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Improving Evidence Generation from Rare Disease Registries: Need for Harmonization of Data

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Poster Session Time: 9:00 - 11:30
Discussion Period: 9:00 - 10:00

BACKGROUND

- Rare disease registries represent an important source of knowledge to better understand the natural history and clinical trial endpoints for diseases that are often phenotypically and genetically diverse.
- However, registries for the same disease indication often differ in scope, objectives, and recruitment criteria, as well as data elements captured. [1]
- Efforts to standardize the type and definitions of data elements across rare disease registries have been minimal, related in part to their geographic variability.

OBJECTIVE

This research explores an approach called a Variable Gap Analysis that enables a detailed comparison of data elements and other registry characteristics across multinational rare disease registries.

METHODS

The Variable Gap Analysis consists of 4 steps described in Figure 1.

Figure 1. 4 Steps Involved to Conduct a Variable Gap Analysis.

01 Conduct Literature Review
- Identify current registries and other potential data sources for disease(s) of interest who have already published results from studies or related research efforts

02 Develop Customized Feasibility Questionnaire
- Develop a customized Feasibility Questionnaire (FQ) to provide to selected registries
- FQ requests information on population characterizes, data relevance, population size, data quality, and data sharing/governance polices

03 Perform Outreach and Engagement
- Performed outreach and engagement to selected registries with relevant populations
- Request data owner to complete FQ and provide data dictionary/CRF/etc.

04 Conduct Variable Gap Analysis
- Compare variables in each registries database with critical variables needed for clinical development programs and/or HTA evaluations
- Each critical variable will be evaluated as Exact Match, Logical Match, Omitted

Figure 2. Sample Questions from a Feasibility Questionnaire for Registries Assessment.

2. What entities contribute patient to your data source?

☐ Individual Participants (e.g., Patients/guardians only enter data)
Please specify details (e.g., countries):

☐ Individual Clinical Sites (e.g., Sites only enter data)
Please Specify details (e.g., number of sites and country locations):

☐ Individual Clinical Sites and Participants (e.g., Sites and Patients enter data)Please specify details (e.g., countries):

☐ A consortium of established registries/institutionsPlease list all names and locations (e.g., countries):

3. What is the Inclusion and/or Exclusion requirements for a patient to be eligible for your data source?

15. What data does your data source collect?

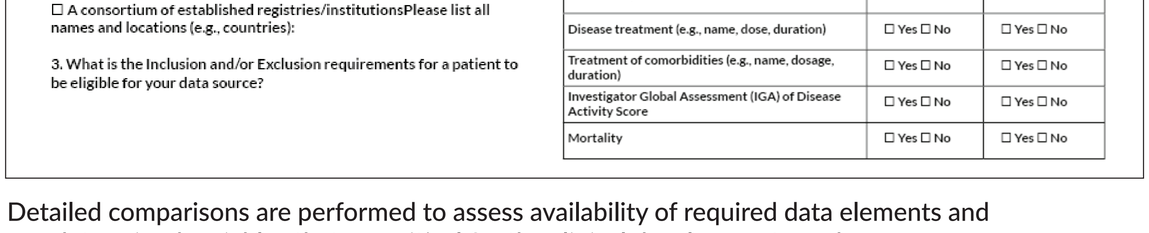
Information	Disease Subtype 1 please tick Yes/No	Disease Subtype 1 please tick Yes/No
Genetic mutation confirmation	☐ Yes ☐ No	☐ Yes ☐ No
Pulmonary function testing	☐ Yes ☐ No	☐ Yes ☐ No
Radiological assessment (e.g., MRI, CT scan, HRCT)	☐ Yes ☐ No	☐ Yes ☐ No
Current or prior medical conditions	☐ Yes ☐ No	☐ Yes ☐ No
Disease treatment (e.g., name, dose, duration)	☐ Yes ☐ No	☐ Yes ☐ No
Treatment of comorbidities (e.g., name, dosage, duration)	☐ Yes ☐ No	☐ Yes ☐ No
Investigator Global Assessment (IGA) of Disease Activity Score	☐ Yes ☐ No	☐ Yes ☐ No
Mortality	☐ Yes ☐ No	☐ Yes ☐ No

Detailed comparisons are performed to assess availability of required data elements and pre-determined variables that are critical for the clinical development needs:
(1) between data elements that exist in a single registry
(2) across multiple disease registries

RESULTS

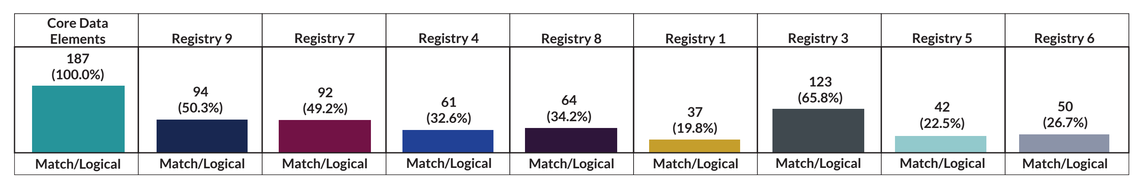
Metrics of variable alignment are presented that display indication of the commonality and/or variance of data elements (i.e., exact match, logical match, omitted).

