LONDON
MELBOURNE
MINNEAPOLIS
MUMBAI
MUNICH
PARIS
SANTIAGO
SÃO PAOLO
SEOUL
SHANGHAI
SINGAPORE
STOCKHOLM
TOKYO
TORONTO
VALENCIA
WARSAW

ISPOR Medical Device SPOTLIGHT Session

Hull Associates LLC
MARKET ACCESS

November
2019

BOSTON
BRUSSELS
BOGOTA
BUENOS AIRES
CHICAGO
ISTANBUL
JERUSALEM

Our panel today covers a broad range of industry, academic and public HTA perspectives

Rachele Busca, PharmD, MSc, MBA

W.L. GORE, Verona, Italy

Lindsay Bockstedt, PhD

Medtronic, Inc., Minneapolis, MN, USA

Hedi Schelleman, PhD

The National Healthcare Institute (ZIN), Diemen, Netherlands

Prof. Giorgio Lorenzo Colombo

Center of Pharmaceuticals Economics and Medical Technologies Evaluation, University of Pavia

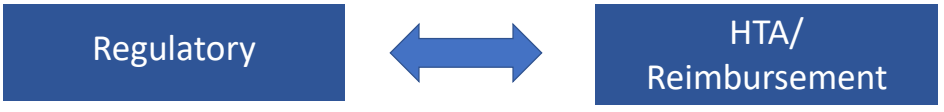
Rossana Alessandrello, MSc

Agency for Health Quality and Assessment of Catalonia (AQuAS), Barcelona, Spain

Themes we will cover today

- Innovator's perspective: What are the challenges in designing evidence strategies that satisfy the multiple evaluators in Europe?
- Evaluators perspective: What are the key hurdles and how is the evaluation of devices evolving or changing?
- Procurement perspective: Is procurement, rather than reimbursement, the primary arena to understand device "value"?

What is the center of the debate over device evidence?



- Regulatory and HTA evaluation processes have different objectives and different perspectives
- Regulatory: Absolute risk and clinical efficacy
- HTA and Reimbursement: Relative "value" and real world effectiveness and safety
- It is common for device evidence to reflect regulatory demands primarily, without addressing those of HTA bodies and payers

Most disconnects in medical device evidence reviews….

- Evolving and diversity of surgical technique and clinical results over time
- Lack of randomization
- Sample sizes
- Duration of follow-up
- Does a “gold standard” exist? Absence of clinical evidence on the standard of care
- Issue of manufacturer bias vs. independent, but improper technique
- Clarity on the mechanism of action

- Altogether, medical devices can present very diverse scenarios for evidence … how do we understand and define “value” for medical technology in today’s world?

Will MDR increase available evidence for HTAs?

- What should the HEOR community understand?

- Key changes or concerns in:
  - Clinical Evaluation ☺
  - Vigilance and post-market surveillance ☺
  - Transparency, UDI and EU database 😐
  - Reclassification of legacy devices 😐
  - Notified Body Capacity ☹

Clinical Evaluation: greater emphasis on clinical evidence in proportion to risk

IN CONCEPT

Additional Clinical Evidence	➔Greater focus on the need for clinical evidence and clinical evaluation, proportionate with the risk (MDR Annex XIV, Part A).
Peer Reviewed Literature	➔Reliance on the scientific literature to demonstrate equivalence to be more tightly regulated; clinical evaluations will be more closely aligned with clinical trials associated with drugs.

KEY IMPLICATIONS

- **More rigorous studies, may help support health economic analyses, true comparative economic evidence.**

SOURCE: THE NEW EU MEDICAL DEVICE REGULATION (MDR): Practical Implications for Manufacturers Peter Rose, Jens Weirsoe, and Mike Wolf June 2017. MAETRICS.

Will MDR vigilance and post-market surveillance enable RWE for health economics?

IN CONCEPT

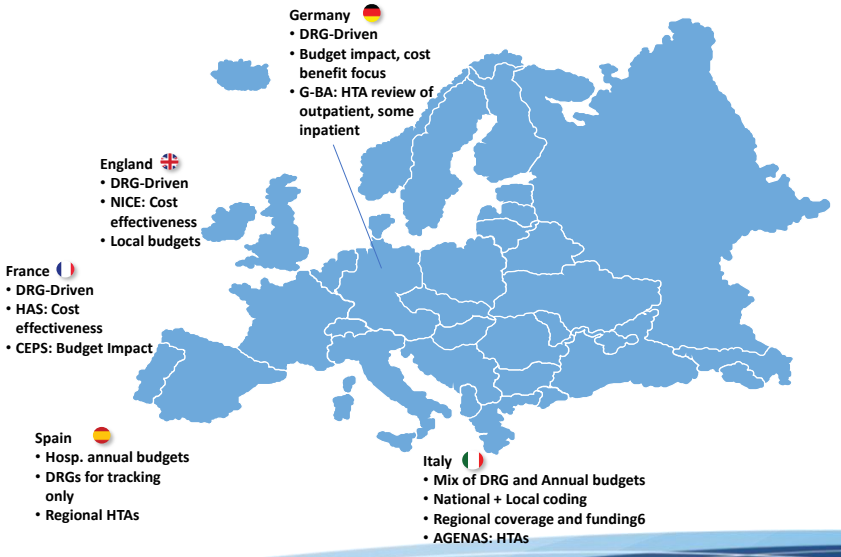
Collection of post-market data	➔ Part of on-going assessment of potential safety risks.
Post Market Clinical Follow up (PMCF)	➔ Continuous process to constantly update the clinical evaluation (MDR Annex XIV, Part B).
Tighter reporting timeframes	➔ Changed from 30 days to 15 days for serious incidents
New electronic vigilance and Periodic Safety Update Reports	➔ Required for all devices (MDR Article 86)

