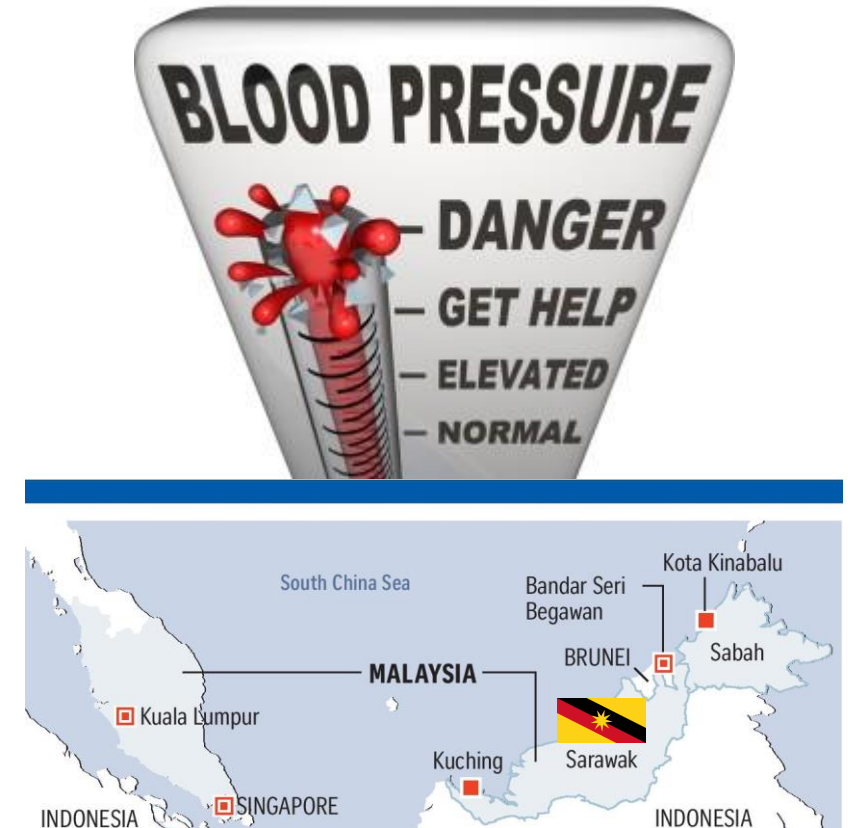


Liquid chromatography-coupled mass spectrometry for antihypertensive treatment adherence assessment

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Kuching, SARAWAK

Overview

- Introduction
- Objective
- Methods
- Results
- Discussion
- Challenges

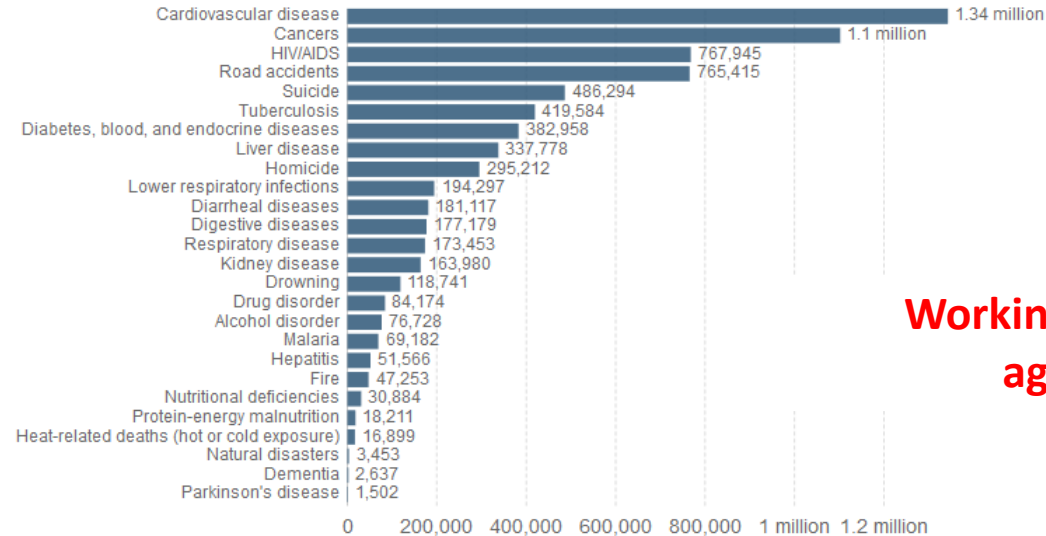


Cardiovascular disease

- Top global killer

Causes of death in 15-49 year olds, World, 2016

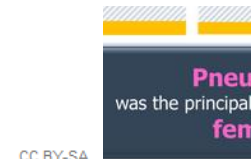
Annual number of deaths by cause in children aged 15 to 49 years old, across both sexes. Data refers to the specific cause of death, which is distinguished from risk factors for death, such as air pollution, diet and other lifestyle factors. See sources for further details on definitions of specific cause categories. Data on deaths related to terrorism and executions are not available by age group, so have been excluded.



