

Work Productivity Assessment in Clinical Trials and Subsequent Economic Modeling in Multiple Sclerosis (MS) in Two Health Technology Assessment (HTA) Archetypes

Poster #PCR17

Elizabeth Hubscher¹, Sharada Harricharan¹
¹Cytel, Inc., Waltham, MA, US

Background

- Productivity loss constitutes a substantial proportion of indirect costs in many health conditions, and may be estimated using different approaches including the human capital approach or friction cost approach.^{1,2}
- For chronic conditions, such as multiple sclerosis (MS), productivity decrements and associated indirect costs may increase with disease progression.³⁻⁴
- In one study of workers with MS, they were more limited in their fitness to work and more working disabled than matched controls.³ Activity impairment in MS has been correlated with fatigue and cognitive function, as well as worse expanded disability status scale (EDSS) scores and higher brain lesion volume.^{3,4}
- Many patients with MS are unemployed, work part-time, or report a substantial activity impairment due to MS.⁵ Trajectories of symptom burden, absenteeism/presenteeism, and costs are not fully characterized in MS.
- Several instruments are available to assess productivity in MS and can be used to capture societal costs for economic modelling and subsequent HTA; however, how they have been employed and accepted has not been reported.

Objective

- To explore the frequency and manner in which measures of productivity are employed in clinical studies and economic models to inform value assessment by HTA agencies.

Methods

Clinicaltrials.gov search

- We conducted a review of trials in MS that included productivity measures on clinicaltrials.gov. The search was conducted as follows:
 - Search term for condition or disease: "Multiple sclerosis"; Other terms: "productivity".
 - Studies could be recruiting, not yet recruiting, active not recruiting, completed, or enrolling by invitation. Terminated studies were excluded. No country or time limits were applied.
- Extracted information included the study design and phase, study location, and productivity instrument employed.

HTA reviews

- Identified trials were then cross-referenced with publicly available HTA assessment reports from two different HTA agencies: National Institute for Health and Care Excellence (NICE; England) and Dental and Pharmaceutical Benefits Agency (Tandvårds- och läkemedelsförmånsverket, TLV; Sweden).
- NICE and TLV were selected as they both publish assessment information and differ in terms of their general approach to considering the societal perspective and indirect costs. This search was expanded to include the Canadian Agency for Drugs and Technologies in Health (CADTH; Canada) and Pharmaceutical Benefits Advisory Committee (PBAC; Australia) for a representative evaluation to make comparisons.

Results

- Of 2131 studies in MS during the search period, only 30 studies reporting a productivity-related outcome were identified. Studies were primarily conducted in the US and European countries (Figure 1).
- Of the 30 included studies, half were interventional and half were observational studies. Interventional studies were primarily phase 4 (n=7) or phase 3 (n=3), though several did not specify a phase (Figure 2).

