Health Technology Assessment: Methods, Tools, and Specific Criteria Applicable to Innovative Medical Devices

How to launch an innovative medical device on the European market?

GERONTE Project
Leuven March 2024

Dr. Nicolas MARTELLI - PharmD, PhD

Groupe de Recherche et d'Accueil en Droit et Économie de la Santé (GRADES)

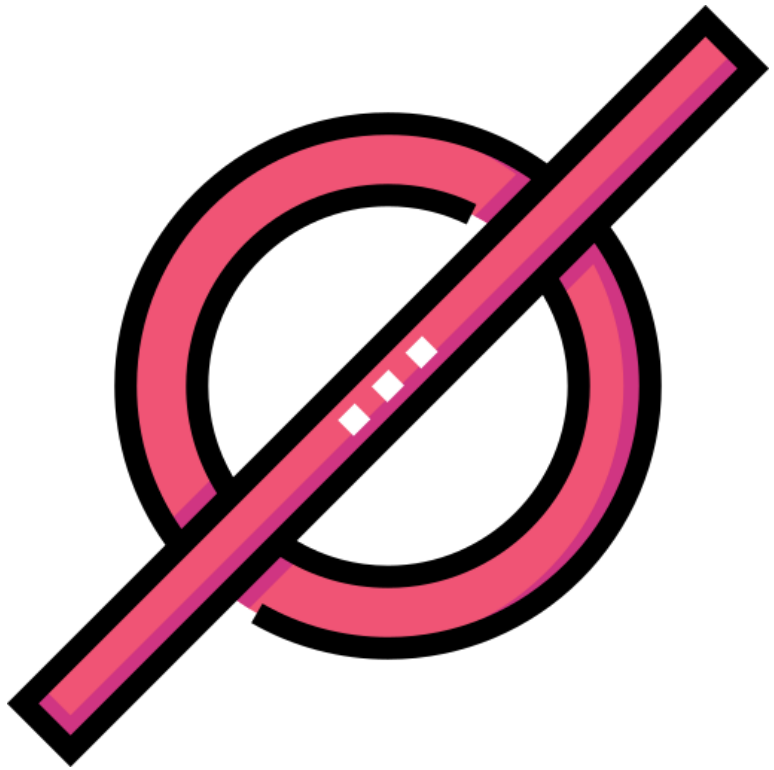
Faculty of Pharmacy - Paris-Saclay University

Georges Pompidou European Hospital – Pharmacy Department

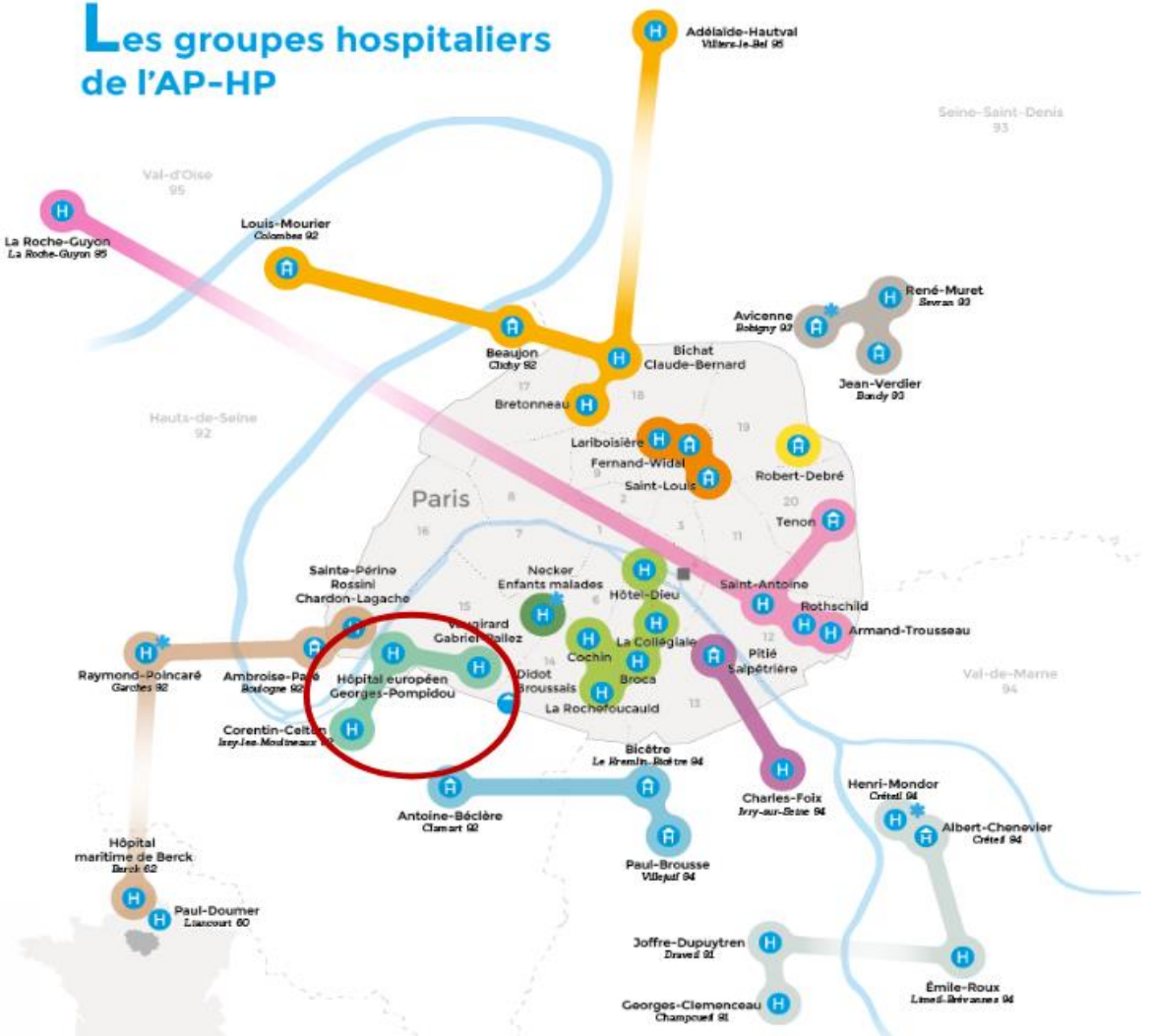
Assistance Publique – Hôpitaux de Paris (AP-HP)

Conflict of interest

Nothing to disclose!



