameters compared to other devices which measure the same parameters in a different way or with a different algorithm, subject to an indirect comparison. An indirect comparison is beyond the scope of this review, but establishing equivalence or superiority with other PWA devices would render it possible to conduct such analysis. Furthermore, it would allow authorities to expand the comparison of the device to real world comparators.

The effectiveness of Mobil-O-Graph® with pulse wave analysis remains unclear after this assessment. In terms of technical efficacy, Mobil-O-Graph®, using reliability and consistency measures, as well as comparing accuracy to invasive, and mean values with other devices, seems equivalent to other devices, based on a moderate quality and relatively small body of evidence. However, the effectiveness in triaging patients to better or more timely care for hypertension and cardiovascular disease prevention remains to be studied. Studies may exist which assess the measures such as pulse wave velocity and AIx index and their ability to predict cardiovascular risk. Future studies are needed where the devices such as Mobil-O-Graph® with ARCSolver® are implemented compared to other devices that have pulse wave analysis paramters or currently used cardiovascular risk equations and blood pressure measurement to determine diagnostic accuracy as well as effectiveness in reducing cardiovascular events or reducing hypertension.

One patient population was identified in which the ARCSolver® algorithm appears to underestimate PWV. This is in patients with Marfan syndrome. As this is not the intended population, care should be used when extending the use of ARCSolver® to measure hypertension or cardiovascular risk in Marfan syndrome patients.

There were no studies that addressed safety of Mobil-O-Graph® with ARCSolver® algorithm. This was to be expected as Mobil-O-Graph® already exists without the additional ARCSolver® algorithm. Furthermore, it is a well-known and accepted oscillometric blood pressure measurement

system. Blood pressure devices have a long history and in their past, the safety has mostly related to irritation or burning through the contact points of measurement. A useful measure of safety would be diagnostic accuracy, to include the rate of false positives and false negatives when used in a population compared to other methods of measuring arterial stiffness. Future studies should consider diagnostic accuracy in a population at risk of cardiovascular events or hypertension.

This assessment is not without limitations. The biggest limitation is that the analysis was limited to assessing MOGARC or ARCSolver® coupled with another device compared with other central blood pressure and arterial stiffness measurement devices. The search was conducted in a simple but broad manner to include any studies that mentioned the device or algorithm. However, it is possible that some studies that used Mobil-O-Graph® with the ARCSolver® algorithm were not found if they did not mention it in the title or abstract or it was not tagged as a device used by the databases searched. However, the authors of this assessment are confident that the dearth of evidence found by the broad Mobil-O-Graph® ARCSolver® search is representative of the actual stance of evidence. Importantly, the level of evidence according to the Hierarchical Model of Efficacy adapted from Fryback and Thornberry 1991 was deemed at Level 1: Technical Efficacy. This level of evidence is not sufficient for making population reimbursement decisions or guidelines. Additional searches could have been done for pulse wave analysis in general, as there is currently controversy on the use of pulse wave analysis and the place of it in clinical practice. However, for this study, the goal was not to settle controversies around the use of pulse wave analysis but to determine whether or not this particular algorithm was more effective and safer in the identification of arterial stiffness for better management of hypertension and cardiovascular risk than other devices measuring hypertension and cardiovascular risk. Future research should assess the sensivity and specificity of different parameters from peripheral and central blood pressure measurement tools.

The value of estimating central arterial blood pressure has not been extensively explored. Additionally, the various methods and algorithms to calculate these parameters have not been extensively explored to determine which measures are most useful in avoiding cardiovascular events and identifying and controlling hypertension by triaging patients to better care. Most of the included studies looked at whether or not the measure was accurate, consistent, or responsive compared to invasive or to other measures. This information does not facilitate the jump from a good measure to a clinically useful measure. As this REA meant to assess the place of Mobil-O-Graph® in clinical practice compared to other comaprators, it is possible that other devices or central parameters in general have been explored in terms of accuracy (sensitivity and specificity) in patients in identifying risk of cardiovascular events or helping classify patients as hypertensive. Therefore, as a first step, future studies should assess the usefulness of central measures compared to peripheral measures in these two indications. Once a relevant target population and accuracy is established, it should be compared to non central measures.

Current literature is very technical, focusing on exact measurement. However, the threshold at which the measurement is clinically useful has not been studied.

8 CONCLUSION

Cardiovascular events have a profound effect on activities of daily living due to physical and cognitive symptoms that may persist after a cardiovascular event.[69, 70] If the technology were able to triage patients to more effective therapy, it has been shown that improved control of hypertension can lead to lower cardiovascular events and mortality.[67, 68]

The current literature on ARCSolver® coupled with Mobil-O-Graph® still focuses on technical characteristics and technical efficacy compared to other devices that provide measures of arterial stiffness. There is a lack of evidence on whether or not the measurement of arterial stiffness using Mobil-O-Graph® and ARCSolver® pulse wave analysis leads to improvement in patient outcomes through better treatment pathways in the identification and management of hypertension and assessment of cardiovascular risk. In terms of technical efficiency, there is evidence of moderate quality that Mobil-O-Graph® with ARCSolver® is equivalent to other devices that provide measures of arterial stiffness, whether by algorithm or using carotid-femoral pulse wave velocity. GRADE recommendations were not assessed as this was not the outcome of interest. There is reason to speculate that MOGARC underestimated PWV in patients with Marfan syndrome. There is a lack of evidence to determine if ARCSolver® coupled with Mobil-O-Graph® is more effective and safer in triaging patients to better health care services and medicines to eventually improve outcomes in terms of hypertension control or cardiovascular events. Further research should focus on diagnostic accuracy compared to other cardiovascular risk assessment tools and equations, and diagnostic accuracy compared to regular blood pressure measurement in hypertension.

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among patients on peritoneal dialysis: A preliminary validation study. Peritoneal Dialysis International. 2018;38:S5.

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APPENDIX 1: METHODS AND DESCRIPTION OF THE EVIDENCE USED

DOCUMENTATION OF THE SEARCH STRATEGIES

Search Strategy Embase Platform for Embase and Medline databases

('mobil-o-graph':ti,ab OR 'mobil-o-graph'/dn OR 'arcsolver':ti,ab OR 'arc-solver':ti,ab OR mobilo-graph:ti,ab)

Literature from January 1, 2008 until December 12, 2019

Limitations: none

Results: 547

Search Strategy Clinicaltrials.gov

('mobil-o-graph' OR 'arcsolver')

Conducted on January 24, 2020 without date restrictions.

Limitations: none

Results: 44

Search Strategy Center for Reviews and Dissemination

('mobil-o-graph' OR 'arcsolver' OR (pulse and wave))

Conducted on January 24, 2020 without date restrictions.

Limitations: none

Results: 14

Ad Hoc Search Strategy VaSera

('Vasera':ti,ab)

Conducted on January 31, 2020 without date restrictions.

Limitations: none

Results: 1

DESCRIPTION OF THE EVIDENCE USED

Table A1: Study pool of the Rapid REA

Study	Available documents	Study registry entries
Benas, D. K., M.Triantafyllidi, H.Kostelli, G.Pavlidis, G.Varoudi, M.Vlastos, D.Lambadiari, V.Parissis, J.Ikonomidis, I. (2019). "Pulse wave analysis using the Mobil-O-Graph, Arteriograph and Complior device: a comparative study." Blood Pressure 28(2): 107-113.	(63)	NA
de la Sierra, A. P., J.Yun, S.Acosta, E.Aiello, F.Oliveras, A.Vázquez, S.Armario, P.Blanch, P.Sierra, C.Calero, F.Fernández-Llama, P. (2018). "Central blood pressure variability is increased in hypertensive patients with target organ damage." Journal of Clinical Hypertension 20(2): 266-272.	(56)	NA
Díaz, A. B., D.Zócalo, Y. (2019). "Impact of Methodological and Calibration Approach on the Association of Central and Peripheral Systolic Blood Pressure with Cardiac Structure and Function in Children, Adolescents and Adults." High Blood Pressure and Cardiovascular Prevention 26(6): 509-534.	(22)	NA
Endes, S. B., M.Li, Y.Mayer, C.Hanssen, H.Hametner, B.Schmidt-Trucksäss, A.Wassertheurer, S. (2015). "Feasibility of oscillometric aortic pressure and stiffness assessment using the VaSera VS-1500: Comparison with a common tonometric method." Blood Pressure Monitoring 20(5): 273-279.	(58)	NA
Gotzmann, M. H., M.Seibert, F. S.Rohn, B. J.Bergbauer, M.Babel, N.Bauer, F.Mügge, A.Westhoff, T. H. (2019). "Accuracy of fully automated oscillometric central aortic blood pressure measurement techniques." Journal of Hypertension.	(61)	NA
Grillo, A. P., G.Rovina, M.Moretti, F.Salvi, L.Gao, L.Baldi, C.Sorropago, G.Faini, A.Millasseau, S. C.Scalise, F.Carretta, R.Salvi, P. (2018). "Short-Term Repeatability of Noninvasive Aortic Pulse Wave Velocity Assessment: Comparison between Methods and Devices." American Journal of Hypertension 31(1): 80-88.	(77)	NA
Luzardo, L. L., I.Sottolano, M.Da Rosa, A.Thijs, L.Noboa, O.Staessen, J. A.Boggia, J. (2012). "24-h ambulatory recording of aortic pulse wave velocity and central systolic augmentation: A feasibility study." Hypertension Research 35(10): 980-987.	(59)	NA
Salvi, P. S., F.Rovina, M.Moretti, F.Salvi, L.Grillo, A.Gao, L.Baldi, C.Faini, A.Furlanis, G.Sorropago, A.Millasseau, S. C.Sorropago, G.Carretta, R.Avolio, A. P.Parati, G. (2019). "Noninvasive Estimation of Aortic Stiffness Through Different Approaches: Comparison with Intra-Aortic Recordings." Hypertension 74(1): 117-129.	(21)	NA
Salvi, P. F., G.Grillo, A.Pini, A.Salvi, L.Marelli, S.Rovina, M.Moretti, F.Gaetano, R.Pintassilgo, I.Faini, A.Fabris, B.Carretta, R.Parati, G. (2019). "Unreliable Estimation of Aortic Pulse Wave Velocity Provided by the Mobil-O-Graph Algorithm-Based System in Marfan Syndrome." Journal of the American Heart Association 8(9).	(64)	NA
Sarafidis, P. A. L., A. A.Imprialos, K. P.Georgianos, P. I.Avranas, K. A.Protogerou, A. D.Doumas, M. N.Athyros, V. G.Karagiannis, A. I. (2016). "A comparison study of brachial blood pressure recorded with Spacelabs 90217A and Mobil-O-Graph NG devices under static and ambulatory conditions." Journal of Human Hypertension 30(12): 742-749.	(78)	NA
Sarafidis, P. A. L., C.Mayer, C. C.Karpetas, A.Pagkopoulou, E.Bikos, A.Faitatzidou, D.Wassertheurer, S.Schmaderer, C.Liakopoulos, V.Papagianni, A.London, G. (2019). "Weak within-individual association of blood pressure and pulse wave velocity in hemodialysis is related to adverse outcomes." Journal of Hypertension 37(11): 2200-2208.	(79)	NA
Vaios, V. G., P. I.Pikilidou, M. I.Eleftheriadis, T.Zarogiannis,	(60)	NA

S.Papagianni, A.Zebekakis, P. E.Liakopoulos, V. (2018). "Accuracy of a Newly-Introduced Oscillometric Device for the Estimation of Arterial Stiffness Indices in Patients on Peritoneal Dialysis: A Preliminary Validation Study." Advances in peritoneal dialysis. Conference on Peritoneal Dialysis 34(2018): 24-31.		
Wassertheurer, S. K., J.Weber, T.Van Der Giet, M.Baulmann, J.Ammer, M.Hametner, B.Mayer, C. C.Eber, B.Magometschnigg, D. (2010). "A new oscillometric method for pulse wave analysis: Comparison with a common tonometric method." Journal of Human Hypertension 24(8): 498-504.	(20)	NA
Weber, T. W., S.Rammer, M.Maurer, E.Hametner, B.Mayer, C. C.Kropf, J.Eber, B. (2011). "Validation of a brachial cuff-based method for estimating central systolic blood pressure." Hypertension 58(5): 825-832.	(62)	NA

Table A2: List of excluded studies (full text level) with reasons for exclusion

Reference	Main reason for exclusion
Exclusion key: *2 no comparator,* *4 invasive comparison,* *5 not central blood pressure measures,* *6 background,* *9 calibration comparison,* *11 comparison with imaging*	
Aissopou, E. K. A., A. A.Nasothimiou, E. G.Konstantonis, G. D.Tampakis, K.Tentolouris, N.Papathanassiou, M.Theodossiadis, P. G.Papaioannou, T. G.Stehouwer, C. D. A.Sfikakis, P. P.Protogerou, A. D. (2016). "Ambulatory Aortic Stiffness Is Associated With Narrow Retinal Arteriolar Caliber in Hypertensives: The SAFAR Study." American Journal of Hypertension 29(5): 626-633.	2
Almeida De Faria, R. A. B., A.Pozzan, R.Gomes Paiva, A.Campos Magalhaes, M. E.Gonc¸alves Campana, E. M.Lopes Fonseca, F.Mota Gomes, M. A. (2015). "24h central blood pressure and pulse wave velocity monitoring in normotensive, hypertensive, white coat hypertension and masked hypertension young adults." Journal of Hypertension 33: e39.	2
Blanch, P. A., P.Oliveras, A.Fernández-Llama, P.Vázquez, S.Pareja, J.Álvarez, E.Calero, F.Sierra, C.De La Sierra, A. (2018). "Association of either left ventricular hypertrophy or diastolic dysfunction with 24-hour central and peripheral blood pressure." American Journal of Hypertension 31(12): 1293-1299.	2
Buelvas-Herazo, J. U.-T., M.Mantilla-Morrón, M.Urina-Jassir, D.Galeano-Muñoz, L.Urina-Triana, M.Quintero-Baiz, A. (2018). "Pulse wave velocity and arterial aging in subjects with and without type 2 diabetes mellitus." Revista Latinoamericana de Hipertension 13(4): 380-383.	2
Chi, C. Y., S. K.Auckle, R.Argyris, A. A.Nasothimiou, E.Tountas, C.Aissopou, E.Blacher, J.Safar, M. E.Sfikakis, P. P.Zhang, Y.Protogerou, A. D. (2017). "Association of left ventricular structural and functional abnormalities with aortic and brachial blood pressure variability in hypertensive patients: The SAFAR study." Journal of Human Hypertension 31(10): 633-639.	2
Çörtük, M. A., S.Baykan, A. O.Kiraz, K.Uçar, H.Çaylı, M.Kandiş, H. (2016). "Aortic stiffness increases in proportion to the severity of apnoea–hypopnea index in patients with obstructive sleep apnoea syndrome." Clinical Respiratory Journal 10(4): 455-461.	2
Danninger, K. H., A.Binder, R. K.Aichberger, M.Hametner, B.Wassertheurer, S.Weber, T. (2019). "High prevalence of hypertension and early vascular aging: a screening program in pharmacies in Upper Austria." Journal of Human Hypertension.	2
Elmenhorst, J. H.-W., M.Barta, C.Dalla Pozza, R.Springer, S.Oberhoffer, R. (2015). "Percentiles for central blood pressure and pulse wave velocity in children and adolescents recorded with an oscillometric device." Atherosclerosis 238(1): 9-16.	2