Source: IHME, Global Burden of Disease (GBD)



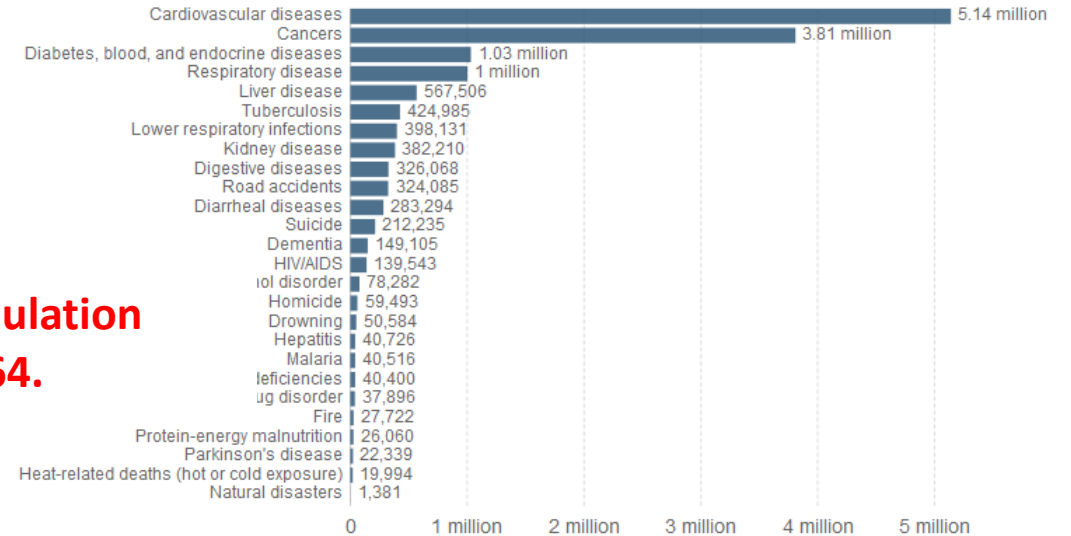
Working age population aged 15 to 64.



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Causes of death in 50-69 year olds, World, 2016

Annual number of deaths by cause in children aged 50 to 69 years old, across both sexes. Data refers to the specific cause of death, which is distinguished from risk factors for death, such as air pollution, diet and other lifestyle factors. See sources for further details on definitions of specific cause categories. Data on deaths related to terrorism and executions are not available by age group, so have been excluded.



Source: IHME, Global Burden of Disease (GBD)

Our World in Data

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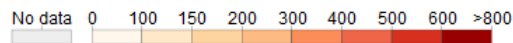
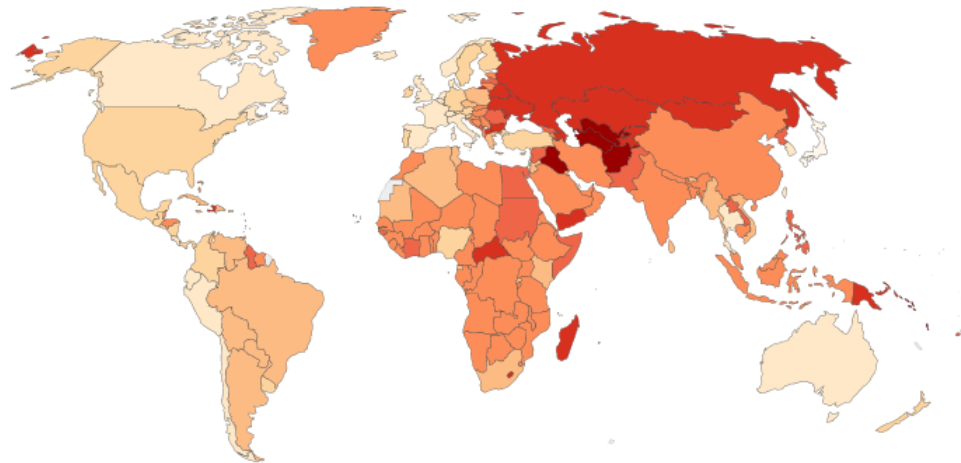
Cardiovascular disease

- Mainly in LMICS
- Stroke predominates in South East Asia

Cardiovascular disease death rates (per 100,000), 2016

Age-standardized death rates from cardiovascular disease, measured as the number of deaths per 100,000 individuals across both sexes. Age-standardization assumes a constant population age & structure to allow for comparisons between countries and with time without the effects of a changing age distribution within a population (e.g. aging).

