HTA43

Assessing the Added Value of Fixed-Dose Combinations in Non-Communicable Diseases: A Comparative HTA Analysis Across Canada, Scotland, France, and Germany (2014–2024)

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Background

- Fixed-dose combinations can provide a range of benefits including improved adherence and quality of life, particularly in an NCD context.
- Reimbursement and access to FDCs remain inconsistent.[1] HTA of FDCs is fragmented and varied standards and cost thresholds yield inconsistent outcomes. Often seen as incremental innovations, they require robust trial evidence to prove added benefit.[2]
- Prices often reflect summed component costs with mandated discounts, while access is restricted by subgroup or treatment history.[3] This gap between trials and real-world value fuels disparities and limits FDCs' public health impact.[2]

Objectives

- This study investigates factors influencing approval and reimbursement FDCs targeting common NCDs.
- It explores clinical and economic evidence, stakeholder views, and implementation factors across four HTA agencies from 2014–2024: Scotland (SMC), France (HAS), Germany (G-BA), and Canada (CDA).
- The goal is to understand how these elements interact to impact reimbursement decisions.

Methods

Step 1

Comparative Systematic Review

- 84 HTA reports identified (2014–2024)
- Agencies: SMC, HAS, G-BA, CDA*
- Source: HTA-Hive database

Step 2

Key Elements Analyzed

- Clinical & economic evidence
- Implementation factors (e.g. restrictions applied)
- Stakeholder perspectives

*NICE was excluded due to insufficient reports (n=1)

Step 3

Scenarios Examined

- FDCs replacing monotherapies
- FDCs introducing novel therapeutic advancements

Step 4

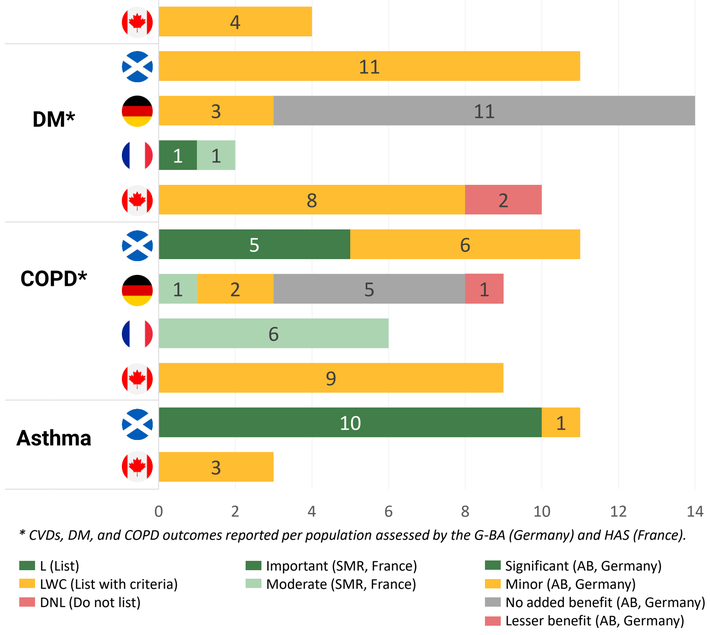
Analysis Techniques

- **Quantitative**: Chi-square tests (associations between HTA decisions and variables such as disease area and country)
- **Qualitative**: Thematic analysis (explore convergent and divergent decision drivers across agencies)

