

Evidence-Based Design and Evaluation of a Whole Genome Sequencing Clinical Report for the Reference Microbiology Laboratory

Anamaria Crisan, Geoffery McKee, Tamara Munzner, & Jennifer L. Gardy
University of British Columbia



<https://doi.org/10.1101/199570>



@amcrisan | @ DrGWM | @tamaramunzner | @jennifergardy

Mycobacterium Whole Genome Sequencing Report from MGIT Positive Samples

Not for diagnostic use

01/02/1915

Sample Details			
Sequencing Location	Oxford	Date received in Lab	
Local Lims Specimen ID	123456789	Run date	01/01/19150115
Guuid	123456-79aab-910abr-15243hg		

Organism Identification	
Predicted/closest match	
TBCOMP/microti	100%
TBCOMP	100%
TBCOMP/TB	96.77%
TBCOMP/tuberculosis-canettii	35.71%
MACCOMP	21.21%

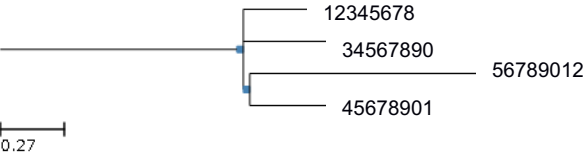
Sample/Sequencing Quality			
Total reads (~millions)	Mapped %	No reads mapped (~millions)	Coverage %
4.73	99.47	4.7	91.99

Resistance Summary						
INH	RIF	EMB	PZA	QUI	SM	AG
U	S	S	S	S	S	S

Resistotype					
Drug	Mutation	Nucleotides	Support (ACGT)	Source – (R/Total)	Prediction
INH	katG_A727T	GCC->ACC	(160/0/1/0) (0/164/0/0) (0/167/0/0)	Unclassified	UNK

Relatedness			
NB: This data may be added or updated at a later date			
Nearest neighbour(s)			
Sample -Plate Name	Date received in Lab	Centre	No. of SNPs apart
123456789		Oxford	0
34567890	1900-01-01		10
45678901	1015-01-31	Oxford	15
56789012		London	8

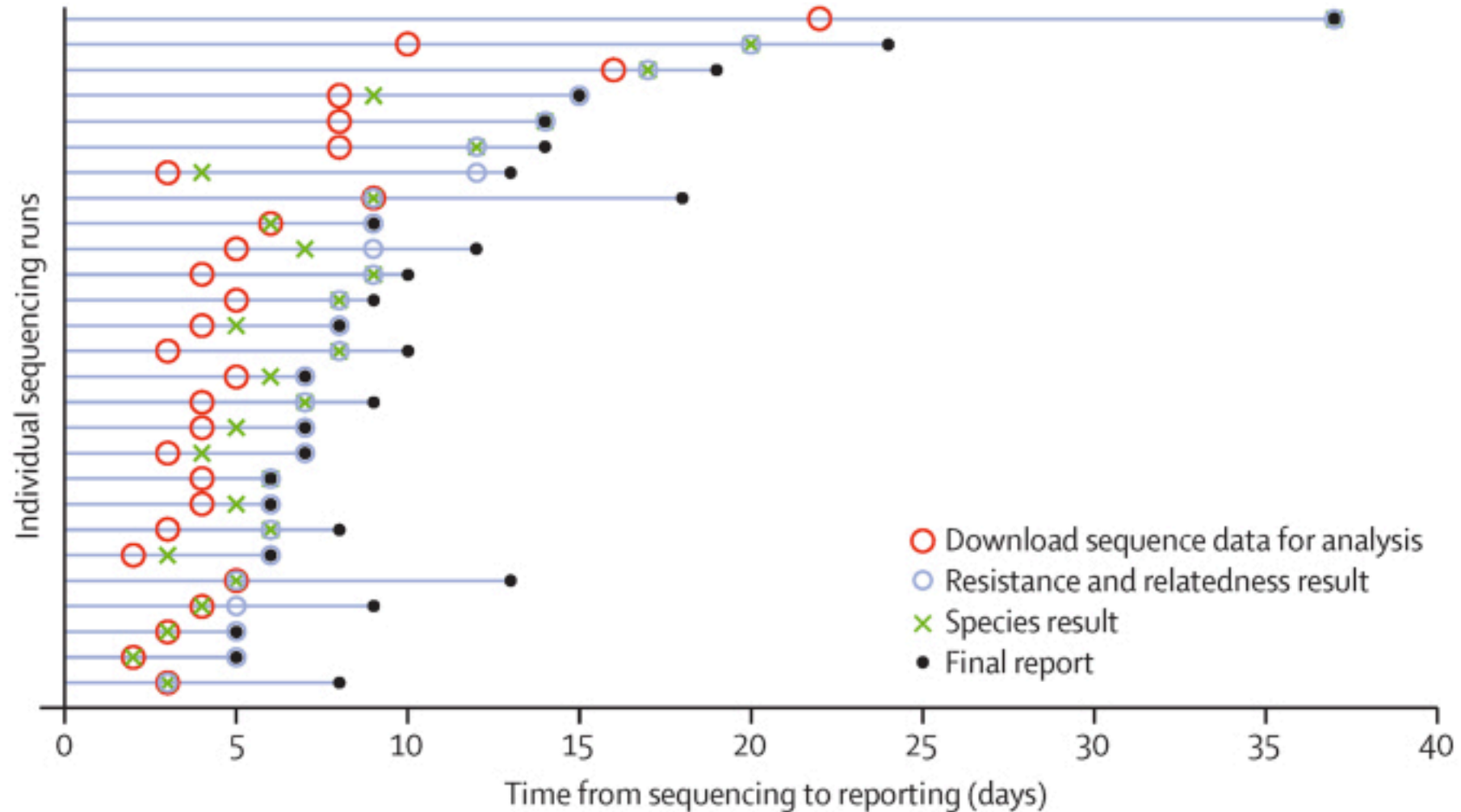
The alignment width is 285. Multiply this number by the tree metrics.



Comments

Authorised	
Signature:	Print name:
Position:	Date:

COMPASS-TB : Clinical WGS for Mycobacteria



COLLABORATION



THE UNIVERSITY
OF BRITISH COLUMBIA



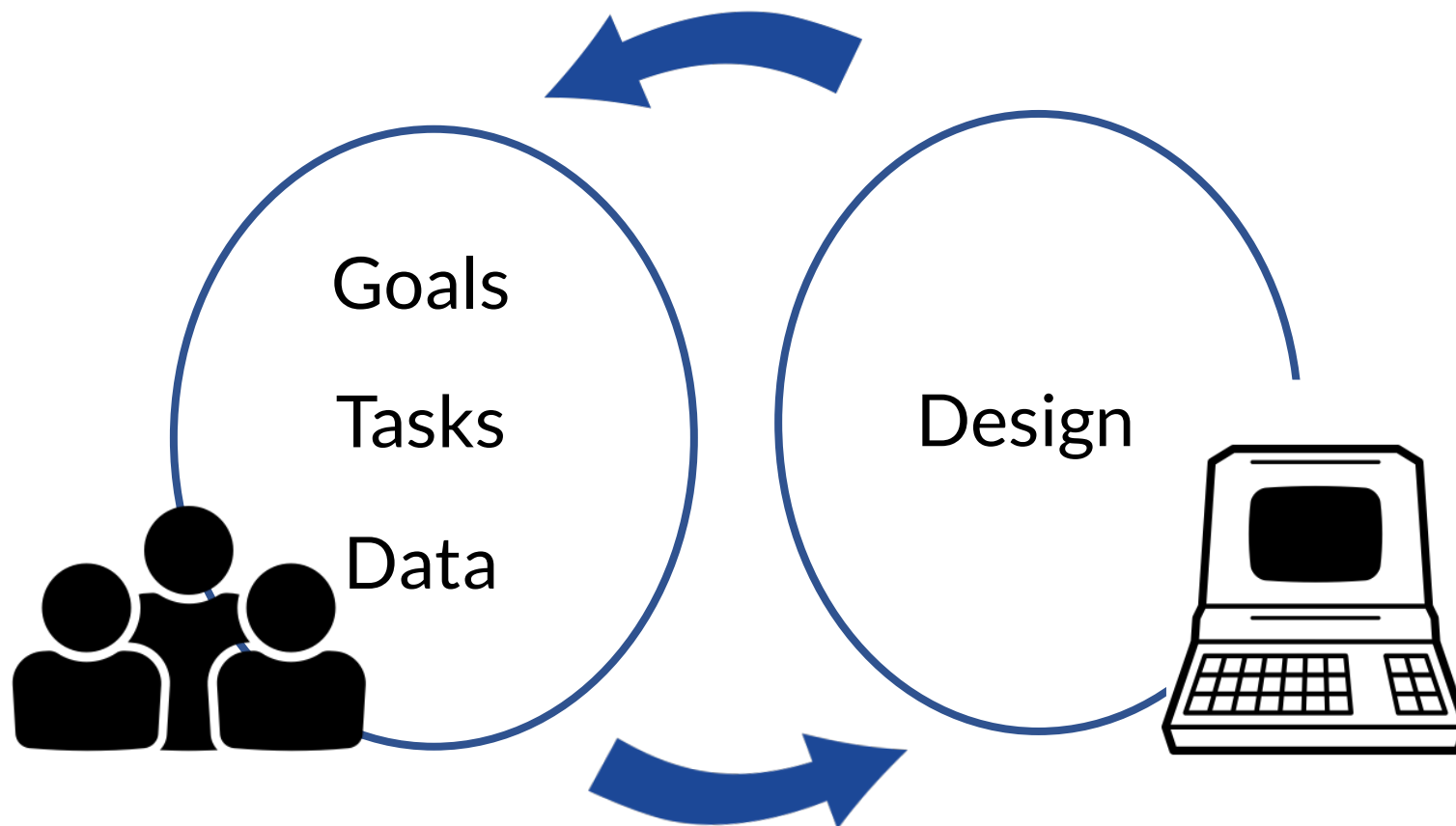
BC Centre for Disease Control



Public Health
England

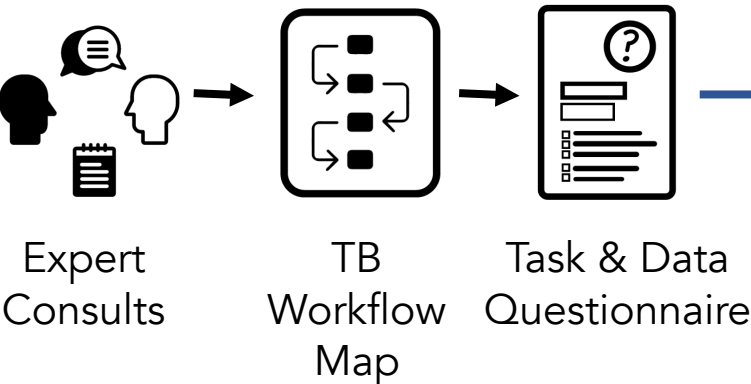
Our Approach: a Human Centered Design Process

“Design is not just what it looks like and feels like – design is how it works”
Steve Jobs

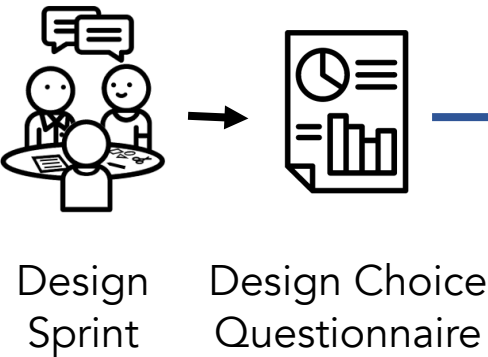


Using a Design Study Methodology + Mixed Methods Approaches

Discovery *Information Gathering*



Design *Design & Evaluation*



Implement *Finalize Design*

MYCOBACTERIUM TUBERCULOSIS
GENOME SEQUENCING REPORT
NOT FOR DIAGNOSTIC USE

Patent Name	JOHN DOE	Barcode	
Birth Date	2000-01-01	Patient ID	12345678910
Location	SOMEPLACE	Sample Type	SPUTUM
Sample Source	PULMONARY	Sample Date	2016-12-25
Sample ID	A12345678	Sequenced From	MGIT CULTURED ISOLATE
Reporting Lab	LAB NAME	Report Date/Time	2017-01-01, 15:36
Requested By	REQUESTER NAME	Requester Contact	REQUESTER@EMAIL.COM

Summary
The specimen was positive for *Mycobacterium tuberculosis*. It is resistant to isoniazid and rifampin. It belongs to a cluster, suggesting recent transmission.

Organism
The specimen was positive for *Mycobacterium tuberculosis*, lineage 2.2.1 (East-Asian Beijing).

Drug Susceptibility
Resistance is reported when a high-confidence resistance-conferring mutation is detected. "No mutation detected" does not exclude the possibility of resistance.

Drug class	Interpretation	Drug	Resistance Gene (HIV-1, HIV-2)
First Line	Susceptible	Ethambutol	No mutation detected
		Pyrazinamide	No mutation detected
		Isoniazid	katG (S315T)
First Line	Resistant	Rifampin	rpoB (S531L)
		Streptomycin	No mutation detected
		Ciprofloxacin	No mutation detected
Second Line	Susceptible	Ofloxacin	No mutation detected
		Moxifloxacin	No mutation detected
		Amikacin	No mutation detected
Second Line	Susceptible	Kanamycin	No mutation detected
		Capreomycin	No mutation detected

Page 1 of 2 Patient ID: 12345678910 | Date: 2017-01-01 | Location: Someplace

Data Gathered

Qualitative
Quantitative

Study Design

Exploratory Sequential Model

Embedded Model

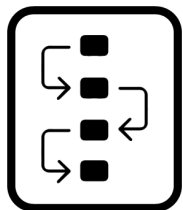


DISCOVERY



Expert Consults

- Map out TB diagnosis, treatment, and surveillance steps
- Assess role of WGS and identify major barriers



TB workflow

- Formalize tasks (what people do) & data used for those tasks
- Not further elaborated on here



Task & Data Questionnaire

- Assess generality of expert findings, workflow tasks & data

Expert Consultations : Participants & Methods



Public Health Role	Total
--------------------	-------

Clinician	2
-----------	---

Nurse	1
-------	---

Laboratorian	2
--------------	---

Researcher	0
------------	---

Surveillance	1
--------------	---

Other	1
-------	---

Total	7
--------------	----------

- **Semi-structured interviews**

- *Sampling*: Experts known to us
- *Data Collected*: Qualitative (interviewer notes)

- **Analyzed for common themes**

- **Used to establish TB workflow**

- Steps from diagnosis to treatment to surveillance
- Intended to link tasks to data
- Identify genomic actionable steps

Common Themes from Expert Consults



Procedural Insights

- Limited time to digest content
- Many documents arriving at different times
- Reporting formats varied considerably :
PDF, EHR, Fax
 - Black & white essential

“10 seconds [to review content] is likely, one minute is luxurious”

Data Insights

- Different data needs (clinicians, non-clinicians)
- Different expectations about level of detail
- Emphasis on clinically actionable results

“my patient’s isolate is 6 SNPs from someone diagnosed 3 years ago. What is the clinical action?”

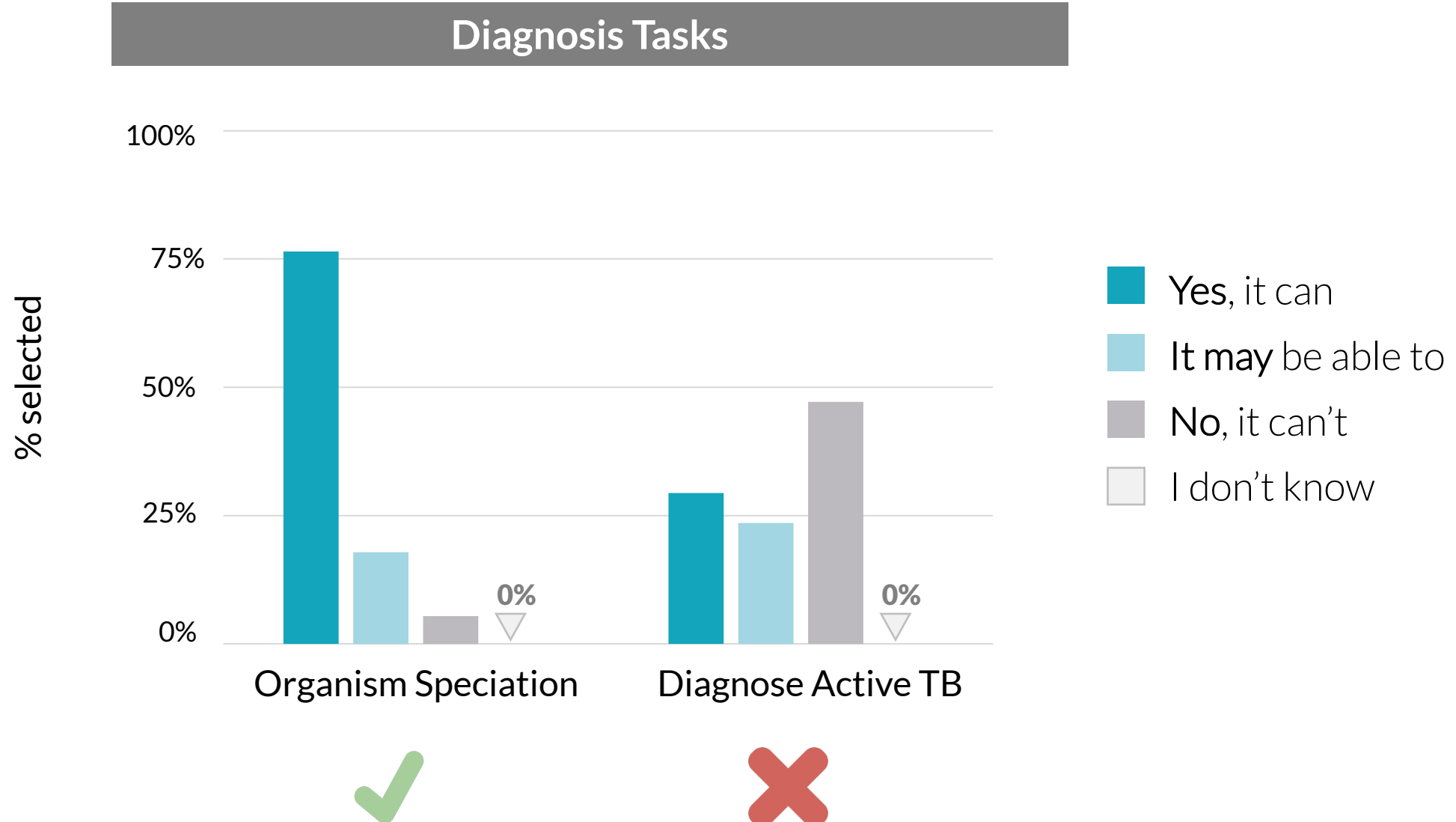
Task & Data Questionnaire: Participants & Methods