Frick, M. S. B., F.Sick, B.Wilkinson, I. B.Amann-Vesti, B.Husmann, M. (2018). "Sensitivities of in vivo markers of arterial organ damage in patients with peripheral atherosclerosis." Vasa - European Journal of Vascular Medicine 47(1): 30-35.	2
García-Ortiz, L. R.-R., J. I.Mora-Simón, S.Guillaumet, J.Martí, R.Agudo-Conde, C.Rodriguez-Sanchez, E.Maderuelo-Fernandez, J. A.Ramos-Blanes, R.Gómez-Marcos, M. A.Ramos, R.Parramon, D.Ponjoan, A.Quesada, M.Garcia-Gil, M.Sidera, M.Camós, L.Montesinos, F.Montoya, I.López, C.Agell, A.Gil, I.Rigo, F.Frontera, G.Rotger, A.Feuerbach, N.Pons, S.Garcia, N.Gómez-Sanchez, L.Castaño-Sanchez, C.Rodriguez-Martín, C.Sanchez-Salgado, B.de Cabo-Laso, A.Gómez-Sánchez, M.Ramos-Delgado, E.Patino-Alonso, C.Recio-Rodriguez, J. I.Gomez-Marcos, M. A.Garcia-Ortiz, L. (2016). "Vascular structure and function and their relationship with health-related quality of life in the MARK study." BMC Cardiovascular Disorders 16(1).	2
Greve, S. V. L., S.Olsen, M. H. (2017). "Estimated Pulse Wave Velocity Calculated from Age and Mean Arterial Blood Pressure." Pulse 4(4): 175-179.	2
Hametner, B. S., M.Parragh, S.Wassertheurer, S. (2017). "Computational assessment of model-based wave separation using a database of virtual subjects." Journal of Biomechanics 64: 26-31.	2
László, A. R., G.Nemcsik, J. (2016). "Ambulatory arterial stiffness in chronic kidney disease: A methodological review." Hypertension Research 39(4): 192-198.	2
Laurent, S. M., L.Boutouyrie, P. (2016). "The Noninvasive Assessment of Vascular Aging." Canadian Journal of Cardiology 32(5): 669-679.	2
Mayer, C. C. M., J.Sarafidis, P. A.Hagmair, S.Lorenz, G.Angermann, S.Braunisch, M. C.Baumann, M.Heemann, U.Wassertheurer, S.Schmaderer, C. (2018). "Association of ambulatory blood pressure with all-cause and cardiovascular mortality in hemodialysis patients: Effects of heart failure and atrial fibrillation." Journal of the American Society of Nephrology 29(9): 2409-2417.	2
Mendes-Pinto, D. R.-M., M. D. G. (2019). "Applications of arterial stiffness markers in peripherarterial disease." Jornal Vascular Brasileiro 18.	2
Miyashita, H. (2012). "Clinical assessment of central blood pressure." Current Hypertension Reviews 8(2): 80-90.	2
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Exclusion key:
2 no comparator,
4 invasive comparison,
5 not central blood pressure measures,
6 background,
9 calibration comparison,
11 comparison with imaging

Guidelines for diagnosis and management

Table A3: Guidelines for diagnosis and management

Name of society/organisation issuing guidance	Date of issue	Country/ies to which applicable	Summary of recommendation
American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines	2019	United States of America	The most important way to prevent atherosclerotic vascular disease, heart failure and artrial fibrillation is to promote a healthy lifestyle throughout life. Adults who are 40 to 75 years of age and are being evaluated for cardiovascular disease prevention should undergo 10-year atherosclerotic cardiovascular disease (ASCVD) risk estimation. In addition to clinician-patient risk discussion before starting pharmacological therapy, assessing for other risk-enhancing factors can help guide decisions about preventive interventions in select individuals.
European Society of Cardiology (ESC) and European Society of Hypertension (ESH)	2018	European Union	Hypertension is usually asymptomatic (hence the term ‘silent killer’). Because of its high prevalence, screening programmes should be established to ensure that BP is measured in all adults at least every 5 years, and more frequently in people with a high–normal BP. When hypertension is suspected because of an elevated screening BP, the diagnosis of hypertension should be confirmed either by repeated office BP measurements over a number of visits or by out-of-office BP measurement using 24 h ABPM or HBPM. Other CV risk factors such as dyslipidaemia and metabolic syndrome frequently cluster with hypertension. Thus, unless the patient is already at high or very high risk due to established CVD, formal CV risk assessment is recommended using the SCORE system. The optimal DBP target has been less well defined, but a DBP target of <80 mmHg is recommended. A key message in these guidelines is the need to do better at improving BP control rates.

European Society of Cardiology and other societies on cardiovascular disease prevention in clinical practice	2016	European Union	Systematic CV risk assessment is recommended in individuals at increased CV risk, i.e. with family history of premature CVD, familial hyperlipidaemia, major CV risk factors (such as smoking, high BP, DM or raised lipid levels) or comorbidities increasing CV risk. In treated hypertensive patients <60 years old, SBP <140 mmHg and DBP <90 mmHg are recommended In patients >60 years old with SBP ≥160 mmHg, it is recommended to reduce SBP to between 150 and 140 mmHg. In individuals >80 years and with initial SBP ≥160 mmHg, it is recommended to reduce SBP to between 150 and 140 mmHg, provided they are in good physical and mental conditions.
UpToDate Cardiovascular disease risk assessment for primary prevention in adults	2019	-	For all individuals, the first step in assessing CVD risk is to determine whether one or more of the traditional risk factors (hypertension, cigarette smoking, diabetes mellitus [DM], premature family history of CVD, chronic kidney disease, obesity) for CVD is present. Subsequently, for individuals ≥20 years of age, a baseline lipid profile is generally obtained. Once all of the relevant risk factors have been identified and data acquired (ie, blood pressure and lipid profile), all patients from 40 to 79 years of age should have CVD risk estimated using a validated CVD risk calculator.
UpToDate Overview of hypertension in adults	2019	-	The diagnosis of hypertension requires integration of home or ambulatory blood pressure monitoring (ABPM) in addition to measurements made in the clinical setting. Meeting one or more of these criteria using ABPM qualifies as hypertension: • A 24-hour mean of 125/75 mmHg or above • Daytime (awake) mean of 130/80 mmHg or above • Nighttime (asleep) mean of 110/65 mmHg or above Proper technique and interpretation of the blood pressure is essential in the diagnosis and management of hypertension
UpToDate Patient adherence and the treatment of hypertension	2019	-	More sophisticated techniques for assessing adherence include measurements of medications in urine or blood samples, electronic medication monitors, and the use of pills that emit a small electrical signal triggered by gastric acid. However, these options are not available for routine clinical practice and may not be feasible in primary care.

UpToDate Cardiovascular disease risk assessment for primary prevention: Risk calculators	2018	-	A number of multivariate risk models have been developed for estimating the risk of cardiovascular events in apparently healthy, asymptomatic individuals based upon assessment of multiple variables. While all of the risk models have advantages and disadvantages, no single risk model will be appropriate for all patients. The choice of a specific risk model for CVD risk assessment should be individualized based on patient-specific characteristics (eg, age, gender, ethnicity). However, our experts feel that the use of risk models that predict hard events (ie, death, myocardial infarction, stroke) are preferred over those that include other endpoints (ie, revascularization).
UpToDate Treatment of hypertension in patients with diabetes mellitus	2017	-	In patients with diabetes, we suggest a goal blood pressure of 120 to 125/<80 mmHg (if unattended, automated oscillometric blood pressure readings are used to measure blood pressure), or a goal blood pressure of 125 to 130/<80 mmHg (if manual auscultatory measurements are used), rather than a goal blood pressure of <140/<90 mmHg (using manual auscultatory measurements)

Abbreviations: ABPM = ambulatory blood pressure measurement, AIx = augmentation index, ASCVD = atherosclerotic cardiovascular disease,BP = Blood pressure CVD = cardiovascular disease, DBP = diastolic blood pressure, DM = diabetes mellitus, HBPM = home blood pressure measurement, PWA = pulse wave analysis, PWV = pulse wave velocity, SBP = systolic blood pressure

Source: ACC-AHA 2019, ESC-ESH 2019, Piepoli et al. ESC Guidelines 2016, UpToDate Treatment of hypertension, UpToDate Cardiovascular disease risk assessment for primary prevention: Risk calculators, UpToDate Patient adherence and the treatment of hypertension, UpToDate Overview of hypertension in adults, UpTo Date Cardiovascular disease risk assessment for primary prevention in adult

Evidence tables of individual studies included for clinical effectiveness and safety

Table A4: Characteristics of the studies included – non-RCTs, direct comparison: intervention vs. comparator

Author	Year	Title	Patients *n* (mean age) disease area	Study type	Intervention	Comparator(s)	Main endpoints
De La Sierra et. al	2017	Twenty-four-hour central blood pressure is not better associated with hypertensive target organ damage than 24-h peripheral blood pressure	*208* (57 years) target organ damage in heart, brain and kidneys	Consecutive cross-sectional	- Mobil-O-Graph® with ARCSolver®		odds ratio for each mmHg increase of the association of each blood pressure value with the presence of target organ damage
Díaz et al.	2019	Impact of Methodological and Calibration Approach on the Association of Central and Peripheral Systolic Blood Pressure with Cardiac Structure and Function in Children, Adolescents and Adults	*269* (29 years) None – healthy individuals	Part of a population study	- Mobil-O-Graph® (not clear if it is used with ARCSolver® or not)	- Arteriograph - ultrasound	- association between blood pressure levels (peripheral-, brachial- or central-, aortic-) - agreement (Bland-Altman mean error) among aoSBP and/or pSBP obtained with different devices and calibration schemes - association between blood pressure (peripheral-, brachial or central- aortic-) level and cardiac and structural on functional parameters
Sarafidis et al.	2017	Ambulatory pulse wave velocity and augmentation index predict cardiovascular events and all-cause mortality better than office and ambulatory blood pressure in hemodialysis patient	*170* (63.76 years) Hemodialysis patients with endstage renal disease	Cohort study	- Mobil-O-Graph® with ARCSolver®		- combination of all-cause death, nonfatal MI and nonfatal stroke - all-cause mortality - cardiovascular mechanism within 30 days after an MI or fatal stroke - a combined outcome of cardiovascular death, nonfatal MI, nonfatal stroke

Author	Year	Title	Patients *n* (mean age) disease area	Study type	Intervention	Comparator(s)	Outputs measured	Main endpoints
Benas et al.	2019	Pulse wave analysis using the Mobil-O-Graph®, Arteriograph and Complior device: a comparative study	*316* (55 years) patients with several cardiovascular risks	Cross-sectional	- Mobil-O-Graph® with ARCSolver®	- Arteriograph - Complior	- cSBP - PWV	- intraclass correlation coefficient (ICC) PWV - intraclass correlation coefficent (ICC) cSBP - correlation of PWV and cSBP values measured by the 3 devices

Author	Year	Title	Patients *n* (mean age) disease area	Study type	Intervention	Comparator(s)	Outputs measured	Main endpoints
De La Sierra et. al	2017	Twenty-four-hour central blood pressure is not better associated with hypertensive target organ damage than 24-h peripheral blood pressure	*208* (57 years) target organ damage in heart, brain and kidneys	Consecutive cross-sectional	- Mobil-O-Graph®with ARCSolver®	- Mobil-O-Graph®	- Target organ damage	- odds ratio for each mmHg increase of the association of each blood pressure value with the presence of target organ damage
Endes et al.	2015	Feasibility of oscillometric aortic pressure and stiffness assessment using the VaSera® VS-1500: Comparison with a common tonometric method	*68* (51 years) NA	Convenience sample	- ARCSolver® with VaSera®	- SphygmoCor®	- cSBP - PWV	- reproducibility/variation - mean cSBP difference - mean PWV difference
Gotzmann et al.	2019	Accuracy of fully automated oscillometric central aortic blood pressure measurement techniques	*502* (67.9 years) Coronary artery disease (n=287) peripheral occlusive disease (n=45) hypertension (n=454)	Cross-sectional	- Mobil-O-Graph®NG with ARCSolver®	- SphygmoCor® XCEL - Invasively measured aortic BP	- cSBP - cDBP mmHg	- correlations between invasively and noninvasively measured values (cSBP & cDBP)
Grillo et al.	2018	Short-Term Repeatability of Noninvasive Aortic Pulse Wave Velocity Assessment: Comparison between Methods and Devices	*102* (65 years) High cardiovascular risk patients	Cross-sectional	- Mobil-O-Graph®with ARCSolver®	- Complior Analyse - PulsePen® - ET - SphygmoCor® - BPLab	- PWV - MAP - HR	- coefficient of repeatability (differences observed between 2 measurements of PWV according to the mean values
Luzardo et al.	2012	24-h ambulatory recording of aortic pulse wave velocity and central systolic augmentation: A feasibility study	*35/83* (45.6 years) NA	Cross-sectional	- Mobil-O-Graph®PWA with ARCSolver®	- SphygmoCor ®	- cSBP - cDBP - PP - AIx - AIx (75) - PWV	- absolute difference between tonometry vs. oscillometry - relative difference between tonometry vs. oscillometry
Salvi et al.	2019	Noninvasive Estimation of Aortic Stiffness Through Different Approaches: Comparison with Intra-Aortic Recordings	*102* (65 years) patients undergoing angiography	Consecutive cross-sectional	- Mobil-O-Graph®with ARCSolver®	- Complior Analyse - PulsePen® - ET - PulsePen® - ETT - SphygmoCor® - Proprietary Algorithms - BPLab® v.5.03 - BPLab® v.6.02	- PWV	- r (pearson correlation coefficient) and mean differences (SD) between devices - r (pearson correlation coefficient) and mean differences (SD) with invasive for each device - trend association with coronary damage of each device
Salvi et al.	2019	Unreliable Estimation of Aortic Pulse Wave Velocity Provided by the Mobil-O-Graph Algorithm-Based System in	*90* (38.2 years) Marfan Syndrome	Cross-sectional	- Mobil-O-Graph®with ARCSolver®	- PulsePen®	- cSBP - cDBP - Heart rate	- Correlation analysis PWV - Distribution of PWV related to age - Distribution of PWV related to systolic

