A systematic literature review on the drivers of effectiveness and the efficacy-effectiveness gap in hematological malignancies with a focus on Hodgkin’s Lymphoma

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BACKGROUND

- Efficacy is the outcome of treatment observed in clinical trials, which may not be identical to the treatment effectiveness seen in observational and real life studies. (Nordon et al. 2016)
- A superior survival was observed for patients with Hodgkin’s Lymphoma treated inside clinical trials as compared to those treated in the routine settings. (Favier et al. 2009; Monnereau et al. 2003;www.iknl.nl)
- No review of literature has been systematically performed to give an overview on the efficacy and effectiveness gap and its determinants on hematological cancers, in particular Hodgkin’s Lymphoma (HL).

OBJECTIVE

- To systematically review existing literature on the gaps between efficacy and effectiveness and its determinants (i.e. drivers of effectiveness) among patients with HL and other hematological malignancies.

METHODS

- Approach
  - Population, Intervention, Comparison, Outcomes, Study type, and Time horizon (PICOS-T) framework.
  - In- and exclusion criteria
    - Population: patients >18 years with HL or other hematological malignancies
    - Interventions/Comparators: All treatments for HL
    - Outcomes: Progression Free Survival (PFS), Event-Free Survival (EFS), Disease-Free Survival (DFS), Overall survival (OS), Response rates, Treatment discontinuation, Safety (e.g. hematological toxicity, neuropathy, gastro-enterologic toxicity, etc.)
    - Study type: (Observational studies) and/or (Comparison of Clinical Trials vs. Observational /Real life studies)
    - English language
    - Publication in 2000-2015
  - Data sources
  - We searched the EMBASE and MEDLINE databases. Citation screening, full text screening, and data extraction for the studies of interest were performed by two researchers independently. Any discrepancy between reviewers was reconciled by consensus.

RESULTS

- Review results:
  - We included 42 articles among them 11 were on HL (see Figure 1).
- Summary of findings:
  - Age was identified as a key driver of the efficacy-effectiveness gap for Hodgkin’s Lymphoma and other hematological malignancies as older patients are often excluded from clinical trials. In HL, patients > 60 represent 5-10% in trials vs. 20-44% in observational studies while older age was significantly associated with shorter PFS (HR range: 1.76 - 3.97) and survival (HR range: 2.24 -3.90).
  - In HL, comorbidities, disease stage and treatment toxicities were also driving factors for the efficacy-effectiveness gap. More advanced stage and severe treatment-related toxicities were respectively associated with poorer survival outcome and lower remission rates.
  - Interestingly male gender was identified as a prognostic factor for poorer survival in patients with Non-Hodgkin’s Lymphoma.
  - Other factors like compliance to the treatment and histological subtypes of the cancer also explains differences in outcome observed in clinical research and observational studies.

DISCUSSION

- This is the first review investigating the drivers of efficacy-effectiveness gap in patients with hematological malignancies.
- Our review shows that older age is the key driver for all hematological malignancies. It is not only distributed differently in trials and real life studies but also strongly associated with shorter PFS and survival.
- Further research is encouraged to quantify the attributable fractions of all identified explanatory factors to support future designs of clinical research by incorporating real life elements, and therefore decreasing the gap which is often seen between treatment efficacy and effectiveness.

REFERENCES

- http://www.iknl.nl/