



Public Health
England

Protecting and improving the nation's health

Managing TB outbreaks and incidents using WGS

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Outline

1. Summary of process we use to manage information coming from TB labs and ensure clusters are investigated
2. Identify lessons learnt from a number of investigations using WGS

Background

In March 2017, PHE introduced WGS for all culture positive TB cases in North and Central England

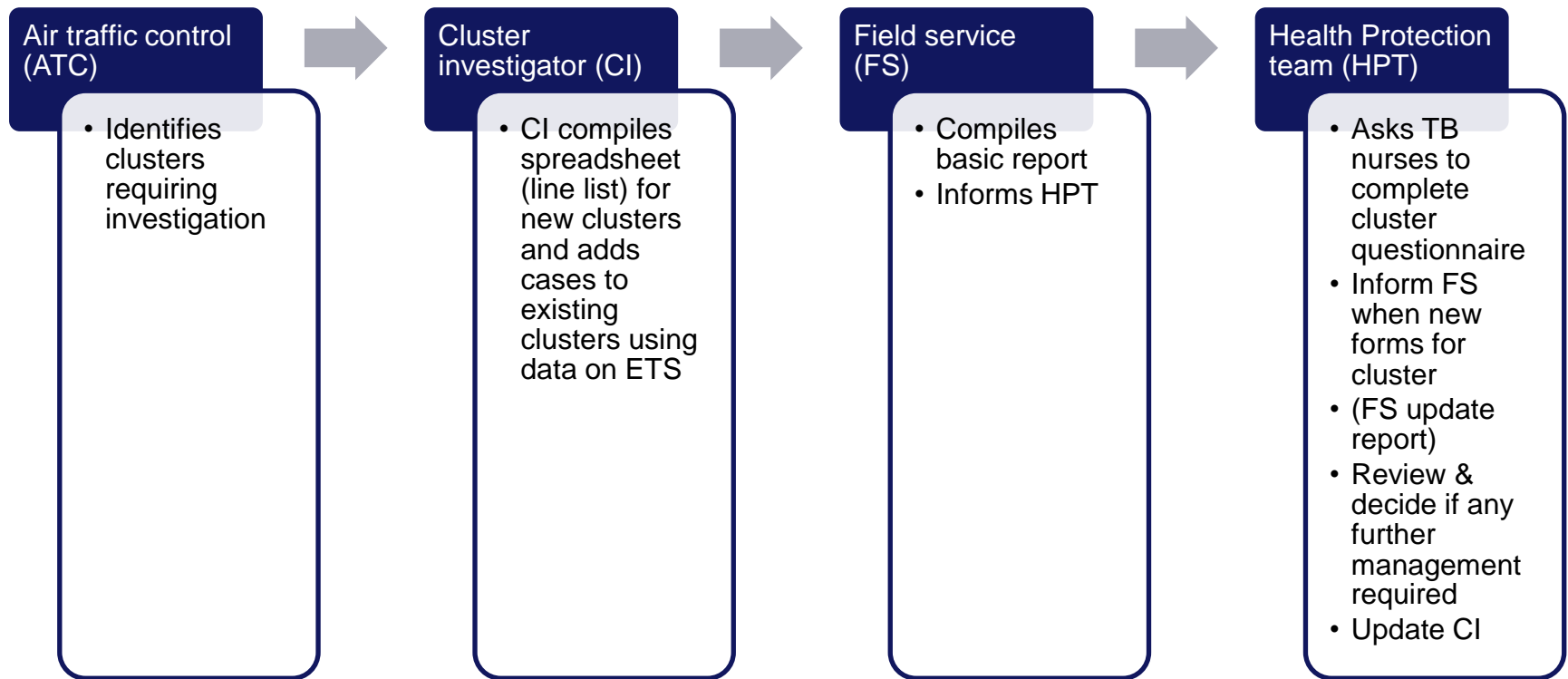
Allows for timely identification of clusters of cases of TB

In the NW, a large number of clusters were identified that required some investigation

- How much investigation should be done for each cluster?
- How do we collect and store information?