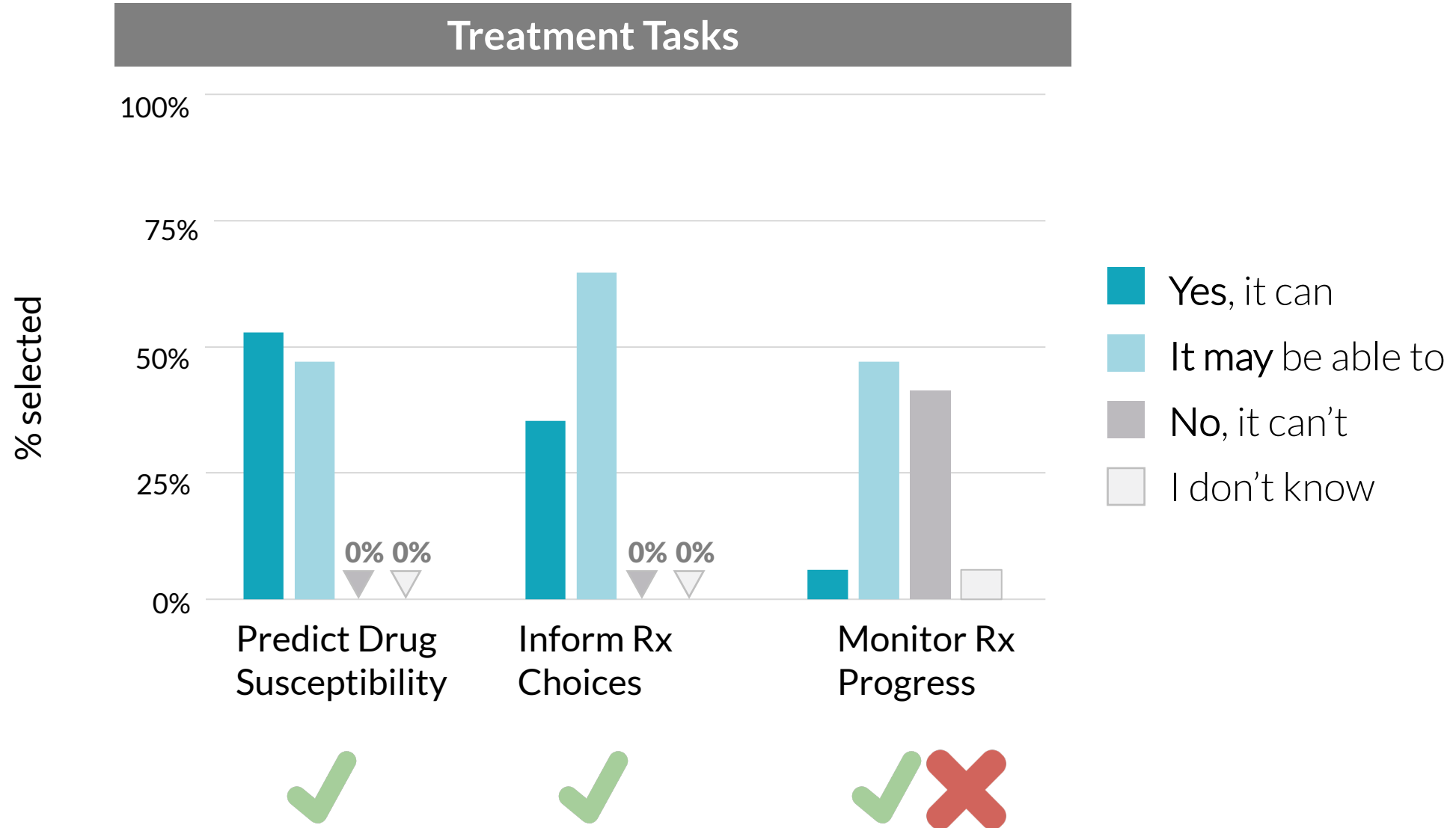
Public Health Role	Total
Clinician	7
Nurse	3
Laboratorian	3
Researcher	1
Surveillance	3
Other	0
Total	17

- **Online survey**
 - *Sampling*: Convenience & Snowball
 - *Data collected*: Quantitative, some qualitative
- **Questions about task & data**
 - Emphasized genomic results
 - Utility of data types
 - Interpretation confidence

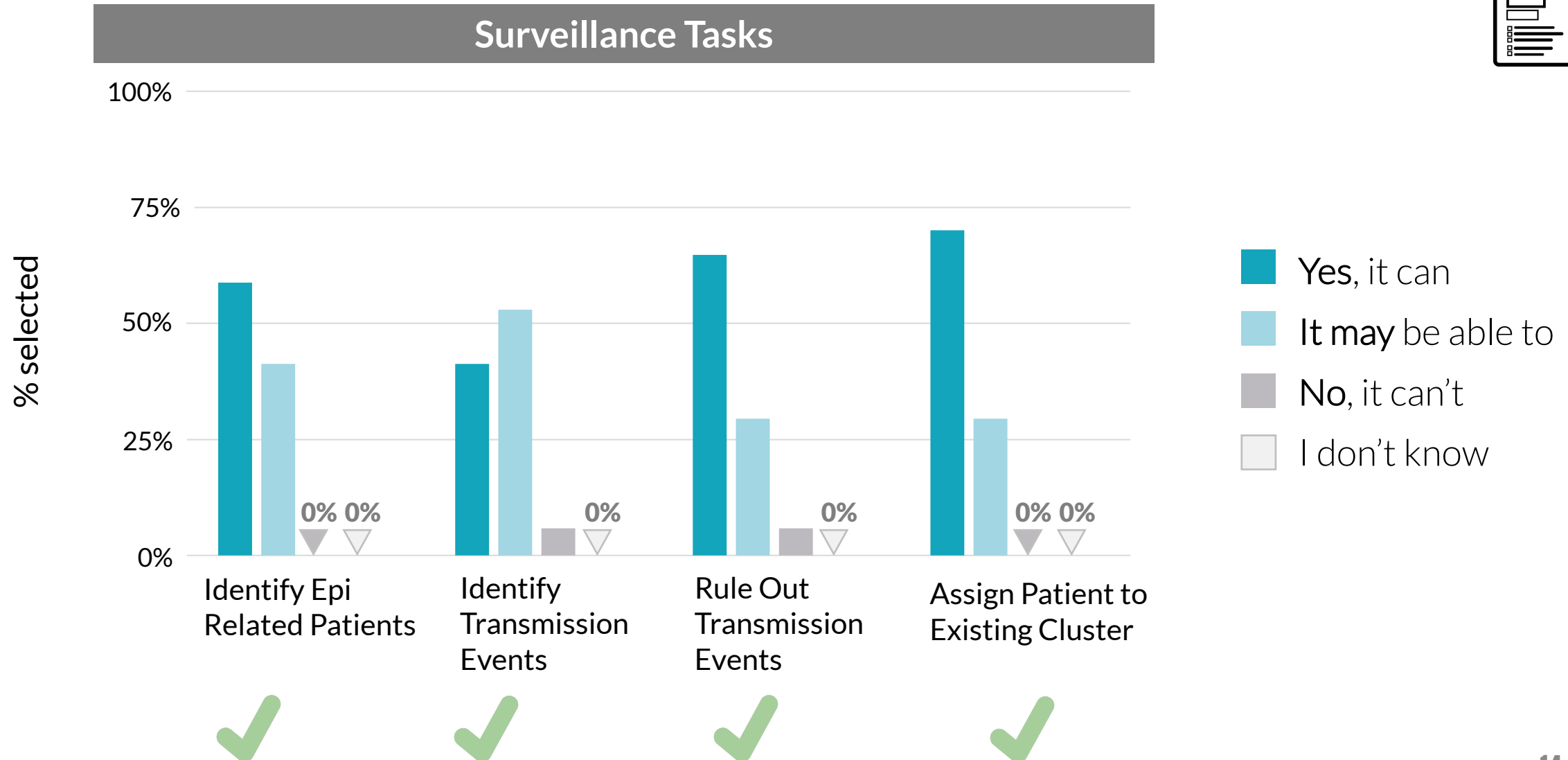
Can Genomic Data be used for this Task (now or eventually)?



Can Genomic Data be used for this Task (now or eventually)?



Can Genomic Data be used for this Task (now or eventually)?



But... Variable Consensus for Data used across Tasks



	WGS equivalent	DIAGNOSIS TASKS				TREATMENT TASKS			SURVEILLANCE TASKS					TOTAL SCORE
		Diagnose Latent TB	Diagnose Active TB	Reactive vs New Infection	Characterize Transmission Risk	Choose Meds	Choose Tx Duration	Assess Response to Tx	Guide Contact Tracing	Report to Public Health	Define a Cluster	Connect Case to Existing Cluster	Guide Public Health Response	
Patient Identifier	Same	3	3	3	3	3	3	3	2	1	1	1	1	26
Sample Collection Date	Same	3	3	2	3	3	3	3	1	1	1	1	1	24
Patient Prior TB Results	Same	3	2	3	3	3	3	3	1	1	1	0	1	23
Speciation	Speciation	1	3	2	3	3	3	3	2	1	1	1	1	23
Sample Type (sputum, fine needle aspirate etc.)	Same	2	3	2	3	3	3	3	1	1	1	0	1	22
Culture results	NA	1	3	2	3	3	3	3	2	1	1	0	1	22
Sample Collection Site (lymph node, lung etc.)	Same	2	3	2	3	3	3	3	1	1	0	0	1	21
Acid Fast Bacilli Smear	Speciation	2	3	2	3	2	3	3	1	1	1	0	1	21
Resistotype	Predicted DST	0	2	3	1	3	3	2	2	1	1	1	1	19
Phenotypic DST	Predicted DST	0	2	3	2	3	3	2	1	1	1	0	1	18
Chest x-ray	NA	3	3	2	3	0	2	3	1	0	0	0	0	17
Report Release Date	Same	2	2	1	2	2	2	2	1	0	1	0	1	15
Requester IDs	Same	2	2	2	2	2	2	2	1	0	0	0	0	15
Interpretation or comments from reviewer	Same	2	2	1	2	2	2	3	1	0	0	0	0	15
Predicted DST	Predicted DST	0	2	2	1	3	3	2	1	0	1	0	0	15
MIRU-VNTR	SNPs	0	2	3	1	1	1	1	1	1	1	1	1	13
Cluster Assignment	Same	0	2	2	1	1	1	0	1	1	1	1	1	11
SNP/variant distance	SNPs	0	1	2	1	1	1	0	1	1	1	1	1	10
Phylogenetic Tree	Same	0	2	1	1	1	1	0	1	0	1	1	1	9
Reviewer ID	Same	1	1	1	1	1	1	1	1	0	0	0	0	8
TST results	Speciation*	3	1	1	1	0	0	0	1	0	0	0	0	7
IGRA results	Speciation*	3	1	1	1	0	0	0	1	0	0	0	0	7
Lab QC	WGS Specific	0	1	2	1	1	1	0	1	0	0	0	0	7
Spoligotype	SNPs	0	1	1	1	0	0	0	0	0	0	0	0	3
RFLP	SNPs	0	1	1	1	0	0	0	0	0	0	0	0	3

Degree of Consensus:

High (3)

Some (2)

Low (1)

Very low (0)

But... Variable Consensus for Data used across Tasks



	WGS equivalent	DIAGNOSIS TASKS				TREATMENT TASKS			SURVEILLANCE TASKS					TOTAL SCORE
		Diagnose Latent TB	Diagnose Active TB	Reactive vs New Infection	Characterize Transmission Risk	Choose Meds	Choose Tx Duration	Assess Response to Tx	Guide Contact Tracing	Report to Public Health	Define a Cluster	Connect Case to Existing Cluster	Guide Public Health Response	
Patient Identifier	Same	3	3	3	3	3	3	3	2	1	1	1	1	25
Sample Collection Date	Same	3	3	2	3	3	3	3	1	1	1	1	1	21
Patient Prior TB Results	Same	3	2	3	3	3	3	3	1	1	1	0	1	23
Speciation	Speciation	1	3	2	3	3	3	3	2	1	1	1	1	20
Sample Type (sputum, fine needle aspirate etc.)	Same	2	3	2	3	3	3	3	1	1	1	0	1	22
Culture results	NA	1	3	2	3	3	3	3	2	1	1	0	1	22
Sample Collection Site (lymph node, lung etc.)	Same	2	3	2	3	3	3	3	1	1	0	0	1	21
Acid Fast Bacilli Smear	Speciation	2	3	2	3	2	3	3	1	1	1	0	1	21
Resistotype	Predicted DST	0	2	3	1	3	3	2	2	1	1	1	1	19
Phenotypic DST	Predicted DST	0	2	3	2	3	3	2	1	1	1	0	1	18
Chest x-ray	NA	3	3	2	3	0	2	3	1	0	0	0	0	17
Report Release Date	Same	2	2	1	2	2	2	2	1	0	1	0	1	15
Requester IDs	Same	2	2	2	2	2	2	2	1	0	0	0	0	15
Interpretation or comments from reviewer	Same	2	2	1	2	2	2	3	1	0	0	0	0	15
Predicted DST	Predicted DST	0	2	2	1	3	3	2	1	0	1	0	0	15
MIRU-VNTR	SNPs	0	2	3	1	1	1	1	1	1	1	1	1	13
Cluster Assignment	Same	0	2	2	1	1	1	0	1	1	1	1	1	11
SNP/variant distance	SNPs	0	1	2	1	1	1	0	1	1	1	1	1	10
Phylogenetic Tree	Same	0	2	1	1	1	1	0	1	0	1	1	1	9
Reviewer ID	Same	1	1	1	1	1	1	1	1	0	0	0	0	8
TST results	Speciation*	3	1	1	1	0	0	0	1	0	0	0	0	7
IGRA results	Speciation*	3	1	1	1	0	0	0	1	0	0	0	0	7
Lab QC	WGS Specific	0	1	2	1	1	1	0	1	0	0	0	0	7
Spoligotype	SNPs	0	1	1	1	0	0	0	0	0	0	0	0	3
RFLP	SNPs	0	1	1	1	0	0	0	0	0	0	0	0	3

- Administrative data is most commonly used data type

Degree of Consensus:

High (3)

Some (2)

Low (1)

Very low (0)

But... Variable Consensus for Data used across Tasks



	WGS equivalent	DIAGNOSIS TASKS				TREATMENT TASKS			SURVEILLANCE TASKS					TOTAL SCORE
		Diagnose Latent TB	Diagnose Active TB	Reactive vs New Infection	Characterize Transmission Risk	Choose Meds	Choose Tx Duration	Assess Response to Tx	Guide Contact Tracing	Report to Public Health	Define a Cluster	Connect Case to Existing Cluster	Guide Public Health Response	
Patient Identifier	Same	3	3	3	3	3	3	3	2	2	1	1	1	25
Sample Collection Date	Same	3	3	2	3	3	3	3	1	1	1	1	1	21
Patient Prior TB Results	Same	3	2	3	3	3	3	3	1	1	1	0	1	23
Speciation	Speciation	1	3	2	3	3	3	3	2	1	1	1	1	23
Sample Type (sputum, fine needle aspirate etc.)	Same	2	3	2	3	3	3	3	1	1	1	0	1	22
Culture results	NA	1	3	2	3	3	3	3	2	1	1	1	1	23
Sample Collection Site (lymph node, lung etc.)	Same	2	3	2	3	3	3	3	1	1	1	0	1	21
Acid Fast Bacilli Smear	Speciation	2	3	2	3	2	3	3	1	1	1	0	1	23
Resistotype	Predicted DST	0	2	3	1	3	3	2	2	1	1	1	1	19
Phenotypic DST	Predicted DST	0	2	3	2	3	3	2	1	1	1	0	1	18
Chest x-ray	NA	3	3	2	3	0	2	3	1	0	0	0	0	17
Report Release Date	Same	2	2	1	2	2	2	2	1	0	1	0	1	15
Requester IDs	Same	2	2	2	2	2	2	2	1	0	0	0	0	15
Interpretation or comments from reviewer	Same	2	2	1	2	2	2	3	1	0	0	0	0	15
Predicted DST	Predicted DST	0	2	2	1	3	3	2	1	0	1	0	0	15
MIRU-VNTR	SNPs	0	2	3	1	1	1	1	1	1	1	1	1	13
Cluster Assignment	Same	0	2	2	1	1	1	0	1	1	1	1	1	11
SNP/variant distance	SNPs	0	1	2	1	1	1	0	1	1	1	1	1	10
Phylogenetic Tree	Same	0	2	1	1	1	1	0	1	0	1	1	1	9
Reviewer ID	Same	1	1	1	1	1	1	1	1	0	0	0	0	8
TST results	Speciation*	3	1	1	1	0	0	0	1	0	0	0	0	7
IGRA results	Speciation*	3	1	1	1	0	0	0	1	0	0	0	0	7
Lab QC	WGS Specific	0	1	2	1	1	1	0	1	0	0	0	0	7
Spoligotype	SNPs	0	1	1	1	0	0	0	0	0	0	0	0	3
RFLP	SNPs	0	1	1	1	0	0	0	0	0	0	0	0	3

■ Administrative data is most commonly used data type

■ Speciation & DST are the most useful WGS derived data

Degree of Consensus:

High (3)

Some (2)

Low (1)

Very low (0)

