HTA91

Indirect comparisons in German AMNOG assessments: Keep the faith

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Background

- In Germany, pharmaceutical companies are required to demonstrate the benefit of newly approved drugs in their respective therapeutic areas compared to an appropriate comparator therapy (ACT) according to the Act on the Reform of the Market for Medicinal Products (AMNOG)
- Although direct evidence via randomized controlled trials (RCTs) is considered the gold standard, in certain circumstances, indirect comparisons (ICs) are the best available alternative evidence.

Objectives

- This study aimed to identify benefit assessments incorporating ICs and to critically evaluate the key parameters influencing these ICs within the context of the benefit assessments.

Methods

- A systematic search for ICs was performed using an internal AMNOG database containing all benefit assessments published on the website of the Federal Joint Committee (G-BA)[1] until April 2024.
- The assessment of the ICs by the G-BA and the associated added medical benefit were obtained from the database.

Conclusions

- The acceptance criteria for ICs are stringent, with success often hinging on special circumstances.
- Methodological deficiencies and insufficient similarity between the compared studies are the main reasons for the rejection of an IC by the G-BA.
- In rapidly evolving therapeutic fields like oncology, in which frequent changes in the definition of the ACT occur, or among highly vulnerable patient populations (e.g. pediatric populations), ICs will continue to provide critical evidence.

References

1. Federal Joint Committee (G-BA). 2024. Benefit Assessments Database. https://www.g-ba.de/ [Accessed 18 April 2024]
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4. Federal Joint Committee (G-BA). 2021. AM-RL-XII Sebelipase-alfa. https://www.g-ba.de/downloads/40-268-7570/2021-06-03_AM-RL-XII_Sebelipase-alfa_D-606_TrG.pdf [Accessed 20 September 2024]

Results

- ICs were present in 222 concluded benefit assessments, encompassing 334 subpopulations.
- The predominant therapeutic fields were oncology (51.2%), metabolic (15.0%) and infectious (11.4%) diseases (**Figure 1**).