A NW task group was set up to develop a process to coordinate cluster investigation of TB

Process



Questionnaire



TB Cluster Investigation Tool (DRAFT v12)

Cluster ID (to be completed by HPT)

Tab/arrow – to move between fields. F4 – to display dropdown menus. Space – to check boxes

1. Patient details

Date form completed: <input type="text"/>	Date of notification: <input type="text"/>	Patient's NHS Number: <input type="text"/>	ETS Number: <input type="text"/>
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The next section asks about places the patient has visited regularly. This is to identify venues where transmission to others may have occurred. This would involve spending a significant amount of time at a venue with other people with prolonged, frequent or intense contact. Please include venues visited in the last 2 years as standard, if a longer time period has been used please provide details in the comments.

2. Patient contexts

Category	Type of venue	Venue name	Town	Postcode	Frequency	Time period From To	Comments
Childcare/ Education	Please select...	<input type="text"/>	<input type="text"/>	<input type="text"/>	Please select...	<input type="text"/> <input type="text"/>	<input type="text"/>
	Please select...	<input type="text"/>	<input type="text"/>	<input type="text"/>	Please select...	<input type="text"/> <input type="text"/>	<input type="text"/>
	Please select...	<input type="text"/>	<input type="text"/>	<input type="text"/>	Please select...	<input type="text"/> <input type="text"/>	<input type="text"/>
	Please select...	<input type="text"/>	<input type="text"/>	<input type="text"/>	Please select...	<input type="text"/> <input type="text"/>	<input type="text"/>
Work place	Please select...	<input type="text"/>	<input type="text"/>	<input type="text"/>	Please select...	<input type="text"/> <input type="text"/>	<input type="text"/>
	Please select...	<input type="text"/>	<input type="text"/>	<input type="text"/>	Please select...	<input type="text"/> <input type="text"/>	<input type="text"/>
	Please select...	<input type="text"/>	<input type="text"/>	<input type="text"/>	Please select...	<input type="text"/> <input type="text"/>	<input type="text"/>
	Please select...	<input type="text"/>	<input type="text"/>	<input type="text"/>	Please select...	<input type="text"/> <input type="text"/>	<input type="text"/>
Place of worship	Please select...	<input type="text"/>	<input type="text"/>	<input type="text"/>	Please select...	<input type="text"/> <input type="text"/>	<input type="text"/>
	Please select...	<input type="text"/>	<input type="text"/>	<input type="text"/>	Please select...	<input type="text"/> <input type="text"/>	<input type="text"/>
	Please select...	<input type="text"/>	<input type="text"/>	<input type="text"/>	Please select...	<input type="text"/> <input type="text"/>	<input type="text"/>
	Please select...	<input type="text"/>	<input type="text"/>	<input type="text"/>	Please select...	<input type="text"/> <input type="text"/>	<input type="text"/>
Detention (e.g. Prison)	Please select...	<input type="text"/>	<input type="text"/>	<input type="text"/>	Please select...	<input type="text"/> <input type="text"/>	<input type="text"/>
	Please select...	<input type="text"/>	<input type="text"/>	<input type="text"/>	Please select...	<input type="text"/> <input type="text"/>	<input type="text"/>
	Please select...	<input type="text"/>	<input type="text"/>	<input type="text"/>	Please select...	<input type="text"/> <input type="text"/>	<input type="text"/>
	Please select...	<input type="text"/>	<input type="text"/>	<input type="text"/>	Please select...	<input type="text"/> <input type="text"/>	<input type="text"/>