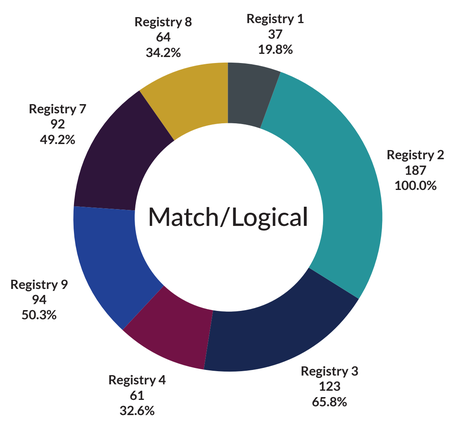
Figure 3. Variable Gap Analysis Results: Comparison of Results for Multiple Disease Registries for Variables that are Exact/Logical Matches or Omitted.



			Core Data Elements	Registry 1	Registry 2	Registry 3	Registry 4	Registry 5	Registry 6	Registry 7	Registry 8
AE	AE	Action taken with treatment	Exact Match	Omitted	Omitted	Omitted	Omitted	Omitted	Logical Match	Omitted	Omitted
		AE term	Exact Match	Logical Match	Logical Match	Omitted	Omitted	Omitted	Logical Match	Omitted	Logical Match
		CTCAE Grade	Exact Match	Omitted	Omitted	Omitted	Omitted	Omitted	Logical Match	Omitted	Omitted
		Outcome	Exact Match	Omitted	Omitted	Omitted	Omitted	Omitted	Logical Match	Omitted	Omitted
		Relationship with Treatment	Exact Match	Omitted	Logical Match	Omitted	Omitted	Omitted	Logical Match	Omitted	Omitted
		Serious AE	Exact Match	Omitted	Logical Match	Omitted	Omitted	Omitted	Logical Match	Omitted	Omitted
		Serious Criteria	Exact Match	Omitted	Omitted	Omitted	Omitted	Omitted	Logical Match	Omitted	Omitted
		Start Date	Exact Match	Logical Match	Logical Match	Omitted	Omitted	Omitted	Logical Match	Omitted	Omitted
		Stop Date	Exact Match	Omitted	Logical Match	Omitted	Omitted	Omitted	Logical Match	Omitted	Omitted
Demog	Caregiver Contact Information	Alternative phone number	Exact Match	Omitted	Omitted	Omitted	Omitted	Logical Match	Omitted	Omitted	Omitted
		Cell (mobile) Phone	Exact Match	Omitted	Omitted	Omitted	Logical Match	Logical Match	Omitted	Omitted	Omitted
		Email	Exact Match	Omitted	Omitted	Omitted	Logical Match	Logical Match	Omitted	Logical Match	Omitted
		First/Last Name	Exact Match	Omitted	Omitted	Omitted	Logical Match	Logical Match	Omitted	Logical Match	Omitted
	Consent/Assent	Assent Acknowledgment	Exact Match	Omitted	Omitted	Omitted	Omitted	Logical Match	Logical Match	Omitted	Omitted

Figure 4. Variable Gap Analysis Results: Alignment Across Multiple Disease Registries for Variables that are Exact or Logical Matches.





