POSTER
#PSY5

ECONOMIC VALUE DRIVERS IN SEVERE RED BLOOD CELL DISORDERS: A REVIEW AND DEVELOPMENT OF AN ECONOMIC CONCEPTUAL FRAMEWORK

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PURPLE SQUIRREL ECONOMICS

BACKGROUND

- Red blood cell (RBC) transfusion was historically the standard of care in the treatment of anemia. This practice has fallen out of favor because of the increased risk of adverse events such as fatal organ failure.
- Erythropoiesis-stimulating agents (ESAs) received initial approval for anemia related to chronic renal failure in 1989. Multiples sources have reported reduction in the need for RBC transfusion in patients treated with an ESA.
- The success of ESAs shows that it is possible to increase clinical benefits to patients through new drugs. This study evaluated newer treatments for severe types of anemia between 2010 and 2020. The objective was to explore the landscape of economic evaluations conducted in the last few years.
- Subsequently, a guideline for future economic evaluations modeling severe types of anemia will be created based on the strengths and weaknesses of the identified studies.

OBJECTIVE

The purpose of this study is to inform the conceptual framework for future economic research in severe anemia by reviewing published economic studies in major RBC disorders including autoimmune hemolytic anemia, beta-thalassemia, chemotherapy-induced anemia, chronic kidney disease anemia, and severe aplastic anemia.

METHODS

Database:
A targeted literature review was conducted via PubMed Central ® (PMC), Google Scholar, and Ovid.

Selection criteria:
The studies were stratified by multiple specifications such as study design and perspective, disease area, treatments, time horizon, and costs.

Selection criteria (CONT'D):
1. The study designs must be a budget impact model (BIM), cost-effectiveness analyses (CEA) or cost-utility analyses (CUA).
2. The disease of interest in the study must be related to any type of severe anemia, and stem cell transplant treatment was excluded.
3. The study must have been published between 2010 and 2020.
4. Only studies published in English were considered.

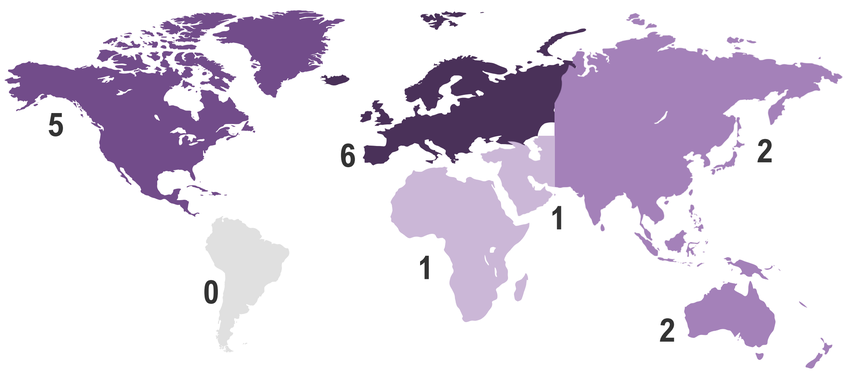
RESULTS

DISEASE	COUNTRY	STUDY	TYPE OF STUDY	TIME HORIZON	PERSPECTIVE	TREATMENT
β-thalassemia	Thailand	Luangasanatip et al.	CUA	Lifetime	Societal	Deferasirox (DFX) vs deferiprone (DFP)
	Australian	Karnon et al.	CUA	50 years	Healthcare payer	DFX vs Deferoxamine (DFO)
	United Kingdom	Bentley et al.	CUA	5 years	Healthcare payer	DFO, DFP, DFX & combination therapy (DFO-DFP)
	China, Taiwan	Ho et al.	CUA	50 years	Healthcare payer	DFX vs DFO
	Iran	Keshtkaran et al	CUA	Lifetime	Societal	DFX vs DFO
	Poland	Walczak et al.	CUA	1 years	Healthcare payer	DFX vs DFO
	Italy	Pepe et al.	CUA	5 years	Healthcare payer	DFX vs DFP
AIHA	Italy	Rognoni et al.	BIM	3 and 5 years	Hospital and taxpayer	Rituximab originator vs rituximab biosimilars and SC vs IV
Chemotherapy-Induced Anemia	Greece	Nikolaidi et al.	BIM	15 weeks	Social Security funds	ESA originator vs ESA biosimilar
SAA	United States	Tremblay et al.	BIM	3 years	Private healthcare system	EPAG + ATGAM + Cyclosporine vs ATGAM + Cyclosporine
	Germany	Heublein et al.	CEA	1 year	Healthcare payer	h-GAM (ATGAM) vs R-GAM (thymoglobulin)
Chronic Kidney Disease-Related Anemia	United States	Yarnoff et al.	CEA	Lifetime	Healthcare payer	ESA for optimal Hb level
	Australia	Wong et al.	CEA	Lifetime	Healthcare payer	IV vs oral iron supplementation
	Canada	Clement et al.	CUA	Lifetime	Healthcare Payer	ESA vs without ESA
	Canada	Tsao et al.	BIM	5 years	Healthcare payer	ESA originator vs ESA biosimilar
	Morocco	Maoujoud et al.	CUA	1 year	Healthcare payer	Continuous erythropoietin receptor activator vs epoetin beta vs Red blood cell transfusion
	United States	Quon et al.	CEA	5 years	Healthcare payer	ESA for optimal Hb level

Database:
17 studies satisfied the inclusion/exclusion criteria. Seven studies evaluated therapies in Beta-thalassemia, one in autoimmune hemolytic anemia (AIHA), one in chemotherapy-induced anemia, two in severe aplastic anemia, and six in chronic-kidney disease anemia.