1

Category	Type of venue	Venue name	Town	Postcode	Frequency	Time period (mm-yy) From To	Comments
Treatment /Rehab Centre	Please select...	<input type="text"/>	<input type="text"/>	<input type="text"/>	Please select...	<input type="text"/> <input type="text"/>	<input type="text"/>
	Please select...	<input type="text"/>	<input type="text"/>	<input type="text"/>	Please select...	<input type="text"/> <input type="text"/>	<input type="text"/>
	Please select...	<input type="text"/>	<input type="text"/>	<input type="text"/>	Please select...	<input type="text"/> <input type="text"/>	<input type="text"/>
	Please select...	<input type="text"/>	<input type="text"/>	<input type="text"/>	Please select...	<input type="text"/> <input type="text"/>	<input type="text"/>
Residential (e.g. nursing home, homeless shelter)	Please select...	<input type="text"/>	<input type="text"/>	<input type="text"/>	Please select...	<input type="text"/> <input type="text"/>	<input type="text"/>
	Please select...	<input type="text"/>	<input type="text"/>	<input type="text"/>	Please select...	<input type="text"/> <input type="text"/>	<input type="text"/>
	Please select...	<input type="text"/>	<input type="text"/>	<input type="text"/>	Please select...	<input type="text"/> <input type="text"/>	<input type="text"/>
	Please select...	<input type="text"/>	<input type="text"/>	<input type="text"/>	Please select...	<input type="text"/> <input type="text"/>	<input type="text"/>
Social venue	Please select...	<input type="text"/>	<input type="text"/>	<input type="text"/>	Please select...	<input type="text"/> <input type="text"/>	<input type="text"/>
	Please select...	<input type="text"/>	<input type="text"/>	<input type="text"/>	Please select...	<input type="text"/> <input type="text"/>	<input type="text"/>
	Please select...	<input type="text"/>	<input type="text"/>	<input type="text"/>	Please select...	<input type="text"/> <input type="text"/>	<input type="text"/>
	Please select...	<input type="text"/>	<input type="text"/>	<input type="text"/>	Please select...	<input type="text"/> <input type="text"/>	<input type="text"/>
Other places of interest	Please select...	<input type="text"/>	<input type="text"/>	<input type="text"/>	Please select...	<input type="text"/> <input type="text"/>	<input type="text"/>
	Please select...	<input type="text"/>	<input type="text"/>	<input type="text"/>	Please select...	<input type="text"/> <input type="text"/>	<input type="text"/>
	Please select...	<input type="text"/>	<input type="text"/>	<input type="text"/>	Please select...	<input type="text"/> <input type="text"/>	<input type="text"/>
	Please select...	<input type="text"/>	<input type="text"/>	<input type="text"/>	Please select...	<input type="text"/> <input type="text"/>	<input type="text"/>

3. Residence

List the addresses where the patient has lived in the previous two years (excluding current address)

	Address 2	Address 3	Address 4
House no. & street	<input type="text"/>	<input type="text"/>	<input type="text"/>
Town	<input type="text"/>	<input type="text"/>	<input type="text"/>
Postcode	<input type="text"/>	<input type="text"/>	<input type="text"/>
Date from (mm-yy)	<input type="text"/>	<input type="text"/>	<input type="text"/>
Date to (mm-yy)	<input type="text"/>	<input type="text"/>	<input type="text"/>

Please provide any further addresses in the following comments box

<input type="text"/>

Outputs of the report to HPTs

Data collected from ETS:

Age and sex

Ethnicity and country of birth

Map of residence in NW

Resistance profiles

Phylogenetic tree

Data collected from questionnaire:

Summary of social context information



TB_Working_NW_V1.html

Figure 1: Epidemic Curve by ethnic group.*

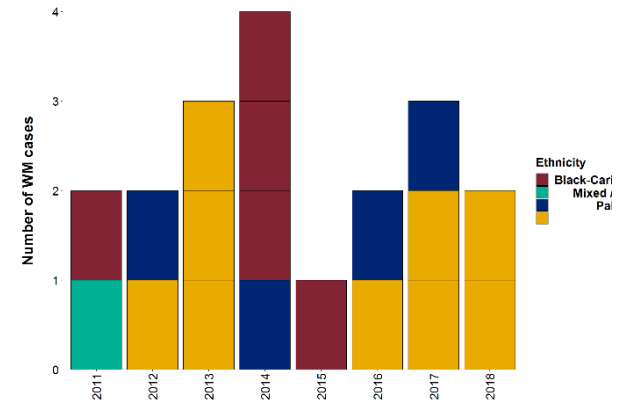
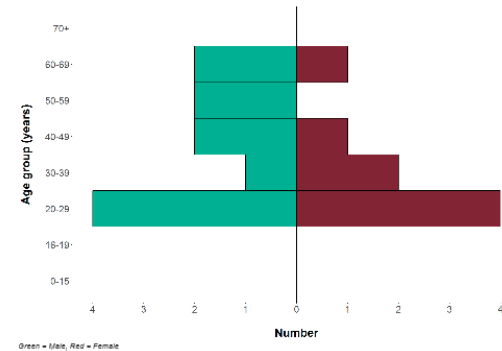