Hôpital européen Georges-Pompidou AP-HP



726 beds

48 medical departments

= Research Group in Health Law and Economics of the faculty of Pharmacy

- 13,000 students
- 2,100 doctoral candidates
- 1,700 teaching researchers

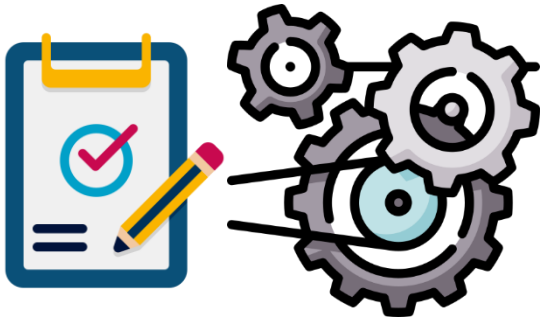
ACADEMIC RANKING OF WORLD UNIVERSITIES SINCE 2003

15th	University in the world
1st	in Mathematics
9th	in Physics
11th	in Agriculture
20th	in Clinical Medicine

2023

Topics we work on!

MEDICAL DEVICES (MDs)



Market access and Health technology assessment (HTA)

1

Evaluation Methods for Non-Clinical Criteria

2

Unique evaluation aspects of disruptive MDs

3

QUIZ

Market Access for innovative MDs: a multi-layered problem?

European market

Regulatory

National market

HTA

Reimbursement/ coverage

Local/Hospital market

HBHTA

Purchase

Market Access for innovative MDs: a multi-layered problem?

European market → Regulatory

National market → HTA → Reimbursement/ coverage

Local/Hospital market → HBHTA → Purchase

Challenge

Bringing medical technology innovations to patients in the EU has become increasingly long and difficult.

Ever-stricter EU regulations.

Lack of harmonised approaches in Member States for facilitating early evidence generations.

Uncertainty for innovators.

Decline in attractiveness of Europe.

Opportunity

What is an early feasibility study (EFS)?

A **limited clinical investigation** of a device early in development

Before the device design has been finalized, for a specific indication

Information obtained from an EFS can guide device modifications = **iterative process**

Harmonised approach to Early Feasibility Studies for medical devices in the European Union (HEU-EFS)

Disclaimer

Funded by the European Union, the private members, and those contributing partners of the IHI JU. Views and opinions expressed are however those of the author(s) only and do not necessarily reflect those of the aforementioned parties. Neither of the aforementioned parties can be held responsible for them.

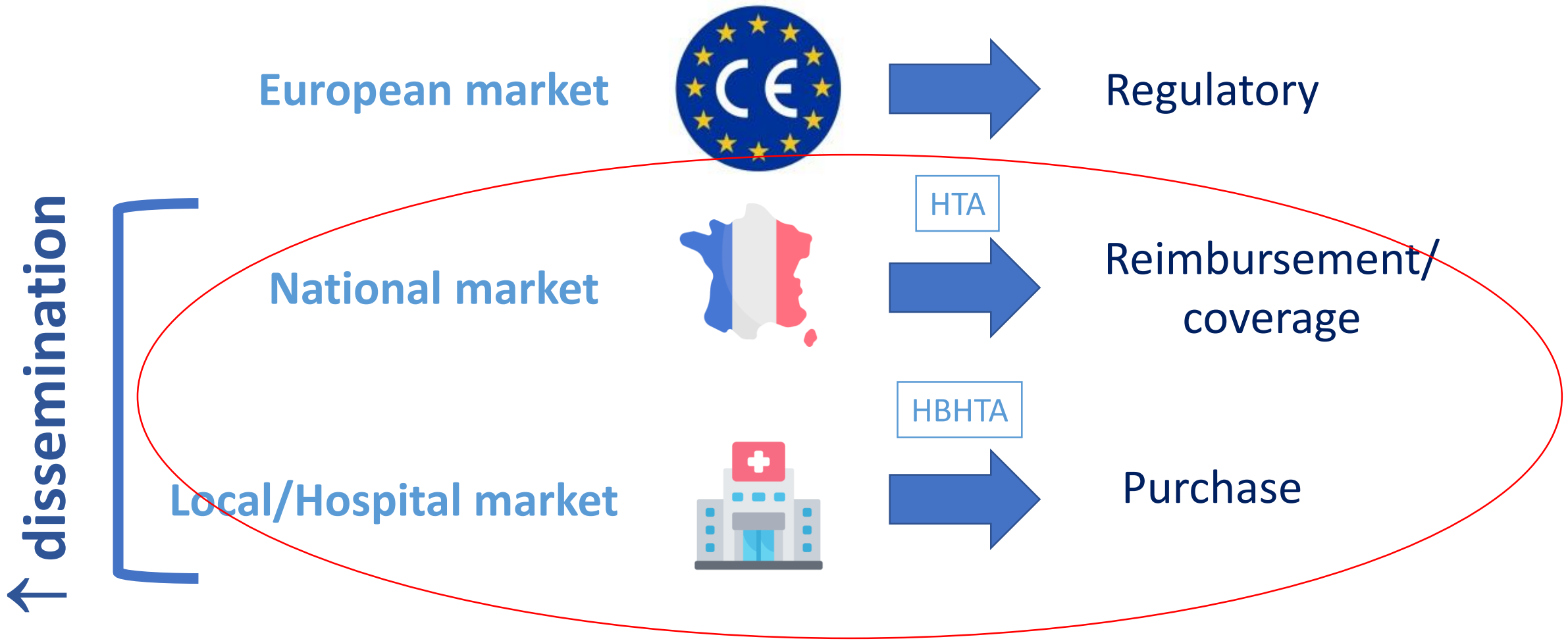
HEU-EFS aim & objectives

- ✓ To define a **methodology for EFS**, involving various stakeholders from different sectors
- ✓ To test, refine, and validate the framework based on pilot use-cases
- ✓ To develop a comprehensive database to track EFS submissions in Europe and assess the impact of the initiative