Author	Year	Title	Patients *n* (mean age) disease area	Study type	Intervention	Comparator(s)	Outputs measured	Main endpoints
		Marfan Syndrome						blood pressure
Sarafidis et al.	2014	Evaluation of a novel brachial cuff-based oscillometric method for estimating central systolic pressure in hemodialysis patients	*73* (61.7 years) Endstage renal disease	Cross-sectional	- Mobil-O-Graph® with ARCSolver®	- SphygmoCor®	- bSBP - bDBP - bPP - aSBP - aDBP - aPP - AIx - AIx (75) - AP - PWV	- Correlation analysis aSBP - Correlation analysis AIx75 - Correlation analysis PWV
Vaios et al.	2018	Accuracy of a Newly-Introduced Oscillometric Device for the Estimation of Arterial Stiffness Indices in Patients on Peritoneal Dialysis: A Preliminary Validation Study	*27* (62.5 years) Endstage renal disease	Cross-sectional	- Mobil-O-Graph® with ARCSolver®	- SphygmoCor®	- bSBP - bDBP - bPP - aSBP - aDBP - aPP - AIx (75) - AP - PWV	- Correlation analysis of the agreement between the Mobil-O-Graph® and SphygmoCor® devices in the estimation of heart-rate-adjusted AIx75, aSBP and PWV
Wassertheurer et al.	2010	A new oscillometric method for pulse wave analysis: comparison with a common tonometric method	*302* (56 years) NA	Cross-sectional	- oscillometric method using ARCSolver® algorithm (not clear if it is Mobil-O-Graph®)	- SphygmoCor®	- AIx - aSBP	- mean difference AIx - mean difference aSBP
Weber et al.	2011	Validation of a brachial cuff-based method for estimating central systolic blood pressure	*131* (59 years) suspected coronary artery disease	Prospective cross-sectional	- Mobil-O-Graph® NG with ARCSolver®	- SphygmoCor ® - Invasively measured aortic BP	- aSBP	- aSBP r2 compared to invasive

Abbreviations: AIx=augmentation index, AIx(75)=Augmentation index at 75 bpm; aSBP=aortic systolic blood pressure, aDBP=aortic diastolic blood pressure, aPP=aortic pulse pressure, bSBP=brachial systolic blood pressure, bDBP=brachial diastolic blood pressure, bPP=brachial pulse pressure, cSBP=central systolic blood pressure, PWV=pulse wave velocity

Table A5: Characteristics of the studies included: non-RCTs, direct comparison: intervention vs. comparator

Study	Study Aim	Setting	Country	Disease area	Study Design	Funding Source	Devices
Benas, D. K., M.Triantafyllidi, H.Kostelli, G.Pavlidis, G.Varoudi, M.Vlastos, D.Lambadiari, V.Parissis, J.Ikonomidis, I. (2019). "Pulse wave analysis using the Mobil-O-Graph, Arteriograph and Complior device: a comparative study." Blood Pressure 28(2): 107-113.	The aim of the study was to compare PWV and cSBP values by the gold standard Complior device with Arteriograph and Mobil-O-Graph® in the same subjects	unclear, department of cardiology	Greece	subjects with several cardiovascular risks	cross-sectional	NA	• Mobil-O-Graph® •Arteriograph •Complior
de la Sierra, A. P., J.Yun, S.Acosta, E.Aiello, F.Oliveras, A.Vázquez, S.Armario, P.Blanch, P.Sierra, C.Calero, F.Fernández-Llama, P. (2018). "Central blood pressure variability is increased in hypertensive patients with target organ damage." Journal of Clinical Hypertension 20(2): 266-272.	To evaluate the association of office and ambulatory central and peripheral BP with the presence of silent TOD, at heart, kidney, and vascular levels, in a group of essential hypertensive patients	office and ambulatory	Spain	target organ damage in heart, brain, and kidneys	consecutive cross-sectional	•Instituto de Salud Carlos III (PI14/00592) •Fundacio´ de Recerca I Doce`ncia Mu´tua Terrassa.	• Mobil-O-Graph® 24-h Peripheral BP ambulatory • Mobil-O-Graph® 24-h Central BP ambulatory • Mobil-O-Graph® Peripheral BP in the office • Mobil-O-Graph® Central BP in the office
Díaz, A. B., D.Zócalo, Y. (2019). "Impact of Methodological and Calibration Approach on the Association of Central and Peripheral Systolic Blood Pressure with Cardiac Structure and Function in Children, Adolescents and Adults." High Blood Pressure and Cardiovascular Prevention 26(6): 509-534.	To analyze the extent to which the methodological approach and/or the calibration scheme determine: (1) the association between pSBP and aoSBP, the (2) agreement between pSBP and/or aSBP levels obtained noninvasively, and (3) the association between pSBP and aoSBP and structural and functional cardiovascular characteristics.	unclear	Argentina	none	cross-sectional	NA	• Mobil-O-Graph® •Arteriograph •RCD, ultrasound

Endes, S. B., M.Li, Y.Mayer, C.Hanssen, H.Hametner, B.Schmidt-Trucksäss, A.Wassertheurer, S. (2015). "Feasibility of oscillometric aortic pressure and stiffness assessment using the VaSera® VS-1500: Comparison with a common tonometric method." Blood Pressure Monitoring 20(5): 273-279.	To estimate central systolic blood pressure and aortic pulse wave velocity using retrospective application of the ARCSolver® algorithm as part of VaSera® VS compared to SphygmoCor®.	outpatient	Switzerland	NA	convenience sample	•Fukuda Denshi	• ARCSolver® with VaSera® •SphygmoCor®
Gotzmann, M. H., M.Seibert, F. S.Rohn, B. J.Bergbauer, M.Babel, N.Bauer, F.Mügge, A.Westhoff, T. H. (2019). "Accuracy of fully automated oscillometric central aortic blood pressure measurement techniques." Journal of Hypertension.	To compare cBP measured noninvasively by the SphygmoCor ® XCEL and Mobil-O-Graph®NG to invasively measured aortic BP patients undergoing coronary angiography	cardiac catheterization laboratory	Germany	Concomitant diseases: Coronary artery disease (n=287) periperal occlusive disease (n=45) hypertension (n=454)	consecutive cross-sectional	NA	•SphygmoCor® XCEL device (software version 1.2, ATCor Medical) • Mobil-O-Graph® NG (software version HMS CS 5.1; IEM) •Invasive
Grillo, A. P., G.Rovina, M.Moretti, F.Salvi, L.Gao, L.Baldi, C.Sorropago, G.Faini, A.Millasseau, S. C.Scalise, F.Carretta, R.Salvi, P. (2018). "Short-Term Repeatability of Noninvasive Aortic Pulse Wave Velocity Assessment: Comparison between Methods and Devices." American Journal of Hypertension 31(1): 80-88.	To characterize the shortterm repeatability of PWV in a population at high cardiovascular risk, using noninvasive measures obtained within a single session, in a controlled environment.	in-hospital, Cardiology Unit	Italy	consecutive patients for suspected coronary artery disease	cross-sectional	one author is consultant for DiaTecne and has received revenue from some companies whose devices have been used in thids study	•Complior Analyse •PulsePen® - ET •SphygmoCor® • BPLab® • Mobil-O-Graph®
Luzardo, L. L., I.Sottolano, M.Da Rosa, A.Thijs, L.Noboa, O.Staessen, J. A.Boggia, J. (2012). "24-h ambulatory recording of aortic pulse wave velocity and central systolic augmentation: A feasibility study." Hypertension Research 35(10): 980-987.	To compare brachial oscillometry(Mobil-O-Graph® 24-h PWA) with radial tonometry (SphygmoCor®)	outpatients and volunteers	Uruguay	NA	convenience cross-sectional	•Atcor Medical and IEM GmbH provided equipment free of charge for use •European Union •Fonds voor Wetenschappelijk Onderzoek Vlaanderen Brussels, Belgium •The Programa para la Formacio´n y Fortalecimiento de los Recursos Humanos de los Prestadores Pu´ blicos de Servicios de Salud, Unidades Docentes Asisten-	•brachial oscillometry method Mobil-O-Graph®24h PWA Monitor •radial tonometry method SphygmoCor®

						ciales gave support to the Unidad de Hipertensio´n Arteri-al.	
Salvi, P. S., F.Rovina, M.Moretti, F.Salvi, L.Grillo, A.Gao, L.Baldi, C.Faini, A.Furlanis, G.Sorropago, A.Millasseau, S. C.Sorropago, G.Carretta, R.Avolio, A. P.Parati, G. (2019). "Noninvasive Estimation of Aortic Stiffness Through Different Approaches: Comparison with Intra-Aortic Recordings." Hypertension 74(1): 117-129.	To determine which devices are reliable approaches for the estimation of aortic stiffness, 7 noninvasive devices were compared with invasive aortic pulse wave velocity.	inpatient	Italy	pateints under-going angiography	consecutive cross-sectional	•Authors consult for DiaTecne srl. And AtCor Medical Pty Ltd, Alam Medical SAS, OOO Petr Telegin, found and owned stock in Flag Vascular srl. •Devices and tech-nical assistance provided in kind from Flag Vascular srl, OOO Petr Telegin, Alam Medical SAS, I.E.M. GmbH, and Axelife.	**Carotid-femoral pulse wave velocity** •Complior Analyse •PulsePen® - ET •PulsePen® - ETT •SphygmoCor® **Proprietary Algorithms** •Mobil-O-Graph •BPLab® v.5.03 •BPLab®v.6.02
Salvi, P. F., G.Grillo, A.Pini, A.Salvi, L.Marelli, S.Rovina, M.Moretti, F.Gaetano, R.Pintassilgo, I.Faini, A.Fabris, B.Carretta, R.Parati, G. (2019). "Unreliable Estimation of Aortic Pulse Wave Velocity Provided by the Mobil-O-Graph Algorithm-Based System in Marfan Syndrome." Journal of the American Heart Association 8(9).	To compare the estimat-ed algorithm-based PWV values, provided by the Mobil-O-Graph® system, with the standard nonin-vasive assessment of aortic PWV in patients with Marfan syndrom	center for Marfan syn-drome	Italy	Marfan Syndrome	cross-sectional	Salvi reported receiv-ing consulting fees from DiaTecne srl (manufacturer of systems for as-sessing the arterial stiffness)	• Mobil-O-Graph® •PulsePen®
Sarafidis, P. A. L., A. A.Imprialos, K. P.Georgianos, P. I.Avranas, K. A.Protogerou, A. D.Doumas, M. N.Athyros, V. G.Karagiannis, A. I. (2016). "A comparison study of brachial blood pressure recorded with Spacelabs 90217A and Mobil-O-Graph NG devices under static and ambulatory conditions." Journal of Human Hypertension 30(12): 742-749.	The aim of the present study was to examine for the first time the agree-ment between the Mobil-O-Graph® and Sphyg-mocor® for measurement of aSBP, AIx and PWV in ESRD patients receiving hemodialysis	in-hospital, Hemodialysis Unit	Greece	endstage renal disease	unclear, as-sumed con-secutive cross-sectional	No conflict of interest disclosed but the authors got two Mobil-O-Graph®devices of-fered by the manu-facturer	• Mobil-O-Graph® •SphygmoCor®

Sarafidis, P. A. L., C.Mayer, C. C.Karpetas, A.Pagkopoulou, E.Bikos, A.Faitatzidou, D.Wassertheurer, S.Schmaderer, C.Liakopoulos, V.Papagianni, A.London, G. (2019). "Weak within-individual association of blood pressure and pulse wave velocity in hemodialysis is related to adverse outcomes." Journal of Hypertension 37(11): 2200-2208.	The aim of the study was to evaluate and compare the prognostic value of ambulatory recording of peripheral and central BP, arterial stiffness and wave reflection parameters for major cardiovascular outcomes and all-cause mortality in hemodialysis patients	in-hospital, 5 affiliated hemodialysis center	Greece	endstage renal disease	prospective cohort study	NA	•Mobil-O-Graph ambulatory BP Monitoring
Vaios, V. G., P. I.Pikilidou, M. I.Eleftheriadis, T.Zarogiannis, S.Papagianni, A.Zebekakis, P. E.Liakopoulos, V. (2018). "Accuracy of a Newly-Introduced Oscillometric Device for the Estimation of Arterial Stiffness Indices in Patients on Peritoneal Dialysis: A Preliminary Validation Study." Advances in peritoneal dialysis. Conference on Peritoneal Dialysis 34(2018): 24-31.	The aim of the study was to assess, for the first time, the accuracy of the Mobil-O-Graph® device in estimating central aortic BP and PWV in a cohort of stable PD patients	in-hospital, peritoneal dialysis unit	Greece	End-stage-renal-disease	cross-sectional	NA	•Mobil-O-Graph® •SphygmoCor
Wassertheurer, S. K., J.Weber, T.Van Der Giet, M.Baulmann, J.Ammer, M.Hametner, B.Mayer, C. C.Eber, B.Magometschnigg, D. (2010). "A new oscillometric method for pulse wave analysis: Comparison with a common tonometric method." Journal of Human Hypertension 24(8): 498-504.	To validate a movel method determining AIx and aSBP based on an oscillometric method using a common cuff (ARCSolver®) against a validated tonometric system (SphygmoCor®)	cardiology departments	Austria	NA	unclear, assumed consecutive cross-sectional	•government of Lower Austria •EFRE European Regional Development Fund • ARCSolver® inventors (COI, in kind contribution)	•oscillometric method using ARCSolver® algorithm •tonometric system using SphygmoCor®
Weber, T. W., S.Rammer, M.Maurer, E.Hametner, B.Mayer, C. C.Kropf, J.Eber, B. (2011). "Validation of a brachial cuff-based method for estimating central systolic blood pressure." Hypertension 58(5): 825-832.	To validate the cSBP provided by ARCSolver® alogrithm within an oscillometric brachial cuff-based sphygmomanometer that has been validated for automated blood pressure against invasive and FDA approved noninvasive system (SphygmoCor®)	tertiary care cardiogogy department of a university teaching hospital	Austria	suspected coronary artery disease	prospective cross-sectional	•government of Lower Austria •EFRE European Regional Development Fund • ARCSolver® inventors (COI, in kind contribution)	•oscillometric method using ARCSolver® algorithm •tonometric system using SphygmoCor ® •invasive central blood pressure measurement