Figure 2: Age and sex pyramid of clustered cases.



Cluster 1: GM MDR (AA726-2_B1006)



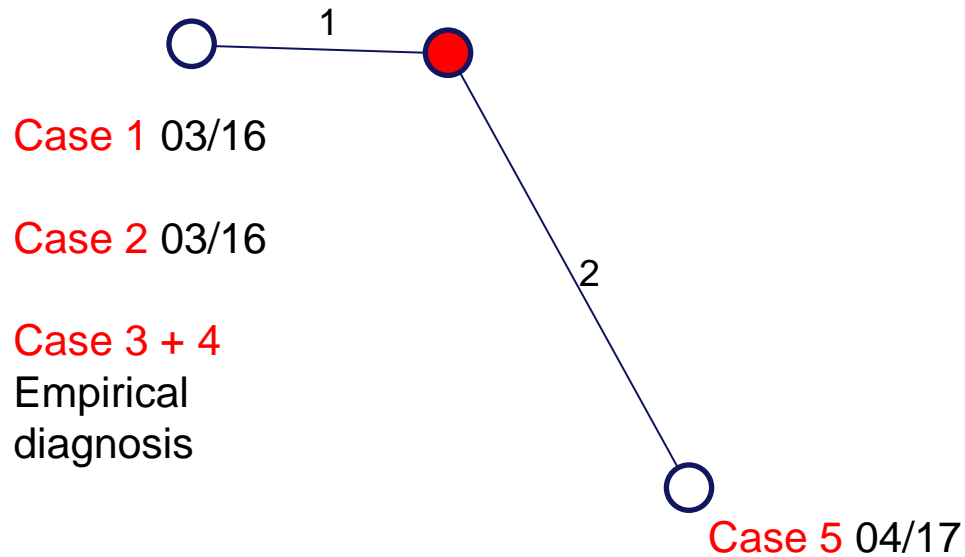
Case 1 03/16

Case 2 03/16

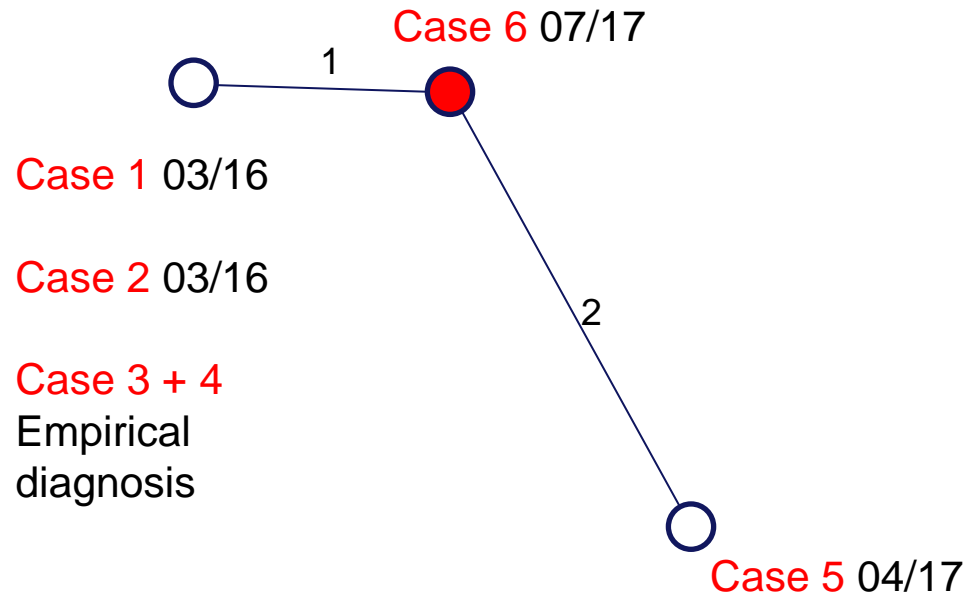