Figure 1. Study types by country

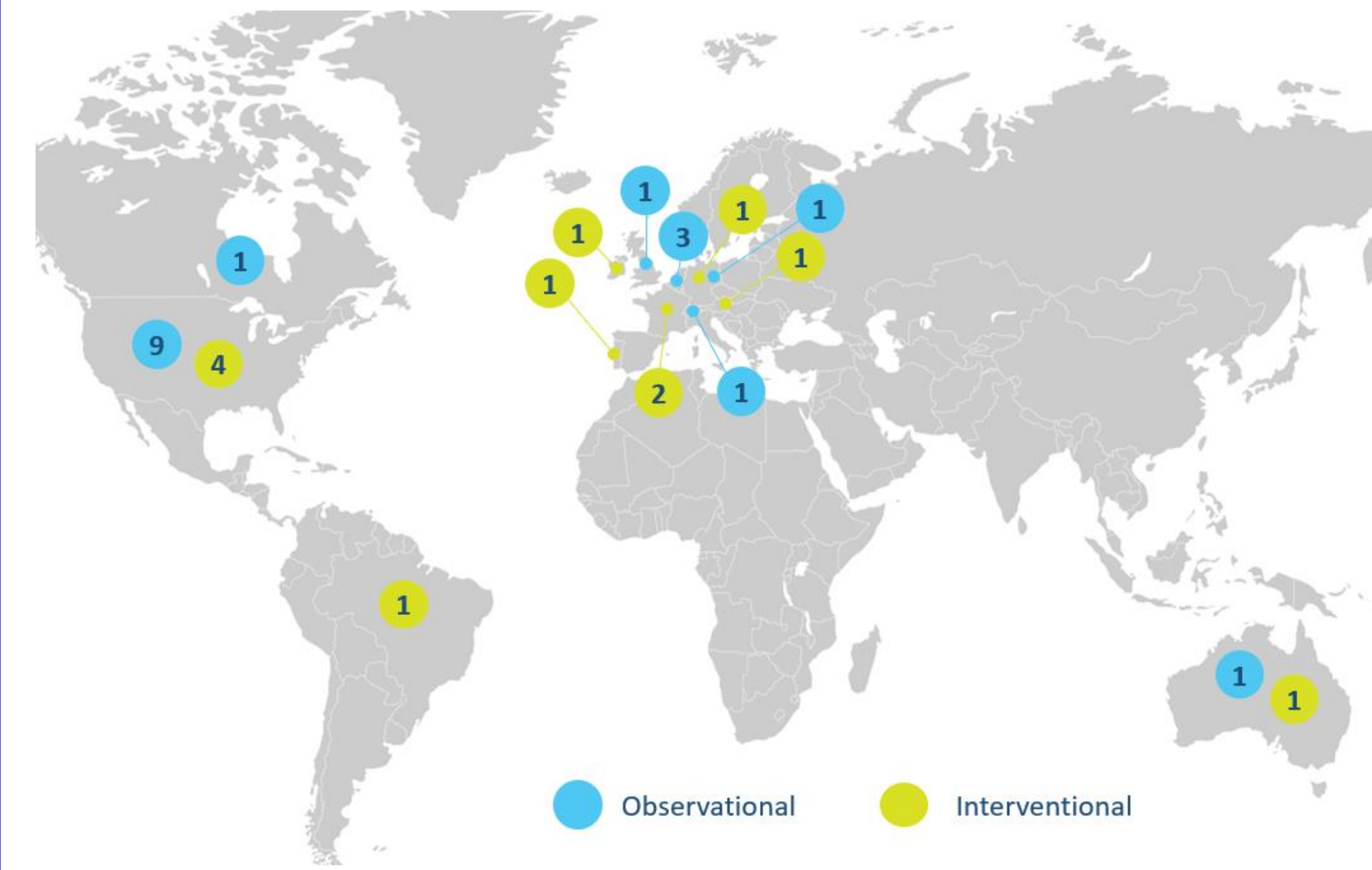