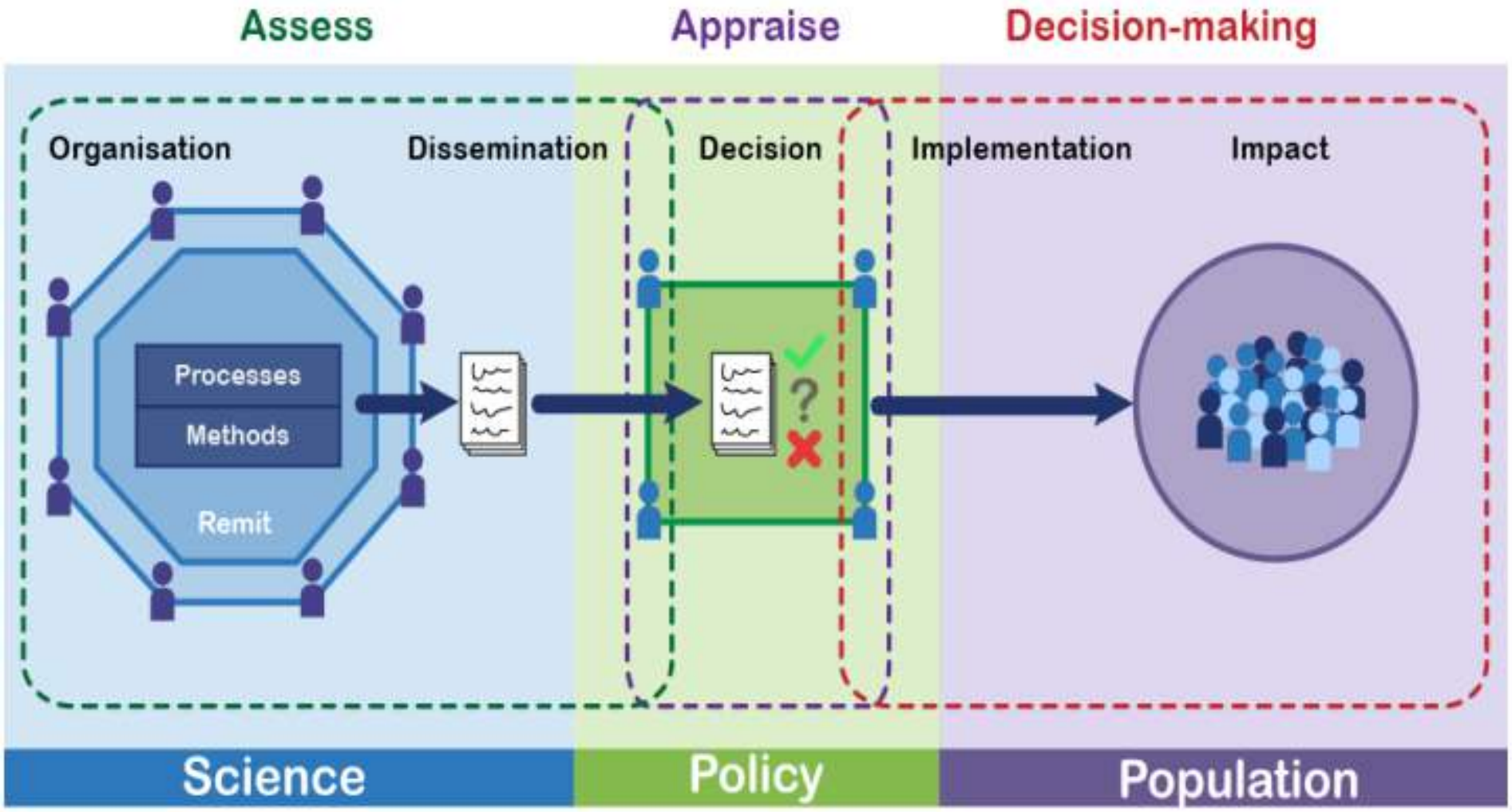
22 public and private consortium partners
4-year project / €19 million grant from the Innovative Health Initiative
Coordinated by Bocconi University - Industrially led by Edwards Lifesciences

Co-leading WP2 (with Trinity College Dublin)
Objective: to define the best possible alignment between the EU EFS program and current and future rules/standards.

Market Access for innovative MDs: a multi-layered problem?