KEY IMPLICATIONS

- **These requirements may coincide with Payer related requirements for coverage with evidence development (Example: France post-inscription studies)**

SOURCE: THE NEW EU MEDICAL DEVICE REGULATION (MDR): Practical Implications for Manufacturers Peter Rose, Jens Weirsoe, and Mike Wolf June 2017. MAETRICS.

European Reimbursement Issues



The status quo in HTA is fragmented, redundant and burdensome.

- Across EU Member States, HTA is used to inform different things.
- HTA approaches also differ:
  - methodologies
  - points-in-time
  - acceptance of types of data
- HTA approaches reflect a very localized market access model, oriented towards local healthcare delivery, and local funding decisions
- Ability for cooperation in HTA has been fairly limited.
  - *The timing of HTA reviews differs for the same technology across different EU markets.*

NEW: EC proposal for joint European HTAs

- **January 2018, European Commission (EC) proposed required joint/centralized clinical assessments for HTAs among member countries.**
- **Individual EU countries would still be responsible for the non-clinical aspects of HTA and ultimately determining pricing and reimbursement.**

Common HTA tools, methodologies and procedures in four main areas:

- **Joint clinical assessments**, focusing on the most innovative health technologies with the most potential impact for patients;
- **Joint scientific consultations**, whereby developers can seek advice from HTA authorities;
- **Identification of emerging health technologies** to identify promising technologies early; and
- **Continuing voluntary cooperation** in other areas.

EUnetHTA

81 partners consisting of national, regional and non-for-profit agencies that produce or contribute to HTA

Project Coordinator: Dutch National Health Care Institute (ZIN)

Early dialogues program also allows companies to understand future HTA evidence requirements.

What is the way forward?

(+)	(-)
Possible increases in comparative studies for higher risk devices in Europe will better support HEOR	EU approvals will demand more evidence, but that does not mean alignment with FDA in the USA!
Surveillance and post market study requirements also may drive opportunity for HE studies	Use of RWE seems unlikely to replace demands for controlled, comparative evidence
Overall, RWE may become more available and accepted, satisfying demands of both payers and regulators	The CE mark process may enable HE studies but may also continue to be out of sink with payer requirements

OPTIMIZING AN EU EVIDENCE STRATEGY FOR A DEVICE LAUNCH

Rachele Busca

November 5th, 2019

Together, improving life

Clinical evidence serve different stakeholders

Stakeholders	Catalyzer of evidence generation	Focus of evidence
Regulators typically single trans-national bodies with similar focus	• Market authorisation	Safety, efficacy, technical requirements, in defined indication
Payers: range of national, regional and local payers by market with different foci	• Appraisal to get access to public funding (coverage decision) at population level (HTA) • Unlock money using local payment schemes (Payment) and maintain those • The presence of health plans that offer coverage and payment for devices, within clinical trials that	Disease, epidemiology, unmet medical needs, burden of disease, safety, Efficacy, Comparative effectiveness, costs-effectiveness, Budget impact
Conventional HTA /unified approach	• Assessment of clinical and economic evidence to provide recommendations to decision makers	Disease, epidemiology, unmet medical needs, burden of disease Safety, Efficacy, Comparative safety and effectiveness, (costs-effectiveness), patient utilities and preferences
Scientific Societies and HCPs	• Converts the abstract exercise of reading and appraising the literature into the pragmatic process of using the literature to benefit individual patients (EBM)	Disease, epidemiology, unmet medical needs, Safety, Efficacy, Comparative safety and effectiveness, medical practice/clinical medicine
Purchasing Organisation or procurement authorities	• Determining whether to grant access or not and the amount of budget to allocate	Efficiency, service solution, patient flow optimisation, care pathways, quality of care, attractiveness, cost-saving

©2019 W. L. Gore & Associates, Inc.

