

Relationship Between the Directness of the Evidence and Identification of Added Therapeutic Value: An Analysis of HTA Procedures

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INTRODUCTION

Relative effectiveness assessment procedures are a critical step of HTA. [1] If there is another intervention to link the two interventions under discussion, indirect comparison approaches can be used to infer the relative efficacy of two interventions in the absence of research that explicitly compare them. [2] Some evaluation procedures may need to resort on adjusted indirect comparisons, such as network meta-analysis (NMA), to assess the therapeutic value of the pharmacological intervention. [3] The aim of this study is to assess if there is a relationship between the directness of evidence supporting the relative effectiveness assessments and the identification of added therapeutic value (ATV).

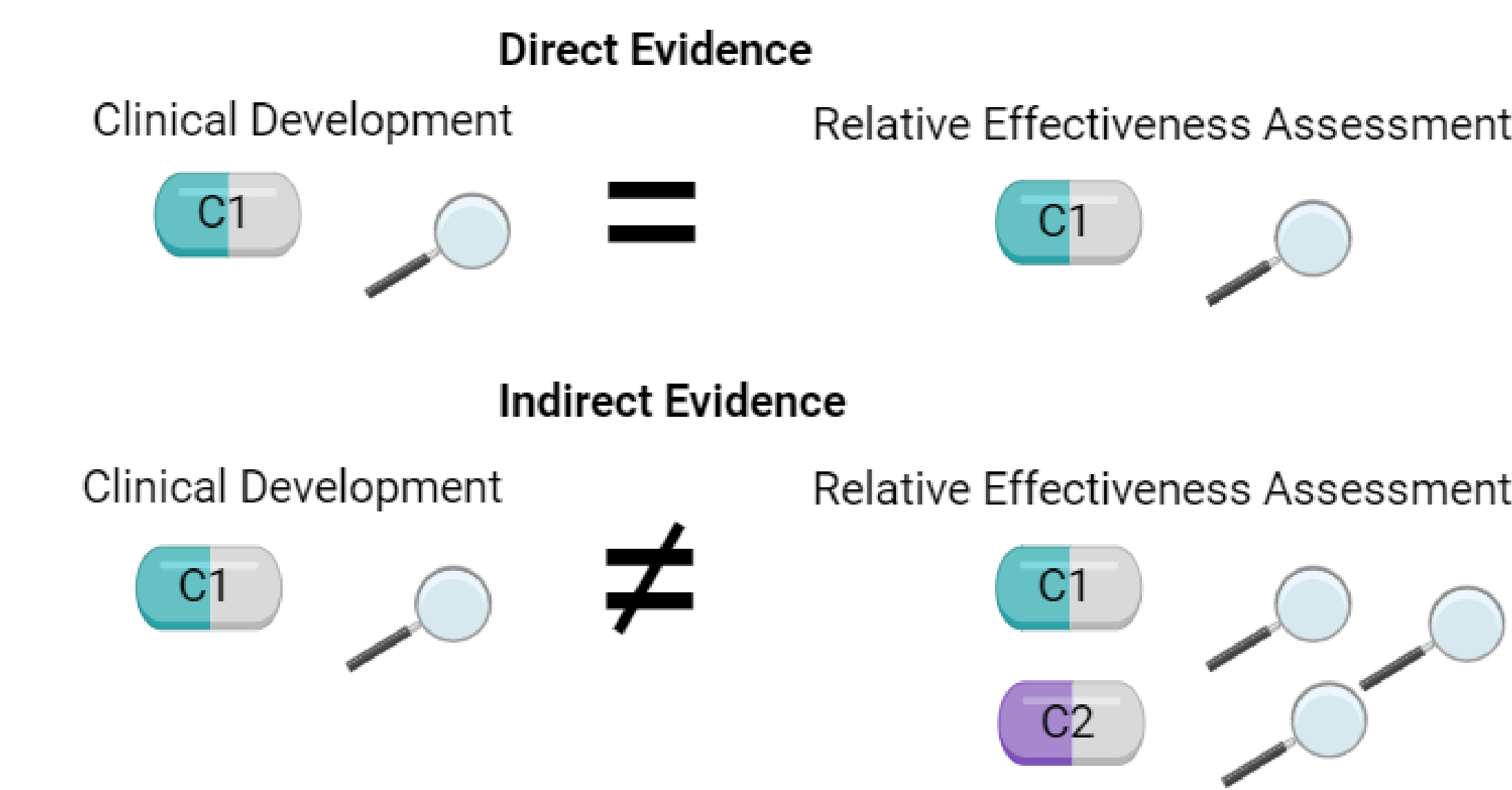


Figure 1 - Differences between direct evidence and indirect evidence. C1 - Comparator 1, C2 - Comparator 2, Magnifier - Represent studies

METHODS

Relative effectiveness assessments produced between 2018 and 2021 by 6 HTA bodies (NICE [England and Wales], SMC [Scotland], HAS [France], AEMPS [Spain], SiNATS [Portugal] and IQWIG [Germany]) were reviewed. Data on the pharmacological intervention, comparator(s), data sources and conclusions of therapeutic value was retrieved. Direct evidence reflects evaluations informed by the same comparator(s) and studies that integrated the clinical development program of the pharmacological intervention, representing direct links to assess the health outcomes. Indirect evidence represents the opposite. The qui-square test was applied to explore a possible relationship between the directness of the evidence and the identification of ATV.

RESULTS

Of the 987 relative effectiveness assessment procedures analyzed, 717 were exclusively supported by the direct evidence. Of those, 515 (71.83%) concluded for ATV, 81 (11.30%) for equivalence, 13 (1.81%) were inconclusive, and 108 (15.06%) did not recognize therapeutic value. A total of 270 procedures were informed by indirect evidence. Of those, 196 (72.59%) concluded for ATV, 35 (12.96%) for equivalence, 12 (4.44%) were inconclusive, and 27 (10.00%) did not recognize therapeutic value. The chi-square test did not find a relationship between the directness of the evidence and identification of ATV, except for IQWIG (indirect evidence was related with less chance of ATV identification) and SMC (direct evidence was related with less chance of ATV identification).