Our World
in Data

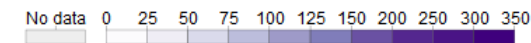
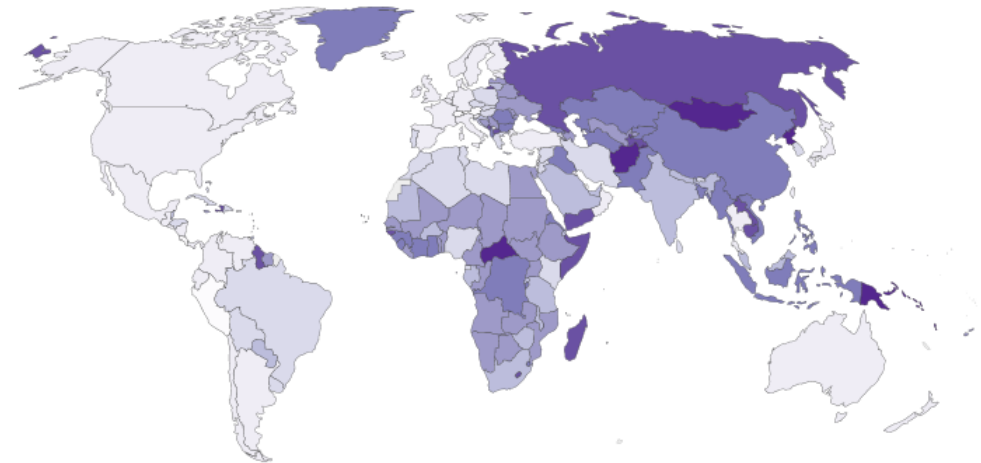


Source: IHME, Global Burden of Disease (GBD)

Stroke death rates (per 100,000), 2016

Age-standardized death rates from cerebrovascular diseases (stroke), measured as the number of deaths per 100,000 individuals. Age-standardization assumes a constant population age & structure to allow for comparisons between countries and with time without the effects of a changing age distribution within a population (e.g. aging).

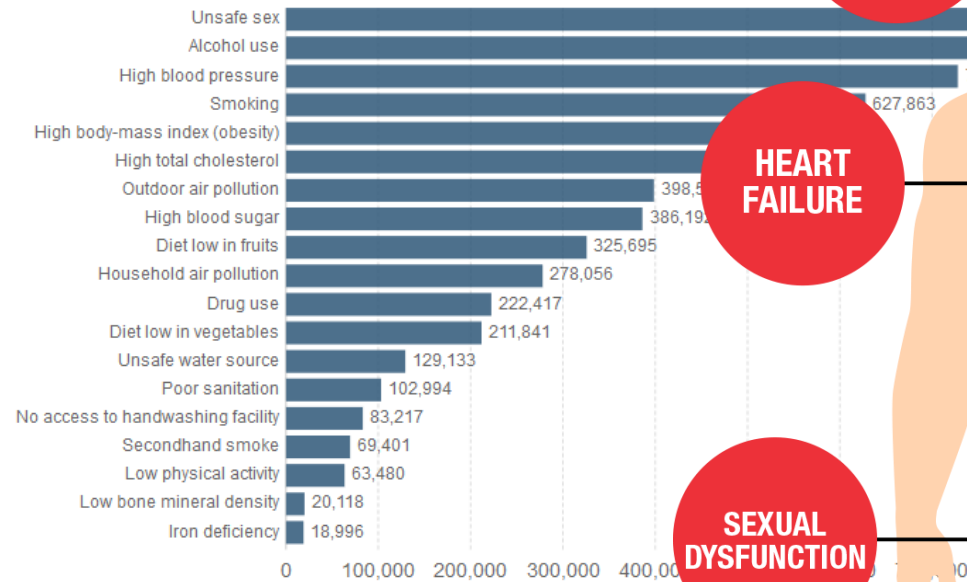
Our World
in Data



Source: IHME, Global Burden of Disease (GBD)