But... Variable Consensus for Data used across Tasks



	WGS equivalent	DIAGNOSIS TASKS				TREATMENT TASKS			SURVEILLANCE TASKS					TOTAL SCORE
		Diagnose Latent TB	Diagnose Active TB	Reactive vs New Infection	Characterize Transmission Risk	Choose Meds	Choose Tx Duration	Assess Response to Tx	Guide Contact Tracing	Report to Public Health	Define a Cluster	Connect Case to Existing Cluster	Guide Public Health Response	
Patient Identifier	Same	3	3	3	3	3	3	3	2	2	1	1	1	25
Sample Collection Date	Same	3	3	2	3	3	3	3	1	1	1	0	1	23
Patient Prior TB Results	Same	3	2	3	3	3	3	3	1	1	1	0	1	23
Speciation	Speciation	1	3	2	3	3	3	3	2	1	1	1	1	23
Sample Type (sputum, fine needle aspirate etc.)	Same	2	3	2	3	3	3	3	1	1	1	0	1	22
Culture results	NA	1	3	2	3	3	3	3	2	1	1	1	1	23
Sample Collection Site (lymph node, lung etc.)	Same	2	3	2	3	3	3	3	1	1	1	0	1	21
Acid Fast Bacilli Smear	Speciation	2	3	2	3	2	3	3	1	1	1	0	1	23
Resistotype	Predicted DST	0	2	3	1	3	3	2	2	1	1	1	1	19
Phenotypic DST	Predicted DST	0	2	3	2	3	3	2	1	1	1	0	1	18
Chest x-ray	NA	3	3	2	3	0	2	3	1	0	0	0	0	17
Report Release Date	Same	2	2	1	2	2	2	2	1	0	1	0	1	15
Requester IDs	Same	2	2	2	2	2	2	2	1	0	0	0	0	15
Interpretation or comments from reviewer	Same	2	2	1	2	2	2	3	1	0	0	0	0	16
Predicted DST	Predicted DST	0	2	2	1	3	3	2	1	0	1	0	0	15
MIRU-VNTR	SNPs	0	2	3	1	1	1	1	1	0	1	1	1	11
Cluster Assignment	Same	0	2	2	1	1	1	0	1	1	1	1	1	10
SNP/variant distance	SNPs	0	1	2	1	1	1	0	1	0	1	1	1	9
Phylogenetic Tree	Same	0	2	1	1	1	1	0	1	0	1	1	1	9
Reviewer ID	Same	1	1	1	1	1	1	1	1	0	0	0	0	8
TST results	Speciation*	3	1	1	1	0	0	0	1	0	0	0	0	7
IGRA results	Speciation*	3	1	1	1	0	0	0	1	0	0	0	0	7
Lab QC	WGS Specific	0	1	2	1	1	1	0	1	0	0	0	0	7
Spoligotype	SNPs	0	1	1	1	0	0	0	0	0	0	0	0	3
RFLP	SNPs	0	1	1	1	0	0	0	0	0	0	0	0	3

- Administrative data is most commonly used data type
- Speciation & DST are the most useful WGS derived data
- Strong consensus for data used in diagnosis and treatment tasks

Degree of Consensus:

High (3)

Some (2)

Low (1)

Very low (0)

But... Variable Consensus for Data used across Tasks



	WGS equivalent	DIAGNOSIS TASKS				TREATMENT TASKS			SURVEILLANCE TASKS					TOTAL SCORE
		Diagnose Latent TB	Diagnose Active TB	Reactive vs New Acquisition	Characterize Transmission Risk	Choose Meds	Choose Rx Duration	Assess Response to Rx	Guide Contact Tracing	Report to Public Health	Define a Cluster	Connect case to Existing Cluster	Guide Public Health Response	
Patient Identifier	Same	3	3	3	3	3	3	3	2	1	1	1	1	26
Sample Collection Date	Same	3	3	2	3	3	3	3	1	1	1	1	1	24
Patient Prior TB Results	Same	3	2	3	3	3	3	3	1	1	1	0	1	23
Speciation	Speciation	1	3	2	3	3	3	3	2	1	1	1	1	23
Sample Type (sputum, fine needle aspirate etc.)	Same	2	3	2	3	3	3	3	1	1	1	0	1	22
Culture results	NA	1	3	2	3	3	3	3	2	1	1	0	1	22
Sample Collection Site (lymph node, blood draw etc.)	Same	2	3	2	3	3	3	3	1	1	0	0	1	21
Acid Fast Bacilli Smear	Speciation	2	3	2	3	2	3	3	1	1	1	0	1	21
Resistotype	Speciation	0	3	3	3	2	3	2	2	1	1	1	1	19
Phenotype DST	Predicted DST	0	2	3	2	3	3	2	1	1	1	0	1	18
Chest x-ray	Same	2	2	1	2	0	2	3	1	0	0	0	0	17
Report Release Date	Same	2	2	1	2	2	2	2	1	0	1	0	1	15
Requester IDs	Same	2	2	2	2	2	2	2	1	0	0	0	0	15
Interpretation or comments from reviewer	Same	2	2	1	2	2	2	3	1	0	0	0	0	15
Predicted DST	Predicted DST	0	2	2	1	3	3	2	1	0	1	0	0	15
MIRU-VNTR	SNPs	0	2	3	1	1	1	1	1	1	1	1	1	13
Cluster Assignment	Same	0	2	2	1	1	1	0	1	1	1	1	1	11
SNP/variant distance	SNPs	0	1	2	1	1	1	0	1	1	1	1	1	10
Phylogenetic Tree	Same	0	2	1	1	1	1	0	1	0	1	1	1	9
Reviewer ID	Same	1	1	1	1	1	1	1	1	0	0	0	0	8
TST results	Speciation*	3	1	1	1	0	0	0	1	0	0	0	0	7
IGRA results	Speciation*	3	1	1	1	0	0	0	1	0	0	0	0	7
Lab QC	WGS Specific	0	1	2	1	1	1	0	1	0	0	0	0	7
Spoligotype	SNPs	0	1	1	1	0	0	0	0	0	0	0	0	3
RFLP	SNPs	0	1	1	1	0	0	0	0	0	0	0	0	3

- Very little consensus for data used in surveillance tasks

Degree of Consensus:

High (3)

Some (2)

Low (1)

Very low (0)

But... Variable Consensus for Data used across Tasks



- Cluster assignments & phylogenetic trees also not frequently used

		DIAGNOSIS TASKS				TREATMENT TASKS			SURVEILLANCE TASKS					TOTAL SCORE
	WGS Equivalent	Diagnose Latent TB	Diagnose Active TB	Reactive vs New Acquisition	Characterize Transmission Risk	Choose Mode	Choose Rx	Assess Response	Guide Contact Tracing	Report to Public Health	Define a Cluster	Connect case to Existing Cluster	Guide Public Health Response	
Patient Identifier	Same	3	3	2	3	3	3	3	1	1	1	1	1	24
Sample Collection Date	Same	3	2	3	3	3	3	3	1	1	1	0	1	23
Patient Prior TB Results	Speciation	1	3	2	3	3	3	3	2	1	1	1	1	23
Sample Type (sputum, fine needle aspirate etc.)	Same	2	3	2	3	3	3	3	1	1	1	0	1	22
Culture results	NA	1	3	2	3	3	3	3	2	1	1	0	1	22
Sample Collection Site (lymph node, blood draw etc.)	Same	2	3	2	3	3	3	3	1	1	0	0	1	21
Acid Fast Bacilli Smear	Speciation	2	3	2	3	2	3	3	1	1	1	0	1	21
Resistotype	Predicted DST	0	2	3	1	3	3	2	2	1	1	1	1	19
Phenotype DST	Predicted DST	0	2	3	2	3	3	2	1	1	1	0	1	18
Chest x-ray	NA	3	3	2	3	0	2	3	1	0	0	0	0	17
Report Release Date	Same	2	2	1	2	2	2	2	1	0	1	0	1	15
Requester IDs	Same	2	2	2	2	2	2	2	1	0	0	0	0	15
Interpretation or comments from reviewer	Same	2	2	1	2	2	2	3	1	0	0	0	0	15
Predicted DST	Predicted DST	0	2	2	1	3	3	2	1	0	1	0	0	15
MIRU-VNTR	SNPs	0	2	3	1	1	1	1	1	1	1	1	1	13
Cluster Assignment	Same	0	2	2	1	1	1	0	1	1	1	1	1	11
SNP/variant distance	SNPs	0	1	2	1	1	1	0	1	1	1	1	1	10
Phylogenetic Tree	Same	0	2	1	1	1	1	0	1	0	1	1	1	9
Reviewer ID	Same	1	1	1	1	1	1	1	1	0	0	0	0	8
TST results	Speciation*	3	1	1	1	0	0	0	1	0	0	0	0	7
IGRA results	Speciation*	3	1	1	1	0	0	0	1	0	0	0	0	7
Lab QC	WGS Specific	0	1	2	1	1	1	0	1	0	0	0	0	7
Spoligotype	SNPs	0	1	1	1	0	0	0	0	0	0	0	0	3
RFLP	SNPs	0	1	1	1	0	0	0	0	0	0	0	0	3

Degree of Consensus:

High (3)

Some (2)

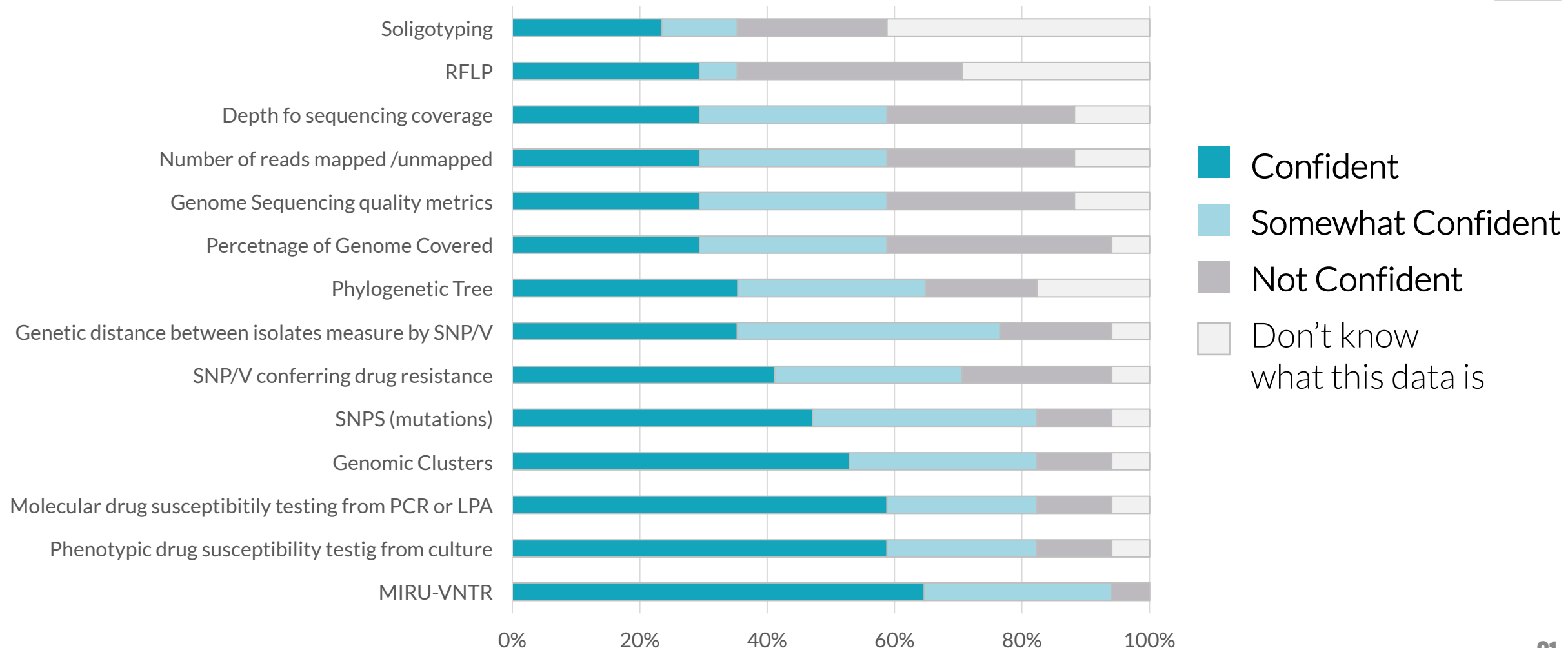
Low (1)

Very low (0)

... and Variable Confidence to Interpret Data



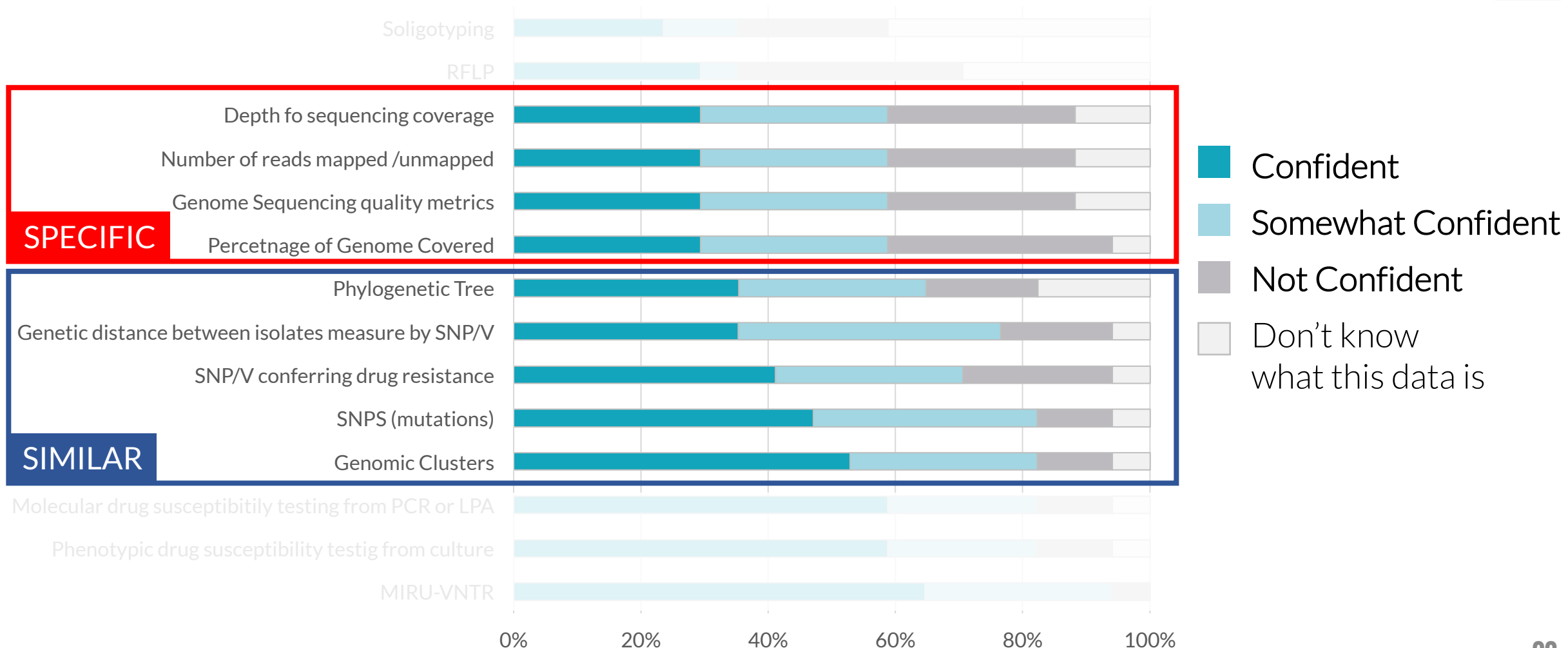
Results are ordered from least confident (top) to most confident (bottom)



... and Variable Confidence to Interpret Data



Emphasis: data **specific** to WGS or **similar** with older genotyping technology



Take away messages



- Prioritizing relevant information is important
- There are variable perceptions on value of different data types
- There's little consensus on data that is useful for surveillance tasks
- WGS data is useful, but some lack confidence to interpret it



DESIGN



Design Sprint

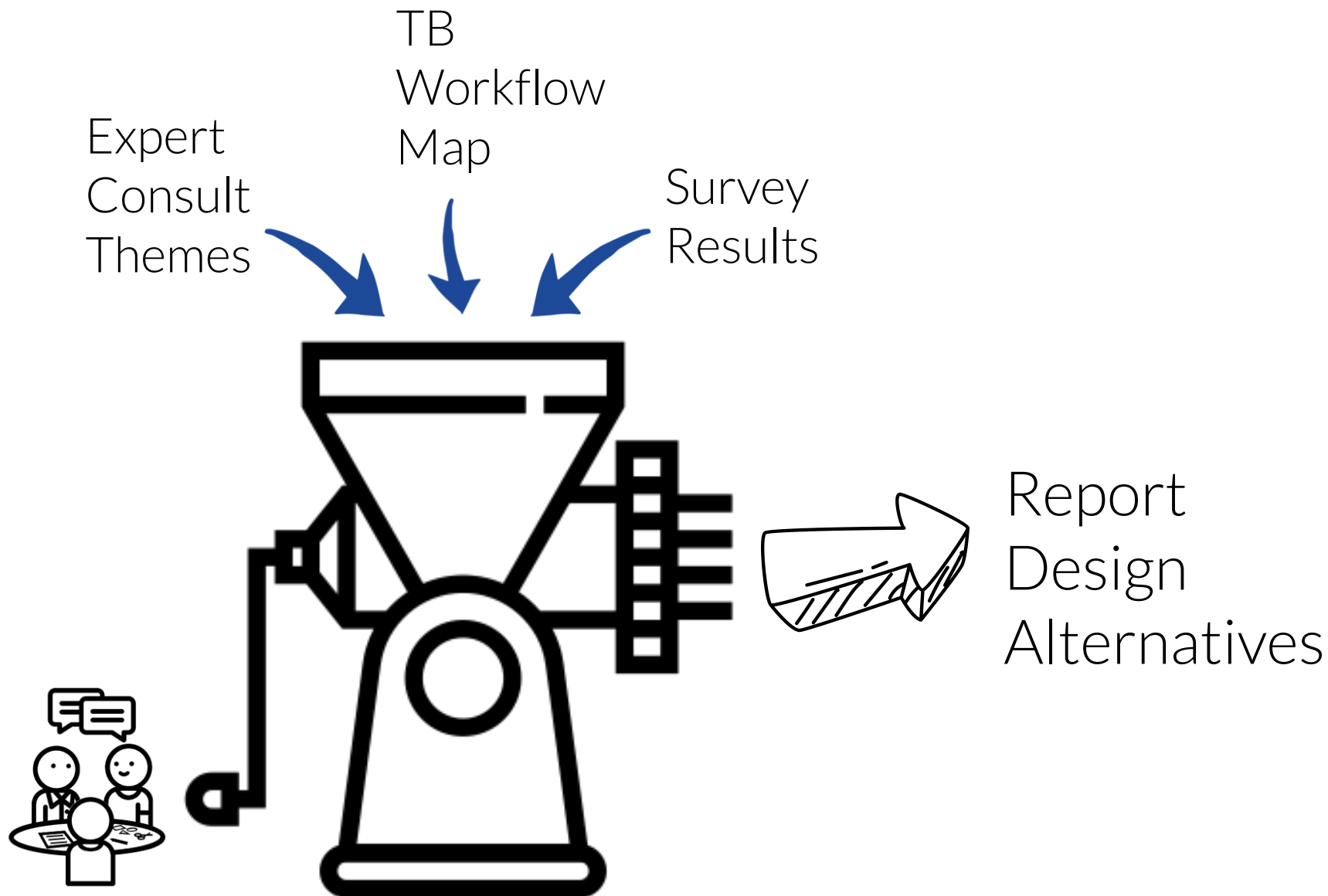
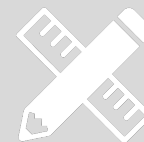
- Using Discovery findings and designing alternative reports