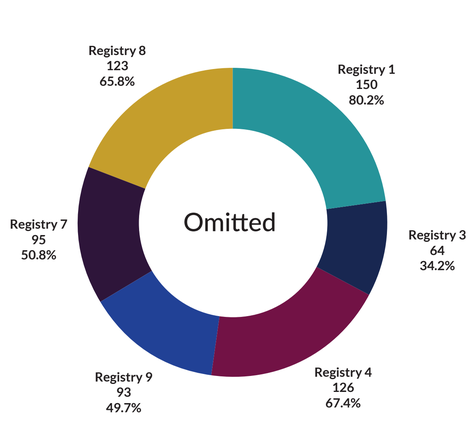


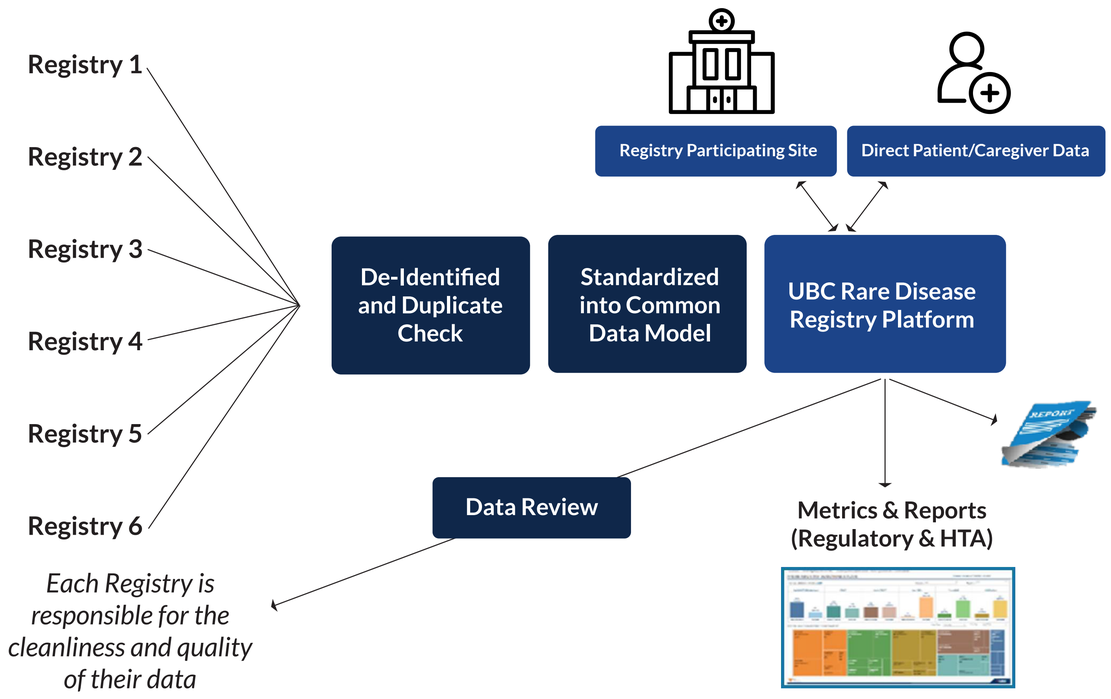
Table 1. Variable Gap Analysis Results: Assessments Across Multiple Disease Registries for Specific Data Elements.

Categories of variables	Time of assessment	Variable	Detailed information	Registry #1	Registry #2 Comments	Registry #2	Registry #2 Comments	Registry #3	Registry #3Comments
Demography and diagnosis	Baseline	Sex	Male/female/unkown	Logical Match	Patients gender male/female collected	Logical Match	Question = Sex. Responses: Female, Male, Currently UNK, Truly UNK.	Omitted	
Demography and diagnosis	Baseline and follow-up	Pulmonary function test	FEV1/FVC	Omitted		Omitted		Logical Match	Collected only at Baseline.
Demography and diagnosis	Baseline and follow-up	Blood sampling	eGFR (and equation)	Omitted		Omitted		Omitted	
Treatments	Baseline and follow-up	Concomitant treatments (e.g. antiplatelets, antihypertensive	brand and generic name	Omitted	Only treatment of rare disease collected	Omitted		Omitted	
Measures of disease activity	Baseline and follow-up	Patient (Caregiver) Global Assessment of Disease (PGA-VAS)	change from baseline	Logical Match	Collected only at Baseline.	Exact Match		Logical Match	Collected only at Baseline.
Death or patient withdrawal	Follow-up	Primary reason for Death	DDMMMYYYY	Logical Match	Question = Main cause of Death. Answer in ICD10	Omitted		Omitted	

CONCLUSION

- Variable Gap Analysis for rare disease registries can play an important role in preparing for harmonization of data to address important clinical questions for developing new therapies to treat patients with unmet medical needs.
- Importantly, harmonization of data across multiple registries, despite challenges, can address research questions that require more generalizable clinical information and larger sample sizes than are available in a single rare disease registry.
- Ultimately, this approach is expected to increase collaboration amongst researchers and reduce the time to medication approval and access to patients.

Figure 5. Variable Gap Results Lead to Development of Integrated Registry Database.



REFERENCES

1. Gisslander et al. Orphanet Journal of Rare Diseases (2023) 18:253, https://doi.org/10.1186/s13023-023-02841-z