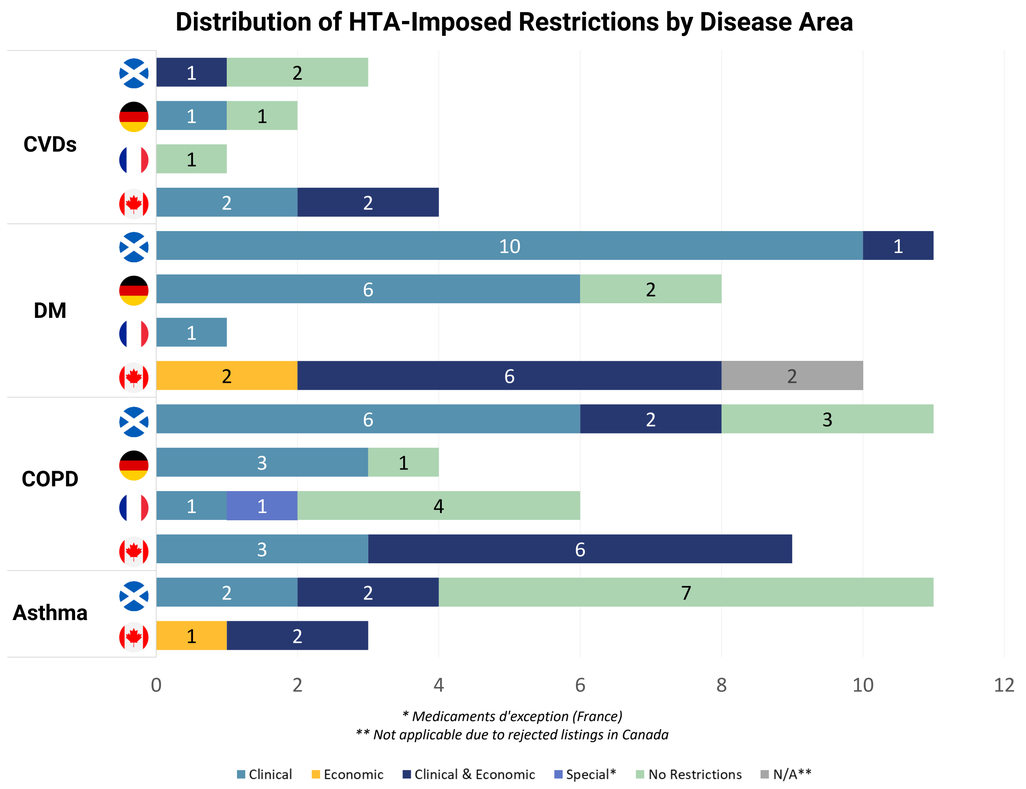
RESULTS

- Chi-square test *(χ^2=19.91, df=6, p≈0.003)* revealed a significant association between HTA outcome and disease area. Post-hoc residual analysis indicated asthma FDCs were associated with more positive outcomes *(+2.24)*, while those for DM were significantly less likely *(−2.35)*.
- No significant differences arose between novel FDCs (n=19) and those replacing monotherapies (n=65), though novel combinations received higher clinical benefit ratings and higher pricing.
- Positive decisions favored FDCs that offered cost savings, improved disease control, addressed higher disease severity or prior treatment failure, and demonstrated efficacy through validated biomarkers.

Distribution of Outcomes Across Agencies by Disease Area



Distribution of HTA-Imposed Restrictions by Disease Area



- Agencies required robust efficacy and clinical benefits (favouring cost-effectiveness) yet diverge on comparator choice, surrogate endpoints, and thresholds for “added benefit”.
- Overdosing inflexibility and insufficient benefit led to two rejections, and no agency explicitly addressed patient adherence or polypharmacy; except in two reports on diabetes medications, which highlighted their potential to reduce overall pill burden and simplify treatment regimens.

Conclusions

- Reimbursement decisions are tied to pricing considerations and tend to favour innovative FDCs that show clear added benefits or cost-savings
- Though HTA agencies converge on requiring robust efficacy and clinical relevance, variations remain in comparator choice and “added benefit” criteria.
- Current HTA frameworks struggle to capture patient-centric benefits: improved adherence and reduced pill burden are seldom accepted as formal endpoints, and methodological challenges hinder quantifying these advantages.[2]
- Addressing patient adherence and polypharmacy could strengthen FDC value demonstrations.

References

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Abbreviations

Canada’s Drug Agency, CDA, CDA; Chronic Obstructive Pulmonary Disease. COPD; Cardiovascular Diseases , CVDs; Diabetes Mellitus, DM; Fixed-Dose Combinations , FDC; Gemeinsamer Bundesausschuss (Federal Joint Committee), G-BA; Haute Autorité de Santé (French National Authority for Health), HAS; Health Technology Assessment, HTA; Non-Communicable Diseases, NCDs; Scottish Medicines Consortium, SMC

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