Table 1 - Conclusion of the reports supported by direct evidence and indirect evidence.

Conclusion	Total supported by direct evidence(%)	Total supported by indirect evidence(%)
ATV	515 (71.83%)	196 (72.59%)
Similar	81 (11.30%)	35 (12.96%)
Inconclusive	13 (1.81%)	12 (4.44%)
No add value	108 (15.06%)	27 (10.00%)
Total	717 (100%)	270 (100%)

When the results of reports using direct evidence were compared with those using indirect evidence, no association was identified (p=0.6062). When the analysis was disaggregated by HTA agency, IQWIG and SMC reported differences in the results. However, the procedures that each of these two agencies adopted for assessing health technologies may explain these findings.

Table 2 - Conclusion of the reports supported by direct evidence and indirect evidence by IQWIG.

Conclusion	Total supported by direct evidence(%)	Total supported by indirect evidence(%)
ATV	94 (61.84%)	2 (15.38%)
Similar	40 (26.32%)	6 (46.15%)
Inconclusive	2 (1.32%)	1 (7.69%)
No add value	16 (10.53%)	4 (30.77%)
Total	152 (100.00%)	13 (100.00%)

In the German HTA agency, using direct evidence is associated with a greater probability of concluding for ATV (p< 0.0001).

Table 3 - Conclusion of the reports supported by direct evidence and indirect evidence by SMC.

Conclusion	Total supported by direct evidence(%)	Total supported by indirect evidence(%)
ATV	89 (77.39%)	48 (92.31%)
Similar	18(15.65%)	4 (7.69%)
Inconclusive	0	0
No add value	8(6.96%)	0
Total	152 (100.00%)	52 (100.00%)

In the Scottish HTA agency, using direct evidence is associated with a less probability of concluding for ATV (p=0.0041).

CONCLUSIONS

These results suggest that there is no relationship between the directness of the evidence supporting the relative effectiveness assessment procedures and the identification of ATV. Some tendencies were identified for two HTA agencies (Germany and Scotland), which can be explained by the HTA methodologies and procedures locally adopted.

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