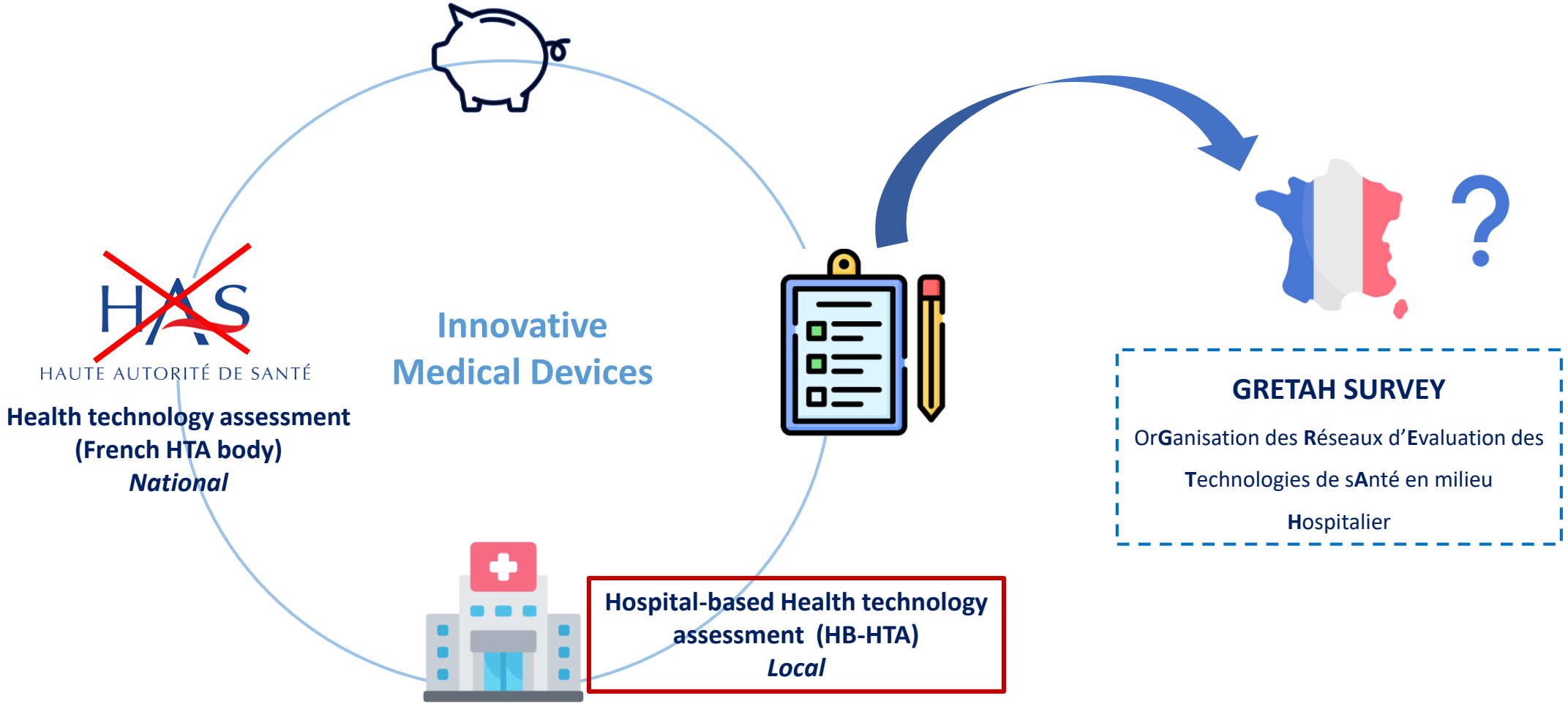


Health technology assessment: Three-phase model



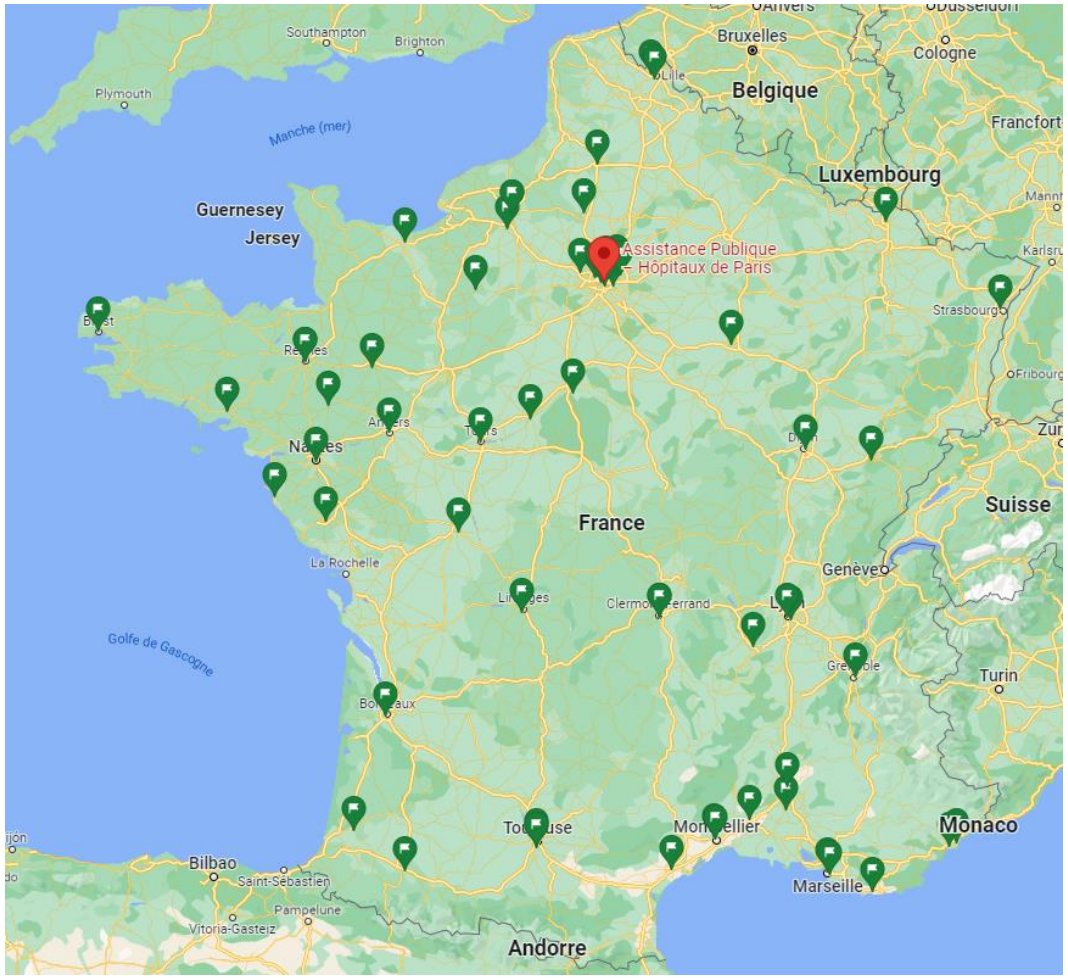
European Patients' Academy on Therapeutic Innovation (EUPATI) https://toolbox.eupati.eu/resources/health-technology-assessment-process-fundamentals

Hb-HTA and technology assessment



Martelli, N. Evaluation des dispositifs médicaux innovants dans les CHU en vue de leur acquisition: état des lieux et élaboration d'un outil d'aide à la décision. 2015. Thèse de doctorat. Université Paris Sud-Paris XI.
Piazza, L., et al. "What are the Most Important Decision-Making Criteria For Innovative Health Technology Integration? A National Survey from French Hospitals Decision-Makers." Value in Health 19.7 (2016): A489.
Martelli, N., Puc, C., Szwarcensztein, K., Beuscart, R., Coulonjou, H., Degrassat-Théas, A., ... & Lechat, P. (2017). Rôle et place de l'évaluation des technologies de santé à l'hôpital: schéma cible appliqué aux dispositifs médicaux. *Thérapie*, *72*(1), 105-113.
Guerre, Pascale. L'évaluation médico-économique des innovations: qualité des études, place d'une nouvelle méthode d'évaluation (mini-HTA), et recommandations pour l'amélioration des pratiques. 2021. Thèse de doctorat. Université de Lyon.