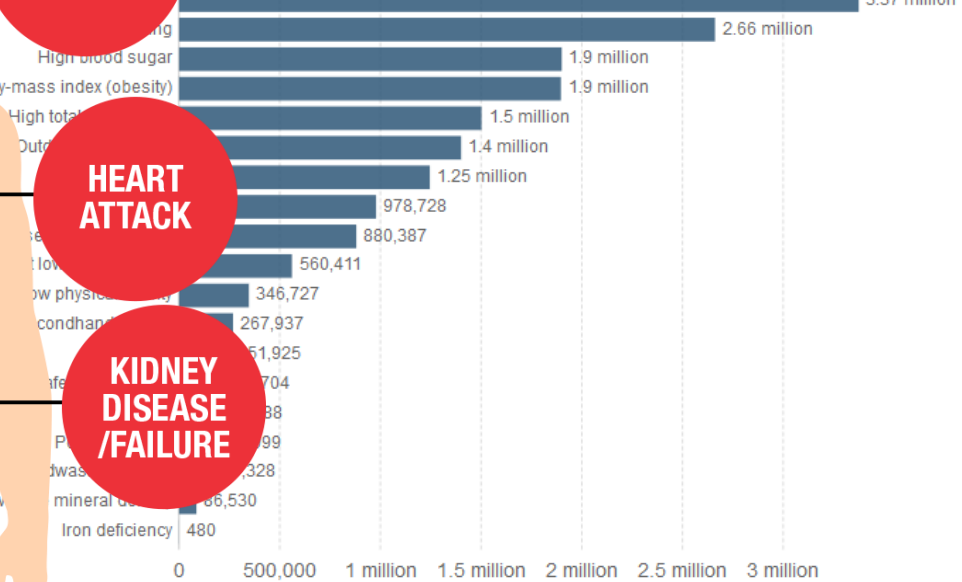
Hypertension - major modifiable risk factor for stroke

Number of deaths by risk factor aged 15-49, World, 2016
Total annual number of deaths by risk factor, measured across both sexes for adolescents and adults aged 15-49 years old.



Source: IHME, Global Burden of Disease (GBD)

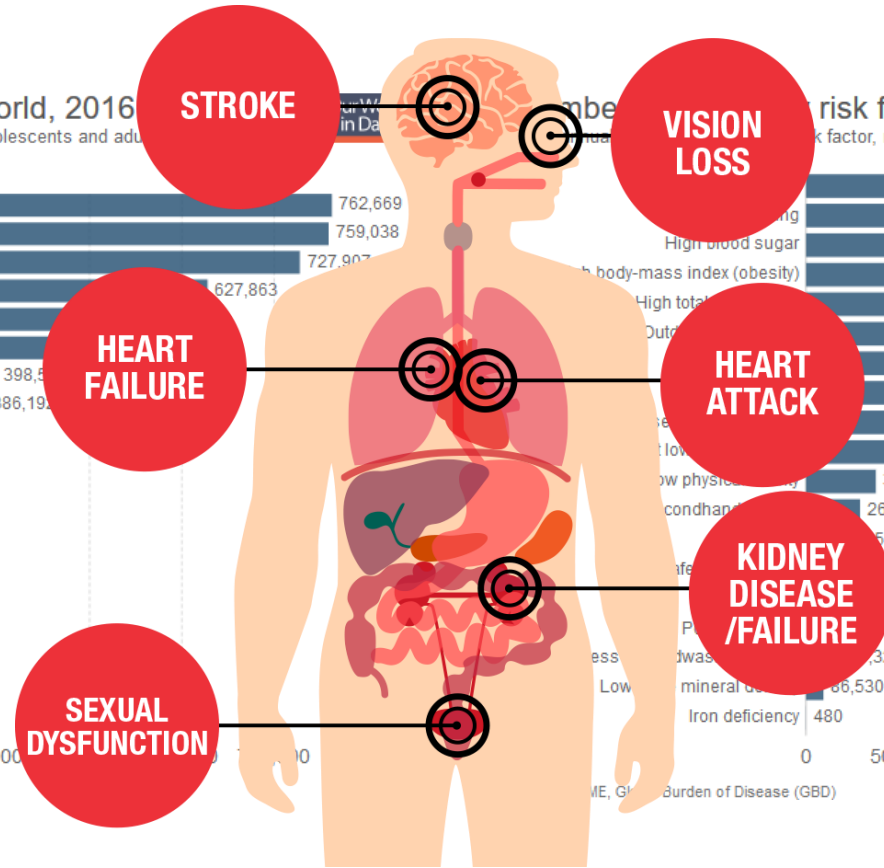
Number of deaths by risk factor aged 50-69, World, 2016
Total annual number of deaths by risk factor, measured across both sexes for adults aged 50-69 years old.