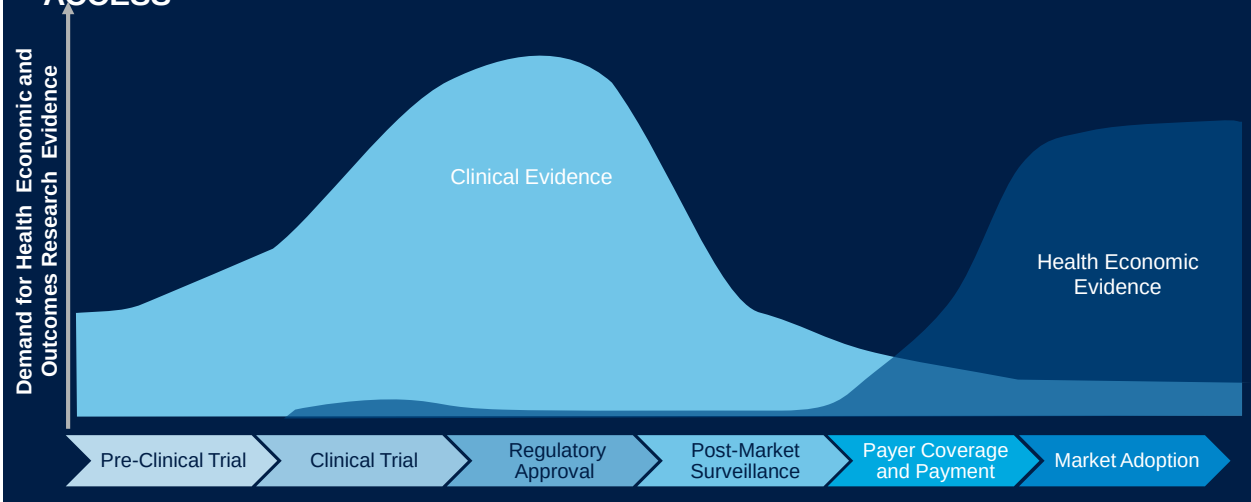
November 5, 2019

THE EVOLVING DEMANDS FOR MEDICAL DEVICE EVIDENCE DEVELOPMENT: WHAT THE FUTURE HOLDS

PRESENTED BY
LINDSAY BOCKSTEDT, PH.D.
VP, HEALTH ECONOMICS AND OUTCOMES RESEARCH
MEDTRONIC, INC.

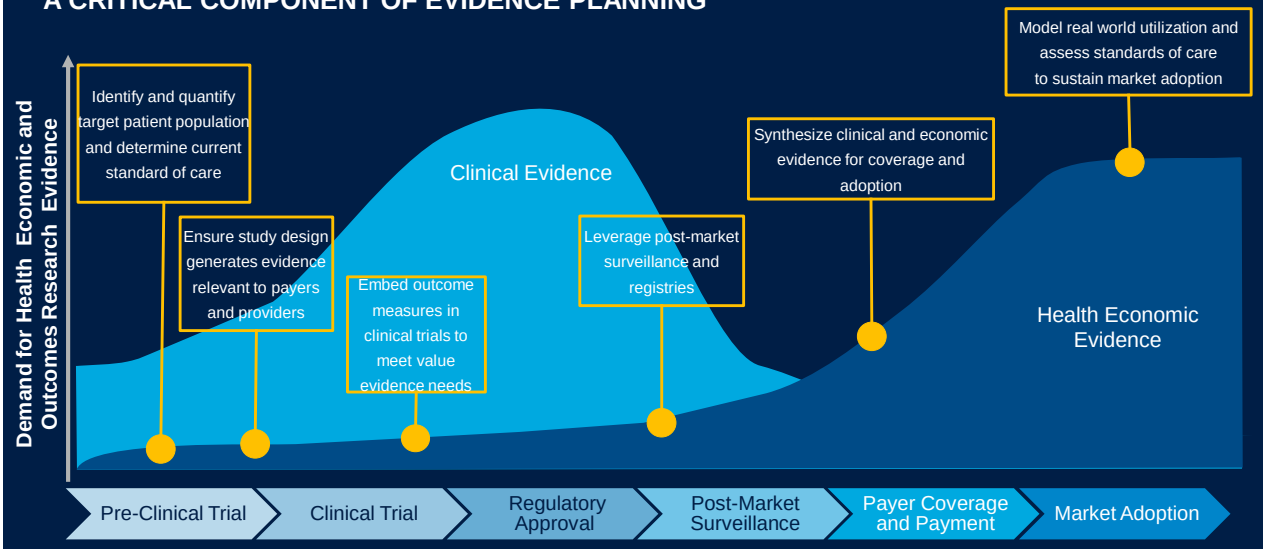
Medtronic
Further, Together

TRADITIONALLY HEALTH ECONOMICS FOCUSED ON GENERATING POST-MARKET EVIDENCE TO SECURE AND EXPAND COVERAGE AND MARKET ACCESS



