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Aligning investigational designs and data sources with evidence needs in healthcare research

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Conflict of interest

Massoud Toussi is an employee of Cytel Inc which provides services to pharmaceutical, biotechnology and medical device industry as well as governmental and non-for-profit organizations. He declares no conflict of interest with regards to the subject of this presentation.



Background and objectives



A Hierarchy of Evidence

A hierarchy of evidence (or levels of evidence) is a heuristic used to rank the relative strength of results obtained from scientific research.



>80 Hierarchies

More than 80 different hierarchies have been proposed for assessing medical evidence. An example is Oxford Centre for Evidence-Based Medicine (CEBM) Levels of Evidence)¹



Criticism

However, they are subject of criticism^{2,3,4}:

- Too much focus on the assessment of efficacy
- Too much emphasis on clinical trials
- Low importance of clinical and epidemiological plausibility
- Lack of consideration for data sources

Goal

To develop a new way of aligning evidence needs with investigational designs and data sources, providing a wider range of possibilities

ALIGN: Aligning investigational designs and data sources with evidence needs in healthcare research

We formed a multidisciplinary group of experts, the « Align working group » from different stakeholders including regulators, HTA bodies, academia, consulting, pharmaceutical and medical device companies.

The working group **defined** categories of evidence needs, study designs and data sources in separate breakout sessions.

Then, they will get together to debate and approve the categories

The working group aligned on its **preference** of study designs and data sources for each of the evidence needs

A group of independent experts and users **reviewed** the result of the previous two steps and provides comments on the relevance of the alignment matrix.

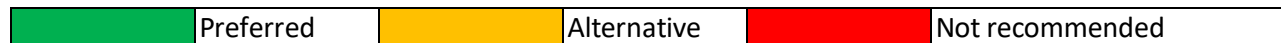
The Align working group reconvened and **adjudicate** on the comments received.

Alignment between evidence needs and study designs

		Study Design												
		Interventional designs					Non-interventional designs							
		Evidence synthesis (meta-analysis of multiple sources)	Randomized controlled trial	Randomized trials with pragmatic aspects	Registry-based RCTs	Single arm trial with and without ECA	Cohort study including case-control sampling	Cross-sectional study (survey)	Case series studies	Ecological studies	Before-after study incl. interrupted time series	Cross-over designs	Qualitative research and implementation designs	Simulation studies for example Monte Carlo and Modelization
Evidence needs	Number of patients exposed to the intervention	Yellow	Red	Red	Red	Red	Green	Green	Red	Red	Green	Red	Red	Yellow
	Characteristics of patients receiving or not the intervention	Red	Red	Yellow	Yellow	Red	Green	Green	Red	Red	Red	Red	Yellow	Yellow
	Ascertainment of short-term comparative safety effects	Green	Green	Green	Green	Green	Green	Red	Green	Yellow	Yellow	Green	Red	Red
	Ascertainment of long-term comparative safety effects	Green	Yellow	Yellow	Yellow	Green	Green	Red	Green	Yellow	Yellow	Red	Red	Red
	Real world effectiveness, including comparative	Green	Red	Green	Green	Green	Green	Red	Red	Red	Green	Green	Red	Red
	Efficacy and effectiveness of the intervention	Green	Green	Yellow	Red	Yellow	Red	Red	Red	Red	Red	Yellow	Red	Yellow
	Measure of compliance, adherence (drugs), acceptability and adoption (medical devices), usability and engagement (digital products)	Red	Red	Red	Red	Red	Green	Red	Red	Yellow	Green	Red	Red	Red
	Patient experience, preference and satisfaction	Green	Green	Green	Green	Green	Green	Green	Red	Red	Red	Red	Green	Red
	Impact of the intervention on the quality of life	Green	Green	Green	Green	Green	Green	Green	Red	Red	Red	Red	Yellow	Red
	Epidemiology of the disease	Red	Red	Red	Red	Red	Green	Green	Red	Red	Red	Red	Red	Yellow
	Understanding the standard of care	Red	Red	Red	Yellow	Red	Green	Green	Red	Red	Green	Red	Yellow	Red
	Burden of illness	Yellow	Yellow	Yellow	Yellow	Yellow	Green	Green	Yellow	Red	Red	Red	Green	Red
	Predictive accuracy of diagnostic tests and devices	Green	Green	Green	Green	Green	Green	Green	Red	Red	Red	Red	Red	Yellow
	Health system impact of the intervention, including environmental, organizational, cultural, and ethical	Red	Red	Red	Red	Red	Green	Green	Red	Yellow	Red	Red	Yellow	Yellow
	Equity and access to the intervention	Red	Red	Red	Red	Red	Green	Green	Red	Yellow	Red	Red	Yellow	Yellow
	Resource utilization	Red	Red	Yellow	Red	Red	Green	Green	Red	Red	Red	Red	Red	Red
	Cost estimation	Red	Red	Red	Red	Red	Green	Green	Red	Red	Red	Red	Red	Yellow


