Considerations for the Representativeness of US EHR Data for HTA Use Cases

	TRANSPORTABILITY ELEMENT	RATIONALE
☑	**Patient characteristic differences**	
☐	Baseline demographics	Demographics may encompass a set of effect-modifying variables — differences in the prevalent and incident population should be considered.
☐	Prevalence of disease	The baseline prevalence of a given disease may affect the transportability of some elements based on the mathematical association with relevant endpoints.
☐	Preference for modifiable risk-factors	Preferences, and thus the prevalence, for modifiable risk factors (smoking, obesity, etc.) within a given population may modify the transportability of outcomes between countries if these risk-factors are known effect modifiers.
☐	Biomarker prevalence	For cancers with a diverse genetic etiology, there may exist significant treatment effect heterogeneity. Therapies indicated for those cancers may lack transportability in populations with a widely different biomarker makeup. Further, because biomarker testing rates may differ between populations, those selected into the cohort may also differ and affect the transportability of outcomes.
☑	**Setting differences**	
☐	Treatment site variation	The distribution of academic and research institutions as well as high- and low-volume sites, may vary between countries, or jurisdictions, and influence the transportability of a given insight.
☐	Differences in time-to-treatment initiation within a disease's natural history	Time-to-treatment initiation may vary dramatically between countries (driven by locality's procedures to confirm diagnosis and/or healthcare system capacity) and therefore change a particular risk set and influence outcomes
☐	Disease assessment frequency	Disease assessment frequency can provide erroneous conclusions about metrics such as progression free survival or other outcomes that rely on monitoring schedules, and thus the time at which observations can be made.
☐	Preference for end of life care	In later lines of therapy, the risk-set a country chooses to treat may be different from that of another country based on differences in preferences for hospice. So, countries that tend to treat more aggressively may treat a sicker risk-set than that of a country that is more likely to choose for alternative end-of-life remedies

Contact us at rwe@flatiron.com
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	TRANSPORTABILITY ELEMENT	RATIONALE
☑	Treatment Differences	
☐	Access to a given treatment	A prevalent population may not be represented in the EHR data given restriction in access based on socio-economic status or variability in payer preferences for a given product. Thus, patients selecting into a given cohort could vary and impact observed outcomes. For example, cost-prohibitive therapies may naturally select healthier populations, and reveal better outcomes, in countries with worse access arrangements.
☐	Access to supportive care	Supportive care is known to improve outcomes for patients in many settings; however, access to supportive care varies within and between countries.
☐	Market share of the pharmaceutical(s) of interest and competitors	Environments with a large diversity of available technologies for a specific indication require contextualization for who selects into a cohort treated with a specific technology.
☐	Market share of backbone therapies used concomitantly with a therapy of interest	Even in situations where the market share for a technology of interest is the same, concomitant therapies of interest (eg. high- versus low- dose dexamethasone) may differ. If these therapies are effect-modifying, the distribution of them in the given data will affect transportability of the outcomes.
☐	Guideline differences between jurisdictions / localities	Because the approved label/reimbursement criteria for a given therapy may vary, the way a product is used between countries may also sometimes differ, which may present itself in what is known as the compound treatment problem. Further, labels may also influence the preceding drugs that patients have been exposed to, complicating the question of transportability.

Note:
This table is intended to be a dynamic, living tool that will change over time. As Flatiron Health develops more learnings from experience with HTA use cases, and transportability nuances that arise, this tool will continue to be updated.

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