Source: IHME, Global Burden of Disease (GBD)

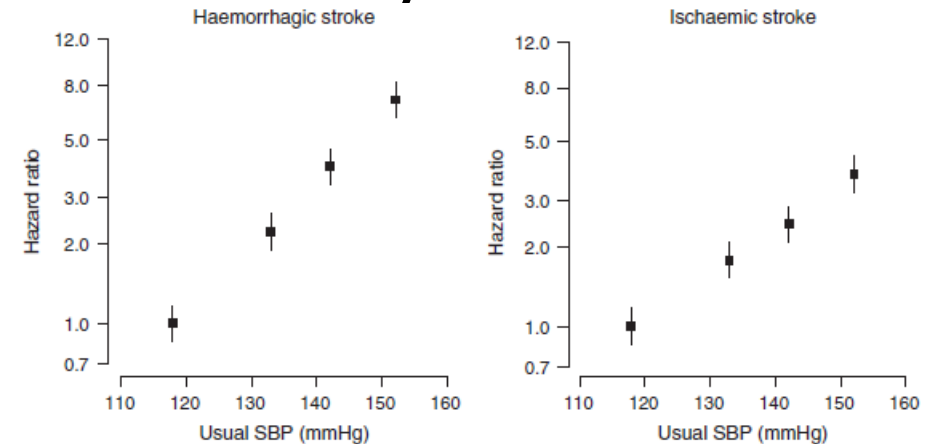
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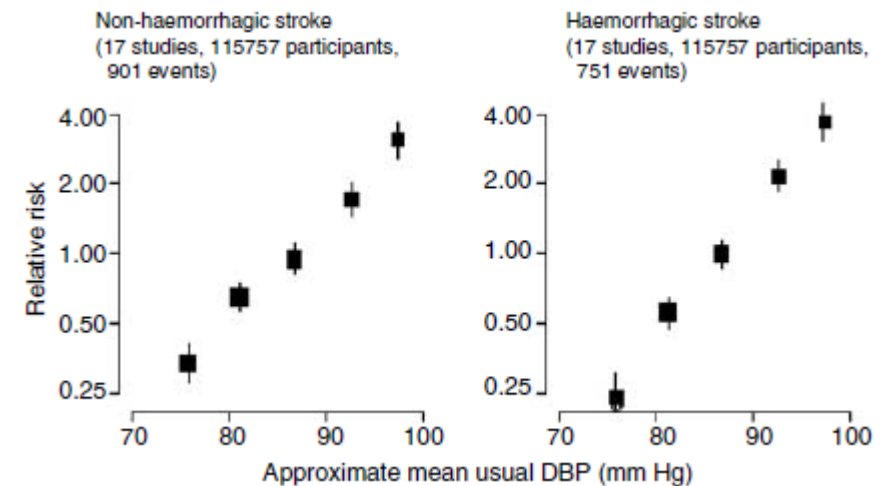


Uncontrolled blood pressure – why??

- \uparrow BP = \uparrow risk of CVD (including stroke) & mortality
 - BP control inadequate amongst Asians
 - Factors affecting BP control:
 - low awareness
 - under-treatment
 - intolerance
- Non-adherence



Park et al 2015 *Hypertens Res.*



Rasool et al 2005 *J Hum Hypertens.*

Treatment (non-)adherence

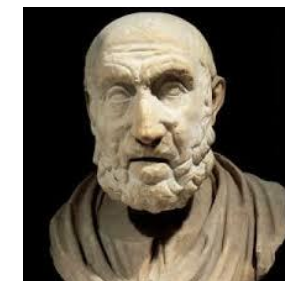
- Treatment non-adherence – major problem in the treatment of hypertension Gascón et al 2004 *Fam Pract.*
- Particularly, delineating true resistant HTN from pseudoresistant HTN
- Consequences of non-adherence:

Unnecessary hospitalization

Financial

Deaths

White-coat adherence



Treatment non-adherence was recorded since the time of Hippocrates (400 BC)