Table A6: Characterisation of the interventions

	Technology	Comparator 1	Comparator 2	Comparator 3	Comparator 4	Comparator 5	Comparator 6	Comparator 7	Comparator 8	Comparator 9
Name	Mobil-O-Graph® PWA	SphygmoCor®	SphygmoCor® Xcel	Complior Analyse	PulsePen®-ETT	PulsePen®-ET	pOpmetre®	BPLab®	Arteriograph	Vicorder®
Manufacturer	I.E.M	AtCor Medical	AtCor Medical	Alam Medical	DiaTecne	DiaTecne	Axelife	Petr Telegin	Tensiomed	Skidomore Medical
Country of Origin	Germany	Australia	Australia	France	Italy	Italy	France	Russia	Hungary	UK
Reference codes										
Class/GMDN code										
Aortic PWV Assessment	Cuff-based method	Carotid-femoral PWV	Carotid-femoral PWV	Carotid-femoral PWV	Carotid-femoral PWV	Carotid-femoral PWV	Finger-toe PWV	Cuff-based method	Cuff-based method	Cuff-based Carotid femoral
Probes	Upper arm cuff oscillometric system	1 tonometer +ECG	1 tonometer	2 piezoelectric sensors	2 tonometers	1 tonometer +ECG	2 photodiode sensors	Upper arm cuff oscillometric system	Upper arm cuff oscillometric system	Upper arm cuff oscillometric system
Recording time	10 s	NA	NA	10 cardiac cycles	10 cardiac cycles	10 cardiac cycles	10 cardiac cycles	4-8 cardiac cycles	NA	NA
Method	Algorithm primarily based on age and systolic blood pressure	Sequential ECG-gated pulse wave recording at carotid and femoral artery	Femoral and carotid signals are acquired simultaneous	Simultaneous pulse wave recording at carotid and femoral artery	Simultaneous pulse wave recording at carotid and femoral artery	Sequential ECG-gated pulse wave recording at carotid and femoral artery	Simultaenous pulse wave recording at finger and toe	5.03 SW: analysis of reflected wave transit time. 6.02 SW: algorithm primary based on age and systolic blood pressure	PWV acquirement is based two systolic peak	Transit time is computed using the maximum of the second derivate, based on the maximum of the second derivative algorithm
Transit time	-	Foot-to-foot method: intersecting tangent algorithm	NA	Foot-to-foot method: intersecting tangent algorithm	Foot-to-foot method: intersecting interpolating algorithm	Foot-to-foot method: intersecting interpolating algorithm	Maximum of the second derivative algorithm	-	NA	NA
Sampling rate	100 Hz	128 Hz	256 Hz	1 kHz	1 kHz	1 kHz	1 kHz	100 Hz	200 Hz	556 Hz
Central BP Assessment	Brachial oscillometric blood pressure cuff-based method	Transfer function from radial artery	NA	Direct method from carotid artery	Direct method from carotid artery	Direct method from carotid artery	From digital volume pulse by photodiode sensor on the finger	Brachial oscillometric blood pressure cuff-based method	NA	NA

	Technology	Comparator 1	Comparator 2	Comparator 3	Comparator 4	Comparator 5	Comparator 6	Comparator 7	Comparator 8	Comparator 9
24-h monitoring	Ambulatory blood pressure monitoring (ABPM)	No	NA	No	LP software allows up to 24-h track recording	LP software allows up to 24-h track recording	No	Ambulatory blood pressure monitoring (ABPM)	Ambulatory blood pressure monitoring (ABPM)	NA
Weight, g	240	800	NA	450	121	88	375	226	250	600
Other characteristics	Handheld system	-	-	-	Pocket-sized wireless system	Pocket-sized wireless system	-	Handheld system	Handheld system	-

Table A7: Baseline characteristics of the study populations – non-RCT, direct comparison: intervention vs. comparator

Study	Devices	Participant Type	N patients	N for each device	Age	Subgroups
Benas, D. K., M.Triantafyllidi, H.Kostelli, G.Pavlidis, G.Varoudi, M.Vlastos, D.Lambadiari, V.Parissis, J.Ikonomidis, I. (2019). "Pulse wave analysis using the Mobil-O-Graph, Arteriograph and Complior device: a comparative study." Blood Pressure 28(2): 107-113.	•MOGARC •Arteriograph •Complior	subjects with several cardiovascular risk factors	316	316	55 (SD 14)	none
de la Sierra, A. P., J.Yun, S.Acosta, E.Aiello, F.Oliveras, A.Vázquez, S.Armario, P.Blanch, P.Sierra, C.Calero, F.Fernández-Llama, P. (2018). "Central blood pressure variability is increased in hypertensive patients with target organ damage." Journal of Clinical Hypertension 20(2): 266-272.	• Mobil-O-Graph® 24-h Peripheral BP ambulatory • Mobil-O-Graph® 24-h Central BP ambulatory • Mobil-O-Graph® Peripheral BP in the office • Mobil-O-Graph® Central BP in the office	patients with essential hypertension	208	• Mobil-O-Graph® 24-h Peripheral BP ambulatory = 208 • Mobil-O-Graph® 24-h Central BP ambulatory = 208 • Mobil-O-Graph® Peripheral BP in the office = 208 • Mobil-O-Graph® Central BP in the office = 208	mean 57 (SD 12)	none
Díaz, A. B., D.Zócalo, Y. (2019). "Impact of Methodological and Calibration Approach on the Association of Central and Peripheral Systolic Blood Pressure with Cardiac Structure and Function in Children, Adolescents and Adults." High Blood Pressure and Cardiovascular Prevention 26(6): 509-534.	•MOGARC •Arteriograph •RCD, ultrasound	asymptomatic subjects from the community	269	NA	29 (SD 16)	young people (< 24y, n=147)
Endes, S. B., M.Li, Y.Mayer, C.Hanssen, H.Hametner, B.Schmidt-Trucksäss, A.Wassertheurer, S. (2015). "Feasibility of oscillometric aortic pressure and stiffness assessment using the VaSera VS-1500: Comparison with a common tonometric method." Blood Pressure Monitoring 20(5): 273-279.	• ARCSolver® with VaSera® •SphygmoCor®	outpatients	68	• ARCSolver® with VaSera® n=68 •SphygmoCor® n=68	mean age 51 (SD 18)	NA

Gotzmann, M. H., M.Seibert, F. S.Rohn, B. J.Bergbauer, M.Babel, N.Bauer, F.Mügge, A.Westhoff, T. H. (2019). "Accuracy of fully automated oscillometric central aortic blood pressure measurement techniques." Journal of Hypertension.	•SphygmoCor® XCEL device (software version 1.2, ATCor Medical) •MOGARC •Invasive	patients with an indication for an elective coronary angiography and at least 18 years	502	•SphygmoCor® XCEL device (software version 1.2, ATCor Medical) = 498 • Mobil-O-Graph® NG (software version HMS CS 5.1; IEM) = 441	Mean 67.9 (SD 11.6)	atrial fibrillation
Grillo, A. P., G.Rovina, M.Moretti, F.Salvi, L.Gao, L.Baldi, C.Sorropago, G.Faini, A.Millasseau, S. C.Scalise, F.Carretta, R.Salvi, P. (2018). "Short-Term Repeatability of Noninvasive Aortic Pulse Wave Velocity Assessment: Comparison between Methods and Devices." American Journal of Hypertension 31(1): 80-88.	•Complior Analyse •PulsePen® ET •SphygmoCor® •BPLab® •MOGARC	high cardiovascular risk patients hospitalized for suspected coronary artery disease	102	•Complior Analyse=85 •PulsePen®-ETT=89 •PulsePen® - ET= 93 •SphygmoCor® Vx=91 •BPLab® =67 •Mobil-O-Graph®=99	Mean 65 (SD 13)	none
Luzardo, L. L., I.Sottolano, M.Da Rosa, A.Thijs, L.Noboa, O.Staessen, J. A.Boggia, J. (2012). "24-h ambulatory recording of aortic pulse wave velocity and central systolic augmentation: A feasibility study." Hypertension Research 35(10): 980-987.	•brachial oscillometry method MOGARC •radial tonometry method SphygmoCor®	outpatients and health staff volunteers without debilitating cardiovascular or other disease	35 / 83	• Mobil-O-Graph® PWA = 35 / 83 •SphygmoCore® = 35/83	mean 45.6 (SD 16.4) mean 49.9 (SD 13.1)	none
Salvi, P. S., F.Rovina, M.Moretti, F.Salvi, L.Grillo, A.Gao, L.Baldi, C.Faini, A.Furlanis, G.Sorropago, A.Millasseau, S. C.Sorropago, G.Carretta, R.Avolio, A. P.Parati, G. (2019). "Noninvasive Estimation of Aortic Stiffness Through Different Approaches: Comparison with Intra-Aortic Recordings." Hypertension 74(1): 117-129.	Carotid-femoral pulse wave velocity •Complior Analyse •PulsePen® -ET •PulsePen® -ETT •SphygmoCor® Proprietary Algorithms •MOGARC • BPLab® v.5.03 • BPLab® v.6.02	patients undergoing angiography at a cardiology unit	102	Carotid-femoral pulse wave velocity •Complior Analyse n=102 •PulsePen® -ET n=102 •PulsePen® - ETT n=102 •SphygmoCor® n=102 Proprietary Algorithms •Mobil-O-Graph® n=102 •BPLab® v.5.03 n=102 •BPLab® v.6.02 n=102	mean 65±13	none
Salvi, P. F., G.Grillo, A.Pini, A.Salvi, L.Marelli, S.Rovina, M.Moretti, F.Gaetano, R.Pintassilgo, I.Faini, A.Fabris, B.Carretta, R.Parati, G. (2019). "Unreliable Estimation of Aortic Pulse Wave Velocity Provided by the Mobil-O-Graph Algorithm-Based System in Marfan Syndrome." Journal of the American Heart Association 8(9).	•MOGARC •PulsePen®	patients with diagnosed Marfan Syndrome	90(103 were enrolled)	90	38.2 (SD 14.9)	none
Sarafidis, P. A. L., A. A.Imprialos, K. P.Georgianos, P. I.Avranas, K. A.Protogerou, A. D.Doumas, M. N.Athyros, V. G.Karagiannis, A. I. (2016). "A comparison study of brachial blood pressure recorded with Spacelabs 90217A and Mobil-O-Graph NG devices under static and ambulatory conditions." Journal of Human Hypertension 30(12): 742-749.	•MOGARC •SphygmoCor®	end stage renal disease patients receiving standard dialysis therapy	73	not clear, assumption 73 each	61.7 (SD 14.7)	none

Sarafidis, P. A. L., C.Mayer, C. C.Karpetas, A.Pagkopoulou, E.Bikos, A.Faitatzidou, D.Wassertheurer, S.Schmaderer, C.Liakopoulos, V.Papagianni, A.London, G. (2019). "Weak within-individual association of blood pressure and pulse wave velocity in hemodialysis is related to adverse outcomes." Journal of Hypertension 37(11): 2200-2208.	•MOGARC	hemodialysis patients	170	170	63.76 (SD 14.32)	none
Vaios, V. G., P. I.Pikilidou, M. I.Eleftheriadis, T.Zarogiannis, S.Papagianni, A.Zebekakis, P. E.Liakopoulos, V. (2018). "Accuracy of a Newly-Introduced Oscillometric Device for the Estimation of Arterial Stiffness Indices in Patients on Peritoneal Dialysis: A Preliminary Validation Study." Advances in peritoneal dialysis. Conference on Peritoneal Dialysis 34(2018): 24-31.	•MOGARC •SphygmoCor®	stable patients on PD	27	not clear, assumption 27 each	mean 62.5 (SD 15.6)	none
Wassertheurer, S. K., J.Weber, T.Van Der Giet, M.Baulmann, J.Ammer, M.Hametner, B.Mayer, C. C.Eber, B.Magometschnigg, D. (2010). "A new oscillometric method for pulse wave analysis: Comparison with a common tonometric method." Journal of Human Hypertension 24(8): 498-504.	•oscillometric method using ARCSolver® algorithm •tonometric system using SphygmoCor®	outpatient and hospital patients (unclear) and healthy volunteers	302	•oscillometric method using ARCSolver® algorithm = 302 •tonometric system using SphygmoCor® = 302	mean 56 (SD 20)	•age group 16-24 •age group 25-39 •age group 40-49 •age group 50-59 •age group 60-69 •age group 70-79 •age group 80+
Weber, T. W., S.Rammer, M.Maurer, E.Hametner, B.Mayer, C. C.Kropf, J.Eber, B. (2011). "Validation of a brachial cuff-based method for estimating central systolic blood pressure." Hypertension 58(5): 825-832.	•oscillometric method using ARCSolver® algorithm •tonometric system using SphygmoCor® •invasive central blood pressure measurement	patients undergoing elective coronary angiography for suspected coronary artery disease	131	•oscillometric method using ARCSolver® algorithm = 111 (noninvasive study) and 30 (invasive study, not included in this review) •tonometric system using SphygmoCor® = 111 (noninvasive study) •invasive central blood pressure measurement = 111 (noninvasive study) and 30 (invasive study, not included in this review)	mean 59 (SD 11)	none

Table A8: Outcomes in the included studies/ RCTs to be assessed– non-RCT, direct comparison intervention vs. comparator

Author	Year	Title	Patients *n* (mean age) disease area	Study type	Intervention	Comparator(s)	Outcomes
De La Sierra et. al	2017	Twenty-four-hour central blood pressure is not better associated with hypertensive target organ damage than 24-h peripheral blood pressure	*208* (57 years) target organ damage in heart, brain and kidneys	Consecutive cross-sectional	- MOGARC	Mobil-O-Graph®	odds ratio for each mmHg increase of the association of each blood pressure value with the presence of target organ damage
Díaz et al.	2019	Impact of Methodological and Calibration Approach on the Association of Central and Peripheral Systolic Blood Pressure with Cardiac Structure and Function in Children, Adolescents and Adults	*269* (29 years) None – healthy individuals	Part of a population study	- MOGARC	- Arteriograph - ultrasound	- association between blood pressure levels (peripheral-, brachial- or central-, aortic-) - agreement (Bland-Altman mean error) among aoSBP and/or pSBP obtained with different devices and calibration schemes - association between blood pressure (peripheral-, brachial or central- aortic-) level and cardiac and structural on functional parameters
Sarafidis et al.	2017	Ambulatory pulse wave velocity and augmentation index predict cardiovascular events and all-cause mortality better than office and ambulatory blood pressure in hemodialysis patient	*170* (63.76 years) Hemodialysis patients with endstage renal disease	Cohort study	- MOGARC	Mobil-O-Graph®	- combination of all-cause death, nonfatal MI and nonfatal stroke - all-cause mortality - cardiovascular mechanism within 30 days after an MI or fatal stroke - a combined outcome of cardiovascular death, nonfatal MI, nonfatal stroke

Author	Year	Title	Patients *n* (mean age) disease area	Study type	Intervention	Comparator(s)	Outputs measured	Outcomes
Benas et al.	2019	Pulse wave analysis using the Mobil-O-Graph, Arteriograph and Complior device: a comparative study	*316* (55 years) patients with several cardiovascular risks	Cross-sectional	- MOGARC	- Arteriograph - Complior	- cSBP - PWV	- intraclass correlation coefficient (ICC) PWV - intraclass correlation coefficent (ICC) cSBP - correlation of PWV and cSBP values measured by the 3 devices
De La Sierra et. al	2017	Twenty-four-hour central blood pressure is not better associated with hypertensive target organ damage than 24-h peripheral blood pressure	*208* (57 years) target organ damage in heart, brain and kidneys	Consecutive cross-sectional	- MOGARC	- Mobil-O-Graph®	- Target organ damage	- odds ratio for each mmHg increase of the association of each blood pressure value with the presence of target organ damage