Reported assessing uncertainty:
Uncertainty could be evaluated through different methods such as scenarios, probabilistic sensitivity analyses, or deterministic sensitivity analyses. 14 studies (82%) reported one of the tools used to assess uncertainty, and three studies didn't report any uncertainty assessment.

Number of studies by continent:



Model structure:
Various cost-analysis models were found in the literature, but Markov models were the most popular, used in nine studies (52%). Micro-simulations were used in two studies (12%), and model type went unreported in two studies (12%). Four of the studies were budget impact models.

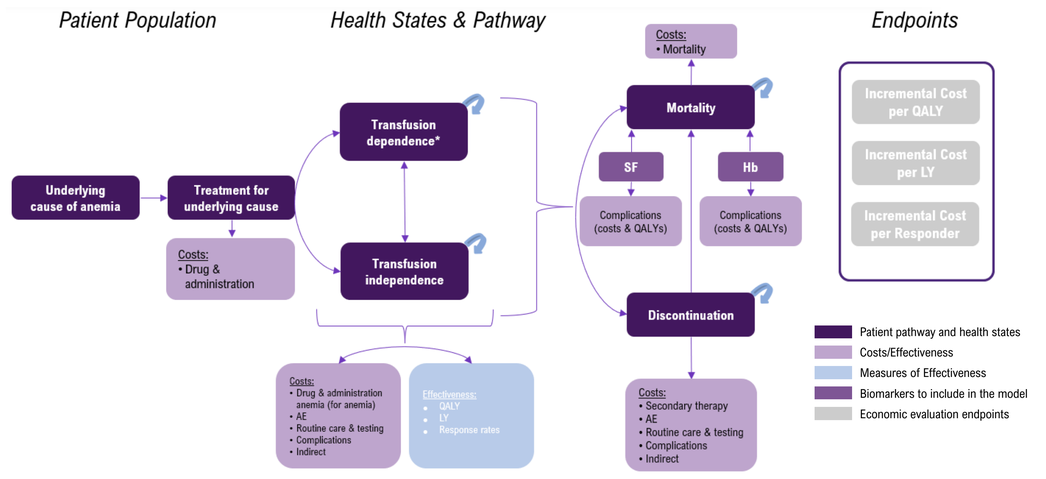
Framework for health economics studies:
A general conceptual framework was developed for CEAs and CUAs in severe anemia from the targeted literature search. The framework is specifically aimed at CEAs and CUAs but should also be considered by health economists creating BIMs.

GUIDELINE

Treatment comparisons
- If multiple trials are used, an indirect treatment comparison (ITC) should be performed.
- An unadjusted ITC could lead to bias if there is significant heterogeneity in evaluated population characteristics.
- The usage of simulated treatment comparison (STC) or matching-adjusted indirect comparison (MAIC) should be
- It is recommended to consult a clinical expert to assess the acuteness of the extrapolated long-term outcomes of the trial data.

Complications and adverse events
- Serum ferritin and hemoglobulin levels should be used as a proxy for complications and adverse events. The hemoglobulin levels were only directly considered in five economic evaluations, mostly chronic kidney diseases anemia related.
- The modeling approach should consider the dynamic rates of long-term complications based on the transfusion burden, serum ferritin, and the hemoglobulin level.

Health states
- Multiple health states should be considered when creating a model related to severe types of anemia.
- Transfusion-dependent patients are more likely to need hospitalization and outpatient visits.
- A decrease in quality of life has been associated with iron overload, which could be estimated through serum ferritin.
- Hemoglobulin also influence patient's quality of life. Patients with elevated/reduced hemoglobulin are prone to adverse events and mortality.



*Transfusion dependent health states should be separated by level of transfusion burden when possible if data permits – this will facilitate a more granular, accurate approach as different levels of transfusion burden area associated with different costs and quality of life Acronyms: AE, adverse event; Hb, hemoglobin; LY, life years; QALY, quality-adjusted life years; SF, serum ferritin.

Costs
- Direct and Indirect costs should be included in the analysis (adverse event, long-term complication, mortality, and productivity costs)
- the analysis should include long term costs since most of the condition evaluated are chronic.

Sensitivity analysis
- Each study should contain an assessment of uncertainty. In each model, multiple assumptions are made and thus should be tested.
- BIMs should have a one-way deterministic sensitivity analysis. CEAs and CUAs should also report one-way deterministic analyses, but also include probabilistic sensitivity analyses.
- The distribution of each variable must be related to the type of variable (costs, odd-ratio, probabilities, utilities, etc.)

FUTURE LANDSCAPE

Key considerations for future analyses:
1- Including hemoglobin and iron concentration level in the model
2- Include indirect costs (adverse events, mortality, and productivity costs)
3- Assess uncertainty through sensitivity analyses.
4- Inclusion of multiple transfusion-dependent health states if possible

Limitations:
The proposed conceptual framework does not include all the disease-specific reality complications. It should be used as a recommendation rather than an exact reality. The modeler might have to face different challenges such as:
- Limited access to data for indirect treatment comparison considering the type of data is not always reported by studies.
- Need to adjust the model for specific treatment related to the disease such as kidney transplant for chronic kidney disease.

CONCLUSIONS

Multiple gaps were found in the published economics literature for severe anemia-related diseases. The objective was to identify those gaps and create a conceptual framework to help future economic evaluations in severe types of anemia. More specifically, key considerations for future economics evaluations consist of the inclusion of Hb and Iron concentrations levels in the model, multiple transfusion-dependent health states if possible, long-term complications, adverse events, early mortality, and productivity costs.

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