Medtronic

AS DEMAND FOR EVIDENCE INCREASES, PAYER, HTA, AND PURCHASER NEEDS BECOME A CRITICAL COMPONENT OF EVIDENCE PLANNING



Medtronic

CONVERGENCE OF GLOBAL EVIDENCE REQUIREMENTS ENABLES A MORE HARMONIZED APPROACH TO EVIDENCE DEVELOPMENT

- US payer and EMEA HTA evidence needs are converging
- Country consultations throughout product development feed in local market evidence needs
  - What is the appropriate study population?
  - What is the relevant standard of care?
  - What are the specific evidence requirements for coverage and adoption (e.g., endpoints, CEA, budget impact, etc.)?
- Global business units develop an informed harmonized evidence strategy

Medtronic

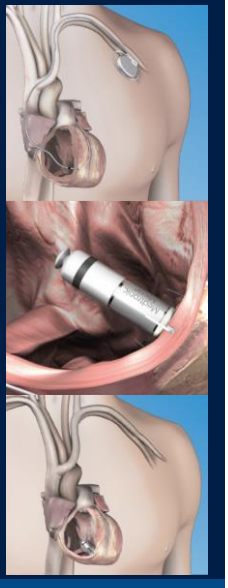
EXTERNAL TRENDS ARE ENABLING ACCESS TO DATA NEEDED TO GENERATE VALUE EVIDENCE BUT ALSO INCREASING OVERSIGHT BY REGULATORY BODIES

Changing Payment Paradigms Emphasizing Value and Outcomes	Increased Access, Demand, and Acceptance of Real World Data, Real World Evidence, Linking Capabilities, and Technology	Government Investment in Advancing Science and Applications of RWE and RWD	Heightened Regulatory Oversight on Scientific Rigor and Patient Privacy

Medtronic

MICRA CED STUDY: A NOVEL APPROACH TO COVERAGE WITH EVIDENCE DEVELOPMENT (CED) FOR US MEDICARE AND MEDTRONIC

- Medicare's leadless pacemaker National Coverage Determination (NCD) is one of the first NCDs to call for CED through prospective longitudinal studies using RWE
- Study objectives designed to address evidence questions and gaps identified by the Centers for Medicare and Medicaid Services (CMS) and includes a comparative effectiveness analysis
- Micra CED Study is conducted through real world data (RWD): Medicare administrative claims data linked to Medtronic device registration data (DART) to identify patients and measure clinical outcomes
- This approach to CED is enabling broad access to breakthrough technology while simultaneously generating evidence for CMS



Medtronic

Zorginstituut Nederland

Netherlands: what the future holds

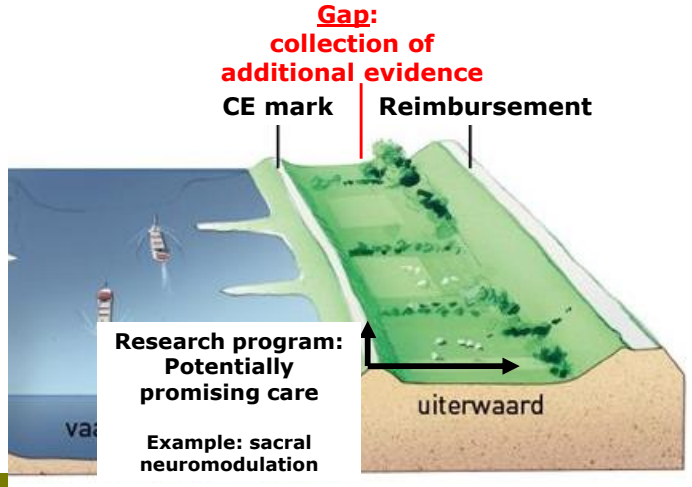
Hedi Schelleman, PhD
Advisor and Programme Officer
Zorginstituut Nederland

| Van goede zorg verzekerd |

Open (reimbursement) system

- Payer => ZIN
- Technique (≠ individual MD)
- Law: versus standard of care
  - Preferably RCT => CED

The Netherlands: now and future?



Other developments:

- Pilots: CEA
  - Goverment: price negotiations?
- Horizon Scanning
- EUDAMED => indication?
  - Improves implementation EUnetHTA assessments?
- More funding of research
  - EU guidelines for state aid

