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Annex No. 10 to the MU Directive on Habilitation Procedures and Professor Appointment Procedures

HABILITATION THESIS REVIEWER'S REPORT

Masaryk University	
Applicant	Jakub Hlávka, Ph.D.
Habilitation thesis	Economics to the Rescue: Balancing Innovation and Access to High-Cost Therapies
Reviewer	Sabine Grimm, PhD
Reviewer's home unit, institution	Care and Public Health Research Institute Maastricht University

I have been asked to prepare a review of the habilitation thesis of Jakub Hlávka, Ph.D., submitted in the field of Public Economics at Masaryk University. The submitted materials include the habilitation thesis entitled " Economics to the Rescue: Balancing Innovation and Access to High-Cost Therapies ", the candidate's list of publications in this thesis, scholarly and policy implications of the work undertaken, and authorship contribution statements.

The habilitation thesis explores the intersection of health economics, regulatory policy, and innovation, focusing on the real-world challenges posed by high-cost, potentially transformative medical therapies. The candidate has published five articles in international peer-reviewed journals included in this thesis.

Chapter 2 explores in what scenarios uniform pricing results in inefficiencies and finds that the rise of high-cost therapies may be intensifying market failures in healthcare. Findings imply that variable treatment effects alone do not justify variable pricing over uniform pricing. Efficiency gains from variable pricing occur only when specific market failures occur.

Chapter 3 presents an empirical assessment of both clinical and financial outcomes of deferred payment for a hypothetical gene therapy in congestive heart failure. It showed that deferred payment may improve patient outcomes through providing earlier access, allow aligning costs with patient outcomes and reduce budget impact.

Chapter 4 investigates the potential of alternative payment models to address market failures due to asynchronous accrual of benefits and costs of Alzheimer's disease-modifying treatments. While there is potential, challenges include the real-world measurement of treatment effectiveness and capacity issues in diagnosis and treatment.

Chapter 5 develops a method for evaluating the impact of FDA guidance on trial endpoint selection and applied it in Alzheimer's disease trials. It showed that FDA guidance indeed shaped trial practices, and developed hypotheses as to why this was the case.

Chapter 6 examines trends in Alzheimer's disease trials and finds that amyloid remains the dominant target despite trials showing modest benefits. The work suggests that expanding trial diversity and investing in non-amyloid approaches may be critical to advance the field.

The thesis demonstrates theoretical reasoning, methodological rigor and practical application. The research contributes significantly to the field of health economics, particularly in the economic implications of high-cost therapies, and regulatory science. It is forward-looking in nature – preparing us for a world in which the sustainability of health care systems is threatened by high cost therapies that promise real but at times uncertain or heterogeneous improvements in patient outcomes. The true impact of this thesis can be substantial. The candidate's work is recognized not only in the Czech academic context, but also internationally, as evidenced by close collaboration with international scholars. The quantity and quality of the publications meet, and in fact exceed, the criteria for habilitation in this field.

Strengths

- The use of a wide range of methods: economic modeling and optimization to Markov models, microsimulation modeling, regression analysis and systematic reviews.
- The relevance of this topic, given the emergence of very costly cell and gene therapies.
- The examination of different aspects relevant for research and development through to market access including trial endpoint selection and pricing.
- This thesis provides methodological advances in the analysis of regulator's trial endpoints and theoretical modelling of pricing mechanisms.

Weaknesses

- Chapters 2 and 3 remain theoretical and the true impact could not be empirically tested. This is a limitation that is owed to the forward-looking nature of this work, which includes theoretical and hypothetical experiments.
- Chapter 5 is a valuable quantitative study on trial endpoints used in Alzheimer's disease and how these may have been influenced by FDA guidance. Some hypotheses on causes for recent uptake of certain endpoints were generated, including that trialists interpreted FDA guidance as binding. It would have likely been valuable to explore this further through qualitative research with key stakeholders.

These weaknesses, however, do not diminish the overall high quality of the candidate's academic profile or the habilitation thesis.

Reviewer's questions for the habilitation thesis defence:

Paulden (2024) (DOI: 10.1007/s40273-023-01325-z) highlighted that value-based pricing leads to a consumer surplus of 0, as prices are set such that the value that is gained from using the new technology is exactly equal to the value that is displaced (elsewhere in the health care system, given that budgets are finite). In contrast, fair prices allow a positive consumer surplus. What is the author's view on these statements and how was or could this be addressed within their research?

The author found that deferred payment under a fixed budget constraint may allow for more patients to receive treatment sooner (Chapter 3). However, the emergence of competing cell and gene therapies were not modelled and neither were future time periods, in which the health care system would have to pay for patients that initiate treatment and those that initiated treatment in previous time periods. Such a future may result in the whole health care budget being used for deferred payments for patients in previous periods. How risky does the author think deferred payments would be for health care systems, and how might their conclusions change if they formally incorporated this in their analysis?

Key issues in pharmaceutical pricing are the discrepancy between list prices and actual prices agreed per individual jurisdiction, the confidentiality of these 'real' prices, and the pharmaceutical industry's lack of transparency on their R&D costs per pharmaceutical. What is the author's view on the importance of these issues and how to overcome them?

How feasible is indication-based pricing, what are the barriers and how could it be enforced?

Given that often times the first indication of a drug is the one in which it is most effective, are drug prices generally too high?

Since there is a lot of uncertainty about the long term effect of disease modifying treatments in Alzheimer's disease, pay-for-performance schemes may be an attractive solution for payers. This would however require continuous monitoring of patients' (e.g. CDR-SB) health state, which would add to the cost as this is currently not standard practice. How would the author evaluate whether pay-for-performance schemes would be worth the trouble?

Throughout the thesis, patient access was mostly linked to hurdles imposed by health care payers: but isn't excessive pricing at the heart of the problem? How can R&D be made more efficient? What does the author think about the substantial part of the innovation chain that occurs in publicly funded settings?

Conclusion

The habilitation thesis entitled *Economics to the Rescue: Balancing Innovation and Access to High-Cost Therapies* by Jakub Hlávka, Ph.D. **fulfils** requirements expected of a habilitation thesis in the field of Public Economics.

Date: Signature:

27-08-2025