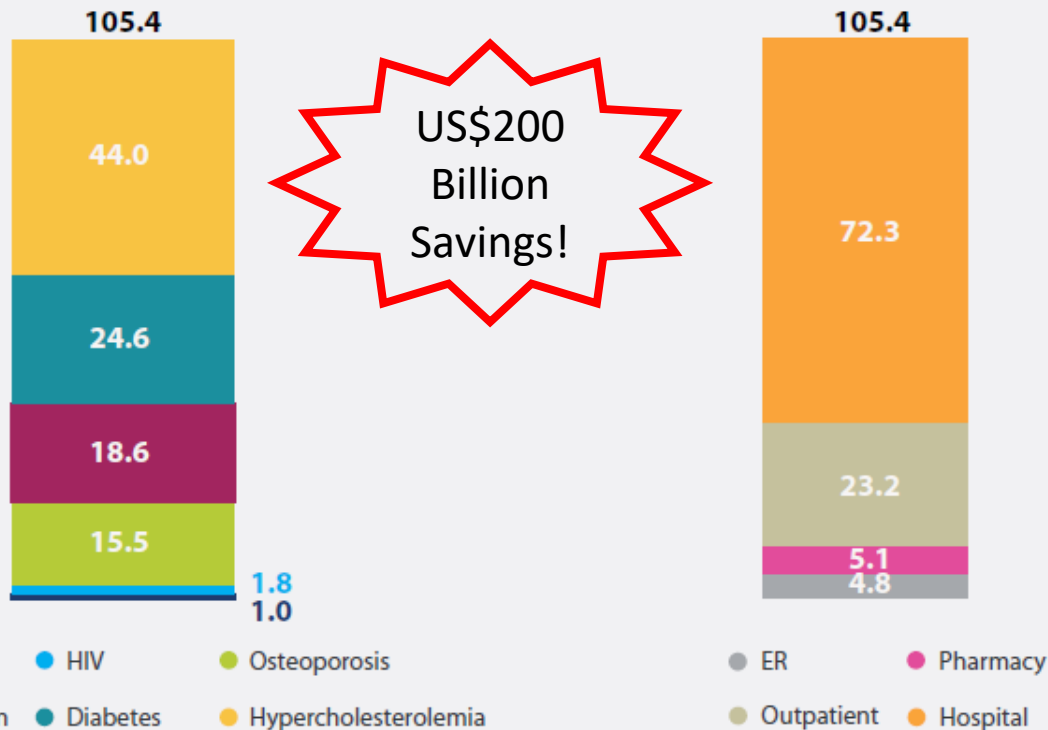
12/13/2018

Treatment (non-)adherence

Avoidable costs by disease, US\$Bn

2013

Avoidable costs by settings of care, US\$Bn



Source: Avoidable costs in healthcare study

Cost of Prescription Drug-Related Morbidity and Mortality

Jonathan H. Watanabe, PharmD, MS, PhD¹,
Terry McInnis, MD, MPH², and Jan D. Hirsch, PhD¹

2016

- Cost of non-optimized meds:
US\$528.4 billion per year
275,689 deaths per year

Annals of Pharmacotherapy
2018, Vol. 52(9) 829-837
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Adherence assessment

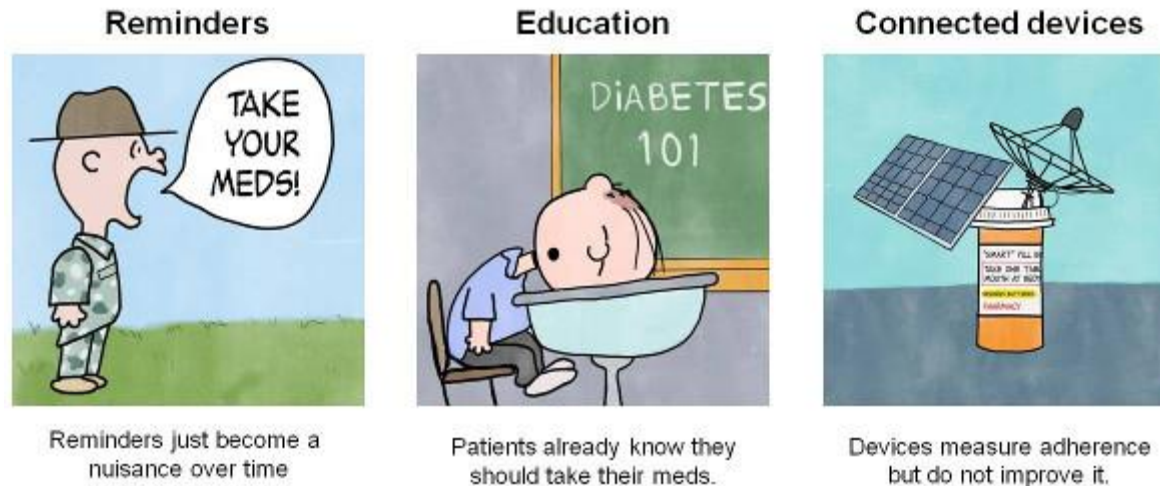
Subjective, inaccurate, over reporting adherence

- Patient interview
- Patient diary
- Adherence Q'aire (MAQ, BMQ, MARS, etc)
- Pill count
- Prescription record
- Electronic monitoring
- Analytical instrumentation & biomarkers



Objective

- To establish the use of LC-MS for antihypertensive treatment adherence assessment by doing a literature search in the electronic database PubMed