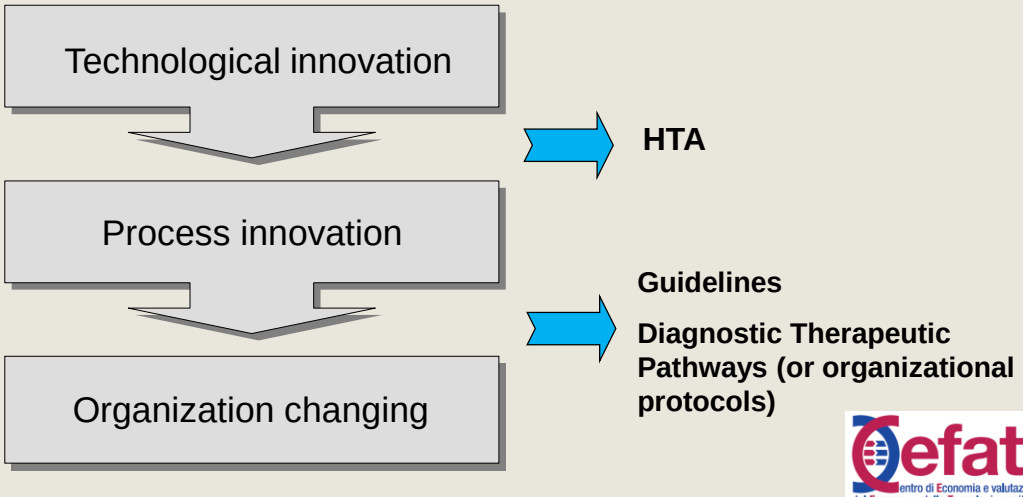
Regional Device Evaluation in an interconnected Europe

Prof. Giorgio Lorenzo Colombo
CEFAT - *Center of Pharmaceuticals Economics and Medical Technologies Evaluation*
Department of Drug Sciences, University of Pavia, ITALY
www.cefat.unipv.it

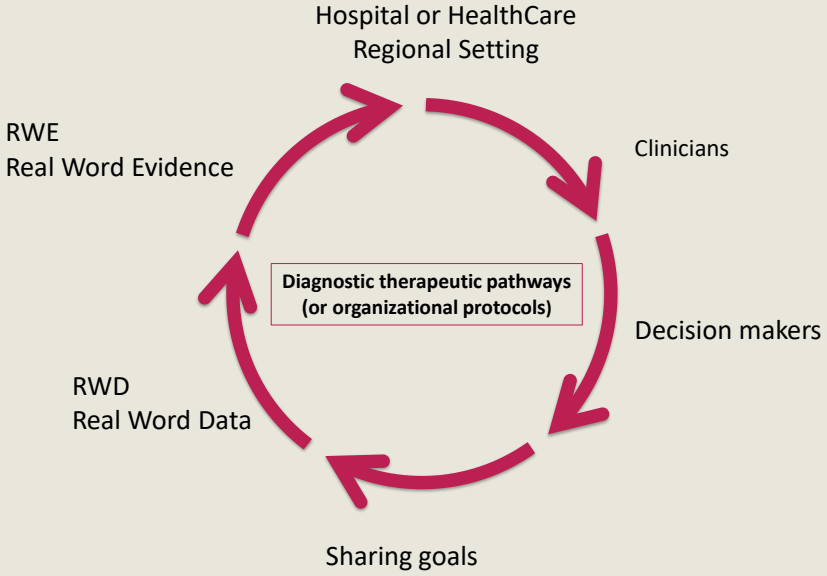
Outline of the presentation

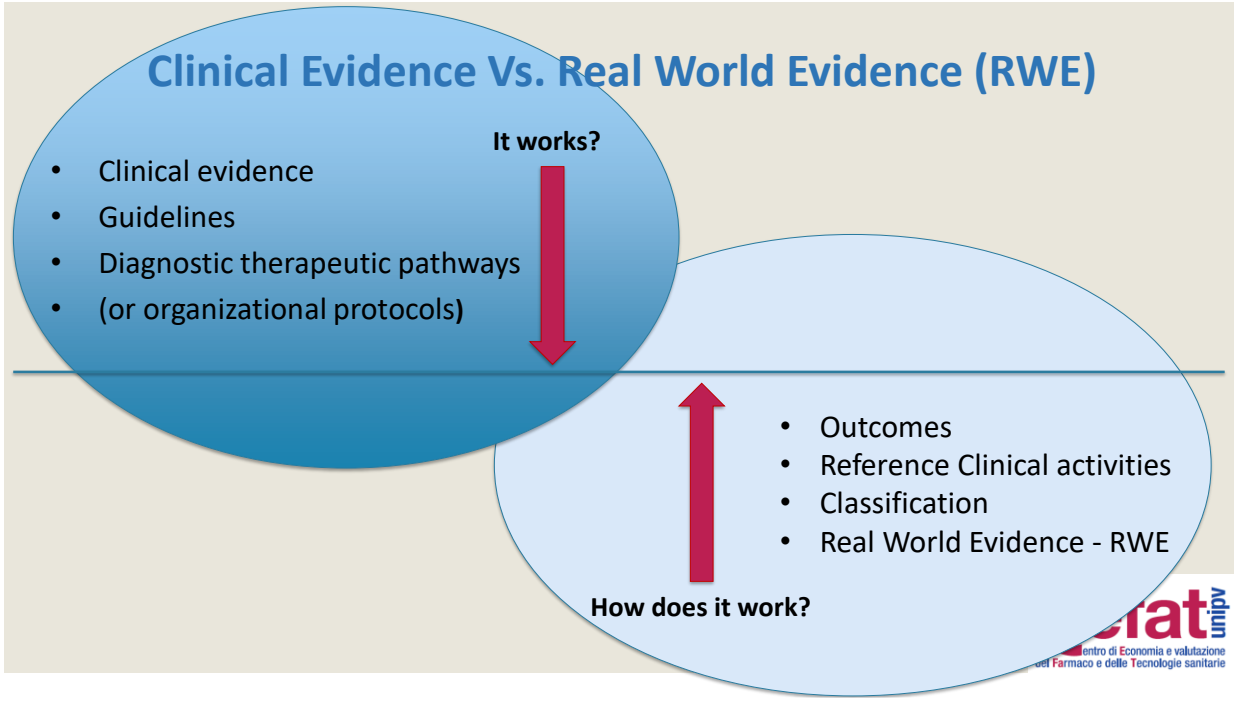
- Relationship between technological innovation, process innovation and organization changing
- Clinical Evidence vs. Real World Evidence (RWE)
  - Some cases studies
  - Breaking the addiction to technology adoption
- Discussion