Figure 1. ICs in German benefit assessments by therapeutic field

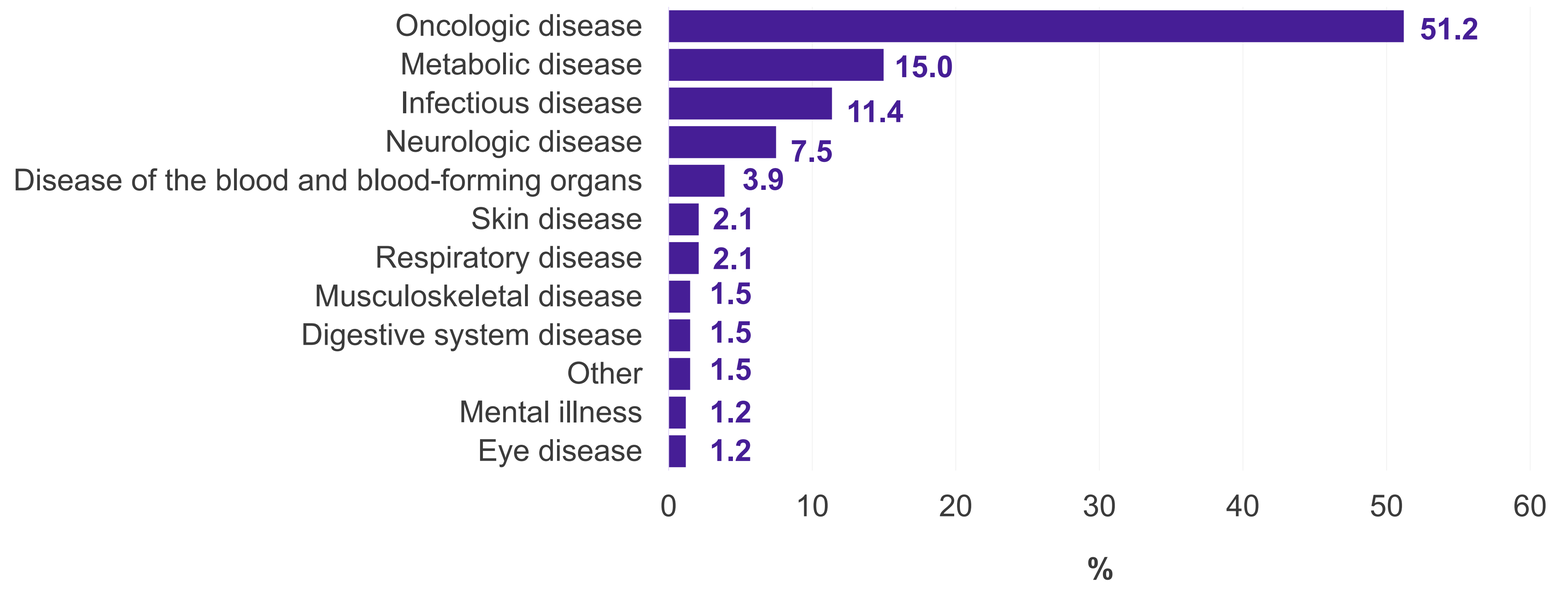
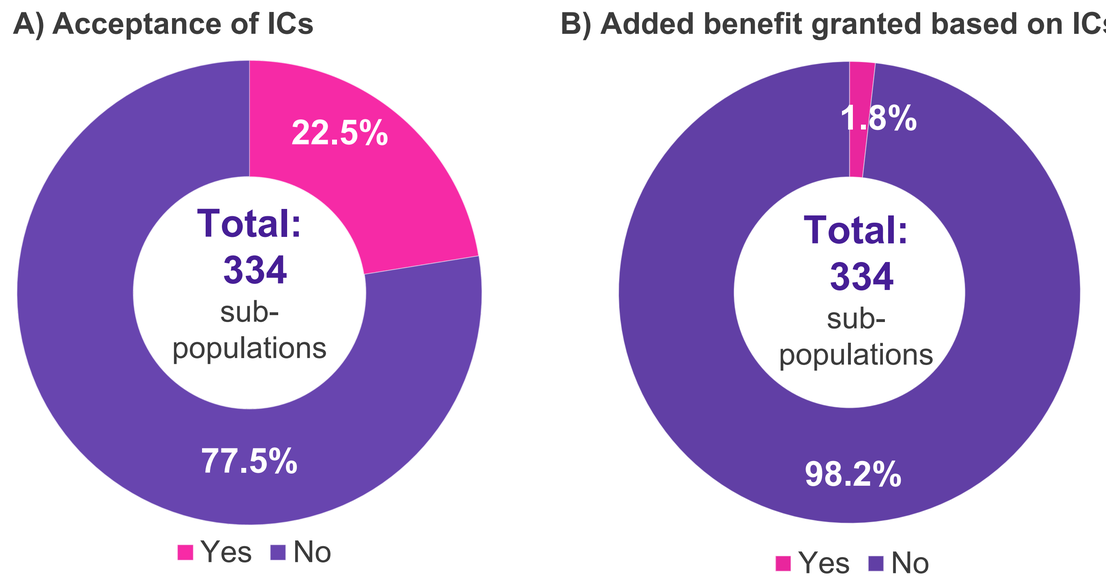
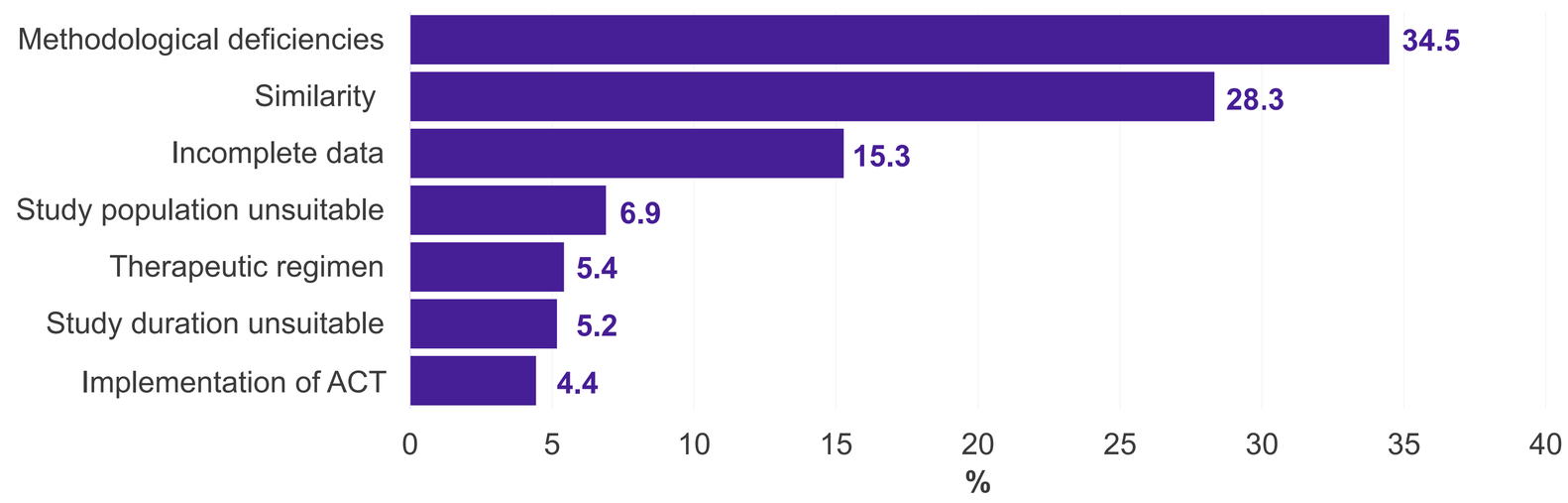


Figure 2. Assessment of ICs by the G-BA



- In 22.5% of the cases, the IC was accepted by the G-BA.
- An added benefit was granted in 1.8% of all assessed subpopulations (**Figure 2**).
- Methodological deficiencies and insufficient similarity of the compared studies were the main reasons for the rejection of an IC by the G-BA (**Figure 3**).
- Among the accepted ICs, only adjusted and unadjusted comparisons were identified. Other methods, such as network meta-analyses or propensity score matching, were not considered to be methodologically appropriate.
- Non-adjusted ICs accepted by the G-BA were considered under additional exceptional circumstances; examples are given in the **Info Box**.

Figure 3. Reasons for rejection of ICs by the G-BA



Info Box: Exceptional circumstances – cases of non-adjusted ICs accepted by the G-BA

Chronic hepatitis C virus infection[2,3]

- Interferon-containing combination therapies have been defined as ACT. These therapies can have significant side effects, such as depression and suicidal thoughts.
- Given the treatment success that can be achieved with the new drug, the possible shortening of the duration of therapy, and the avoidance of the severe side effects of interferon, it was deemed necessary for ethical reasons to consider uncontrolled, single-arm studies compared with historical controls.
- Interferon-containing combination therapies are no longer regarded as standard therapy according to the current state of medical knowledge.

Deficiency of lysosomal acid lipase deficiency[4]

- Rare disease, which in the natural course of the disease is very likely to lead to the death of the patient within the first year of life, and for which there are no treatment alternatives (particularly vulnerable patient population).
- Large treatment effect regarding the outcome mortality, which cannot be explained by random effects.

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Presented at: ISPOR Annual European Congress; 17-20 November 2024; Barcelona, Spain.