Author	Year	Title	Patients *n* (mean age) disease area	Study type	Intervention	Comparator(s)	Outputs measured	Outcomes
Endes et al.	2015	Feasibility of oscillometric aortic pressure and stiffness assessment using the VaSera VS-1500: Comparison with a common tonometric method	*68* (51 years) NA	Convenience sample	- ARCSolver® with VaSera®	- SphygmoCor®	- cSBP - PWV	- reproducibility/variation - mean cSBP difference - mean PWV difference
Gotzmann et al.	2019	Accuracy of fully automated oscillometric central aortic blood pressure measurement techniques	*502* (67.9 years) Coronary artery disease (n=287) periperal occlusive disease (n=45) hypertension (n=454)	Cross-sectional	- MOGARC	- SphygmoCor ® XCEL - Invasively measured aortic BP	- cSBP - cDBP mmHg	- correlations between invasively and noninvasively measured values (cSBP & cDBP)
Grillo et al.	2018	Short-Term Repeatability of Noninvasive Aortic Pulse Wave Velocity Assessment: Comparison between Methods and Devices	*102* (65 years) High cardiovascular risk patients	Cross-sectional	- MOGARC	- Complior Analyse - PulsePen® - ET - SphygmoCor® - BPLab®	- PWV - MAP - HR	- coefficient of repeatability (differences observed between 2 measurements of PWV according to the mean values
Luzardo et al.	2012	24-h ambulatory recording of aortic pulse wave velocity and central systolic augmentation: A feasibility study	*35/83* (45.6 years) NA	Cross-sectional	- MOGARC	- SphygmoCor®	- cSBP - cDBP - PP - AIx - AIx (75) - PWV	- absolute difference between tonometry vs. oscillometry - relative difference between tonometry vs. oscillometry
Salvi et al.	2019	Noninvasive Estimation of Aortic Stiffness Through Different Approaches: Comparison with Intra-Aortic Recordings	*102* (65 years) patients undergoing angiography	Consecutive cross-sectional	- MOGARC	- Complior Analyse - PulsePen® - ET - PulsePen® - ETT - SphygmoCor® - Proprietary Algorithms - BPLab® v.5.03 - BPLab® v.6.02	- PWV	- r (pearson correlation coefficient) and mean differences (SD) between devices - r (pearson correlation coefficient) and mean differences (SD) with invasive for each device - trend association with coronary damage of each device
Salvi et al.	2019	Unreliable Estimation of Aortic Pulse Wave Velocity Provided by the Mobil-O-Graph Algorithm-Based System in Marfan Syndrome	*90* (38.2 years) Marfan Syndrome	Cross-sectional	- MOGARC	- PulsePen®	- cSBP - cDBP - Heart rate	- Correlation analysis PWV - Distribution of PWV related to age - Distribution of PWV related to systolic blood pressure
Sarafidis et al.	2014	Evaluation of a novel brachial cuff-based oscillometric method for estimating central systolic pressure in	*73* (61.7 years) Endstage renal disease	Cross-sectional	- MOGARC	- SphygmoCor®	- bSBP - bDBP - bPP - aSBP	- Correlation analysis aSBP - Correlation analysis AIx75 - Correlation analysis PWV

Author	Year	Title	Patients *n* (mean age) disease area	Study type	Intervention	Comparator(s)	Outputs measured	Outcomes
		hemodialysis patients					- aDBP - aPP - AIx - AIx (75) - AP - PWV	
Vaios et al.	2018	Accuracy of a Newly-Introduced Oscillometric Device for the Estimation of Arterial Stiffness Indices in Patients on Peritoneal Dialysis: A Preliminary Validation Study	*27* (62.5 years) Endstage renal disease	Cross-sectional	- MOGARC	- SphygmoCor®	- bSBP - bDBP - bPP - aSBP - aDBP - aPP - AIx (75) - AP - PWV	- Correlation analysis of the agreement between the Mobil-O-Graph® and SphygmoCor devices in the estimation of heart-rate-adjusted AIx75, aSBP and PWV
Wassertheurer et al.	2010	A new oscillometric method for pulse wave analysis: comparison with a common tonometric method	*302* (56 years) NA	Cross-sectional	- oscillometric method using ARCSolver® algorithm	- SphygmoCor®	- AIx - aSBP	- mean difference AIx - mean difference aSBP
Weber et al.	2011	Validation of a brachial cuff-based method for estimating central systolic blood pressure	*131* (59 years) suspected coronary artery disease	Prospective cross-sectional	- MOGARC	- SphygmoCor ® - Invasively measured aortic BP	- aSBP	- aSBP r2 compared to invasive

Abbreviations: AIx=augmentation index, AIx(75)=Augmentation index at 75 bpm; aSBP=aortic systolic blood pressure, aDBP=aortic diastolic blood pressure, aPP=aortic pulse pressure, bSBP=brachial systolic blood pressure, bDBP=brachial diastolic blood pressure, bPP=brachial pulse pressure, cSBP=central systolic blood pressure, PWV=pulse wave velocity

Table A9: Results summary for outcome (continuous) – non-RCT, direct comparison: intervention vs. comparator

Title	Devices	Methods	Primary outcomes	Each outcome result
Benas, D. K., M.Triantafyllidi, H.Kostelli, G.Pavlidis, G.Varoudi, M.Vlastos, D.Lambadiari, V.Parissis, J.Ikonomidis, I. (2019). "Pulse wave analysis using the Mobil-O-Graph, Arteriograph and Complior device: a comparative study." Blood	•Mobil-O-Graph •Arteriograph •Complior	F and P value Bland-Altmann methodology intraclass correlation coefficient (ICC) Pearson correlation anylisis	•Intraclass correlation coefficient (ICC) PWV •Intraclass correlation coefficient (ICC) cSBP •correlation of PWV and cSBP values measured by the 3 devices	* PWV (m/s) Intraclass correlation coefficient (ICC): 0.86(CI: 0.826-0.888) between Arteriograph and Mobil-O-Graph®; 0.87 (CI: 0.842-0.895) between Complior & Mobil-O-Graph®) and 0.86 (CI 0.82-0.89) between Arteriograph and Complior *cSBP (mmHg): Intraclass correlation coefficient (ICC): 0.92 (CI: 0.9--0.936) between Arteriograph and Mobil-O-Graph®; 0.91 (CI: 0.891-0.929) between Complior & Mobil-O-Graph®) and 0.92 (CI 0.9-0.894) between Arteriograph and Complior *correlation PWV and cSBP values measured by the 3 devices with their respective differences: Arteriograph were related with greater difference in PWV and cSBP values between Arteriograph

Title	Devices	Methods	Primary outcomes	Each outcome result
Pressure 28(2): 107-113.				and Mobil-O-Graph® (r ¼ 0.51 and r ¼ 0.58, p<.01) as well as between Arteriograph and Complior (r ¼ 0.47 and r ¼ 0.41, p<.01), (b) increasing PWV and cSBP measured by Complior was related with greater difference in PWV and cSBP between Arteriograph and Complior (r¼0.39 and r¼0.22, p<.01) as well as between Complior and Mobil-O-Graph® (r¼0.31 and r¼0.26, p<.01), (c) Increasing PWV and cSBP measured by Mobil-O-Graph® were related with greater difference in PWV and cSBP between Arteriograph and Mobil-O-Graph (r¼0.38 and r¼0.31, p<.01) as well as between Complior and Mobil-O-Graph® (r¼0.40 and r¼0.36, p<.01). By univariate and multivariate analysis, we did not find any statistically significant association between the differences in the values of PWV and central BP among the 3 devices and age, sex, disease state and body mass index or of the order of study performance in each patient (p>.05, data not shown) with the exception of height. Increased height was associated with greater difference in PWV values between Arteriograph and Mobil-O-Graph® (standardized coefficient b¼0.14, p¼.02) as well as between Complior and Mobil-O-Graph® (b¼0.16, p<.01). This finding suggest that the variability in the measurement of jugular to symphysis or carotid to femoral distance respectively used for the measurement of PWV may account for the differences observed between Mobil-O-Graph® and Arteriograph or Complior as the greater distance inserted in the formula for PWV the greater the calculated PWV value provided a similar transit time. We also observed that regarding the PWV and cSBP measurement: (a) the PWV and cSBP values by Arteriograph were higher compared to the PWV and cSBP values by Mobil-O-Graph®, in and 64% and 69% of the subjects respectively (b) the PWV and cSBP values by Complior were higher compared to the respective values by Mobil-O-Graph® in 59% and 55% of the subjects respectively and (c) the PWV and cSBP values by Arteriograph were higher compared to the respective values by Complior in 55% and 60% of the subjects respectively.
de la Sierra, A. P., J.Yun, S.Acosta, E.Aiello, F.Oliveras, A.Vázquez, S.Armario, P.Blanch, P.Sierra, C.Calero, F.Fernández-Llama, P. (2018). "Central blood pressure variability is increased in hypertensive patients with target organ damage." Journal of Clinical Hypertension 20(2): 266-272.	• Mobil-O-Graph® 24-h Peripheral BP ambulatory • Mobil-O-Graph® 24-h Central BP ambulatory • Mobil-O-Graph® Peripheral BP in the office • Mobil-O-Graph® Central BP in the office	The association of each BP estimate with the presence of TOD was assessed by means of logistic regression analyses, with odds ratio (OD) calculation adjusted for age, sex, and the use of antihypertensive treatment. Furthermore, the relative impact of central versus peripheral BP estimates was assessed by the simultaneous introduction of each pair of central and peripheral measurements (office, 24-h, daytime, and night-time) in the logistic regression models,	Odds ratio for each mmHg increase (95% confidence interval) of the association of each blood pressure value with the presence of target organ damage	Odds ratio for each mmHg increase (95% CI) association with presence of target organ damage •24-h Peripheral 1.056 (1.025-1.087) •24-h Central 1.053 (1.020-1.086) •24-h Peripheral PP 1.076 (1.034-1.120) •24-h Central PP 1.081 (1.027-1.139) Odds ratio for each mmHg increase (95% CI) association after adjustment for central or peripheral values, with presence of target organ damage •24-h Peripheral 1.079 (1.008-1.156) •24-h Central 0.976 (0.911-1.044) •24-h Peripheral PP 1.124 (1.014-1.246) •24-h Central PP 0.938 (0.820-1.073)

Title	Devices	Methods	Primary outcomes	Each outcome result
		and then calculating the adjusted ODs.		
Díaz, A. B., D.Zócalo, Y. (2019). "Impact of Methodological and Calibration Approach on the Association of Central and Peripheral Systolic Blood Pressure with Cardiac Structure and Function in Children, Adolescents and Adults." High Blood Pressure and Cardiovascular Prevention 26(6): 509-534.	• Mobil-O-Graph® •Arteriograph •RCD, ultrasound	*simple bivariate correlation analyses were performed * analyzes of the agreement between bSBP and/or aoSBP levels Bland-Altman analysis were performed to determine the error between methods * Evaluation and comparison of the strength of the association between cardiac structure and function properties and pSBP and/or aoSBP obtained by different methods and calibrations schemes, simple bivariate correlations and correlations comparisons were performed		•Association between blood pressure levels: The association levels varied, but in almost all the cases, independently of the analyzed group (entire group or < 24 y.o), the levels of aoSBP obtained with the MOG and calibrated to pDBP/MBPc (CM) or pDBP/MBPosc (OscM) were the ones that showed the lowest levels of association with the remaining forms of aoSBP and pSBP determination; In this respect: (1) taking as reference pSBP obtained with the MOG, the minimum and maximum levels of association (R) were 0.56 (aoSBP_MOG_OscM) and 0.899 (aoSBP_MOG_SD) for entire group, and 0.431 (aoSBP_RCD_CM (MOG)) and 0.847 (aoSBP_MOG_SD) for < 24 y.o, and (2) taking as reference pSBP obtained with AGRAPH, the minimum and maximum R were 0.451 (aoSBP_MOG_OscM) and 0.901 (aoSBP_AGRAPH) for the entire group, and 0.401 (aoSBP_MOG_OscM) and 0.814 (aoSBP_AGRAPH) for < 24 y.o *Agreement (Bland-Altman mean error) among aoSBP and/or pSBP: There were differences in aoSBP and pSBP levels between the different approaches and/or calibration methods. In this regard, it is to note that for a given approach (e.g. MOG) mean errors for aoSBP data could reach 23 and 25 mmHg (OscM vs. SD) or 17 and 18 mmHg (OscM vs. CM), for the entire group and < 24 y.o, respectively. Similarly, for RCD, mean error levels could be 20 and 21 mmHg (Osc vs. CM) for the entire group and < 24 y.o On the other hand, using the same calibration method (CM or OscM), the differences in values obtained with the different approaches could reach 5 and 3 mmHg (calibration to CM; MOG vs. RCD) or 8 and 6 mmHg (calibration to OscM; MOG vs. RCD), when considering all the subjects and those < 24 y.o, respectively. Jointly analyzing results obtained when comparing values given by the different approaches and/or calibration schemes it was observed that errors (differences) varied noticeably. As an example, for the entire group the differences were − 27 mmHg, − 23 mmHg, − 17 mmHg, − 12 mmHg or 8 mmHg when aoSBP data obtained with MOG (calibration to OscM) were compared with data from other approaches and calibration schemes *Association between blood pressure (peripheral-, brachial or central- aortic-) level and cardiac and structural on functional parameters: For the entire group, the highest levels of association between SBP and LV diameters (LVEDD, LVESD, and LVOT) were obtained for aoSBP_MOG_CM and aoSBP_ MOG_OscM data. In addition, compared to aoSBP_MOG_CM, the aoSBP_MOG_OscM showed higher levels of association with the structural parameters. LV wall thicknesses values tend to show greater association with aoSBP_MOG_CM and aoSBP_MOG_OscM, than with pSBP_MOG (for the entire group and < 24 y.o). In turn, regardless of the calibration scheme, aoSBP_RCD levels reached a statistically significant association with LV wall thicknesses only in the entire group; the association was not greater than that obtained for pSBP. *When analyzing MOG data it was observed that compared to pSBP, aoSBP values obtained calibrating to CM or OscM showed: (1) greater association with LVOT-VTI, LV SV, E/A ratio, mitral valve close to open time and LV ejection time, in both groups, (2) greater ssociation with right ventricular outflow tract-VTI (RVOT-VTI) and E wave in the entire group, (3) lower association with LV CO (Doppler and B-Mode derived) and A wave two-dimension, in both groups (Tables 5, 6, Figs. 3, 4). In turn, the analysis of AGRAPH records for the entire group showed that, contrarily to that

Title	Devices	Methods	Primary outcomes	Each outcome result
				previously described, the associations with LVOT-VTI, RVOT-VTI, LV SV and CO (Doppler and B-Mode derived), E and E/A ratio were stronger for pSBP_AGRAPH levels than for aoSBP_ AGRAPH values. The only ariables with grater association with aoSBP_AGRAPH than with pSBP_AGRAPH were A, mitral valve close to open ratio and TEI Index. It is to note, that when the group of < 24 y.o was analyzed, none of the functional parameters showed greater association with aoSBP_AGRAPH. LVOT-VTI, LV CO (Doppler-derived) and SV showed a major association with pSBP_AGRAPH ($p < 0.05$) than with aoSBP_AGRAPH (Tables 5, 6, Figs. 3, 4). LV functional parameters did not show a clear, systematic pattern of association with pSBP or aoSBP.
Endes, S. B., M.Li, Y.Mayer, C.Hanssen, H.Hametner, B.Schmidt-Trucksäss, A.Wassertheurer, S. (2015). "Feasibility of oscillometric aortic pressure and stiffness assessment using the VaSera VS-1500: Comparison with a common tonometric method." Blood Pressure Monitoring 20(5): 273-279.	• ARCSolver® with VaSera® •SphygmoCor®	Data are expressed as mean with standard deviation. We used the Bland-Altman method to analyze the agreement between the two methods. Person's linear correlation coefficient was calculated for correlation analysies. T-tests were applied for examination of age group-related differences between the measurements. Reporducability of the methods was quantified as variation estimate, as described by Bland and Altman.	•reproducibility/variation •mean cSBP difference •mean PWV difference	cSBP reporducibility expressed as variability was 14.9% for ARCSolver® and 11.6% for SyphymoCor. PWV reproducibility was better for ARCSolver® with a variation estimate of 6.5% compared with 20.9% using SphygmoCor®. The mean cSBP difference was 0.5 mmHg (SD 6.9 mmHg) and 0.32 m/s (SD 1.20 m/s) for PWV.