Relationship between technological innovation, process innovation and organization changing



The circle for access (at national or regional level)





High-sensitivity cardiac troponin I at presentation in patients with suspected acute coronary syndrome: a cohort study

Anoop S V Shah, Atul Anand*, Yader Sandoval, Kuan Ken Lee, Stephen W Smith, Philip D Adamson, Andrew R Chapman, Timothy Langdon, Dennis Sandeman, Amar Vaswani, Fiona E Strachan, Amy Ferry, Alexandra G Stirzaker, Alan Reid, Alasdair J Gray, Paul O Collinson, David A McAllister, Fred S Apple, David E Newby, Nicholas L Mills; on behalf of the High-STEACS investigators†*

Summary

Background Suspected acute coronary syndrome is the commonest reason for emergency admission to hospital and is a large burden on health-care resources. Strategies to identify low-risk patients suitable for immediate discharge would have major benefits.

Methods We did a prospective cohort study of 6304 consecutively enrolled patients with suspected acute coronary syndrome presenting to four secondary and tertiary care hospitals in Scotland. We measured plasma troponin concentrations at presentation using a high-sensitivity cardiac troponin I assay. In derivation and validation cohorts, we evaluated the negative predictive value of a range of troponin concentrations for the primary outcome of index myocardial infarction, or subsequent myocardial infarction or cardiac death at 30 days. This trial is registered with ClinicalTrials.gov (number NCT01852123).

Findings 782 (16%) of 4870 patients in the derivation cohort had index myocardial infarction, with a further 32 (1%) re-presenting with myocardial infarction and 75 (2%) cardiac deaths at 30 days. In patients without myocardial infarction at presentation, troponin concentrations were less than 5 ng/L in 2311 (61%) of 3799 patients, with a negative predictive value of 99·6% (95% CI 99·3–99·8) for the primary outcome. The negative predictive value was consistent across groups stratified by age, sex, risk factors, and previous cardiovascular disease. In two independent validation cohorts, troponin concentrations were less than 5 ng/L in 594 (56%) of 1061 patients, with an overall negative predictive value of 99·4% (98·8–99·9). At 1 year, these patients had a lower risk of myocardial infarction and cardiac death than did those with a troponin concentration of 5 ng/L or more (0·6% *vs* 3·3%; adjusted hazard ratio 0·41, 95% CI 0·21–0·80; p<0·0001).

Interpretation Low plasma troponin concentrations identify two-thirds of patients at very low risk of cardiac events who could be discharged from hospital. Implementation of this approach could substantially reduce hospital admissions and have major benefits for both patients and health-care providers.

www.thelancet.com Published online October 8, 2015 http://dx.doi.org/10.1016/S0140-6736(15)00391-8

efat unipv
Centro di Economia e valutazione del Farmaco e delle Tecnologie sanitarie

Breaking the addiction to technology adoption (1)

Bryan et al,Health Econ. 23: 379–383 (2014)

- A major driver of cost growth in health care is the rapid increase in the utilization of existing technology and
  - not simply the adoption of new technology.
- Health economists and their health technology assessment colleagues have become obsessed by technology adoption questions and have largely ignored 'technology management' questions.
- Technology management would include the life-cycle assessment of technologies in use, to assess their real-world performance; and monitoring of technology indication creep.