« HOSPITAL-BASED HEALTH TECHNOLOGY ASSESSMENT OF INNOVATIVE MEDICAL DEVICES: INSIGHTS FROM A NATIONWIDE SURVEY IN FRANCE »*

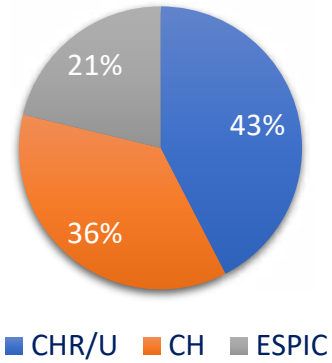


Main Objective: **To study the current organization of the evaluation of innovative MDs in French hospitals.**

Method: **Quantitative survey among targeted Hospitals (2022)**

67 hospitals*:

- ❑ **29** Teaching Hospitals (UH's)
- ❑ **24** Local Hospitals
- ❑ **14** non-profit private hospitals



* 51,1% response rate

Martin, T., Guercio, A., Besseau, H., Huot, L., Guerre, P., Atfeh, J., ... & Martelli, N. (2023). Hospital-based health technology assessment of innovative medical devices: insights from a nationwide survey in France. International Journal of Technology Assessment in Health Care, 39(1), e58.

Results overview– How Hb-HTA is currently implanted in France?*

Most French Hospitals are doing Hb-HTA for the acquisition of innovative MDs

(61 Hospitals, 91%)*

Variety of organizations linked to the category of hospitals

Only 16 hospitals (24%) stated the existence of a dedicated unit* for MD assessment

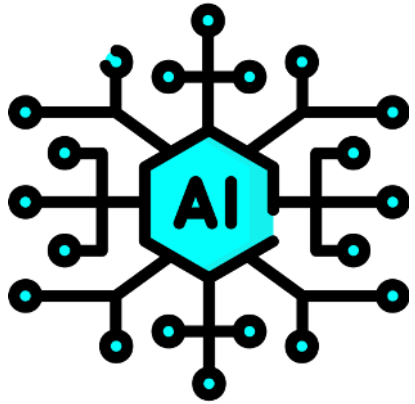
(More common in hospitals > 500 beds : n= 15, p=0,0160 and in Teaching Hospitals n= 11, p=0,0158)

HAS
HAUTE AUTORITÉ DE SANTÉ

Lack of collaboration between French hospitals and national authorities

(0/67 hospitals stated a collaboration with the HAS)

*67 responding hospitals



What are the assessment criteria for innovative MDs?

Artificial Intelligence In Medicine 140 (2023) 102547

Contents lists available at ScienceDirect

Artificial Intelligence In Medicine

journal homepage: www.elsevier.com/locate/artmed

Are current clinical studies on artificial intelligence-based medical devices comprehensive enough to support a full health technology assessment? A systematic review

Line Farah [a,b,*], Julie Davaze-Schneider [c], Tess Martin [a,c], Pierre Nguyen [c], Isabelle Borget [a,d,e], Nicolas Martelli [a,c]

[a] Groupe de Recherche et d'accueil en Droit et Economie de la Santé (GRADES) Department, University Paris-Saclay, Orsay, France
[b] Innovation Center for Medical Devices, Foch Hospital, 40 Rue Worth, 92150 Suresnes, France
[c] Pharmacy Department, Georges Pompidou European Hospital, AP-HP, 20 Rue Leblanc, 75015 Paris, France
[d] Department of Biostatistics and Epidemiology, Gustave Roussy, University Paris-Saclay, 94805 Villejuif, France
[e] Oncostat U1018, Inserm, University Paris-Saclay, Equipe Labellisée Ligue Contre le Cancer, Villejuif, France

ARTICLE INFO

Keywords:
Artificial intelligence
Machine learning
Artificial intelligence-based medical device
Health technology assessment
Clinical trial
Economic evaluation

ABSTRACT

Introduction: Artificial Intelligence-based Medical Devices (AI-based MDs) are experiencing exponential growth in healthcare. This study aimed to investigate whether current studies assessing AI contain the information required for health technology assessment (HTA) by HTA bodies.

Methods: We conducted a systematic literature review based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses methodology to extract articles published between 2016 and 2021 related to the assessment of AI-based MDs. Data extraction focused on study characteristics, technology, algorithms, comparators, and results. AI quality assessment and HTA scores were calculated to evaluate whether the items present in the included studies were concordant with the HTA requirements. We performed a linear regression for the HTA and AI scores with the explanatory variables of the impact factor, publication date, and medical specialty. We conducted a univariate analysis of the HTA score and a multivariate analysis of the AI score with an alpha risk of 5 %.