Title	Devices	Methods	Primary outcomes	Each outcome result
Gotzmann, M. H., M.Seibert, F. S.Rohn, B. J.Bergbauer, M.Babel, N.Bauer, F.Mügge, A.Westhoff, T. H. (2019). "Accuracy of fully automated oscillometric central aortic blood pressure measurement techniques." Journal of Hypertension.	•SphygmoCor® XCEL device (software version 1.2, ATCor Medical) • Mobil-O-Graph® NG (software version HMS CS 5.1; IEM) •Invasive	The performance of the different noninvasively cBP measurement techniques was analyzed using two different approaches: correlations between invasively and noninvasively measured values, assessment of bias and limits of agreement in a Bland-Altman analysis	Correlations between invasively and noninvasively measured values (cSBP & cDBP)	•Correlation invasive to noninvasive Systolic (cSBP): SphygmoCor® R2=0.864, p<0.001, Mobil-O-Graph® R2=0.763, p<0.001 •Correlation invasiv to noninvasive Diastolic (cDBP): SphygmoCor® R2=0.772, p<0.001, Mobil-O-Graph® R2= 0.618, p<0.001 ->Correlations were highly significant for both sBP and DBP with both devices. The correlation coefficients in systolic and diastolic cBP were significantly higher for the SphygmoCor® device compared with the Mobil-O-Graph® •Mean systolic bias to invasively assessed cBP: SphygmoCor® -5.0 (SD 7.7) mmHg, Mobil-O-Graph®-6.0 (SD 10.4) mmHg -> systolic bias is larger in Mobil-O-Graph® •Mean diastolic bias to invasively assessed cBP: SphygmoCor® 0.5 (SD 6.2) mmHg, Mobil-O-Graph 3.6 (SD 8.3) mmHg -> diastolic bias is significantly larger in Mobil-O-Graph®

Title	Devices	Methods	Primary outcomes	Each outcome result
Grillo, A. P., G.Rovina, M.Moretti, F.Salvi, L.Gao, L.Baldi, C.Sorropago, G.Faini, A.Millasseau, S. C.Scalise, F.Carretta, R.Salvi, P. (2018). "Short-Term Repeatability of Noninvasive Aortic Pulse Wave Velocity Assessment: Comparison between Methods and Devices." American Journal of Hypertension 31(1): 80-88.	•Complior Analyse •PulsePen® - ET •SphygmoCor® •BPLab® •Mobil-O-Graph®	The correlations between 2 consecutive measurements were analyzed in 2 steps. In the first step, the correlation between measurements values (equation of the linear relationship, correlation coefficent and P value) was investigated. Secondly, the relative differences within each pair of measurements were plotted against the mean of the pair. The repeatability was expressed as coefficent of repeatability and intraclass correlation coefficients.	Coefficient of repeatability (differences observed between 2 measurements of PWV according to the mean values	All devices evaluating carotid-femoral PWV (PulsePen®, SphygmoCor®, Complior) revealed higher variability for higher PWV values. CV [confidence interval] for PWV more than 10 m/s was 9.72% [7.2–11.7] for Complior Analyse, 9.21% [6.5–11.3] for PulsePen®-ETT, 6.54% [5.3–7.6] for PulsePen®-ET, 10.29% [7.7–12.3] for SphygmoCor®. On the other hand, no such differences were observed with cuff-based devices for PWV <10 m/s vs. PWV ≥10 m/s: BPLab® 6.03% [3.6–7.7] vs. 5.14% [3.5–6.4], Mobil-OGraph 3.52% [2.8–4.1] vs. 3.20% [2.6–3.7]. *Coefficient of Repeatability (Difference PWTT in relation to Average of first and second PWTT measurement):Complior: 12.5 ms; PulsePen® ETT: 10.1 ms; SphygmoCor®: 13.3 ms; PulsePen® ET: 7.8

Title	Devices	Methods	Primary outcomes	Each outcome result
Luzardo, L. L., I.Sottolano, M.Da Rosa, A.Thijs, L.Noboa, O.Staessen, J. A.Boggia, J. (2012). "24-h ambulatory recording of aortic pulse wave velocity and central systolic augmentation: A feasibility study." Hypertension Research 35(10): 980-987.	•brachial oscillometry method Mobil-O-Graph® 24h PWA Monitor •radial tonometry method SphygmoCor®	For comparison of means and proportions, we applied the Student's t-test for paired observations and the w2 statistic, respectively. We assessed the agreement between paired measurements by the Bland and Altman's method.14 Reproducibility was twice the standard deviation of the pairwise differences between duplicate measurements, expressed as a percentage of the average of first and repeat measurements in all participants.14 Using single regression, we also assessed the departure of the slope of repeated on first measurements from the line of identity (slope¼1).	At rest •absolute difference between tonometry vs. oscillometry •relative difference between tonometry vs. oscillometry At rest and during daytime ambulatory monitoring •absolute difference between tonometry vs. oscillometry •relative difference between tonometry vs. oscillometry	At rest n=35 (absolute difference tonometry vs oscillmetry) •central systolic BP (-1.2 ± 3.1, p=0.22) •central diastolic BP (-0.1 ± 2.4, p=0.72) •pulse pressure (-1.1 ± 4.1, p=0.12) •augmentation index % (0.5 ± 9.5, p=0.65) •augmentation index at 75 bpm % (1.1 ± 11.5, p=0.57) •PWV (0.3 ± 1.1, p=0.11) At rest and during daytime ambulatory monitoring n=83 (absolute difference tonometry vs. oscillometry) •central systolic BP (1.4 ± 10.0, p=0.19) •central diastolic BP (-4.0 ± 7.3, p<0.0001) •pulse pressure (5.5 ± 7.4, p<0.0001) •augmentation index % (0.7 ± 9.3, p=0.65) •augmentation index at 75 bpm % (-4.6 ± 9.4, p<0.0001) •PWV (0.6 ± 1.3, p=0.0002)
Salvi, P. S., F.Rovina, M.Moretti, F.Salvi, L.Grillo, A.Gao, L.Baldi, C.Faini, A.Furlanis, G.Sorropago, A.Millasseau, S. C.Sorropago, G.Carretta, R.Avolio, A. P.Parati, G. (2019). "Noninvasive Estimation of Aortic Stiffness Through Different Approaches: Comparison with Intra-Aortic Recordings." Hypertension 74(1): 117-129.	Carotid-femoral pulse wave velocity •Complior Analyse •PulsePen® - ET •PulsePen® - ETT •SphygmoCor® Proprietary Algorithms • Mobil-O-Graph® •BPLab® v.5.03 •BPLab® v.6.02	The relationship between measurements provided by any couple of noninvasive devices as well as between measurements provided by each noninvasive device and the intraarterial recording was assessed with r or r-squared where apporpirate. The relatoinship between PWV and age was analyzed by exponential regression. The agreement between the invasive aortic PWV or PWTT and the corresponding parameters obetained from noninvasive devices was evaluated using the Bland-Altman plots, as-	r (pearson correlation coefficient) and mean differences (SD) between devices r (pearson correlation coefficient) and mean differences (SD) with invasive for each device trend association with coronary damage of each device	•Inter-Operator Repeatability (not tested for Mobil-O-Graph®) •Agreement between devices for PWA measures (correlation and mean difference) Mobil-O-Graph® vs. Complior r=0.46 (p<0.0001), mean difference 0.28±2.94 Mobil-O-Graph® vs. PulsePen® - ETT r=0.62 (p<0.0001), mean difference 1.17±2.59 Mobil-O-Graph® vs. Pulsepen® - ET r=0.61 (p<0.0001), mean difference 1.00±2.77 Mobil-O-Graph® vs. SphygmoCor® r=0.64 (p<0.0001), mean difference 0.40±2.23 Mobil-O-Graph® vs. pOpmetre r=0.21 (p=0.1136), mean difference 0.08±4.69 Mobil-O-Graph® vs. BPLab® 5.03 r=0.17 (p=0.0892), mean difference -0.29±2.84 Mobil-O-Graph® vs. BPLab® 6.02 r=0.94 (p<0.0001), mean difference 2.00±1.00 •Agreement between devices for PWA measures 1/PWV (correlation and mean difference) Mobil-O-Graph® vs. Complior r=0.51 (p<0.0001), mean difference -0.1±29.2 Mobil-O-Graph® vs. PulsePen® -ETT r=0.68 (p<0.0001), mean difference -8.7±22.2 Mobil-O-Graph® vs. Pulsepen® -ET r=0.71 (p<0.0001), mean difference -6.7±21.5 Mobil-O-Graph® vs. SphygmoCor® r=0.70 (p<0.0001), mean difference -2.4±21.8 Mobil-O-Graph® vs. pOpmetre r=0.10 (p=0.4551), mean difference 9.7±46.6 Mobil-O-Graph® vs. BPLab® 5.03 r=0.26 (p=0.0086), mean difference 7.3±30.9 Mobil-O-Graph® vs. BPLab® 6.02 r=0.96 (p<0.0001), mean difference -17.4±8.2 •Agreement between invasive and noninvasive PWA measures Complior: r=0.64 (p<0.0001), mean difference -0.73±2.83

Title	Devices	Methods	Primary outcomes	Each outcome result
		sessing the limits of agreement both for the entire population and for low and high PWV groups. The latter were identified with reference to the median (11 m/s) of the entire population PWV values. A multivariate analysis was performed to evaluate the role of age, peripheral systolic BP, and heart rate in affecting PWV for each device. Normal distribution of variables entering multivariate analysis was confirmed by Shapiro-Wilk test. A further analysis of the differences between non-invasive devices and the gold standard method was accomplished by stratifying the population for PWV and age quartiles. After discarding the Gaussianity hypothesis in single quartiles, data were compared by the Wilcoxon rank-sum test for independent data. Results were reported with P values on a box plot. The relationship between PWV estimated by noninvasive methods and severity of the coronary artery disease was analysed by ANOVA with posterior contrasts. For multiple comparisons, the algorithm which controls the expected rate of false positive results for all positive results (false discovery rate)was used. In		PulsePen® - ETT: r=0.71 (p<0.0001), mean difference 0.20±2.54 PulsePen® - ET: r=0.78 (p<0.0001), mean difference -0.04±2.23 SphygmoCor®: r=0.70 (p<0.0001), mean difference -0.61±2.57 pOpmetre: r=0.41 (p=0.0021), mean difference -0.44±4.44 BPLab® (Vasotens 5.03): r=0.23 (p=0.0283), mean difference -0.71±3.55 BPLab® (Vasotens 6.02): r=0.77(p<0.0001), mean difference 1.04±2.27 Mobil-O-Graph®: r=0.71 (p<0.0001), mean difference -1.01±2.54 •Agreement between invasive and noninvasive inverse of PWA measures (1/PWV) Complior: r=0.57 (p<0.0001), mean difference 6.1±27.6 PulsePen® - ETT: r=0.72 (p<0.0001), mean difference -2.8±21.3 PulsePen® - ET: r=0.78 (p<0.0001), mean difference -0.8±19.2 SphygmoCor®: r=0.66 (p<0.0001), mean difference 3.0±23.5 pOpmetre: r=0.29 (p=0.0334), mean difference 13.1±44.4 BPLab® (Vasotens 5.03): r=0.25 (p=0.0168), mean difference 0.6±31.3 BPLab® (Vasotens 6.02): r=0.80(p<0.0001), mean difference -12.3±18.2 Mobil-O-Graph®: r=0.76 (p<0.0001), mean difference 4.9±19.5