Design Choice Questionnaire

- Test designs from sprint with stakeholders
- Assess preferences for wording, information design, & data visualization
- Assess consistency between clinicians and non-clinicians

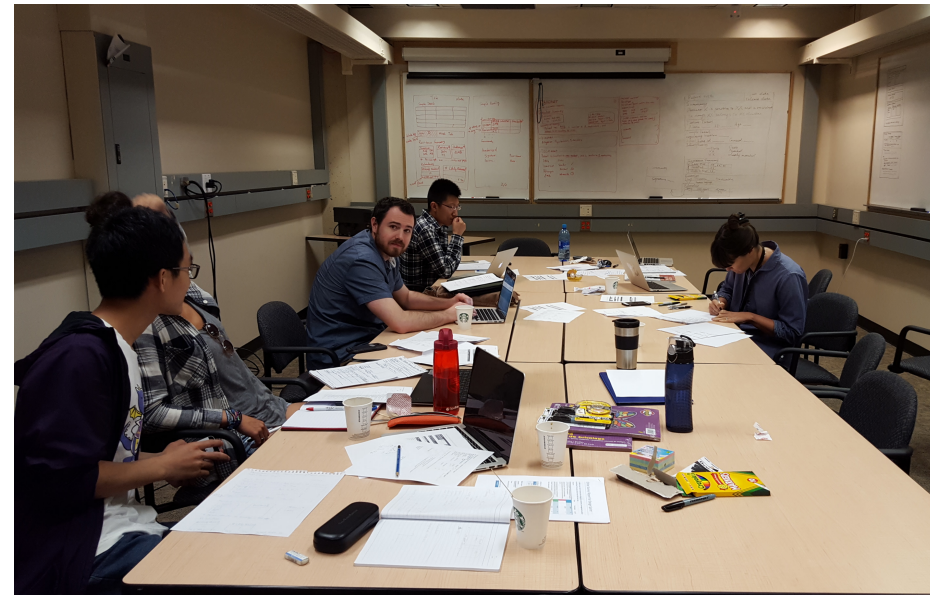
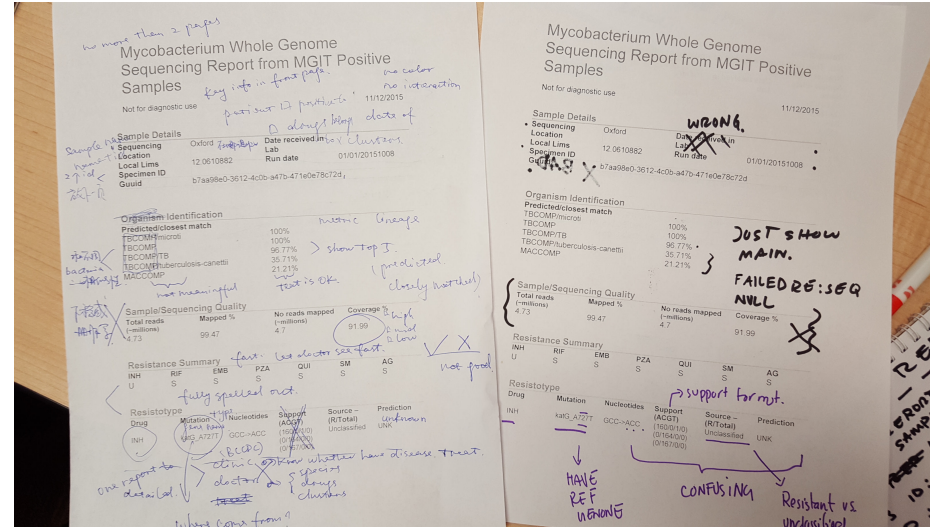
Design Sprint: Half Day Interactive Design Session



Design Sprint: Half Day Interactive Design Session



- Participants
 - 4 UBC infovis group students + us
- Built paper prototypes
- Discussed design choices
- Developed digital mock-ups afterwards



Patient Details
ID: NAME, DOB, LOCATION
RECEIVED: CONTACT, CC

Organism Species
MTB

Resistance Summary
SENSITIVE, RESISTANT, INTERMEDIATE
INH, RIF, QIN, SM, AG

SEE ATTACH FOR MUTATION DETAILS

RELATED ISOLATES

ISOLATES	LINEAGE RELATED LS SNP	SEQUENCE RELATED 6-30 SNP
	2	8

FOR INFORMATION ON RELATED SAMPLES CALL PUBLIC HEALTH AT

REVIEWER COMMENTS:

APP.
RESISTOTYPE: THE FOLLOWING MUTATIONS WERE IDENTIFIED:

DATE	PREDICTION	GENE	MUTATION
2015	RESISTANT	~	~

SEQUENCE QUALITY COMMENTS

Digital Mock-ups of Paper Prototypes

Example of digital mock-ups for 2 out of 4 whole report prototypes



Example 1

01-01-1900 / Bob Johnson Not for diagnostic Use

Public Health England

Mycobacterium Whole Genome Sequencing Report

Report Date

01-01-1900

Laboratory

Oxford

Reviewed by

Dr. John Smith

Patient Details

Patient Name

Bob Johnson

Patient ID

123456789

Patient DOB

01-01-1900

Location

Oxford

Requester Details

Requester

Dr. Paul
1234 Smith St
Birmingham, UK

Copy to

Sample Details

Sample Type

Sputum

Sample Date

01-01-1900

Sample Site

-

Specimen ID

123456789

Speciation

Organism Species

Mycobacterium Tuberculosis

Drug Sensitivities

Ethambutol

Isoniazid¹

Rifampin¹

SUSCEPTIBLE

RESISTANT

INDETERMINATE

Relatedness

Likely Related (less than 3 SNP difference)

Possibly Related (6-50 SNP differences)

Number of Isolates

2

6

Resistotype

Drug

Prediction

Gene

Mutation

Isoniazid

Resistant

katG

S315T

Rifampin

Resistant

rpoB

S531L

Sequence Quality

The whole genome sequence analysis of the isolate was considered **High Quality** as the number of reads was greater than 4.7 million with 95.47% mapped and a coverage of 91.99%.

Reviewer Comments

No additional comments

Authorization

Signature

Print Name

Dr. John Smith

Date

01-01-1900

Position

Lab Director

01-01-1900 / Bob Johnson Not for diagnostic Use

Public Health England

Mycobacterial Genome Sequencing Results

Patient Name

BOB JOHNSON

Patient ID

123456789

Birth Date

1 JAN 1900

Gender

M

Location

OXFORD

Sample Type

SPUTUM

Sample Date

1 JAN 1900

Reporting Lab

OXFORD

Report Date

1 JAN 1900

DIAGNOSIS

The specimen is positive for *Mycobacterium tuberculosis*.

TREATMENT

Based on predicted antibiotic sensitivities, this individual has **multidrug-resistant (MDR) TB**.

First-Line Drugs

Isoniazid

Resistant (katG S315T)

Rifampin

Resistant (rpoB S531L)

Ethambutol

Sensitive

Pyrazinamide

Sensitive

Second-Line Drugs

Streptomycin

Sensitive

Capreomycin

Sensitive

Ofloxacin

Sensitive

Moxifloxacin

Sensitive

Amikacin

Sensitive

Kanamycin

Sensitive

Capreomycin

Sensitive

EPIDEMIOLOGY

This isolate belongs to a cluster of 8 genetically related cases, suggesting recent transmission.

COMMENTS

This sample was sequenced twice; the initial sequencing run did not provide high quality data for further analysis.

GENOME SEQUENCING DETAILS

LOCAL LIMS ID

123456789

RUN DATE

1 JAN 1900

TOTAL READS

4.73M

REFERENCE GENOME

H37Rv (NC_000962.2)

QUALITY

ILLUMINA MISEQ

MAPTED READS (%)

4.73M (99.47%)

Example 2

01-01-1900 / Bob Johnson Not for diagnostic Use

Public Health England

Mycobacterial Genome Sequencing Results

Patient Name

BOB JOHNSON

Patient ID

123456789

Birth Date

1 JAN 1900

Gender

M

Location

OXFORD

Sample Type

SPUTUM

Sample Date

1 JAN 1900

Reporting Lab

OXFORD

Report Date

1 JAN 1900

DIAGNOSIS DETAILS

Species

% Identity

Mycobacterium tuberculosis

100%

Mycobacterium avium complex

40%

Mycobacterium canettii

20%

TREATMENT DETAILS

Drug

Gene

Mutation

Catalog

Coverage

Support

Isoniazid

katG

S315T

Mykrobe v2

47x

40/47 reads

Rifampin

rpoB

S531L

Walker et al

38x

35/38 reads

EPIDEMIOLOGY DETAILS

Isolate

Year

SNP Distance

2015_A

2015

3

2014_A

2014

4

2013_A

2013

8

2013_B

2013

7

2012_A

2012

10

2012_B

2012

5

2012_C

2012

10

2012_D

2012

9

COMMENTS

This sample was sequenced twice; the initial sequencing run did not provide high quality data for further analysis.

GENOME SEQUENCING DETAILS

LOCAL LIMS ID

123456789

RUN DATE

1 JAN 1900

TOTAL READS

4.73M

REFERENCE GENOME

H37Rv (NC_000962.2)

QUALITY

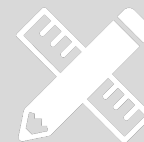
ILLUMINA MISEQ

MAPTED READS (%)

4.73M (99.47%)

28

Isolated Components Derived from Design Sprint



Original Report Element



1 Resistance Summary									
INH	RIF	EMB	PZA	QUI	SM	AG	2	4	5
U	S	S	S	S	S	S	3		

Tested Design Element

1. Alternative titles

- A - Drug Resistance
- B - Drug Sensitivity
- C - Drug Susceptibility
- D - Treatment

2. Drug name format

- A - 3 letter abbreviation (Ex. INH)
- B - Full Name (Ex. Isoniazid)
- C - Show me everything (Ex. Isonizaid (INH,H))
- D - The are equally informative

3. Susceptibility status format

- A - 1 letter abbreviation (Ex. S,R,U)
- B - Full Name (Ex. Susceptible, Resistant, Unknown)
- C - They are equally informative

Isolated Components Derived from Design Sprint



Original Report Element



1 Resistance Summary							2	4	5
INH	RIF	EMB	PZA	QUI	SM	AG			
U	S	S	S	S	S	S	3		

Tested Design Element

4. Presentation order or categorization of drugs

A – Drugs by category

Drug Susceptibility	
Drug	Prediction
Sensitive	Ethambutol, Pyrazinamide
Resistant	Isoniazid, Rifampin
Indeterminate	-

B – Listed by drug

Drug Susceptibility	
Drug	Prediction
Isoniazid	Resistant
Rifampin	Resistant
Ethambutol	Sensitive
Pyrazinimide	Sensitive

C – Summary Sentence

Drug Susceptibility	
The specimen was resistant to isoniazid and rifampin, and sensitive to ethambutol and pyrazinamide	

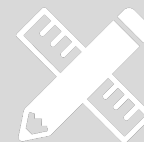
D – Drugs by category bin

Drug Susceptibility		
Isoniazid Rifampin	Ethambutol Pyrazinamide	
Resistant	Sensitive	Indeterminate

E – Abbreviation listed by drug

Drug Susceptibility			
INH	RIF	EMB	PZE
R	R	S	S

Isolated Components Derived from Design Sprint



Original Report Element



1 Resistance Summary						
INH	RIF	EMB	PZA	QUI	SM	AG
U	S	S	S	S	S	S

2 4 5 3

Tested Design Element

5. Summary Statement

A - None

Drug Susceptibility	
Drug	Prediction
Isoniazid	Resistant
Rifampin	Resistant
Ethambutol	Resistant
Pyrazinamide	Resistant

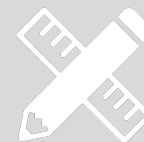
B - Summary sentence

Drug Susceptibility	
Based on predicted antibiotic mutations, the individual has multidrug resistant TB	
Drug	Prediction
Isoniazid	Resistant
Rifampin	Resistant
Ethambutol	Resistant
Pyrazinamide	Resistant

C - Tick boxes

Drug Susceptibility	
Mono-resistant	<input type="checkbox"/>
Multidrug-resistant (MDR)	<input type="checkbox"/>
Extremely Drug Resistant (XDR)	<input checked="" type="checkbox"/>
Drug	Prediction
Isoniazid	Resistant
Rifampin	Resistant
Ethambutol	Resistant
Pyrazinamide	Resistant

Design Choice Questionnaire : Participants & Methods



Public Health Role	Total
--------------------	-------

Clinician	13
-----------	----

Nurse	5
-------	---

Laboratorian	3
--------------	---

Researcher	8
------------	---

Surveillance	8
--------------	---

Other*	12
--------	----

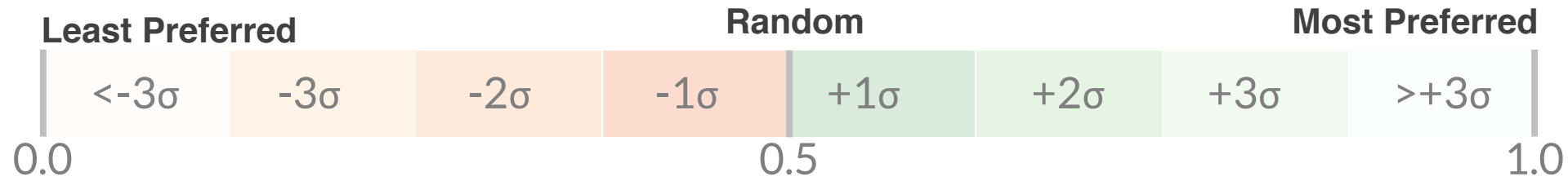
Total	54
--------------	-----------

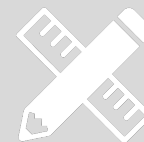
- **Online survey**
 - *Sampling*: Convenience & Snowball
 - *Data collected*: Quantitative and qualitative
- **Questions about design preferences**
 - Wording, information design, and data visualization preferences
 - Consensus between clinicians and non-clinicians
- **Analytic approach varied by question type**

*Others were individuals that were involved in communicable disease research, but not tuberculosis specifically



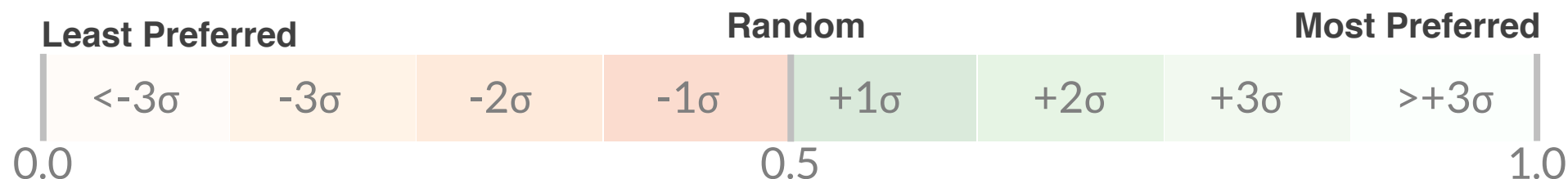
- Reference distribution for all quantitative responses
 - Random distribution, with mean and standard deviation informed by questionnaire results





■ Reference distribution for all quantitative responses

- Random distribution, with mean and standard deviation informed by questionnaire results



■ Some “mathy” details

- *Multiple choice questions*: report proportion of participants selecting option
- *Rank score*: rescale the rank scores

$$= \frac{\left(\sum_{p=1}^P R_{i,p} \right) - P}{P \times (N - 1)}$$

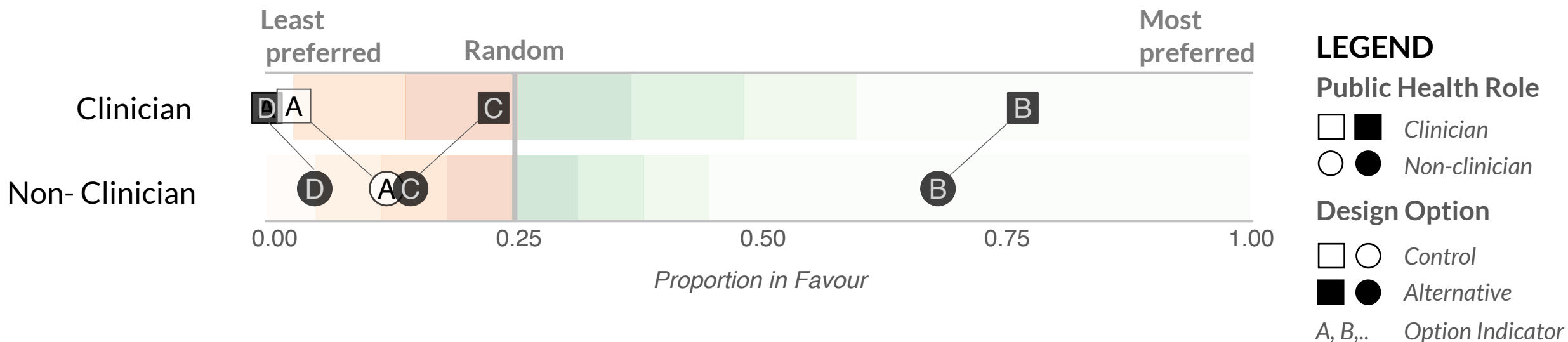
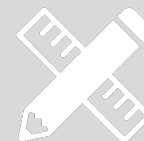
Where for each design choice (D_i)