Case 3 + 4

Empirical diagnosis

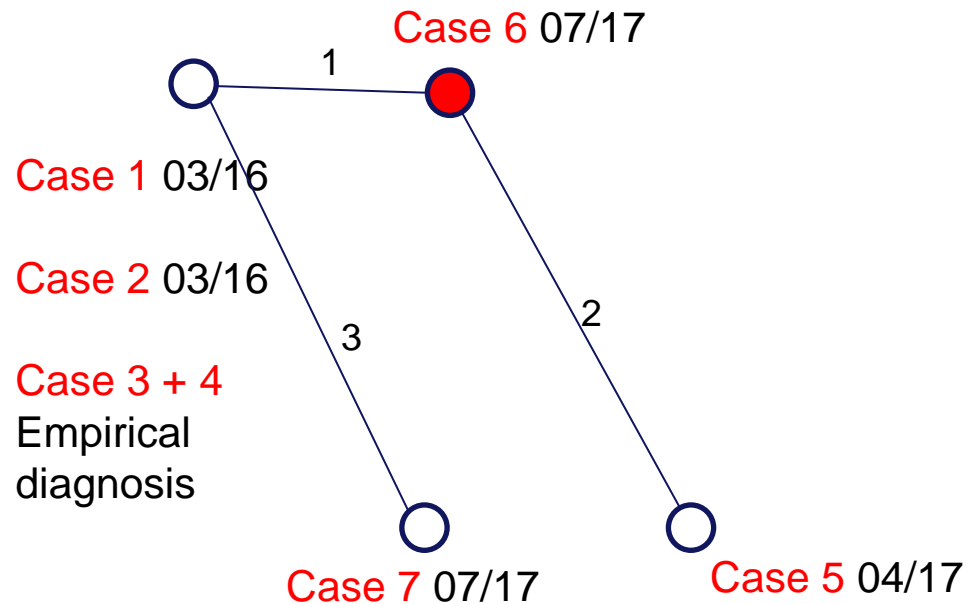
Cluster 1: GM MDR (AA726-2_B1006)



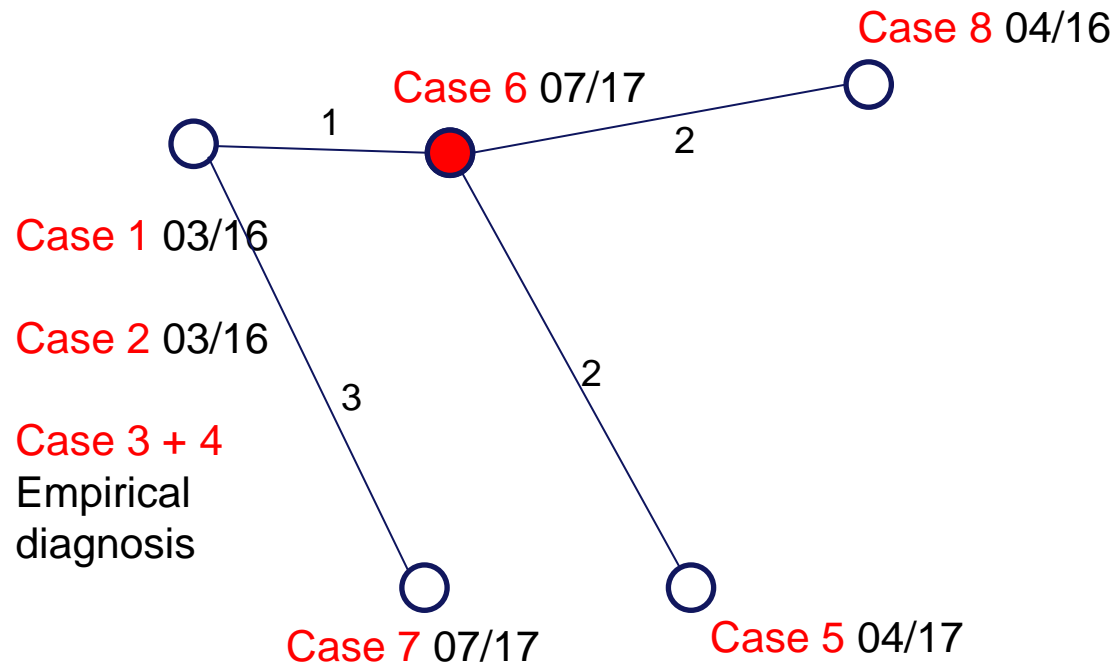
Cluster 1: GM MDR (AA726-2_B1006)