Breaking the addiction to technology adoption (2)

Bryan et al,Health Econ. 23: 379–383 (2014)

- A rebalancing of focus might serve to encourage a more self-critical and learning culture amongst those involved in technology evaluation analysis.
- Further, health economists and health technology assessment analysts could make a more significant contribution to
  - system efficiency through rebalancing their efforts away from technology adoption questions towards technology management issues

According to Dr. H. James Harrington, a pioneer in process improvement methodology:

"…measurement is the first step that leads to control and eventually to improvement."

Harrington HJ, Hoffherr GD, Reid RP. Area activity analysis: aligning work activities and measurements to enhance business performance. New York, NY: McGraw-Hill, 1999.

Center of Pharmaceuticals Economics and Medical Technologies Evaluation

www.cefat.unipv.it

«…Real Word Data to make health»

ISPOR Europe 2019 2-6 November 2019 Copenhagen, Denmark

Understanding device "value" in procurement

SPOTLIGHT SESSION 3
THE EVOLVING DEMANDS FOR MEDICAL DEVICE EVIDENCE DEVELOPMENT-WHAT THE FUTURE HOLDS

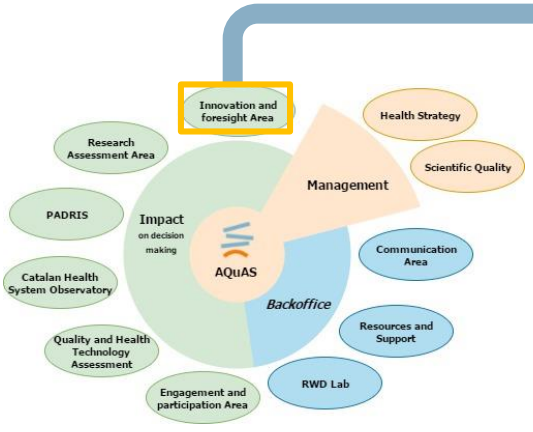
Rossana Alessandrello
Value Based Procurement Director
AQuAS

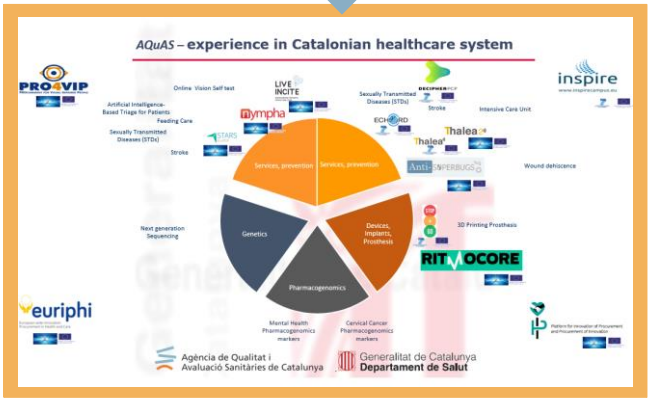
Agència de Qualitat i Avaluació Sanitàries de Catalunya
Generalitat de Catalunya Departament de Salut

AQuAS Agència de Qualitat i Avaluació Sanitàries de Catalunya
Agency for health quality and assessment of Catalonia

Mission

Generating **relevant knowledge**
through the **evaluation and analysis of data** for decision-making
in order to contribute to the **improvement of the health of citizens**
and the **sustainability of the health system** of Catalonia

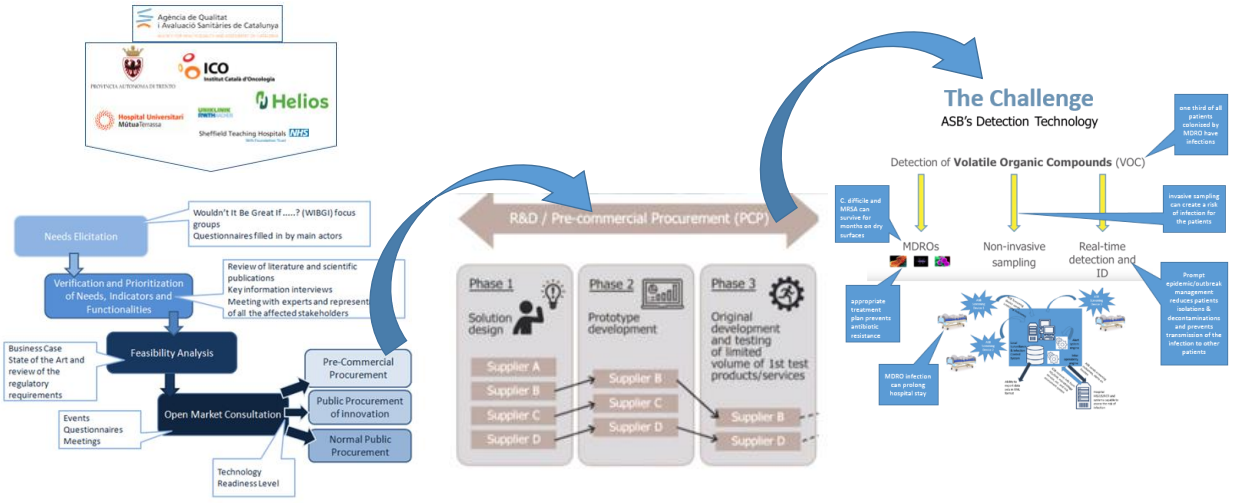




Agència de Qualitat i Avaluació Sanitàries de Catalunya
Generalitat de Catalunya Departament de Salut