$i = \{1..N\}$, where N is the total number of design choices

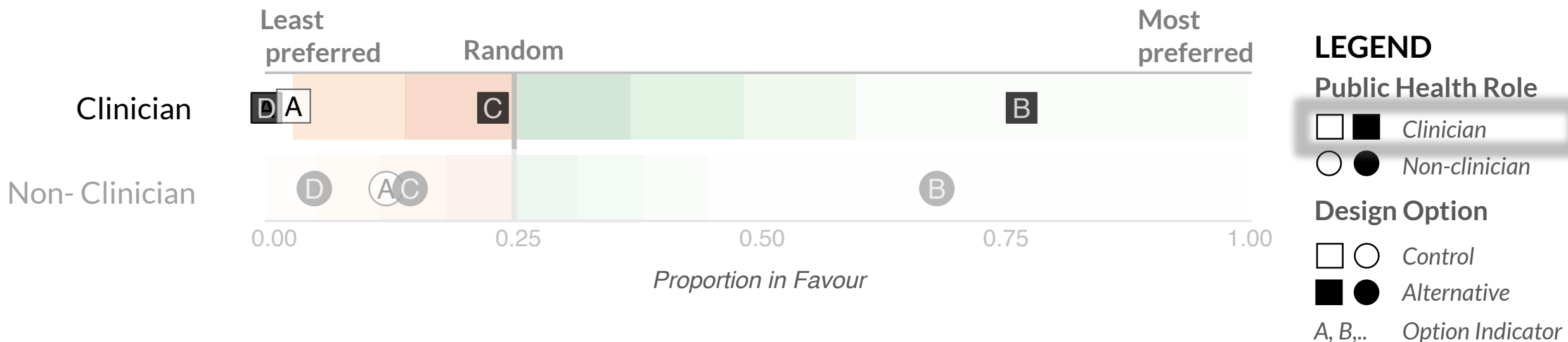
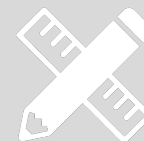
$R = \{1..N\}$, and is the chosen rank

P = is the total number of participants

[Wording] Report Drug Names as Abbreviations, or Not?

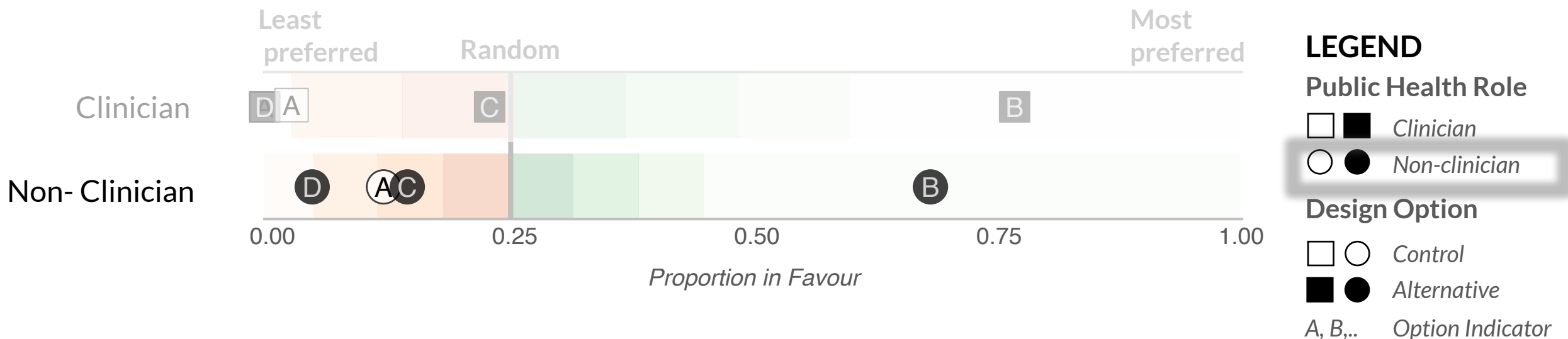
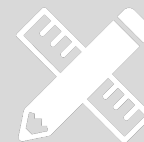


[Wording] Report Drug Names as Abbreviations, or Not?



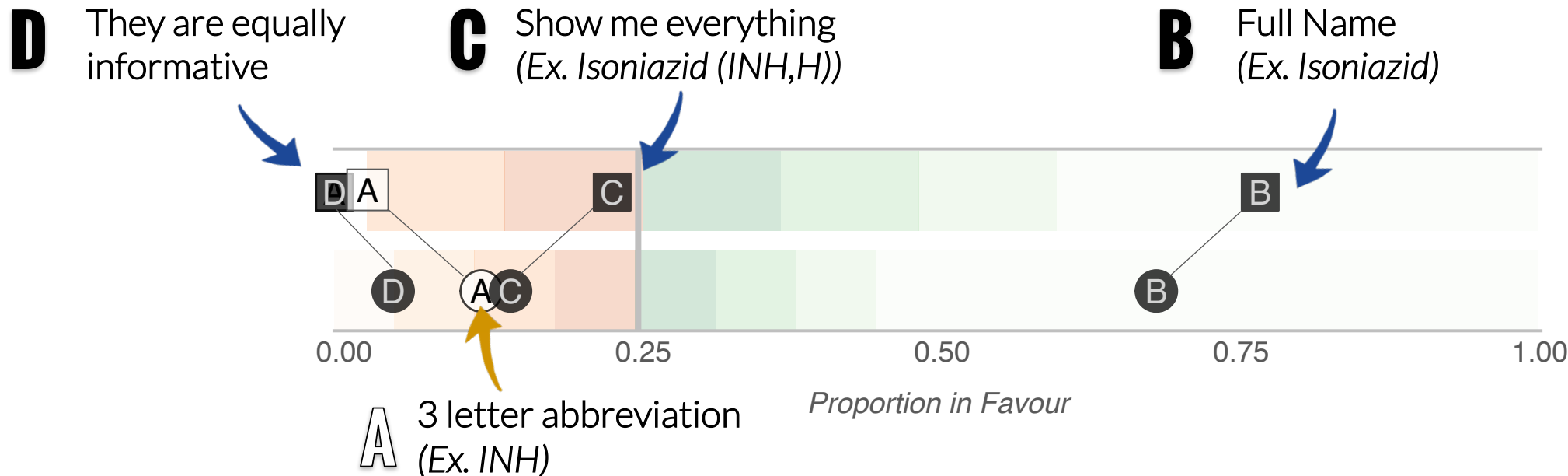
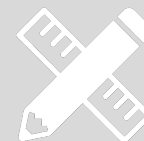
Top row (*square shape*) : Selections made by clinicians

[Wording] Report Drug Names as Abbreviations, or Not?



Bottom row (*circle shape*) : Selections made by non-clinicians

[Wording] Report Drug Names as Abbreviations, or Not?



LEGEND

Public Health Role

- ☐ ☐ Clinician
- ☐ ☐ Non-clinician

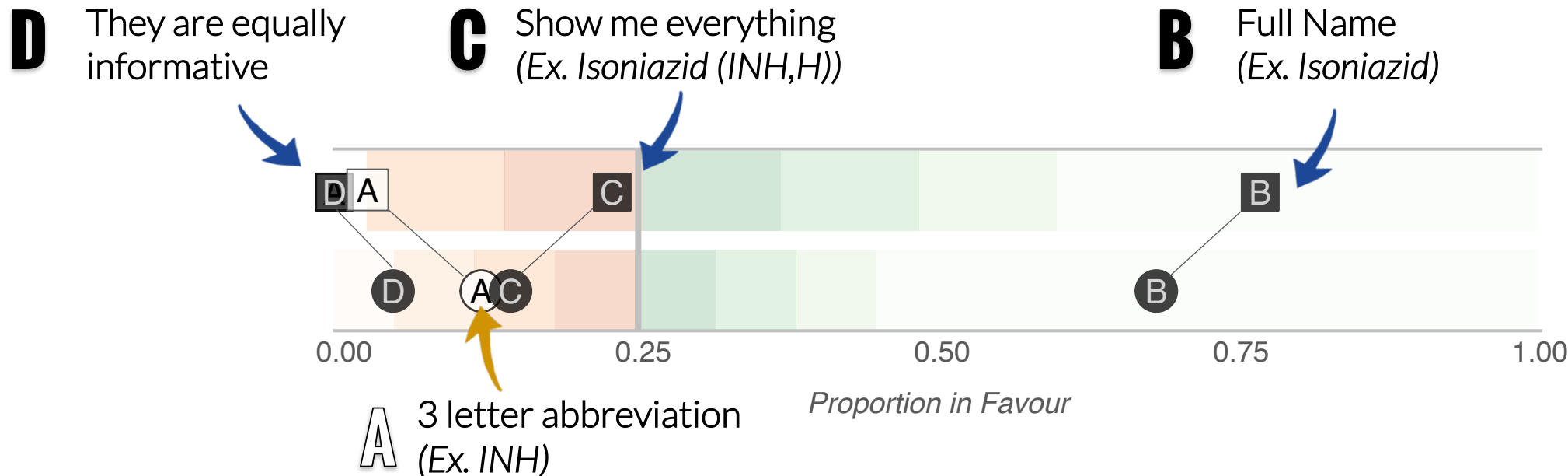
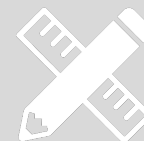
Design Option

- ☐ ☐ Control
- ☐ ☐ Alternative

A, B,... Option Indicator

Letters within shapes link to options on survey

[Wording] Report Drug Names as Abbreviations, or Not?



LEGEND

Public Health Role

- ■ Clinician
- ● Non-clinician

Design Option

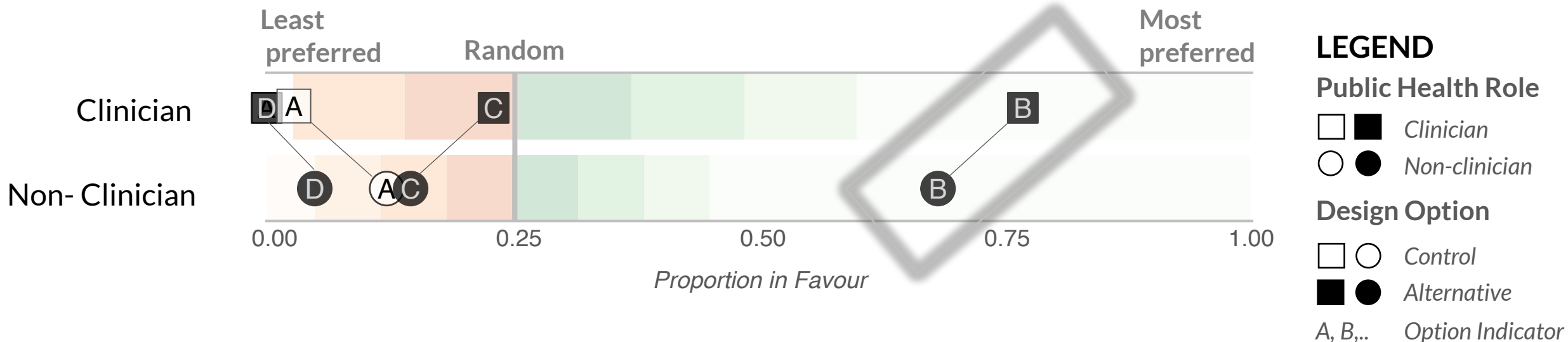
- ○ Control
- ● Alternative
- A, B,... Option Indicator

The *fill* of the shape indicates alternative (black) and control (white) designs

Control: Option A (3 letter abbreviation)

Alternative: Options B,C,D

[Wording] Report Drug Names as Abbreviations, or Not?

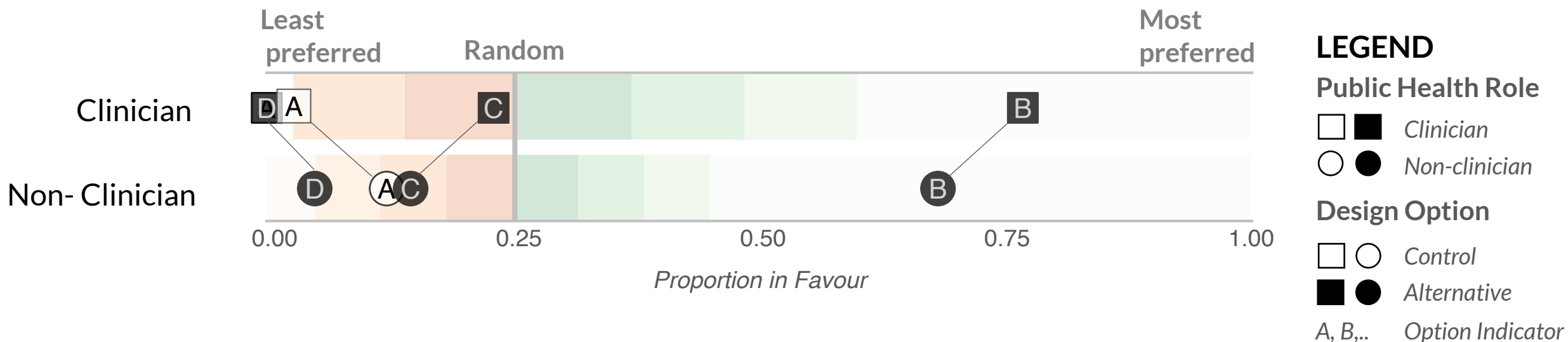
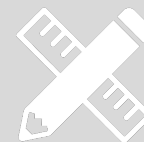


Lines connect design options between clinicians and non clinicians

Non-crossing lines : consensus between clinicians and non-clinicians

Crossing lines : discordance between clinicians and non-clinicians

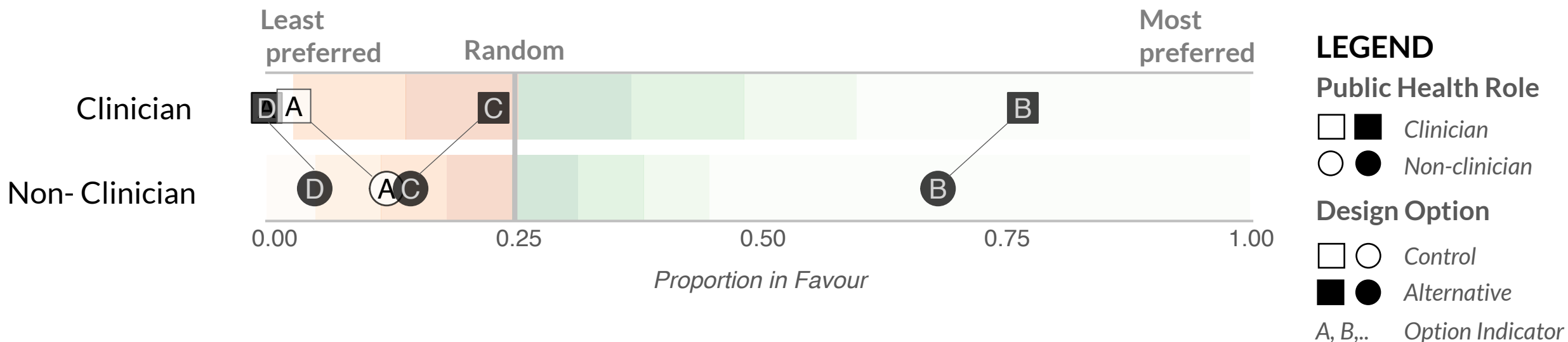
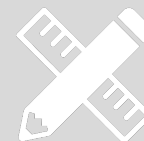
[Wording] Report Drug Names as Abbreviations, or Not?



Interpretation:

- Clinicians & non-clinicians preferred option *B* (*provide full drug name*)
- Option B was an alternative suggestion
- There is general consensus between clinicians and non-clinicians

[Wording] Report Drug Names as Abbreviations, or Not?



Comments from respondents:

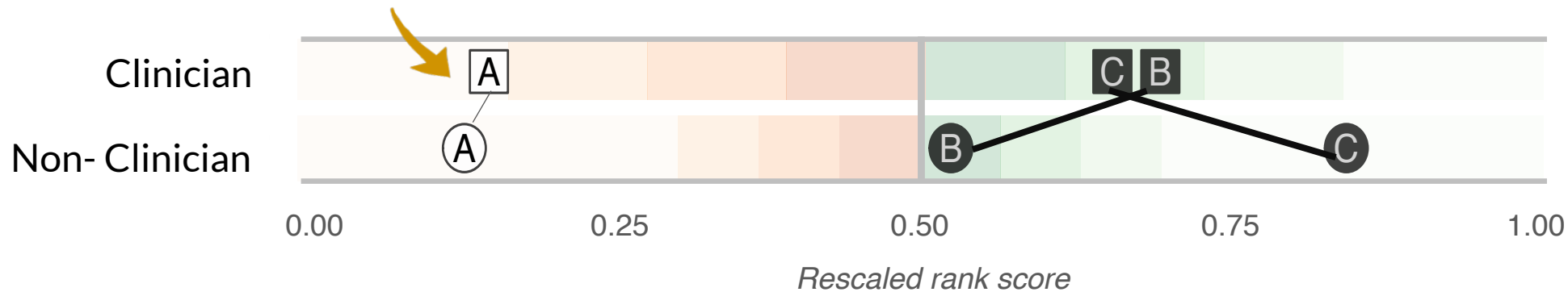
“not all clinicians [are] likely to recognize the abbreviations”

“[using the full name] reduces the risk of errors, especially if new to TB”

[Design] Show Summary of Resistance Results ?