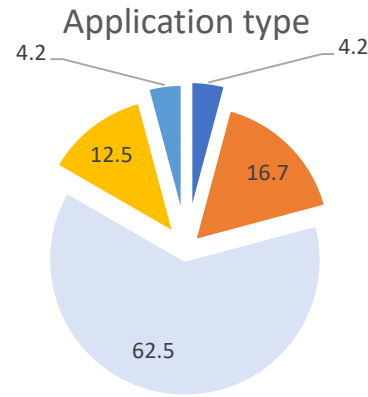
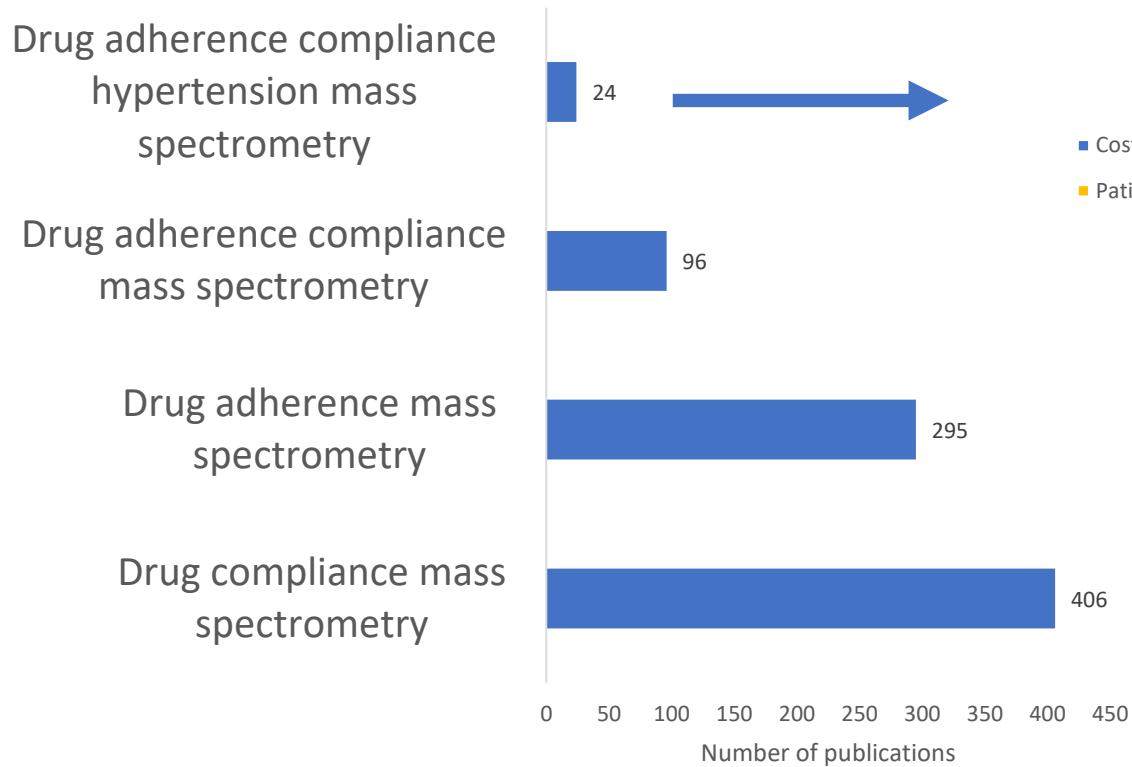


Methods

- Literature review in the electronic database PubMed was carried out.
- Publications between the year of 2011 – 2018 was evaluated
- Studies were identified by the term “drug adherence” and/or “treatment adherence” combined with studies identified by “hypertension” and “mass spectrometry”.
- Descriptive statistics were presented.

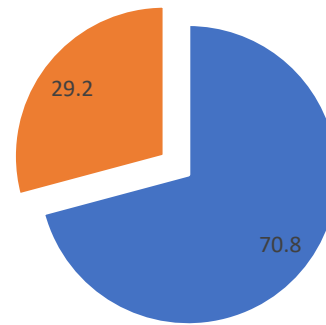
Results

Publications 2011 - 2018



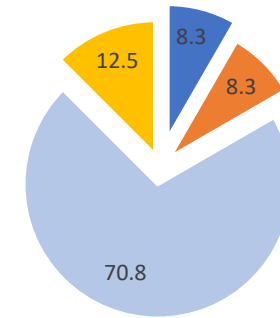
- Cost effectiveness
- Method development
- Treatment adherence
- Patient selection
- RDN effectiveness