Title	Devices	Methods	Primary outcomes	Each outcome result
		the presence of either residual not normally distributed or heterscedasticity, analysis was done after logarithmic transofrmation of PWV variables.		
Salvi, P. F., G.Grillo, A.Pini, A.Salvi, L.Marelli, S.Rovina, M.Moretti, F.Gaetano, R.Pintassilgo, I.Faini, A.Fabris, B.Carretta, R.Parati, G. (2019). "Unreliable Estimation of Aortic Pulse Wave Velocity Provided by the Mobil-O-Graph Algorithm-Based System in Marfan Syndrome." Journal of the American Heart Association 8(9).	• Mobil-O-Graph® •PulsePen®	The average difference between 2 sets of PWV measurements was assessed with a 2-tailed paired t test. A multivariate regression analysis was performed to evaluate the role of BP, heart rate, age and age2 in affecting PWV for each device. The agreement between PWV measurements was analyzed according to the analysis described by Bland and Altman.	•Correlation analysis PWV •Distribution of PWV related to age •Distribution of PWV related to systolic blood pressure	•Correlation in PWV: r=0.35; •PWV mean SD=6.1 1.3 m/s versus 8.8 3.1 m/s, respectively (average of differences between PWV values provided by the 2 methods 1.969SD= 2.7 5.6 m/s), with a greater underestimation for high values of PWV •Distribution of PWV related to age: cf-PWV in patients with MFS was only weakly affected by age (r2=0.21), aortic PWV estimated by Mobil-O-Graph® was strongly related with age (r2=0.86) •Distribution of PWV related to systolic blood pressure: df-PWV (r2=0.00), Mobil-O-Graph® (r2=0.02) In both cases, a significant underestimation of PWV assessed by Mobil-O-Graph® compared with cf-PWV is evident (p<0.0001). cf-PWV in patients with MFS was only weakly affected by age (r2=0.21). On the contrary, aortic PWV, estimated by Mobil-O-Graph® was strongly related with age (r2=0.86) Determinant factors of PWV values, estimated by PulsePen® and Mobil-O-Graph®, were investigated by multivariate analysis, considering as independent variables heart rate, systolic blood pressure, diastolic blood pressure, age, and age2. This multivariate analysis showed that in this population with MFS, cf-PWV was significantly affected by heart rate. The coefficient of correlation of this model was 18.4%. cf-PWV was not affected by age and blood pressure. On the other hand, Mobil-O-Graph® was strongly affected by age, age2, and systolic blood pressure, with a minor contribution of diastolic blood pressure. The coefficient of correlation of this model was 98.6%. A multivariate regression analysis considering only age2 and systolic BP showed a coefficient of determination of PWV estimated by Mobil-O-Graph® of 98%
Sarafidis, P. A. L., A. A.Imprialos, K. P.Georgianos, P. I.Avranas, K. A.Protogerou, A. D.Doumas, M. N.Athyros, V. G.Karagiannis, A. I. (2016). "A comparison study of brachial blood pressure recorded with Spacelabs 90217A and Mobil-O-Graph NG devices under static and ambulatory conditions."	• Mobil-O-Graph® •SphygmoCor®	continuous variables were checked for normality with the one-sample Kolmogorov-Smirnov test. Comparison between the test deivice were performed with the Student's t test or with the Wilcoxon's Signed Rank test. Bivariate correlation coefficients r were calculated using the Pearson's product formula. The agreement	•Correlation analysis aSBP •Correlation analysis AIx75 •Correlation analysis PWV	• Mobil-O-Graph® and SphygmoCor® devices in the estimation of aorSBP: Correlation r=0.770, P<0.001; Bland-Altman mean difference: 2.8mmHg, 95% limits of agreement: -23.6mmHg to 29.2mmHg • Mobil-O-Graph® and SphygmoCor® devices in the estimation of AIx75: Correlation r=0.400, P<0.001; Bland-Altman mean difference: -1.6%, 95% limits of agreement: -25.0% and 21.8% • Mobil-O-Graph® and SphygmoCor® devices in the estimation of PWV: Correlation r=0.739, P<0.001; Bland-Altman mean difference: no evidence of systematic bias, 95% limits of agreement: -3.8 m/s and 5.4 m/s

Title	Devices	Methods	Primary outcomes	Each outcome result
Journal of Human Hypertension 30(12): 742-749.		between the paired measurements of aSBP, AIx(75) and PWV was tested by constructing Bland-Altman plots A p value level <0.05 was considered statistically significant		
Sarafidis, P. A. L., C.Mayer, C. C.Karpetas, A.Pagkopoulou, E.Bikos, A.Faitatzidou, D.Wassertheurer, S.Schmaderer, C.Liakopoulos, V.Papagianni, A.London, G. (2019). "Weak within-individual association of blood pressure and pulse wave velocity in hemodialysis is related to adverse outcomes." Journal of Hypertension 37(11): 2200-2208.	• Mobil-O-Graph® ambulatory BP Monitoring	*Shaprio-Wilk test was applied to examine the normality of distribution for continuous variables *Kaplan-Meier curves were created *log-rank test was applied to compare the differences among the quartiles *Univariate and multivariate Cox regression analyses were performed to evaluate the impact of various demographic and clinical characteristics *variables were tested for interactions and included in the multivariate model if P<0.2 in univariate analysis *values of P<0.05 were considered statistically significant	Primary endpoint: •combination of all-cause death, nonfatal MI and nonfatal stroke •Quartile 1: reference group in all comparisons	•Freedom from primary endpoint of 48-hour central SBP: 65.1% for patients in quartile 1, 69% for patients in quartile 2, 76.2% for patients in quartile 3 and 76.7% for patients in quartile 4 (log-rank P=0.324) •Freedom from primary endpoint of 48-hour central DBP: 55.8% for patients in quartile 1, 73.8% for patients in quartile 2, 76.2% for patients in quartile3 and 81.4% for patients in quartile 4 (log-rank P=0.024) •Freedom from primary endpoint of 48-hour central PP: 83.7% for patients in quartile 1, 71.4% for patients in quartile 2, 69.0% for patients in quartile3 and 69.2% for patients in quartile 4 (log-rank P=0.024) •Freedom from primary endpoint of 48-hour PWV: 93.0% for patients in quartile 1, 81.0% for patients in quartile 2, 57.1% for patients in quartile3 and 55.8% for patients in quartile 4 (log-rank P<0.001) *Freedom from primary endpoint of 48 hour AIx (75): 88.4% for patients in quartile 1, 66.7% for patients in quartile 2, 69.0% for patients in quartile3 and 62.8% for patients in quartile 4 (log-rank P=0.014) *Hazard RAtio of freedom from primary end point were 3.022 (95% CI, 1.077-8.480) and 3.784 (95% CI, 1.386-10.336) for quartiles 3 and 4 compared with quartile 1 * As shown in Figure 3, no significant differences in the future risk of death between quartiles of predialysis BP or ambulatory brachial SBP and DBP were evident. With regards to central SBP and DBP (Figure 3), no significant differences in the HR for all-cause mortality were noted. Future risk of death was marginally different for quartiles of 48-hour central PP, as HR was 1.895 (95% CI, 0.689–5.214) for quartile 3 and 2.216 (95% CI, 0.831–5.907) for quartile 4 (log-rank P=0.089). In contrast, future risk was significantly different for quartiles of ambulatory PWV 10.417 (95% CI, 2.392–45.360) and 8.495 (95% CI, 1.912–37.740) for quartiles 3 and 4 compared with quartile 1.

Title	Devices	Methods	Primary outcomes	Each outcome result
Vaios, V. G., P. I.Pikilidou, M. I.Eleftheriadis, T.Zarogiannis, S.Papagianni, A.Zebekakis, P. E.Liakopoulos, V. (2018). "Accuracy of a Newly-Introduced Oscillometric Device for the Estimation of Arterial Stiffness Indices in Patients on Peritoneal Dialysis: A Preliminary Validation Study." Advances in peritoneal dialysis. Conference on Peritoneal Dialysis 34(2018): 24-31.	• Mobil-O-Graph® •SphygmoCor®	All continous variables were checked for normality, using the Kolmogorov-Smirnov test. Comparison between the SphygmoCor® and Mobil-O-Graph® devices were performed using unpaired t-tests or Mann-Whitney-U-tests. To assess the strenght of the association the pearson product formula to calculate bivariate correlation coefficent (r). Bland-Altman analysis was performed to explore the agreement between the tonometric and oscillometric measurements of aSBP, AIx75 and PWV. A two tailed p value less than 0.05 was considered as statistically significant	•Correlation analysis of the agreement between the Mobil-O-Graph® and SphygmoCor® devices in the estimation of Aortic systolic blood pressure (aorSBP) •Correlation analysis of the agreement between the Mobil-O-Graph® and SphygmoCor® devices in the estimation of heart-rate-adjusted augmentation index (AIx75) •Correlation analysis of the agreement between the Mobil-O-Graph® and SphygmoCor® devices in the estimation of pulse wave velocity (PWV)	*Agreement between the Mobil-O-Graph® and SphygmoCor® devices in the estimation of aorSBP: Correlation r=0.889, P<0.001; Bland-Altman mean difference: 3.9mmHg, 95% limits of agreement: -13.3mmHg to 21.2mmHg *Agreement between the Mobil-O-Graph® and SphygmoCor® devices in the estimation of AIx75: Correlation r=0.816, P<0.001; Bland-Altman mean difference: -2.5%, 95% limits of agreement: -16.7% and 11.6% *Agreement between the Mobil-O-Graph® and SphygmoCor® devices in the estimation of PWV: Correlation r=0.794, P<0.001; Bland-Altman mean difference: no evidence of systematic bias, 95% limits of agreement: -3.1 m/s and 4.4 m/s

Title	Devices	Methods	Primary outcomes	Each outcome result
Wassertheurer, S. K., J.Weber, T.Van Der Giet, M.Baulmann, J.Ammer, M.Hametner, B.Mayer, C. C.Eber, B.Magometschnigg, D. (2010). "A new oscillometric method for pulse wave analysis: Comparison with a common tonometric method." Journal of Human Hypertension 24(8): 498-504.	•oscillometric method using ARCSolver® algorithm •tonometric system using SphygmoCor®	To get a robust estimation of the performance of the system, the measurements were performed within the clinical routine by several examiners. Beside that the international recommendations for the measurement of arterial stiffness were respected. The measurements took place at convenient room temperature and under avoidance of external influences. The systolic and diastolic blood pressure values used for the ARCSolver® method were also entered to the SphygmoCor ® system to calibrate the radial pressure curve. The consecutive recording of the pulse waves was carried out in random order on the left arm. Usually, at least two iterations were performed in each session. This resulted in 749 measurements.	•mean difference AIx • mean difference aSBP	For aSBP the mean difference was 0.1mmHg with an s.d. of 3.1mmHg. The mean difference for AIx was 1.2% with an s.d. of 7.9%. There was no significant difference in reproducibility of AIx for both methods. The variation estimate of inter- and intraobserver measurements was 6.3% for ARCSolver® and 7.5% for SphygmoCor®. For the age group below 25, we observed a moderate over estimation of AIx for negative values by ARCSolver®. This effect seems to result from a different AIx calculation method used by SphygmoCor® for negative values but may be of minor clinical relevance.

Title	Devices	Methods	Primary outcomes	Each outcome result
Weber, T. W., S.Rammer, M.Maurer, E.Hametner, B.Mayer, C. C.Kropf, J.Eber, B. (2011). "Validation of a brachial cuff-based method for estimating central systolic blood pressure." Hypertension 58(5): 825-832.	•oscillometric method using ARCSolver® algorithm •tonometric system using SphygmoCor® •invasive central blood pressure measurement	All of the measurements are presented as mean1 SD. Linearregression was applied to determine the coefficient of determination (R2). Furthermore, data was analyzed using the method presented by Bland and Altman. Those are mainly helpful to represent the data graphically and to investigate the agreement of measurements according to the different methods. To examine the difference in the strength of correlation, z statistic is applied.	•aSBP r2 compared to invasive	The correlation between cSBP (invasive) and cSBP (osc/ ARCSolver®) was close, with R2 0.899 (P 0.0001). Bland-Altman plots are shown in Figure 1, revealing good agreement (mean difference: 3.0 6.0 mm Hg) without any systematic bias.

Risk of bias tables

Table A10: Risk of bias – outcome-level of non-randomised studies

Title	Devices	Quality assessment (risk of bias)
Benas, D. K., M.Triantafyllidi, H.Kostelli, G.Pavlidis, G.Varoudi, M.Vlastos, D.Lambadiari, V.Parissis, J.Ikonomidis, I. (2019). "Pulse wave analysis using the Mobil-O-Graph, Arteriograph and Complior device: a comparative study." Blood Pressure 28(2): 107-113.	•Mobil-O-Graph® •Arteriograph •Complior	Low quality Intended outcomes not fully reported
de la Sierra, A. P., J.Yun, S.Acosta, E.Aiello, F.Oliveras, A.Vázquez, S.Armario, P.Blanch, P.Sierra, C.Calero, F.Fernández-Llama, P. (2018). "Central blood pressure variability is increased in hypertensive patients with target organ damage." Journal of Clinical Hypertension 20(2): 266-272.	• Mobil-O-Graph® 24-h Peripheral BP ambulatory • Mobil-O-Graph® 24-h Central BP ambulatory • Mobil-O-Graph® Peripheral BP in the office • Mobil-O-Graph® Central BP in the office	Low quality Methodology not appropriate. Association of PWA with ABP, which is calculated from ABP. Conclusions do not match methodology.
Díaz, A. B., D.Zócalo, Y. (2019). "Impact of Methodological and Calibration Approach on the Association of Central and Peripheral Systolic Blood Pressure with Cardiac Structure and Function in Children, Adolescents and Adults." High Blood Pressure and Cardiovascular Prevention 26(6): 509-534.	• Mobil-O-Graph® •Arteriograph •RCD, ultrasound	Low quality Unclear reporting of results.

Endes, S. B., M.Li, Y.Mayer, C.Hanssen, H.Hametner, B.Schmidt-Trucksäss, A.Wassertheurer, S. (2015). "Feasibility of oscillometric aortic pressure and stiffness assessment using the VaSera VS-1500: Comparison with a common tonometric method." Blood Pressure Monitoring 20(5): 273-279.	• ARCSolver® with VaSera® •SphygmoCor®	Moderate Some evidence of strong conclusions compared to results.
Gotzmann, M. H., M.Seibert, F. S.Rohn, B. J.Bergbauer, M.Babel, N.Bauer, F.Mügge, A.Westhoff, T. H. (2019). "Accuracy of fully automated oscillometric central aortic blood pressure measurement techniques." Journal of Hypertension.	•SphygmoCor® XCEL device (software version 1.2, ATCor Medical) • Mobil-O-Graph® NG (software version HMS CS 5.1; IEM) •Invasive	Good Outcomes clearly reported. Methods clearly stated. Population described.
Grillo, A. P., G.Rovina, M.Moretti, F.Salvi, L.Gao, L.Baldi, C.Sorropago, G.Faini, A.Millasseau, S. C.Scalise, F.Carretta, R.Salvi, P. (2018). "Short-Term Repeatability of Noninvasive Aortic Pulse Wave Velocity Assessment: Comparison between Methods and Devices." American Journal of Hypertension 31(1): 80-88.	•Complior Analyse •PulsePen®-ET •SphygmoCor® • BPLab® • Mobil-O-Graph®	Moderate Outcomes clearly reported. Methods clearly stated. Population described. Methods not condusive to answering all research questions.
Luzardo, L. L., I.Sottolano, M.Da Rosa, A.Thijs, L.Noboa, O.Staessen, J. A.Boggia, J. (2012). "24-h ambulatory recording of aortic pulse wave velocity and central systolic augmentation: A feasibility study." Hypertension Research 35(10): 980-987.	•brachial oscillometry method Mobil-O-Graph® 24h PWA Monitor •radial tonometry method SphygmoCor®	Moderate Outcomes clearly reported. Methods clearly stated. Population described. Some evidence of strong conclusions.
Salvi, P. S., F.Rovina, M.Moretti, F.Salvi, L.Grillo, A.Gao, L.Baldi, C.Faini, A.Furlanis, G.Sorropago, A.Millasseau, S. C.Sorropago, G.Carretta, R.Avolio, A. P.Parati, G. (2019). "Noninvasive Estimation of Aortic Stiffness Through Different Approaches: Comparison with Intra-Aortic Recordings." Hypertension 74(1): 117-129.	**Carotid-femoral pulse wave velocity** •Complior Analyse •PulsePen®-ET •PulsePen®-ETT •SphygmoCor® **Proprietary Algorithms**	Moderate Evidence of strong conclusions not directly stemming from evidence reported. Methods partially not appropriate for answering research question. Generally results well reported and described.