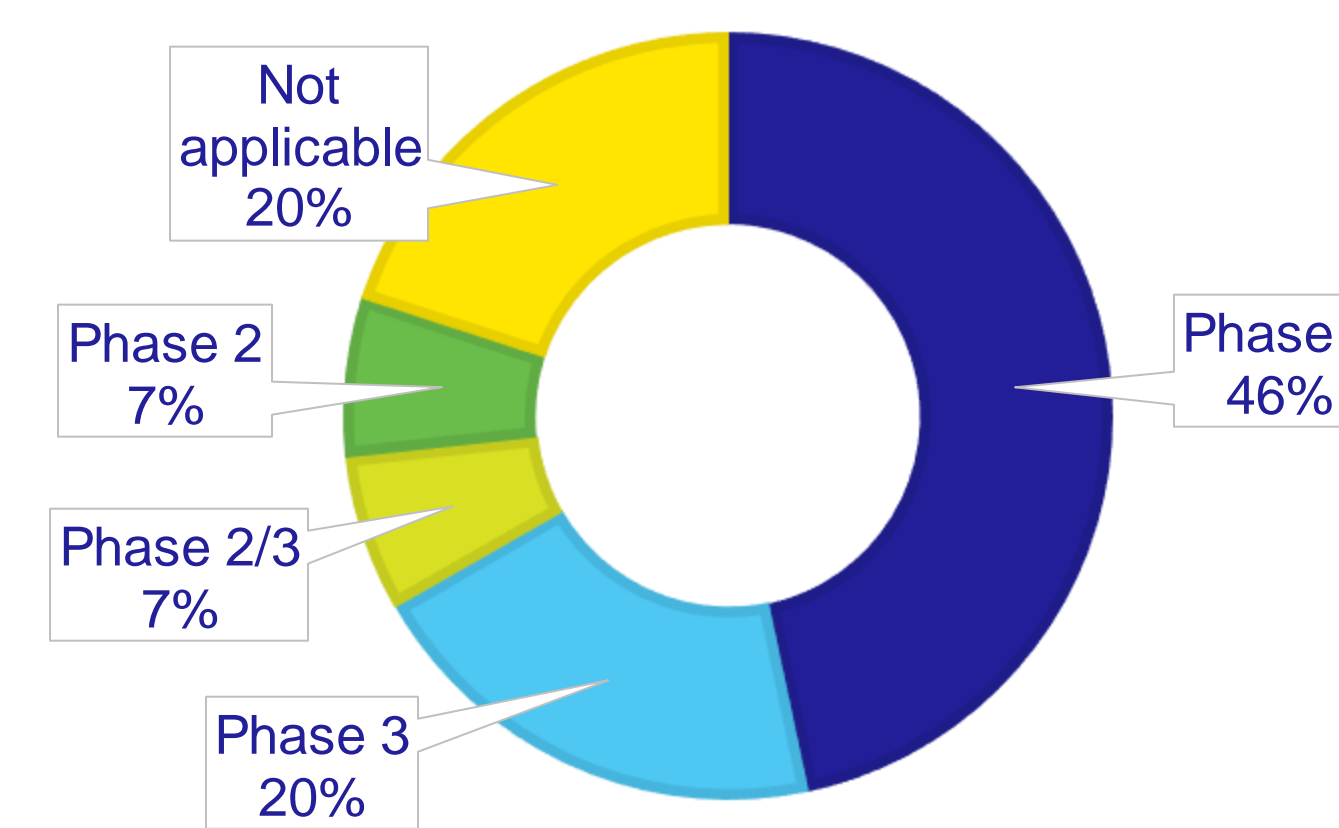
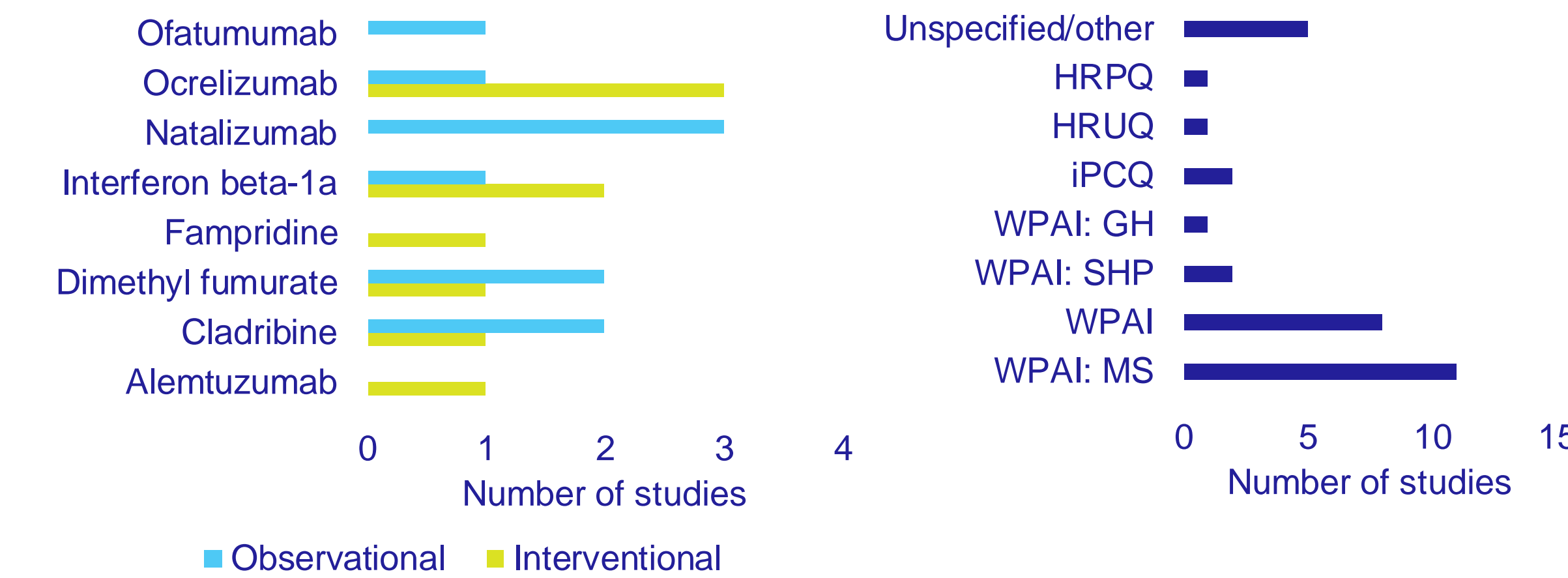