Drug Susceptibility	
Drug	Prediction
Isonazid	Resistant
Rifampin	Resistant
Ethambutol	Resistant
Pyrazinimide	Resistant



Control design : no summary information, just table

[Design] Show Summary of Resistance Results ?



Alternative designs :

Tick-boxes

Drug Susceptibility	
Mono-resistant	<input type="checkbox"/>
Multidrug-resistant (MDR)	<input type="checkbox"/>
Extremely Drug Resistant (XDR)	<input checked="" type="checkbox"/>
Drug	Prediction
Isonazid	Resistant
Rifampin	Resistant
Ethambutol	Resistant
Pyrazinimde	Resistant

Summary Sentence

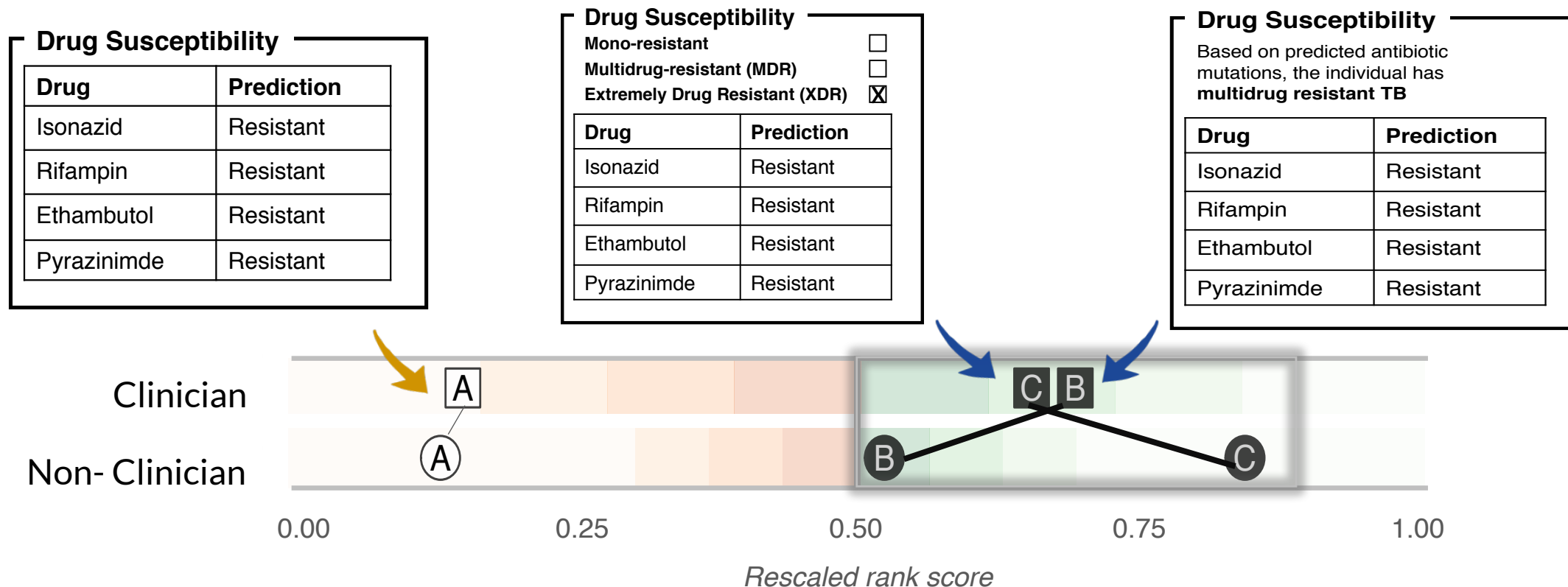
Drug Susceptibility	
Based on predicted antibiotic mutations, the individual has multidrug resistant TB	
Drug	Prediction
Isonazid	Resistant
Rifampin	Resistant
Ethambutol	Resistant
Pyrazinimde	Resistant



Clinician
Non- Clinician



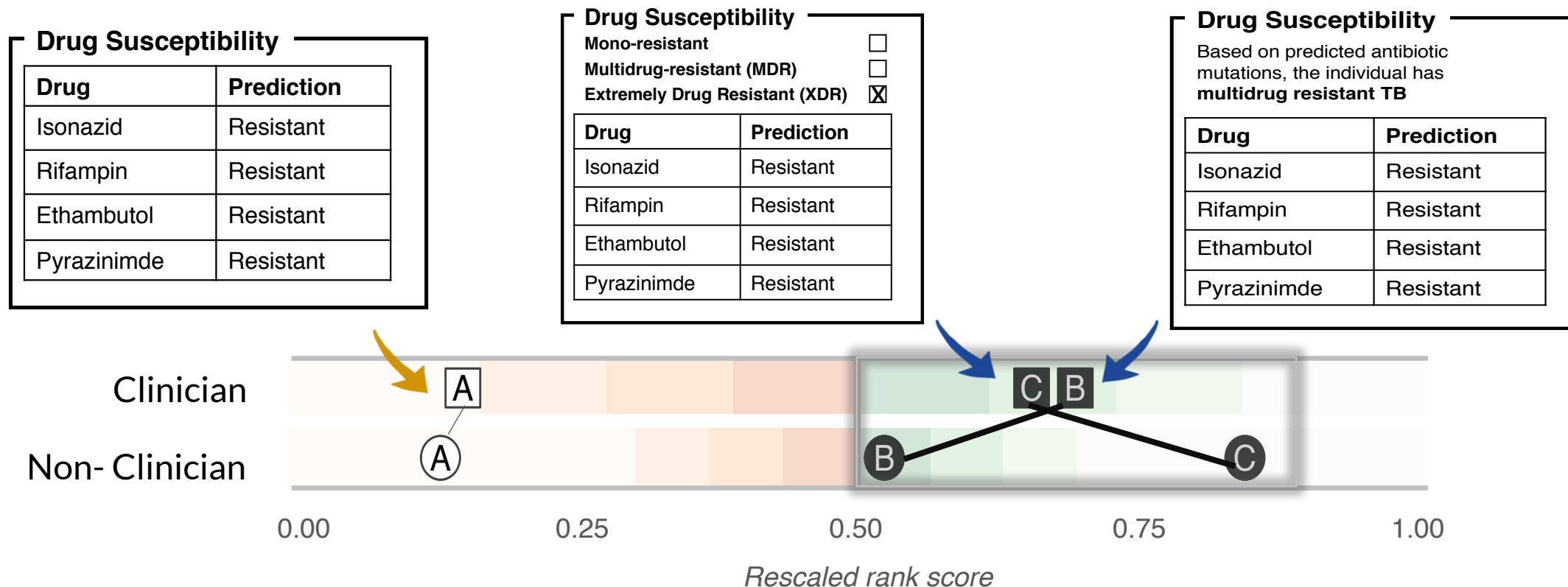
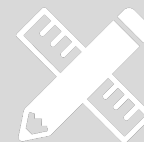
[Design] Show Summary of Resistance Results ?



Interpretation:

- Alternative design preferred (C or B)
- Some difference between clinicians & non-clinicians preferences

[Design] Show Summary of Resistance Results ?



Comments from respondents:

“the check boxes provide an at-a-glance result”

*“tick boxes may cause confusion when clinicians read XDR without realizing that option is **not** selected.”*

Full Results : Summary of Findings



Random permutation reference

<-3σ -2σ -1σ +1σ +2σ +3σ >+3σ

A) Isolated Wording Choices

Rank Questions

[Q6] Wording - Speciation
Preferred: B (Organism)

[Q8] Wording - Resistance
Preferred: C (Drug Susceptibility)

[Q14] Wording - Relatedness
Preferred: C (Cluster Detection)

Multiple Choice Questions

[Q7] Wording - Speciation Results
Preferred: A (Full Sentence)

[Q9] Abbreviation - Drug Names
Preferred: B (Full Name)

[Q10] Abbreviation - Resistance
Preferred: B (Full Name)

B) Isolated Design Choices

Rank Questions

[Q12] Emphasis - Drug Resistance
Preferred: C (Shading)

[Q13] Emphasis - Resistance Overview
Preferred: C (Tick Boxes)

[Q16] Layout - Drug Resistance
Preferred: B (Prediction by drug)
A (Drug listed by category)

[Q17] Visualization - Clusters
Preferred: D (Phylogenetic tree + table)

Multiple Choice Questions

[Q5] Emphasis - Bolding
Preferred: A (With bolding, for relevant content)

[Q11] Data - Mutation Data
Preferred: C (Include, but on second report page)

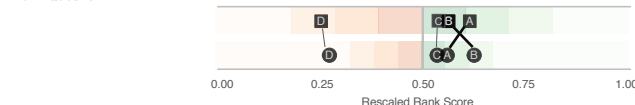
[Q15] Design - Speciation
Preferred: A (Organism name only)

[Q18] Design - Summary Statement
Preferred: B (Include Summary)

[Q19] Layout - Columns
Preferred: B (Two Columns)

C) Full Reports

Rank Question



LEGEND

Public Health Role

□ Clinician
○ Non-clinician

Design Option

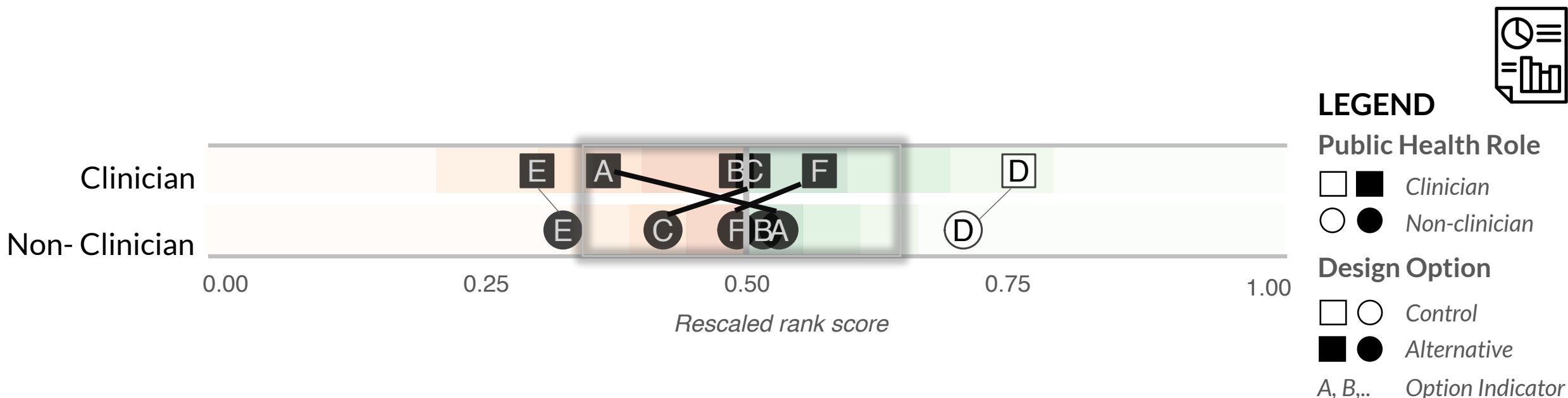
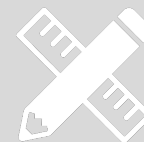
□ Control
● Alternative

A, B, ... Option Indicator

- Generally, alternative designs preferred
 - in 12 out of 14 comparisons to control
- Designs should promote patient safety & precise interpretability
 - Abbreviations should be avoided
 - Debate about prioritizing susceptible vs. resistant drugs
- Clinically actionable data to be given priority
 - Surveillance tasks aren't clinically actionable
- Sometimes we didn't provide good alternatives
 - Example: visualizing cluster results
- Isolated components showed clearer preferences than comparing full reports



Interesting Finding : Uncertainty over Data Visualization

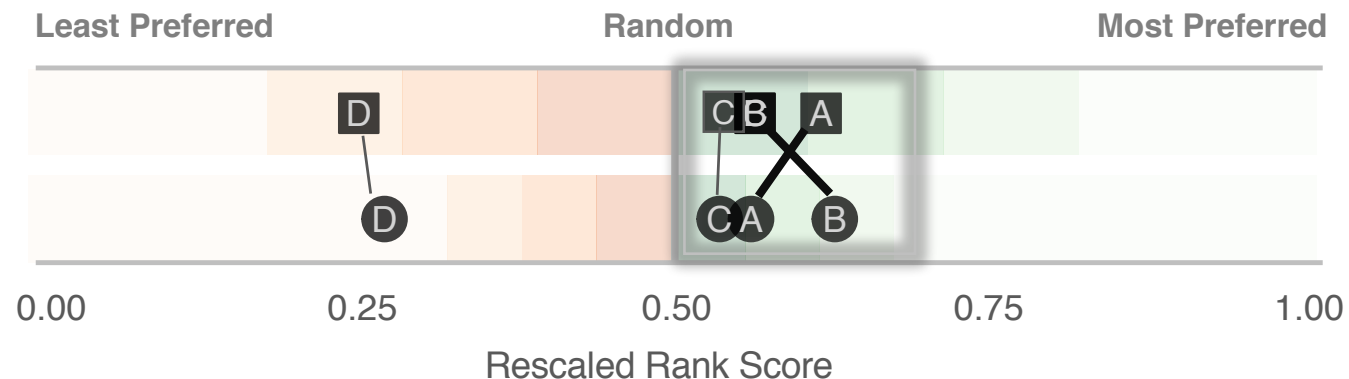
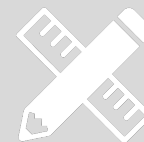


Few good alternatives were suggested

"If you can combine the phylogenetic tree with some kind of graph showing temporal spread that would be perfect. Adding geographical data would be a really helpful bonus too."

"Not useful for clinician. you need to refer this question to public health officials who do contact tracing"

Full Report Comparison : No Real Preference Consensus



LEGEND

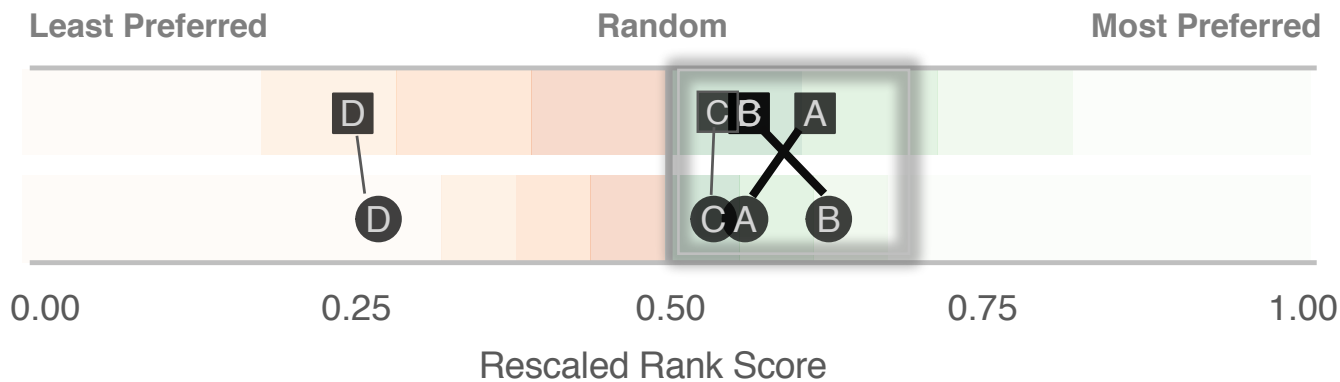
Public Health Role

- Clinician
- Non-clinician

Design Option

- Control
- Alternative
- A, B,.. Option Indicator

Full Report Comparison : No Real Preference Consensus



LEGEND

Public Health Role

- ☐ ☐ Clinician
- ☐ ☐ Non-clinician

Design Option

- ☐ ☐ Control
- ☐ ☐ Alternative

Option A

01-01-1900 / Bob Johnson Not for diagnostic Use

Public Health England

Mycobacterium Whole Genome Sequencing Report

Report Date

01-01-1900

Laboratory

Oxford

Reviewed by

Dr. John Smith

Patient Details

Patient Name

Bob Johnson

Patient ID

123456789

Patient DOB

01-01-1900

Location

Oxford

Requester Details

Requester

Dr. Paul 1234 Smith St Birmingham, UK

Copy to

Sample Details

Sample Type

Sputum

Sample Date

01-01-2000

Sample Site

-

Specimen ID

123456789

Speciation

Organism Species

Mycobacterium Tuberculosis

Drug Sensitivities

Ethambutol

Pyrazinamide

Isoniazid

Rifampin

SUSCEPTIBLE

RESISTANT

INDETERMINATE

Relatedness

Likely Related (less than 5 SNP difference)

Possibly Related (6-50 SNP difference)

Number of isolates

2

6

Resistotype

Drug	Prediction	Gene	Mutation
Isoniazid	Resistant	katG	S315T
Rifampin	Resistant	rpoB	S531L

Sequence Quality

The whole genome sequence analysis of the isolate was considered **HIGH QUALITY** as the number of reads was greater than 4.7 million with 99.47% mapped and a coverage of 91.99%.

Reviewer Comments

No additional comments

Authorization

Signature

Print Name

Dr. John Smith

Date

01-01-1900

Position

Lab Director

01-01-1900 / Bob Johnson Not for diagnostic Use

Public Health England

Tuberculosis Genome Sequencing Results

Page 1 of 2

Patient Information

Patient Name

Bob Johnson

Patient ID

123456789

Patient DOB

01-01-1900

Location

Oxford

Sample Type

Sputum

Sample Site

-

Sample Date

01-01-1900

Specimen ID

123456789

Summary of Findings

Based upon an analysis of the specimen's genomic data, this patient has **mycobacterium tuberculosis** that is predicted to be resistant to 2 antibiotics (**Isoniazid, Rifampin**). This case belongs to a **cluster** of cases with similar genomic findings.

Diagnosis

Methodology: genomic data from the specimen was compared to mycobacterium and non-mycobacterium tuberculosis genomes for speciation/reference published paper).

The specimen was speciated as **mycobacterium tuberculosis**

Treatment

Methodology: Drug sensitivities were predicted using the genomic sequence data in accordance to the method reported in published paper ref.

The specimen was considered to be **multi-drug resistant (MDR) TB**.