Application Mode



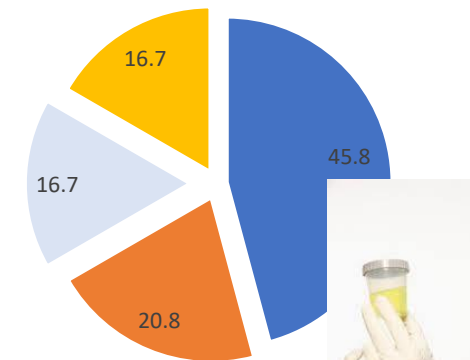
- Qualitative
- Quantitative

Clinical setting



- Clinical Trials
- Primary Care
- Tertiary Hospital
- University/RI

Sample matrix

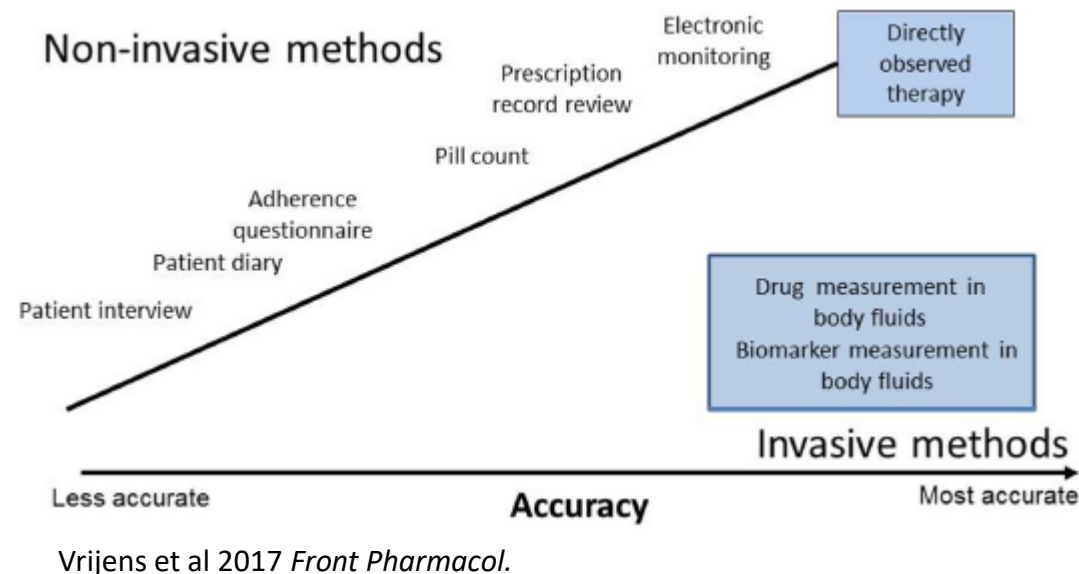


- Urine
- Plasma
- Serum
- Plasma & urine



Discussion

- LC-MSⁿ approach applicable in patient selection for advance treatment
de Jager et al 2018 Br J Clin Pharmacol
- Potentially applicable to a wider population with poor treatment adherence.
- However, further study is needed



Challenges

- White coat adherence?
- Individual therapeutic steady state differs
- Digital Medication Adherence Programs?
 - Works but can it be applied in rural settings?



DigitalMember
RAMADAN Q & A

DOES TAKING
MEDICATION
BREAK YOUR FAST?



Acknowledgement

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Dr Yeoh Leh Siang

Mr King Teck Long

... the RHS team

CRC SGH!

Thank You



References

- Avataneo et al 2018 Br J Clin Pharmacol.
Ceral et al 2011 Hypertens Res.
de Jager et al 2018 Br J Clin Pharmacol.
De Nicolò et al 2016 J Pharm Biomed Anal.
De Nicolò et al 2017 J Pharm Biomed Anal.
Ewen et al 2015 Clin Res Cardiol.
Ewen et al 2015 J Hypertens.
Florczak et al 2015 Pol Arch Med Wewn.
Gascón et al 2004 Fam Pract.
Gupta et al 2017a Hypertension.
Gupta et al 2017b Hypertension.
Hamdidouche et al 2017 J Hypertens.
Helfer et al 2015 Anal Chim Acta.
Jones et al 2017 S Afr Med J.
Jung et al 2013 J Hypertens.
Lawson et al 2016 J Anal Toxicol.
McNaughton et al 2017 Hypertension.
Patel et al 2016 J Hum Hypertens.
Petit et al 2018 Blood Press.
Pucci & Martin 2017 J Hum Hypertens.
Sandbaumhüter et al 2018 Ann Cardiol Angeiol (Paris).
Schmieder et al 2016 J Am Heart Assoc.
Tomaszewski et al 2014 Heart.
van der Nagel et al 2017 J Chromatogr B Analyt Technol Biomed Life Sci.
van Schoonhoven et al 2018 Hypertension
Vrijens et al 2017 Front Pharmacol
Watanabe et al 2018 Ann Pharmacother.