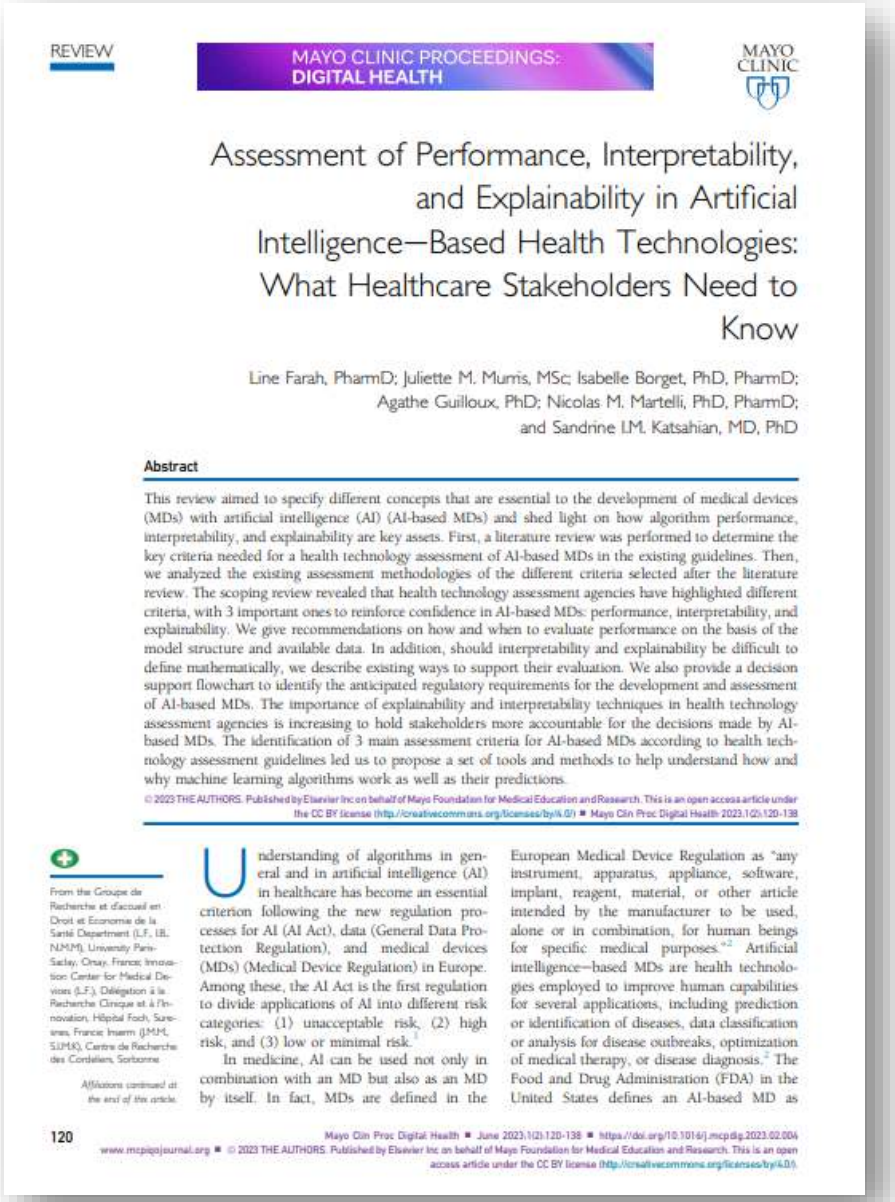
Results: Of 5578 retrieved records, 56 were included. The mean AI quality assessment score was 67 %; 32 % of articles had an AI quality score ≥ 70 %, 50 % had a score between 50 % and 70 %, and 18 % had a score under 50 %. The highest quality scores were observed for the study design (82 %) and optimisation (69 %) categories, whereas the scores were lowest in the clinical practice category (23 %). The mean HTA score was 52 % for all seven domains. 100 % of the studies assessed clinical effectiveness, whereas only 9 % evaluated safety, and 20 % evaluated economic issues. There was a statistically significant relationship between the impact factor and the HTA and AI scores (both $p = 0.046$).

Discussion: Clinical studies on AI-based MDs have limitations and often lack adapted, robust, and complete evidence. High-quality datasets are also required because the output data can only be trusted if the inputs are reliable. The existing assessment frameworks are not specifically designed to assess AI-based MDs. From the perspective of regulatory authorities, we suggest that these frameworks should be adapted to assess the interpretability, explainability, cybersecurity, and safety of ongoing updates. From the perspective of HTA agencies, we highlight that transparency, professional and patient acceptance, ethical issues, and organizational changes are required for the implementation of these devices. Economic assessments of AI should rely on a robust methodology (business impact or health economic models) to provide decision-makers with more reliable evidence.

Abbreviations: AI, Artificial intelligence; AI-based MD, Artificial intelligence-based medical device; AUC, Area under the curve; MD, Medical device; ML, Machine learning; SaMD, Software as a Medical Device; ITFoC, Information Technology: The Future of Cancer; Bfarm, Bundesinstitut Fur Arzneimittel und Medizinprodukte German Ministry of Health; CADTH, Canadian Agency for Drugs and Technologies in Health; FDA., Food and Drug administration; HAS, Haute Autorité de Santé; NHS, National Health Service; NICE, National Institute for Health & Care Excellence; NIPH, Norwegian Institute of Public Health; INAHTA, International Network of Agencies for Health Technology Assessment; EUnetHTA, European network for Health Technology Assessment Joint Action.

* Corresponding author at: Groupe de Recherche et d'accueil en Droit et Economie de la Santé (GRADES) Department, University Paris-Saclay, Orsay, France.
E-mail addresses: line.farah1@gmail.com, l.farah@hopital-foch.com (L. Farah).

https://doi.org/10.1016/j.artmed.2023.102547
Received 31 May 2022; Received in revised form 28 March 2023; Accepted 4 April 2023
Available online 23 April 2023
0933-3657/© 2023 The Author(s). Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).



REVIEW

MAYO CLINIC PROCEEDINGS: DIGITAL HEALTH

MAYO CLINIC

Assessment of Performance, Interpretability, and Explainability in Artificial Intelligence–Based Health Technologies: What Healthcare Stakeholders Need to Know

Line Farah, PharmD; Juliette M. Murris, MSc; Isabelle Borget, PhD, PharmD; Agathe Guilloux, PhD; Nicolas M. Martelli, PhD, PharmD; and Sandrine I.M. Katsahian, MD, PhD

Abstract

This review aimed to specify different concepts that are essential to the development of medical devices (MDs) with artificial intelligence (AI) (AI-based MDs) and shed light on how algorithm performance, interpretability, and explainability are key assets. First, a literature review was performed to determine the key criteria needed for a health technology assessment of AI-based MDs in the existing guidelines. Then, we analyzed the existing assessment methodologies of the different criteria selected after the literature review. The scoping review revealed that health technology assessment agencies have highlighted different criteria, with 3 important ones to reinforce confidence in AI-based MDs: performance, interpretability, and explainability. We give recommendations on how and when to evaluate performance on the basis of the model structure and available data. In addition, should interpretability and explainability be difficult to define mathematically, we describe existing ways to support their evaluation. We also provide a decision support flowchart to identify the anticipated regulatory requirements for the development and assessment of AI-based MDs. The importance of explainability and interpretability techniques in health technology assessment agencies is increasing to hold stakeholders more accountable for the decisions made by AI-based MDs. The identification of 3 main assessment criteria for AI-based MDs according to health technology assessment guidelines led us to propose a set of tools and methods to help understand how and why machine learning algorithms work as well as their predictions.