Figure 2. Phase of study



- Among reported instruments, WPAI:MS (n=11) was used most often, followed by other forms of WPAI (either WPAI, WPAI: general health, or WPAI: specific health problem; n=11) (Figure 3).
- Other instruments included the iMTA Productivity Cost Questionnaire⁶ (iPCQ) (n=2), the Health-related Productivity Questionnaire (HRPQ) (n=1), and the Healthcare Resource Utilization Questionnaire (HRUQ) (n=1). Several studies examined productivity but did not report the outcome measure used.
- A number of different treatments were included in both the interventional and observational studies; ocrelizumab was the most studied.

Figure 3. Interventions and productivity measures in MS studies



- The consideration and acceptance of indirect cost and productivity data, as well as the recommended approach for valuation, varies by HTA agency (Table 1).

Table 1. Indirect cost, productivity, and valuation by HTA agency

Country	Reference or additional analysis	Patient indirect cost consideration	Non-health outcomes considered	Approach to productivity cost
Austria	Not clear	Yes	Non-health excluded	Human capital approach
Australia	Additional	Yes	All	Not stated
Canada	Additional	Yes	All	Friction cost approach
Denmark	Reference	Yes	Patient only	Not reported
England	Additional	Yes	Non-health excluded	Not stated
Germany	Additional	Yes	Patients only	Friction cost approach
Ireland	Additional	Yes	All	Not stated
Netherlands	Reference	Yes	All	Friction cost approach
Norway	Reference	Yes	Patient only	Any
Portugal	Reference	Yes	Patient-only	Human capital approach
Scotland	Additional	No	All	Not reported
Spain	Reference	Yes	Non-health excluded	Any
Sweden	Reference	Yes	Non-health excluded	Human capital approach

Adapted from: ⁷Avşar et al. 2023

- As expected, in all seven applicable MS HTA reports identified from NICE, productivity did not inform the economic model.
- A positive TLV assessment of cladribine reported on the cost minimization analysis; details regarding productivity were not reported.⁸ Likewise, an assessment of natalizumab did not discuss productivity in the economic model.⁹ A TLV assessment of ocrelizumab reported uncertainty in the representativeness of published work-absence data in the model; of note, this data was not derived from studies identified in our search. Examination of other published HTAs for ocrelizumab did not identify specific details regarding productivity in the models, and reimbursement decisions were mixed (Table 2).

Table 2. Case study - ocrelizumab assessments by HTA agency

Agency	Considerations from HTA committee reporting	Reimbursed (Y/N)
NICE ¹⁰	No content related to productivity as not included in model; fatigue disutility and upper limb dysfunction were removed from model; generally considered cost effective vs best supportive care	Yes
TLV ¹¹	Absenteeism included in model; major impact of indirect costs on model results; uncertainty about representativeness of the population, including the patient age being higher in the input study data employed in the model than for the average age of patients with relapsing remitting MS; costs of loss of production seemed high vs TLV's normal assumptions	No
CADTH ¹²	No specific feedback regarding the inclusion of indirect costs/lost productivity (indirect costs included, productivity not mentioned; model was not transparent and was considered overly complex)	Yes
PBAC ¹³	Indirect costs included, but productivity not specifically mentioned in the public summary document; generally, the committee felt costs of care (including nursing home care) were overestimated.	No

Discussion

- The percentage of trials including productivity was low overall, but Nordic countries and the US had higher rates than the UK and other European countries.
- Productivity was more commonly collected in post-marketing studies, with the majority of studies reporting an productivity endpoint being phase 4 studies.
- As expected, in all seven applicable assessment reports identified from NICE, productivity did not inform the economic model. Publicly available assessments from TLV, which considers the societal perspective, were scarce and limited in terms of reporting of productivity considerations.
- This study was limited by the availability of data on searched databases, and is subject to any bias or missing data inherent to the included reports.
- We focused primarily on two HTA agencies and a single health technology case study. As other agencies have important differences in the inclusion of the societal perspective and approach to lost productivity in economic modelling, future study to broaden the scope of included HTAs and interventions is warranted.