	• Mobil-O-Graph® • BPLab® v.5.03 • BPLab® v.6.02	
Salvi, P. F., G.Grillo, A.Pini, A.Salvi, L.Marelli, S.Rovina, M.Moretti, F.Gaetano, R.Pintassilgo, I.Faini, A.Fabris, B.Carretta, R.Parati, G. (2019). "Unreliable Estimation of Aortic Pulse Wave Velocity Provided by the Mobil-O-Graph Algorithm-Based System in Marfan Syndrome." Journal of the American Heart Association 8(9).	•Mobil-O-Graph® •PulsePen®	Moderate Evidence of strong conclusions not directly stemming from evidence reported. Methods partially not appropriate for answering research question. Generally results well reported and described.
Sarafidis, P. A. L., A. A.Imprialos, K. P.Georgianos, P. I.Avranas, K. A.Protogerou, A. D.Doumas, M. N.Athyros, V. G.Karagiannis, A. I. (2016). "A comparison study of brachial blood pressure recorded with Spacelabs 90217A and Mobil-O-Graph NG devices under static and ambulatory conditions." Journal of Human Hypertension 30(12): 742-749.	•Mobil-O-Graph® •SphygmoCor®	Low quality Small sample size and reporting not complete. Methods do not accurately reflect research questions.
Sarafidis, P. A. L., C.Mayer, C. C.Karpetas, A.Pagkopoulou, E.Bikos, A.Faitatzidou, D.Wassertheurer, S.Schmaderer, C.Liakopoulos, V.Papagianni, A.London, G. (2019). "Weak within-individual association of blood pressure and pulse wave velocity in hemodialysis is related to adverse outcomes." Journal of Hypertension 37(11): 2200-2208.	• Mobil-O-Graph® ambulatory BP Monitoring	Low quality Methods and outcomes not adequately reported

Vaios, V. G., P. I.Pikilidou, M. I.Eleftheriadis, T.Zarogiannis, S.Papagianni, A.Zebekakis, P. E.Liakopoulos, V. (2018). "Accuracy of a Newly-Introduced Oscillometric Device for the Estimation of Arterial Stiffness Indices in Patients on Peritoneal Dialysis: A Preliminary Validation Study." Advances in peritoneal dialysis. Conference on Peritoneal Dialysis 34(2018): 24-31.	•Mobil-O-Graph® •SphygmoCor®	Low quality Small sample size. Conclusions too strong for evidence provided.
Wassertheurer, S. K., J.Weber, T.Van Der Giet, M.Baulmann, J.Ammer, M.Hametner, B.Mayer, C. C.Eber, B.Magometschnigg, D. (2010). "A new oscillometric method for pulse wave analysis: Comparison with a common tonometric method." Journal of Human Hypertension 24(8): 498-504.	•oscillometric method using ARCSolver® algorithm •tonometric system using SphygmoCor®	Low quality Outcomes not clearly reported. Method of recruitment not clearly defined.
Weber, T. W., S.Rammer, M.Maurer, E.Hametner, B.Mayer, C. C.Kropf, J.Eber, B. (2011). "Validation of a brachial cuff-based method for estimating central systolic blood pressure." Hypertension 58(5): 825-832.	•oscillometric method using ARCSolver® algorithm •tonometric system using SphygmoCor® •invasive central blood pressure measurement	Moderate Methods matched research question. Adequate reporting.

Table A11: Risk of bias using ROBINS-I from Cochrane

Title	Quality assessment by reviewers	Overall risk of bias	Pre Intervention Bias due to confounding	Pre Intervention Bias in selection of participants into the study	At Intervention Bias in classification of interventions	Post Intervention Bias due to deviations from intended interventions	Post Intervention Bias due to missing data	Post Intervention Bias in measurement of outcomes	Post Intervention Bias in selection of the reported result
Benas, D. K., M.Triantafyllidi, H.Kostelli, G.Pavlidis, G.Varoudi, M.Vlastos, D.Lambadiari, V.Parissis, J.Ikonomidis, I. (2019). "Pulse wave analysis using the Mobil-O-Graph, Arteriograph and Complior device: a comparative study." Blood Pressure 28(2): 107-113.	**Low quality** **Intended outcomes not fully reported**	**Moderate**	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias	Serious risk of bias
de la Sierra, A. P., J.Yun, S.Acosta, E.Aiello, F.Oliveras, A.Vázquez, S.Armario, P.Blanch, P.Sierra, C.Calero, F.Fernández-Llama, P. (2018). "Central blood pressure variability is increased in hypertensive patients with target organ damage." Journal of Clinical Hypertension 20(2): 266-272.	**Low quality** **Methodology not appropriate. Association of PWA with ABP, which is calculated from ABP. Conclusions do not match methodology.**	**Moderate**	Serious risk of bias	Moderate risk of bias	Serious risk of bias	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias

Díaz, A. B., D.Zócalo, Y. (2019). "Impact of Methodological and Calibration Approach on the Association of Central and Peripheral Systolic Blood Pressure with Cardiac Structure and Function in Children, Adolescents and Adults." High Blood Pressure and Cardiovascular Prevention 26(6): 509-534.	**Low quality** **Unclear reporting of results.**	**Moderate**	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias
Endes, S. B., M.Li, Y.Mayer, C.Hanssen, H.Hametner, B.Schmidt-Trucksäss, A.Wassertheurer, S. (2015). "Feasibility of oscillometric aortic pressure and stiffness assessment using the VaSera VS-1500: Comparison with a common tonometric method." Blood Pressure Monitoring 20(5): 273-279.	**Moderate** **Some evidence of strong conclusions compared to results.**	**Moderate**	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias
Gotzmann, M. H., M.Seibert, F. S.Rohn, B. J.Bergbauer, M.Babel, N.Bauer, F.Mügge, A.Westhoff, T. H. (2019). "Accuracy of fully automated oscillometric central aortic blood pressure measurement techniques." Journal of Hypertension.	**Good** **Outcomes clearly reported. Methods clearly stated. Population described.**	**Moderate**	Moderate risk of bias	Serious risk of bias	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias

Grillo, A. P., G.Rovina, M.Moretti, F.Salvi, L.Gao, L.Baldi, C.Sorropago, G.Faini, A.Millasseau, S. C.Scalise, F.Carretta, R.Salvi, P. (2018). "Short-Term Repeatability of Noninvasive Aortic Pulse Wave Velocity Assessment: Comparison between Methods and Devices." American Journal of Hypertension 31(1): 80-88.	**Moderate** **Outcomes clearly reported. Methods clearly stated. Population described. Methods not condusive to answering all research questions.**	**Low**	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias
Luzardo, L. L., I.Sottolano, M.Da Rosa, A.Thijs, L.Noboa, O.Staessen, J. A.Boggia, J. (2012). "24-h ambulatory recording of aortic pulse wave velocity and central systolic augmentation: A feasibility study." Hypertension Research 35(10): 980-987.	**Moderate** **Outcomes clearly reported. Methods clearly stated. Population described. Some evidence of strong conclusions.**	**Low**	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Moderate risk of bias	Serious risk of bias

Salvi, P. S., F.Rovina, M.Moretti, F.Salvi, L.Grillo, A.Gao, L.Baldi, C.Faini, A.Furlanis, G.Sorropago, A.Millasseau, S. C.Sorropago, G.Carretta, R.Avolio, A. P.Parati, G. (2019). "Noninvasive Estimation of Aortic Stiffness Through Different Approaches: Comparison with Intra-Aortic Recordings." Hypertension 74(1): 117-129.	**Moderate** **Evidence of strong conclu-sions not directly stemming from evidence reported. Methods partially not appropriate for answering research question. Generally results well reported and described.**	**Moderate**	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias

Salvi, P. F., G.Grillo, A.Pini, A.Salvi, L.Marelli, S.Rovina, M.Moretti, F.Gaetano, R.Pintassilgo, I.Faini, A.Fabris, B.Carretta, R.Parati, G. (2019). "Unreliable Estimation of Aortic Pulse Wave Velocity Provided by the Mobil-O-Graph Algorithm-Based System in Marfan Syndrome." Journal of the American Heart Association 8(9).	**Moderate** **Evidence of strong conclusions not directly stemming from evidence reported. Methods partially not appropriate for answering research question. Generally results well reported and described.**	**Moderate**	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias
Sarafidis, P. A. L., A. A.Imprialos, K. P.Georgianos, P. I.Avranas, K. A.Protogerou, A. D.Doumas, M. N.Athyros, V. G.Karagiannis, A. I. (2016). "A comparison study of brachial blood pressure recorded with Spacelabs 90217A and Mobil-O-Graph NG devices under static and ambulatory conditions." Journal of Human Hypertension 30(12): 742-749.	**Low quality** **Small sample size and reporting not complete. Methods do not accurately reflect research questions.**	**Moderate**	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias

Sarafidis, P. A. L., C.Mayer, C. C.Karpetas, A.Pagkopoulou, E.Bikos, A.Faitatzidou, D.Wassertheurer, S.Schmaderer, C.Liakopoulos, V.Papagianni, A.London, G. (2019). "Weak within-individual association of blood pressure and pulse wave velocity in hemodialysis is related to adverse outcomes." Journal of Hypertension 37(11): 2200-2208.	**Low quality** **Methods and outcomes not adequately reported**	**Moderate**	Serious risk of bias	Serious risk of bias	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias	Serious risk of bias	Serious risk of bias
Vaios, V. G., P. I.Pikilidou, M. I.Eleftheriadis, T.Zarogiannis, S.Papagianni, A.Zebekakis, P. E.Liakopoulos, V. (2018). "Accuracy of a Newly-Introduced Oscillometric Device for the Estimation of Arterial Stiffness Indices in Patients on Peritoneal Dialysis: A Preliminary Validation Study." Advances in peritoneal dialysis. Conference on Peritoneal Dialysis 34(2018): 24-31.	**Low quality** **Small sample size. Conclusions too strong for evidence provided.**	**Moderate**	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias
Wassertheurer, S. K., J.Weber, T.Van Der Giet, M.Baulmann, J.Ammer, M.Hametner, B.Mayer, C. C.Eber, B.Magometschnigg, D. (2010). "A new oscillometric method for pulse wave analysis: Comparison with a common tonometric method." Journal of Human Hypertension 24(8): 498-504.	**Low quality** **Outcomes not clearly reported. Method of recruitment not clearly defined.**	**Moderate**	Moderate risk of bias	No information	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias

Weber, T. W., S.Rammer, M.Maurer, E.Hametner, B.Mayer, C. C.Kropf, J.Eber, B. (2011). "Validation of a brachial cuff-based method for estimating central systolic blood pressure." Hypertension 58(5): 825-832.	**Moderate** **Methods matched research question. Adequate reporting.**	**Moderate**	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias

Applicability tables

Table A12: Summary table characterising the applicability of a body of studies

Domain	Description of applicability of evidence
Population	Adult population 18 and over as intended, but in one case, studies combined adults with adolescents and children. This was still included due to dearth of evidence.
Intervention	Intervention was not limited to Mobil-O-Graph®, but also coupled with other ways of deriving peripheral blood pressure.
Comparators	No cardiovascular risk equations were compared. 24-h ABPM not the sole comparator, as measurement also can be done at the office.
Outcomes	None of the EFF and SAF outcomes intended were found. Studies were validation and accuracy of measurement compared to invasive.
Setting	Setting was not yet relevant, as the studies were still in the validation or accuracy compared to invasive analysis phase. Study types were not clinical trials.

APPENDIX 2: CHECKLIST FOR POTENTIAL ETHICAL, ORGANISATIONAL, PATIENT AND SOCIAL AND LEGAL ASPECTS

1	**Ethical**	
1.1	Does the introduction of the new technology and its potential use/non-use instead of the defined, existing comparator(s) give rise to any new ethical issues?	No
	If answered with 'yes', please provide a short statement explaining why. *Example:* Routine introduction of prenatal genetic screening tests, which could lead to pregnancy termination, may cause ethical issues for the couple as well as for the health-care provider.	
1.2	Does comparing the new technology to the defined, existing comparators point to any differences that may be ethically relevant?	No
	If answered with 'yes', please provide a short statement explaining why. *Example:* The marketing authorisation holder claims that its product is superior, but has decided to limit the amount of the new medicine, which means that it has to be rationed and not all patients who need it can receive it. The comparator is freely available.	
2	**Organisational**	
2.1	Does the introduction of the new technology and its potential use/non-use instead of the defined, existing comparator(s) require organisational changes?	No
	If answered with 'yes', please provide a short statement explaining why. *Example:* The new intervention requires the establishment of specialised centres for administration.	
2.2	Does comparing the new technology to the defined, existing comparator(s) point to any differences that may be organisationally relevant?	No
	If answered with 'yes', please provide a short statement explaining why. *Example:* The new technology will replace a surgical intervention, which may lead to excess capacity in relevant areas.	
3	**Social**	
3.1	Does the introduction of the new technology and its potential use/non-use instead of the defined, existing comparator(s) give rise to any new social issues?	No
	If answered with 'yes', please provide a short statement explaining why. *Example:* A new technology allows patients to return to the workplace, but since the technology can be seen by co-workers, it may lead to stigmatisation.	
3.2	Does comparing the new technology to the defined, existing comparator(s) point to any differences that may be socially relevant?	No
	If answered with 'yes', please provide a short statement explaining why. *Example:* A technology, which is widely used by persons with abuse problems, colours the tongue blue, thus, immediately identifying the user. Comparators do not have this property.	
4	**Legal**	
4.1	Does the introduction of the new technology and its potential use/non-use instead of the defined, existing comparator(s) give rise to any legal issues?	No
	If answered with 'yes', please provide a short statement explaining why. *Example:* The comparator for the new technology is a pharmaceutical that is not licensed for the indication of concern, but is widely in use.	

4.2	Does comparing the new technology to the defined, existing comparator(s) point to any differences that may be legally relevant?	No

If answered with ‘yes’, please provide a short statement explaining why.

Examples:

- The comparator for the new technology is a controlled, restricted substance, but the new medicine is not.
- The most appropriate comparator for the new technology is available as a pharmacy-compounded medicine, but not as a finished product with marketing authorisation.

Note: The assessment should not address patent-related issues.