© 2023 THE AUTHORS. Published by Elsevier Inc on behalf of Mayo Foundation for Medical Education and Research. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/) ■ Mayo Clin Proc Digital Health 2023;1(2):120-138

From the Groupe de Recherche et d'accueil en Droit et Economie de la Santé Department (L.F., I.B., N.M.M), University Paris-Saclay, Orsay, France; Innovation Center for Medical Devices (L.F.), Délégation à la Recherche Clinique et à l'Innovation, Hôpital Foch, Suresnes, France; Inserm (J.M.M, S.I.M.K), Centre de Recherche des Cordeliers, Sorbonne

Affiliations continued at the end of this article.

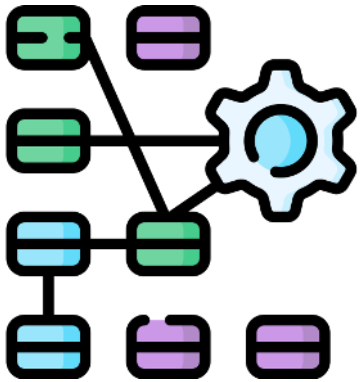
Understanding of algorithms in general and in artificial intelligence (AI) in healthcare has become an essential criterion following the new regulation processes for AI (AI Act), data (General Data Protection Regulation), and medical devices (MDs) (Medical Device Regulation) in Europe. Among these, the AI Act is the first regulation to divide applications of AI into different risk categories: (1) unacceptable risk, (2) high risk, and (3) low or minimal risk.[1]

In medicine, AI can be used not only in combination with an MD but also as an MD by itself. In fact, MDs are defined in the European Medical Device Regulation as "any instrument, apparatus, appliance, software, implant, reagent, material, or other article intended by the manufacturer to be used, alone or in combination, for human beings for specific medical purposes."[2] Artificial intelligence–based MDs are health technologies employed to improve human capabilities for several applications, including prediction or identification of diseases, data classification or analysis for disease outbreaks, optimization of medical therapy, or disease diagnosis.[3] The Food and Drug Administration (FDA) in the United States defines an AI-based MD as

Farah, L., Murris, J. M., Borget, I., Guilloux, A., Martelli, N. M., & Katsahian, S. I. (2023). Assessment of performance, interpretability, and explainability in artificial intelligence–based health technologies: what healthcare stakeholders need to know. *Mayo Clinic Proceedings: Digital Health*, *1*(2), 120-138.

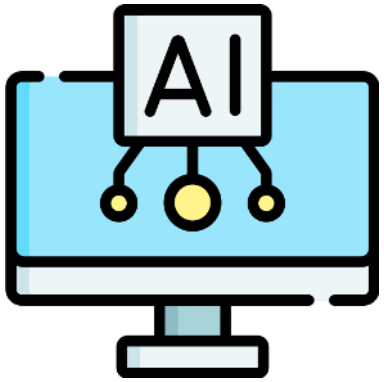
Farah, L., Davaze-Schneider, J., Martin, T., Nguyen, P., Borget, I., & Martelli, N. (2023). Are current clinical studies on artificial intelligence-based medical devices comprehensive enough to support a full health technology assessment? A systematic review. *Artificial Intelligence in Medicine*, 102547.

Take home messages



Market access for innovative MDs = a multi-layered problem!