Conclusions

- Productivity measures may be valuable to inform representative economic modelling in geographies that consider the societal perspective and can impact assessment results; however, current use, and consideration and acceptance by HTA bodies is variable.
- Harmonization of both approach to productivity outcome measures and valuation of related costs may help ensure equitable access across geographies.

References

- Rashdan O, Brodsky V. Productivity Loss in Patients With Chronic Diseases: A Pooled Economic Analysis of Hungarian Cost-of-Illness Studies. *Value Health Reg Issues*. 2020 Sep;22:75-82. doi: 10.1016/j.vhri.2020.07.572.
- Pike J, Grosse SD. Friction Cost Estimates of Productivity Costs in Cost-of-Illness Studies in Comparison with Human Capital Estimates: A Review. *Appl Health Econ Health Policy*. 2018 Dec;16(6):765-778. doi: 10.1007/s40258-018-0416-4. 3. Moccia M, Fontana L, Palladino R, Falco F, Finiello F, Fedele M, Lanzillo R, Reppucci L, Triassi M, Brescia Morra V, Iavicoli I. Determinants of early working impairments in multiple sclerosis. *Front Neurol*. 2022 Dec 9;13:1062847. doi: 10.3389/fneur.2022.1062847. 4. Tauhid S, Chu R, Sasane R, Glanz BI, Neema M, Miller JR, Kim G, Signorovitch JE, Healy BC, Chitnis T, Weiner HL, Bakshi R. Brain MRI lesions and atrophy are associated with employment status in patients with multiple sclerosis. *J Neurol*. 2015 Nov;262(11):2425-32. doi: 10.1007/s00415-015-7853-x. 5. Theodorsdottir A, Nielsen HH, Ravnbrun MH, Illes Z. Patient reported outcomes in a secondary progressive MS cohort related to cognition, MRI and physical outcomes. *Mult Scler Relat Disord*. 2023 Mar;71:104550. doi: 10.1016/j.msard.2023.104550. 6. Bouwmans C, Krol M, Severens H, Koopmanschap M, Brouwer W, Hakkaart-van Roijen L. The iMTA Productivity Cost Questionnaire: A Standardized Instrument for Measuring and Valuing Health-Related Productivity Losses. *Value Health*. 2015 Sep;18(6):753-8. doi: 10.1016/j.jval.2015.05.009. 7. Avşar TS, Yang X, Lorgelly P. How is the Societal Perspective Defined in Health Technology Assessment? Guidelines from Around the Globe. *Pharmacoeconomics*. 2023 Feb;41(2):123-138. doi: 10.1007/s40273-022-01221-y. 8. <https://www.tlv.se/bslut/bslut-lakemedel/generell-subvention/arkiv/2018-03-28-mavenclad-ingar-i-hogkostnadsstykdel.html?query=mavenclad>. 9. <https://www.tlv.se/bslut/bslut-lakemedel/generell-subvention/arkiv/2006-12-23-tysabri-in-i-formanerna.html?query=tysabri>. 10. <https://www.nice.org.uk/guidance/ta585/resources/ocrelizumab-for-treating-primary-progressive-multiple-sclerosis-pdf-82607204950981>. 11. <https://www.tlv.se/bslut/bslut-lakemedel/generell-subvention/arkiv/2006-12-23-tysabri-in-i-formanerna.html?query=tysabri>. 12. https://www.cadth.ca/sites/default/files/cdr/complete/SR0519_Ocrevus_RMS_complete_Nov-23-17.pdf. 13. <https://www.pbs.gov.au/industry/listing/elements/pbac-meetings/psd2020-07/files/ocrelizumab-psd-july-2020.pdf>

Abbreviations

CADTH, Canadian Agency for Drugs and Technologies in Health; EDSS, expanded disability status scale; GH, general health; HTA, health technology assessment; HRPQ, Health-related Productivity Questionnaire; HRUQ, Healthcare Resource Utilization Questionnaire; MS, multiple sclerosis; NICE, National Institute for Health and Care Excellence; PBAC, Pharmaceutical Benefits Advisory Committee; SH, specific health problem; TLV, Tandvårds- och läkemedelsförmånsverket; WPAI, Work Productivity and Activity Impairment Questionnaire

Disclosures

- None