Alignment between evidence needs and data sources

	Data sources									
	Primary data collected for a specific research study	Secondary (data that were collected for purposes other than the specific research study under consideration)								Synthetic
Evidence needs	(The investigator controls what to measure, when to measure, and how to measure)	Patient or drug registry	Claims data	Electronic medical records	Pharmacy data	Medical Device / consumer digital health technology (DHT), mobile device and wearables data	Social media and platforms	Biobanks and genomics data	Aggregated data (environmental and government)	synthetic/simulated data
Number of patients exposed to the intervention	Green	Green	Green	Green	Green	Red	Yellow	Red	Red	Yellow
Characteristics of patients receiving or not the intervention	Green	Green	Green	Green	Yellow	Yellow	Yellow	Green	Red	Red
Ascertainment of short-term comparative safety effects	Green	Green	Green	Green	Red	Red	Red	Red	Red	Red
Ascertainment of long-term comparative safety effects	Green	Green	Green	Green	Red	Red	Red	Red	Red	Red
Real world effectiveness, including comparative	Green	Green	Green	Green	Red	Red	Red	Yellow	Red	Red
Measure of compliance, adherence (drugs), acceptability and adoption (medical devices), usability and engagement (digital products)	Green	Green	Green	Green	Green	Red	Red	Yellow	Red	Red
Patient experience, preference and satisfaction	Green	Green	Green	Green	Green	Green	Green	Red	Red	Red
Impact of the intervention on the quality of life	Green	Green	Red	Red	Red	Green	Green	Red	Red	Red
Epidemiology of the disease	Green	Green	Red	Red	Red	Yellow	Yellow	Red	Red	Red
Understanding the standard of care	Green	Green	Red	Green	Red	Red	Red	Red	Red	Red
Burden of illness	Yellow	Green	Green	Green	Red	Red	Red	Red	Red	Red
Measure of compliance, adherence (drugs), acceptability and adoption (medical devices), usability and engagement (digital products)	Green	Green	Green	Green	Green	Green	Yellow	Red	Red	Red
Patient experience, preference and satisfaction	Green	Green	Yellow	Green	Red	Red	Red	Red	Green	Red
Predictive accuracy of diagnostic tests and devices	Green	Green	Green	Green	Red	Red	Red	Red	Red	Red
Health system impact of the intervention, including environmental, organizational, cultural, and ethical	Green	Green	Yellow	Yellow	Red	Red	Red	Red	Red	Red
Equity and access to the intervention	Green	Yellow	Red	Red	Yellow	Red	Yellow	Red	Red	Red
Resource utilization	Green	Green	Green	Yellow	Yellow	Red	Yellow	Red	Red	Red
Cost estimation	Green	Green	Green	Green	Yellow	Red	Red	Red	Red	Red
Predictive accuracy of diagnostic tests and devices	Green	Yellow	Green	Yellow	Yellow	Red	Red	Red	Green	Red



Question for the audience

What are the use cases of ALIGN matrix?

A black smartphone is shown vertically, centered on the right side of the slide. The screen is white and displays the text "Please use your app to answer the question" in a bold, orange-to-red gradient font. The phone is set against a large, semi-circular background that transitions from white on the left to a vibrant pink on the right.

**Please use
your app to
answer the
question**

Conclusion

The value of the ALIGN matrix

- More Inclusive of various evidence needs
- Provides a more comprehensive view on the study designs and data sources
- Dynamic grading possible as the data sources and methods progress

The quality of data or the execution of the study is not taken into the account; and will be subject of future work. The current alignment is suggested under the assumption of standard quality.

Use cases

- HTA and HTA modeling
- Evidence strategy planning
- Stakeholder communication
- Data asset evaluation

Publication under preparation

Acknowledgments

Name	Surname	Stakeholder category	Affiliation
Massoud	Toussi	Consultancy	Cytel
Alessandra	Blonda	Academia	KU Leuven
Lieven	Annemans	Academia	TRUST4RD, UGent
Marc	Berger	Consultancy	Freelance
Elise	Berliner	Pharmaceutical	Cerner Envisa
Robyn	Bluhm	Academia	Michigan State University and Lyman Briggs College
Christopher	Blunt	Academia	London School of Economics
Gracy	Crane	Pharmaceutical	Roche
Gianmario	Candore	Pharmaceutical	Bayer
Chiara	De Waure	Professional societies	HTAi
Nancy	Dreyer	Consultancy	Dreyer Strategies
Karen	Facey	Consultancy	RWE4Decisions, FIPRA
Jennifer	Graff	Farma	NPC
Amanda	Hodgson	HTA	HTAi / CADTH

Name	Surname	Stakeholder category	Affiliation
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Usha	Kraeden	Medical device	Intuitive Surgical
Laurie	Lambert	HTA	CADTH
Francois	Meyer	Freelance	RWE4Decisions, FIPRA
Motiur	Rahman	Regulator	FDA
Mats	Rosenlund	Pharma	Daichi Synkyo
Laura	Sampietro Colom	Hospital HTA	Hospital Clinic Barcelona
Anja	Schiel	HTA	NoMa (Norway)
Sebastien	Schneeweiss	Academia	Harvard/Aetion
Montse	Soriano Gaborro	Pharma	Bayer Pharmaceuticals
Patrice	Verpillat	Regulatory	EMA
Nicola	Vicari	HTAi	HTAi
Shirley	Wang	Academia	Harvard
Shahid	Hanif	Consultancy	GetReal Institute

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Thank you