Anti-SUPERBUGS

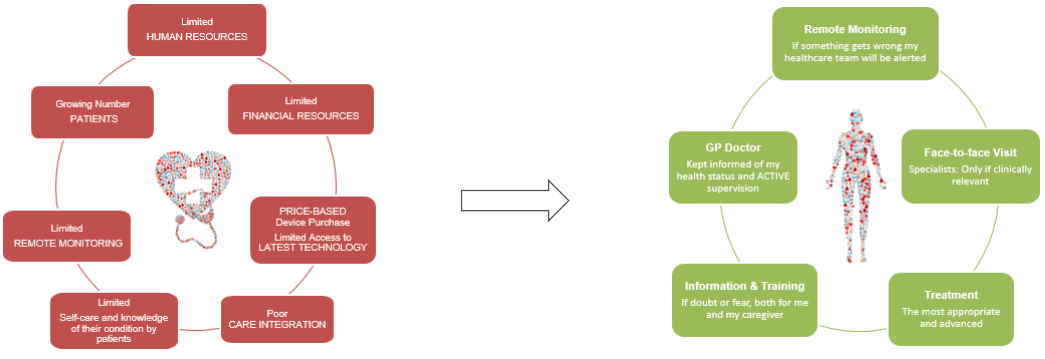
Pre-Commercial Procurement



Co-funded by the Horizon 2020 Framework Programme of the European Union

RITMOCORE

Innovation for a healthy heartbeat



From Hospital centred to Patient-centred care

Co-funded by the European Union

Different stages of the same strategy

Hospital Sant Pau – Implantable Defibrillators

- Individual
- 3% outputs/outcomes dependents (18 indicators)
- Activity variation 10%
- Remote Monitoring and Support Centre
- Stock management
- Technical support
- Training
- Complication management (explantations)
- 12 M€

Hospital Sant Pau, Hospital Bellvitge, Mutua de Terrassa, Liverpool - Pacemakers

- Buyers group
- 5% outputs/outcomes dependents
- Activity variation 10%
- Coordinated care (Hospitals-GPs)
- Remote Monitoring and Support Centre
- Stock management
- Technical support
- Training
- Complication management (explantations)
- 20M€

Hospital Clinic Aortic stenosis

- Individual
- Aortic stenosis
  - TAVI
  - Open surgery
  - Pharmacologic treatment
- % outcomes ?
- Indicators ?
- No remote monitoring
- Ex-ante services:
  - Patient surgical pre-habilitation
  - 3D Simulation
  - Target patient identification system

Agència de Qualitat i Avaluació Sanitàries de Catalunya

Generalitat de Catalunya **Departament de Salut**

Rossana Alessandrello
ralessandrello@gencat.cat

Catsalut: Public Procurement of Innovation Program
18 public procurements of innovation – 30M Euros

30M Euros in Public Procurement of Innovation project to modernize the healthcare services

18 projects granted with the 50% of their budget to improve the quality and the efficiency of the healthcare service

Agència de Qualitat i Avaluació Sanitàries de Catalunya

Generalitat de Catalunya **Departament de Salut**

Rossana Alessandrello
ralessandrello@gencat.cat

Innovation adoption as instrument to bring value to the health system

Demand-driven Innovation

- identification of needs,
- creation of the 'Business case'
- Study of the SoA and Open Market Consultation
- Value Based Public Procurement of Innovation

Supply side innovation
& all the actors of the Department of Health developing innovative projects

Rossana Alessandrello
ralessandrello@gencat.cat

Innovation adoption as instrument to bring value to the health system

Value:

satisfaction of needs currently not satisfied

to improve

the **health of citizens**

and the **sustainability of the health system**

Rossana Alessandrello
ralessandrello@gencat.cat

Value based procurement key elements

Basic ingredients

1. Clear definition of **needs currently unmet**
2. Clear definition of the **'business case'**
3. Evaluation of the **replicability** of the intervention at **systemic** level
4. Strategic and economic alignment between the **buyer(s)** and the **insurer**
5. Strategic and economic alignment between the **buyer(s)** and the **industry**
6. **Horizon scanning**
7. **Contract monitoring** (including PREMs and PROMs)

Enablers

1. **Prospective analysis** of future needs not yet met, **innovation experiences in health management** and changes in the **regulatory** field
2. **Community of practices** (including international buyer network)
3. **Financing schemes**

Rossana Alessandrello
ralessandrello@gencat.cat