EFS for MDs = a new hope for making the EU more attractive



AI and MDs = new criteria for the HTA process

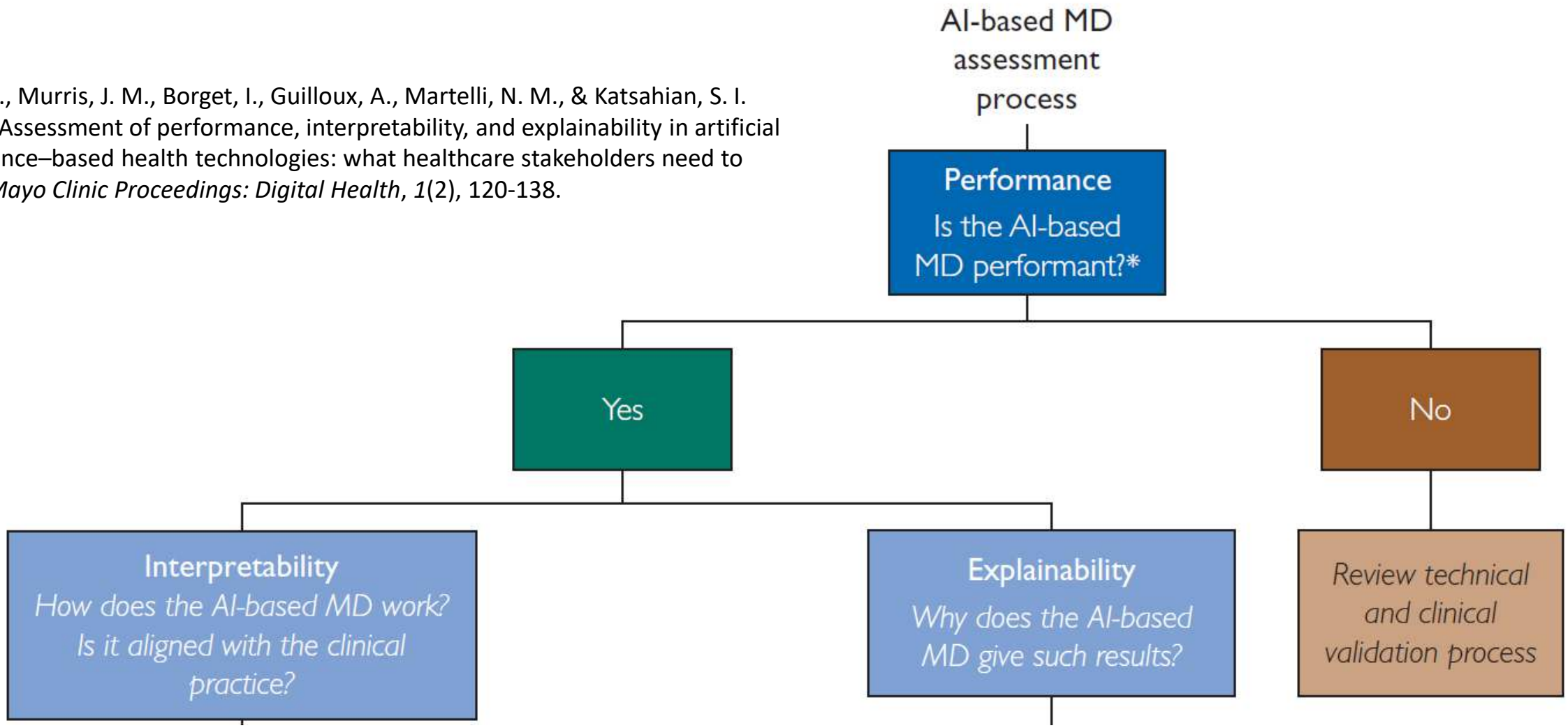
GRADES
UNIVERSITE PARIS-SACLAY

université
PARIS-SACLAY

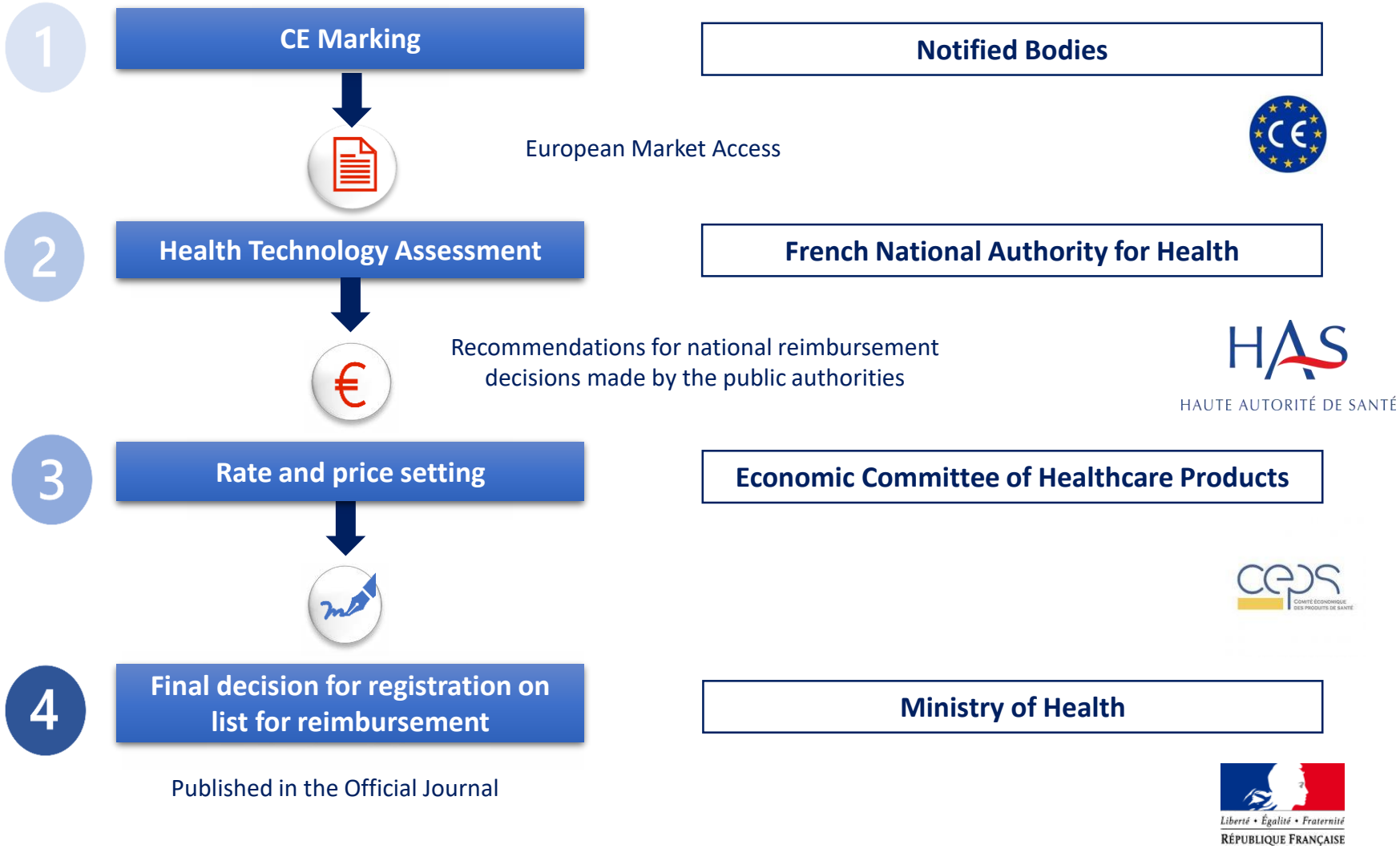
Thank you for your interest and attention!

Hôpital européen
Georges-Pompidou
AP-HP

Farah, L., Murris, J. M., Borget, I., Guilloux, A., Martelli, N. M., & Katsahian, S. I. (2023). Assessment of performance, interpretability, and explainability in artificial intelligence–based health technologies: what healthcare stakeholders need to know. *Mayo Clinic Proceedings: Digital Health*, *1*(2), 120-138.



Market Access Process for Reimbursed Medical Devices in France



Pesqué, R., Percheron, R., Cordonnier, A. L., Steelandt, J., Paubel, P., Pineau, J., ... & Martelli, N. (2019, November). Health technology assessment of innovative medical devices: timing and decision at national and local level. In Annales Pharmaceutiques Francaises (Vol. 78, No. 2, pp. 189-197).