Summary of sensitive findings

Drugs	Prediction	Status	Comment
Isoniazid	Resistant	1	Gene: katG, Amino Acid Change: S315T
Rifampin	Resistant	1	Gene: rpoB, Amino Acid Change: S531L
Ethambutol	Sensitive	✓	-
Pyrazinamide	Sensitive	✓	-
QOI	Sensitive	✓	-
SM	Sensitive	✓	-
AG	Sensitive	✓	-

Epidemiologic Summary

Methodology: Patients are automatically assigned to clusters based upon single nucleotide polymorphism differences. Clustering thresholds are defined according to [the referenced paper](#).

The specimen belongs to a previously existing cluster

Similarity	SNP difference	Cluster trend (past 5 years)	Membership (#cases)
Highly	0 to 5		2
Peripheral	6 to 12		6

Quality Summary

The whole genome sequence analysis of the isolate was considered **HIGH QUALITY** as the number of reads was greater than 4.7 million with 99.47% mapped and a coverage of 91.99%.

Comments

Authorized By

Dr. John Smith

Position

Laboratory Director

Signature

Date

01-01-1901

Page 1 of 2

01-01-1900 / Bob Johnson Not for diagnostic Use

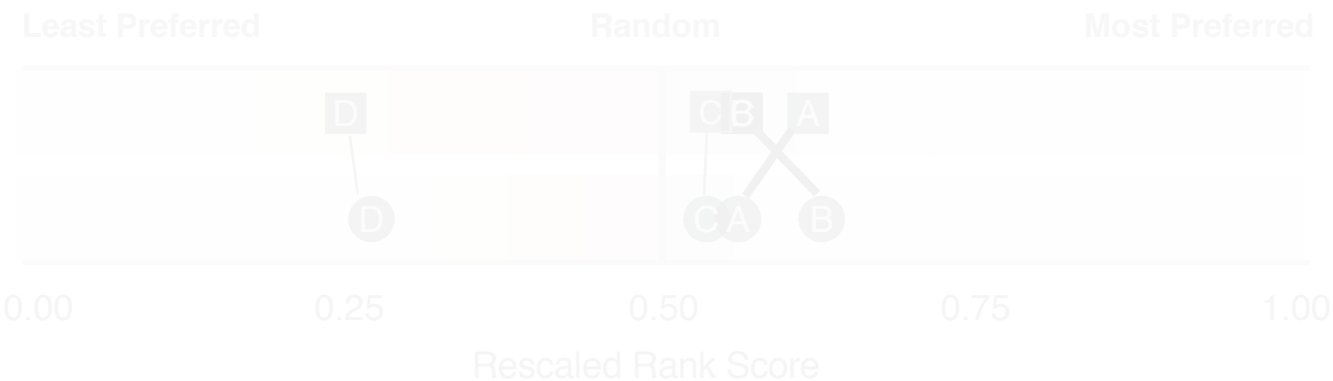
Public Health England

Tuberculosis Genome Sequencing Results

Page 2 of 2

50

Full Report Comparison : No Real Preference Consensus



LEGEND

Public Health Role

☐ ☒ Clinician

☐ ☒ Non-clinician

Design Option

☐ ☒ Control

☐ ☒ Alternative

Option “None are especially good (see previous comments on individual parts)”

- Participant Comment

Mycobacterium Whole Genome Sequencing Report

Patient Details

Patient Name	John Doe
Patient ID	123456789
Patient DOB	01-01-1980
Location	London

Requester Details

Requester	Dr. John Doe
Requester ID	123456789
Requester DOB	01-01-1980
Requester Location	London

Sample Details

Sample Type	Sputum
Sample Date	01-01-2020
Sample ID	123456789

Speciation

Drug Sensitivities

Isoniazid	Resistant
Rifampin	Resistant
Fluoroquinolones	Resistant
Second-line Aminoglycosides	Resistant

Relatedness

Number of isolates	1
Number of isolates	1
Number of isolates	1

Tuberculosis Genome Sequencing Results

Patient Information

Patient Name	John Doe
Patient ID	123456789
Patient DOB	01-01-1980
Location	London

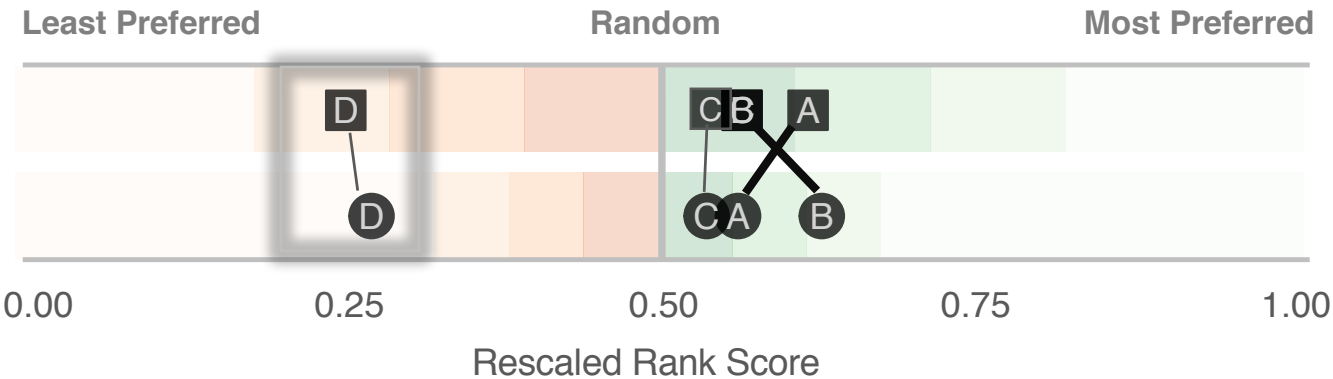
Summary of Findings

Diagnosis

Treatment

Drug	Prediction	Status	Comment
Isoniazid	Resistant	1	Genotype: Isoniazid Resistance (INH ^r)
Rifampin	Resistant	1	Genotype: Rifampin Resistance (RIF ^r)
Fluoroquinolones	Resistant	1	Genotype: Fluoroquinolone Resistance (FQ ^r)
Second-line Aminoglycosides	Resistant	1	Genotype: Second-line Aminoglycoside Resistance (SLA ^r)
Other	Resistant	1	Genotype: Other Resistance (Other ^r)

Full Report Comparison : No Real Preference Consensus



LEGEND

Public Health Role

- ☐ ☒ Clinician
- ☐ ☒ Non-clinician

Design Option

- ☐ ☐ Control
- ☒ ☒ Alternative
- A, B,.. Option Indicator

Option D

MYCOBACTERIAL GENOME SEQUENCING REPORT

Report Issued By: OXFORD Report Date: 1 JAN 1900

Public Health England

1

PATIENT INFORMATION
Name: Bob Johnson Identifier: 123456789
Birth Date: 1 Jan 1900 Sample Date: 1 Jan 1900
Location: Birmingham Gender: M

2

SPECIES IDENTIFIED BY SEQUENCING
100% identical to *Mycobacterium tuberculosis*

3

PREDICTED ANTIBIOTIC RESISTANCE
Resistant to isoniazid, rifampin.

4

EPIDEMIOLOGICAL RELATIONSHIPS
Belongs to a cluster of 8 genetically related cases, suggesting recent transmission.

5

SEQUENCING QUALITY
Sequenced 4 Aug 2016 on an Illumina MiSeq, yielding 4.73M reads, 4.70M (99.47%) mapped to the H37Rv (NC00962.2) reference genome.

6

COMMENTS
The sample was sequenced twice; the initial sequencing run did not provide high quality data for analysis.

MYCOBACTERIAL GENOME SEQUENCING REPORT

Report Issued By: OXFORD Report Date: 1 JAN 1900

Public Health England

7

Technical Details
This section of the report provides the technical details for the summaries presented on the first page.

Resistotype
The resistotype describes the mutations that are predicted to confer drug resistance.

Drug	Gene	Mutation	Catalog	Coverage	Support
Isoniazid	katG	S315I	Mykrobe v2	47x	46/47 reads
Rifampin	rpoB	S531L	Walker et al	38x	38/38 reads

Related Isolates
The following graph and table describe isolates that have been identified as being genetically similar to this patient's isolate.

Isolate	Year	SNP Distance
2015_A	2015	3
2014_A	2014	4
2013_A	2013	8
2013_B	2013	7
2012_A	2015	10
2012_B	2015	9
2012_C	2015	10
2012_D	2015	9



- General consensus in clinician & non-clinician preferences
- Alternative elements were preferred when compared against controls
- Some reporting areas need more work (surveillance)
- Isolated components showed clearer preferences than full reports



IMPLEMENT

Input from Stakeholders on Report Design

- Draft of report presented to a global TB working group
- Revised report was approved with minor changes
 - Revising some language (chiefly, sensitive -> susceptible)
 - Adding place for lineage details
 - Adding summary of assay + pipeline details
 - Adding a standard disclaimer

Mycobacterium Whole Genome Sequencing Report from MGIT Positive Samples

Not for diagnostic use

01/02/1915

MYCOBACTERIUM TUBERCULOSIS GENOME SEQUENCING REPORT

NOT FOR DIAGNOSTIC USE



Patient Name	JOHN DOE	Barcode	
Birth Date	2000-01-01	Patient ID	12345678910
Location	SOMEPLACE	Sample Type	SPUTUM
Sample Source	PULMONARY	Sample Date	2016-12-25
Sample ID	A12345678	Sequenced From	MGIT CULTURED ISOLATE
Reporting Lab	LAB NAME	Report Date/Time	2017-01-01, 15:36
Requested By	REQUESTER NAME	Requester Contact	REQUESTER@EMAIL.COM

Summary

The specimen was positive for **Mycobacterium tuberculosis**. It is **resistant to isoniazid and rifampin**. It belongs to a cluster, suggesting **recent transmission**.

Sample Details			
Sequencing Location	Oxford	Date received in Lab	
Local Lims Specimen ID	123456789	Run date	01/01/19150115
Guuid	123456-79aab-910abr-15243hg		

Organism Identification	
Predicted closest match	
TBCOMP/ microti	100%
TBCOMP/	100%
TBCOMP/	96.7%
TBCOMP/ tuberculosis-netti	35.1%
MACCOM	21.1%

Sample/Sequencing Quality			
Total reads (~millions)	Mapped %	No reads mapped (~millions)	Coverage %
4.73	99.47	4.7	91.99

Resistance Summary						
INH	RIF	EMB	PZA	QUI	SM	AG
U	S	S	S	S	S	S

Resistotype					
Drug	Mutation	Nucleotides	Support (ACGT)	Source – (R/Total)	Prediction
INH	katG_A727T	GCC->ACC	(160/0/1/0) (0/164/0/0) (0/167/0/0)	Unclassified	UNK

Organism

The specimen was positive for **Mycobacterium tuberculosis** (H37Rv, 2% (Asia)).

Drug Susceptibility

Resistance reported for a high confidence resistance-conferring mutation is detected. “No mutation detected” does not exclude the possibility of resistance.

No mutation detected predicted

☐ Mono-resistance predicted

☒ Multi-drug resistance predicted

☐ Extensive drug resistance predicted

Drug class	Interpretation	Drug	Resistance Gene (Amino Acid Mutation)
First Line	Susceptible	Ethambutol	No mutation detected
		Pyrazinimide	No mutation detected
	Resistant	Isoniazid	katG (S315T)
		Rifampin	rpoB (S531L)
Second Line	Susceptible	Streptomycin	No mutation detected
		Ciprofloxacin	No mutation detected
		Ofloxacin	No mutation detected
		Moxifloxacin	No mutation detected
		Amikacin	No mutation detected
		Kanamycin	No mutation detected
		Capreomycin	No mutation detected

Mycobacterium Whole Genome Sequencing Report from MGIT Positive Samples

Not for diagnostic use

01/02/1915

MYCOBACTERIUM TUBERCULOSIS GENOME SEQUENCING REPORT

NOT FOR DIAGNOSTIC USE



Patient Name	JOHN DOE	Barcode	
Birth Date	2000-01-01	Patient ID	12345678910
Location	SOMEPLACE	Sample Type	SPUTUM
Sample Source	PULMONARY	Sample Date	2016-12-25
Sample ID	A12345678	Sequenced From	MGIT CULTURED ISOLATE
Reporting Lab	LAB NAME	Report Date/Time	2017-01-01, 15:36
Requested By	REQUESTER NAME	Requester Contact	REQUESTER@EMAIL.COM

Summary

The specimen was positive for **Mycobacterium tuberculosis**. It is **resistant to isoniazid and rifampin**. It belongs to a cluster, suggesting **recent transmission**.

Organism

The specimen was positive for **Mycobacterium tuberculosis**, lineage 2.2.1 (**East-Asian Beijing**).

Drug Susceptibility

Resistance is reported when a high-confidence resistance-conferring mutation is detected. **"No mutation detected" does not exclude the possibility of resistance.**

- ☐ No drug resistance predicted
- ☐ Mono-resistance predicted
- ☒ Multi-drug resistance predicted
- ☐ Extensive drug resistance predicted

Drug class	Interpretation	Drug	Resistance Gene (Amino Acid Mutation)
First Line	Susceptible	Ethambutol	No mutation detected
		Pyrazinimide	No mutation detected
	Resistant	Isoniazid	katG (S315T)
		Rifampin	rpoB (S531L)
Second Line	Susceptible	Streptomycin	No mutation detected
		Ciprofloxacin	No mutation detected
		Ofloxacin	No mutation detected
		Moxifloxacin	No mutation detected
		Amikacin	No mutation detected
		Kanamycin	No mutation detected
		Capreomycin	No mutation detected

Sample Details			
Sequencing Location	Oxford	Date received in Lab	
Local Lims Specimen ID	123456789	Run date	01/01/19150115
Guuid	123456-79aab-910abr-15243hg		

Organism Identification	
Predicted/closest match	
TBCOMP/microti	100%
TBCOMP	100%
TBCOMP/TB	96.77%
TBCOMP/tuberculosis-canettii	35.71%
MACCOMP	21.21%

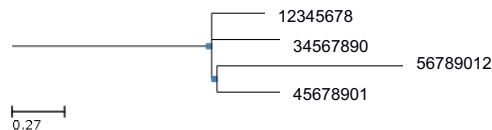
Sample/Sequencing Quality			
Total reads (~millions)	Mapped %	No reads mapped (~millions)	Coverage %
4.73	99.47	4.7	91.99

Resistance Summary						
INH	RIF	EMB	PZA	QUI	SM	AG
U	S	S	S	S	S	S

Resistotype					
Drug	Mutation	Nucleotides	Support (ACGT)	Source – (R/Total)	Prediction
INH	katG_A727T	GCC->ACC	(160/0/1/0) (0/164/0/0) (0/167/0/0)	Unclassified	UNK

Relatedness			
NB: This data may be added or updated at a later date			
Nearest neighbour(s)			
Sample -Plate Name	Date received in Lab	Centre	No. of SNPs apart
123456789		Oxford	0
34567890	1900-01-01		10
45678901	1015-01-31	Oxford	15
56789012		London	8

The alignment width is 285. Multiply this number by the tree metrics.



Comments

Authorised	
Signature:	Print name:
Position:	Date:

MYCOBACTERIUM TUBERCULOSIS GENOME SEQUENCING REPORT

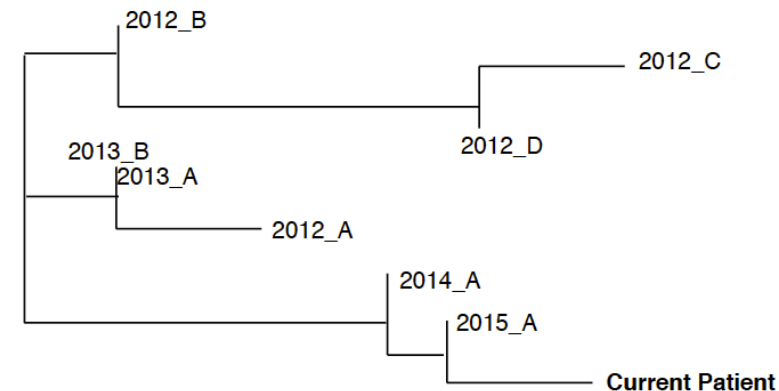
NOT FOR DIAGNOSTIC USE



Cluster Detection

The current isolate was clustered with previously sequenced isolates, suggesting **recent transmission**.

Relatedness	Number of prior matching isolates
Closely Related (< 5 mutations apart)	2 isolates
Related (6 to 30 mutations apart)	6 isolates



Assay Details

Sample ID	A12345678	Barcode	
Sequencer	ILLUMINA HISEQ 2500	Method	WGS
Pipeline	RESEQTB V.3.2C	Reference	H37RV

Comments

No additional comments for this report

Standard Disclaimer: Low frequency hetero-resistance below the limit of detection by sequencing may affect typing results. The interpretation provided is based on the current understanding of genotype-phenotype relationships.

Authorised

Signature	Name
Position	Date

Revised Report Designed through Evidence Collected



MYCOBACTERIUM TUBERCULOSIS GENOME SEQUENCING REPORT NOT FOR DIAGNOSTIC USE



Patient Name	JOHN DOE	Barcode	
Birth Date	2000-01-01	Patient ID	12345678910
Location	SOMEPLACE	Sample Type	SPUTUM
Sample Source	PULMONARY	Sample Date	2016-12-25
Sample ID	A12345678	Sequenced From	MGIT CULTURED ISOLATE
Reporting Lab	LAB NAME	Report Date/Time	2017-01-01, 15:36
Requested By	REQUESTER NAME	Requester Contact	REQUESTER@EMAIL.COM

Summary

The specimen was positive for **Mycobacterium tuberculosis**. It is **resistant to isoniazid and rifampin**. It belongs to a cluster, suggesting **recent transmission**.

Organism

The specimen was positive for **Mycobacterium tuberculosis**, lineage 2.2.1 (**East-Asian Beijing**).

Drug Susceptibility

Resistance is reported when a high-confidence resistance-conferring mutation is detected. "No mutation detected" does not exclude the possibility of resistance.

- ☐ No drug resistance predicted
- ☐ Mono-resistance predicted
- ☒ Multi-drug resistance predicted
- ☐ Extensive drug resistance predicted

Drug class	Interpretation	Drug	Resistance Gene (Amino Acid Mutation)
First Line	Susceptible	Ethambutol	No mutation detected
		Pyrazinimide	No mutation detected
	Resistant	Isoniazid	katG (S315T)
		Rifampin	rpoB (S531L)
Second Line	Susceptible	Streptomycin	No mutation detected
		Ciprofloxacin	No mutation detected
		Ofloxacin	No mutation detected
		Moxifloxacin	No mutation detected
		Amikacin	No mutation detected
		Kanamycin	No mutation detected
		Capreomycin	No mutation detected

- Visual hierarchy that follows a clinical narrative
 - Grouping of common data elements (gestalt)
 - Judicious use of emphasis for “at-a-glance” read
 - Prioritize reading flow for clinical tasks
- Attempts to address timeliness and request for levels of detail



LaTeX Template



<https://goo.gl/t4SMdV>

<https://www.overleaf.com/latex/templates/tb-wgs-report-for-reference-lab/psmnzmcnwrwm>

Example with Sweave (R – LaTeX Interface)



<https://github.com/amcrisan/TB-WGS-MicroReport>



REFLECTION

Why not just hire a Graphic Designer?

“Design is not just what it looks like and feels like – design is how it works”
Steve Jobs

- **Form (visual appeal) should follow function**
 - Visual appeal is important, but does not guarantee functionality
 - *Example:* report design with pictures was pretty but was also the least preferred
- **Functional can also be *beautiful***
 - Report is both functional (*works better*) and also visually appealing
 - Understanding scientific goals, tasks, and data is a scientific problem & linked to function
 - Not necessarily a graphics design issues



Do YOU have to go through all this effort for every report?

It *depends* on what you want to achieve

- Broad data collection can be used for other projects
 - We were also collecting data for future software projects
 - Stayed tuned for more details!

It *depends* on what you want to achieve

- **Broad data collection can be used for other projects**
 - We were also collecting data for future software projects
 - Stayed tuned for more details!
- **At the very least test alternative designs**
 - If you can't do a Discovery stage (time, people, budget) at least to the Design stage
 - Check in with stakeholders to avoid *ad hoc* design issues

It *depends* on what you want to achieve

- **Broad data collection can be used for other projects**
 - We were also collecting data for future software projects
 - Stayed tuned for more details!
- **At the very least test alternative designs**
 - If you can't do a Discovery stage (time, people, budget) at least to the Design stage
 - Check in with stakeholders to avoid *ad hoc* design issues
- **Bioinformaticians : you should use human-centered design for your tools!**
 - Not command line ≠user friendly
 - If you didn't test it with even one user it's not "*user friendly*" or "*intuitive*"
 - Report design is a very simple example of how to use these methods



UBC

Dr. Jennifer Gardy
Dr. Geoff McKee
Dr. Tamara Munzner

COMPASS TB

Dr. Ana Gibertoni-Cruz
Dr. Grace Smith
Dr. Tim Walker

+ UBC infoVis group

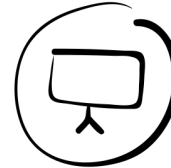
Kimberly Dextras-Romagnino,
Dylan Dong, Georges Hattab,
and Zipeng Liu

+ All of our fantastic
study participants

Pre-Print + Other Stuff



<https://doi.org/10.1101/199570>



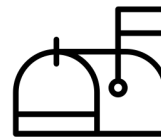
<https://goo.gl/9jt625>

<http://www.cs.ubc.ca/labs/imager/tr/2017/MicroReportDesign/>



<https://goo.gl/6vNqRZ>

<http://www.cs.ubc.ca/labs/imager/tr/2017/MicroReportDesign/>



acrisan@cs.ubc.ca

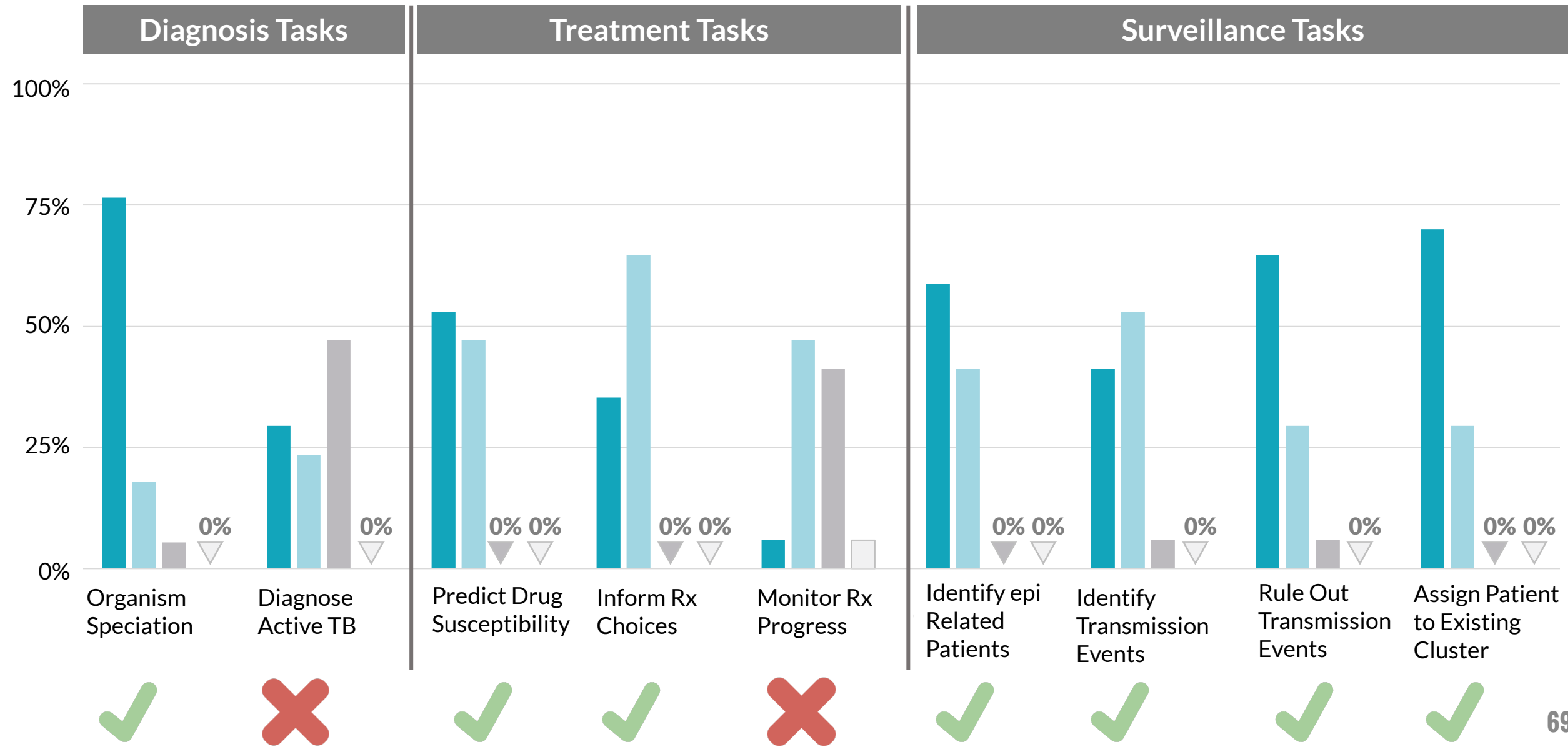


Go forth and analyze!

Additional Materials



CAN GENOMIC DATA PERFORM THE FOLLOWING (NOW OR LATER)?



Results: Wording Preferences

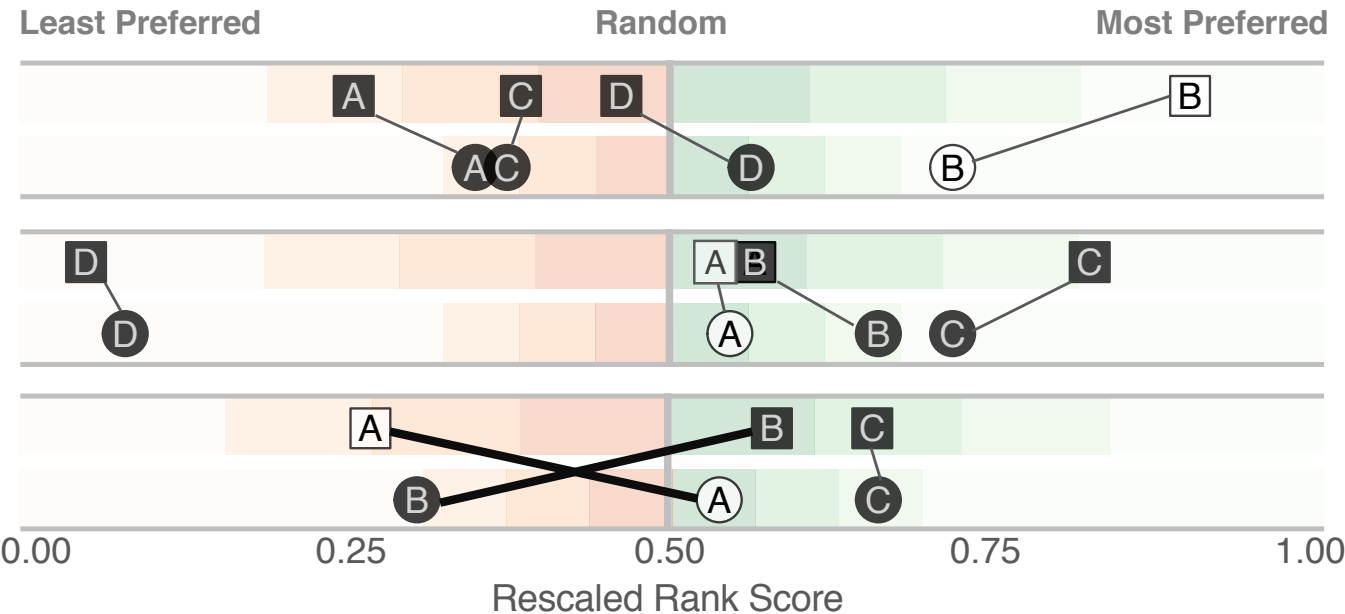


Rank Questions

[Q6] Wording - Speciation
Preferred: B (Organism)

[Q8] Wording - Resistance
Preferred: C (Drug Susceptibility)

[Q14] Wording - Relatedness
Preferred: C (Cluster Detection)

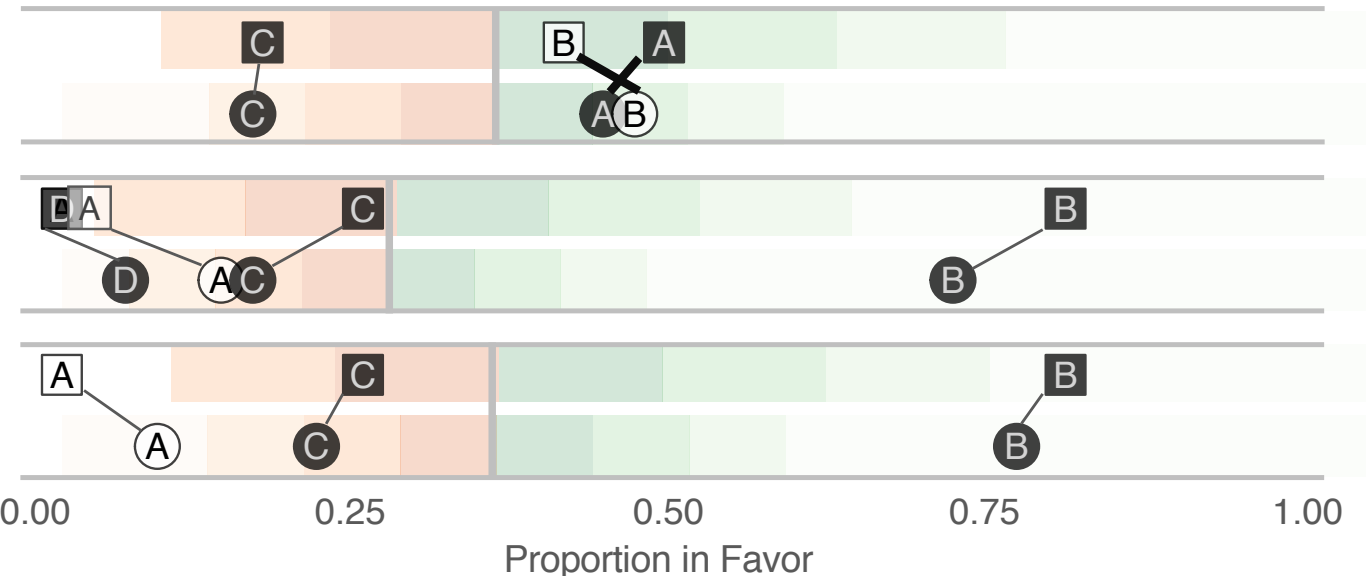


Multiple Choice Questions

[Q7] Wording - Speciation Results
Preferred: A (Full Sentence)

[Q9] Abbreviation - Drug Names
Preferred: B (Full Name)

[Q10] Abbreviation - Resistance
Preferred: B (Full Name)



LEGEND

Public Health Role

- Clinician
- Non-clinician

Design Option

- Control
- Alternative
- A, B,... Option Indicator

Results: Information & Visualization Design Preferences



Rank Questions

[Q12] Emphasis – Drug Resistance
Preferred: C (Shading)

[Q13] Emphasis – Resistance

*Preferred: B (Prediction by drug)
A (Drug listed by category)*

[Q17] Visualization - Clusters
*Preferred: D (Phylogenetic tree
+ table)*

Multiple Choice Questions

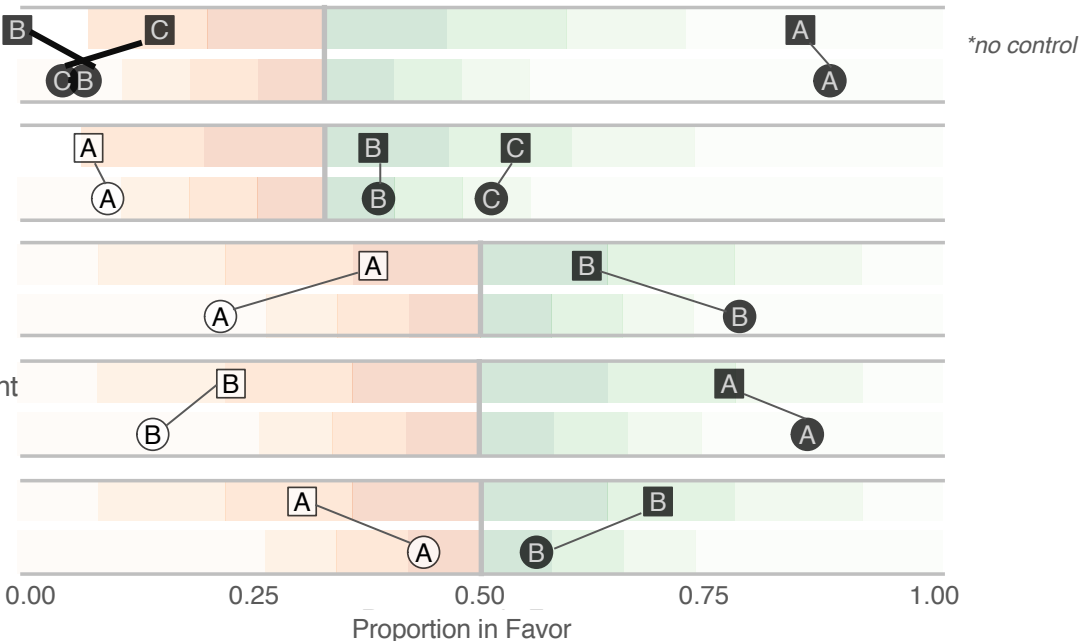
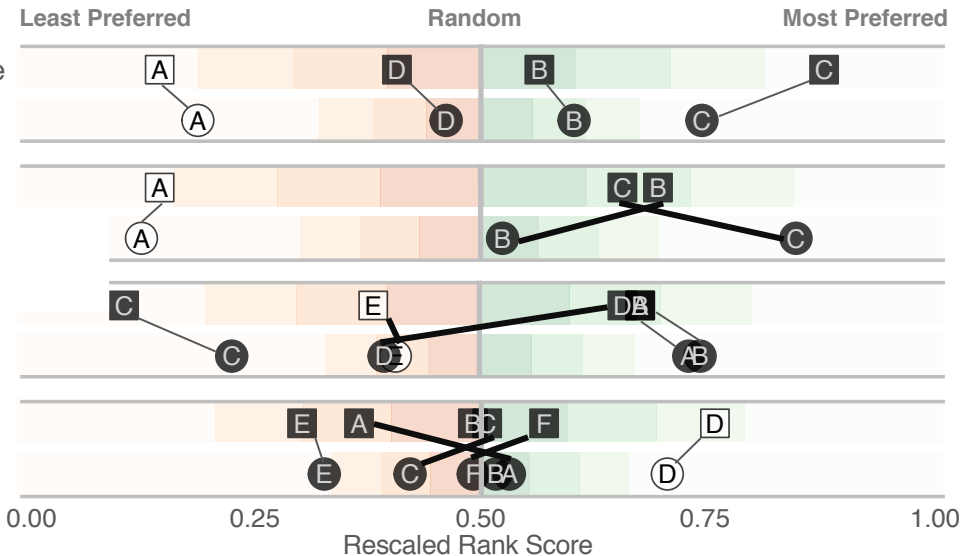
[Q5] Emphasis - Bolding
*Preferred: A (With bolding,
for relevant content)*

[Q11] Data – Mutation Data
*Preferred: C (Include, but on
second report page)*

[Q15] Design - Speciation
Preferred: A (Organism name only)

[Q18] Design – Summary Statement
Preferred: B (Include Summary)

[Q19] Layout – Columns
Preferred: B (Two Columns)



LEGEND

Public Health Role

- Clinician
- Non-clinician

Design Option

- Control
- Alternative
- A, B,... Option Indicator

Some Helpful Tips on Running these Studies

1. Design around tasks
2. Compared components & whole designs
3. Compare against a control

Some Helpful Tips on using Design Techniques

1. Structure data according to a workflow narrative
2. Use emphasis carefully
3. Use words precisely
4. Use images judiciously
5. Information density OK, with caution