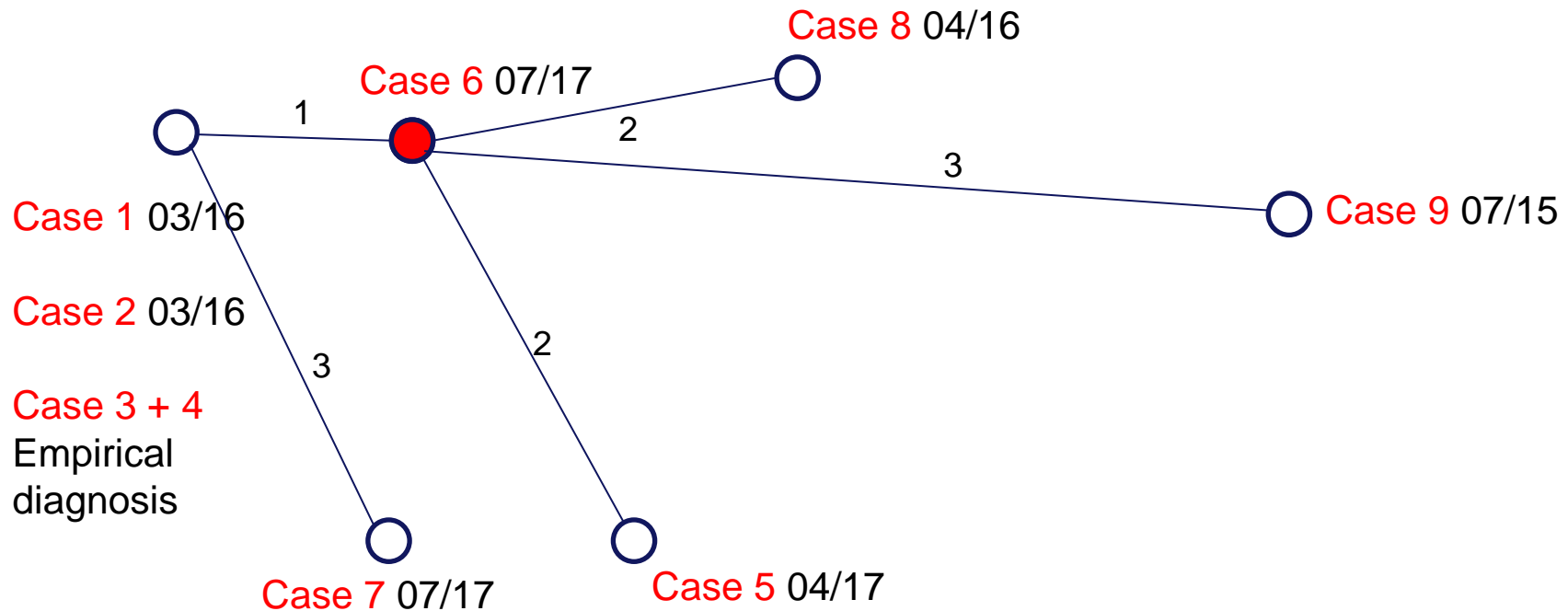
Cluster 1: GM MDR (AA726-2_B1006)



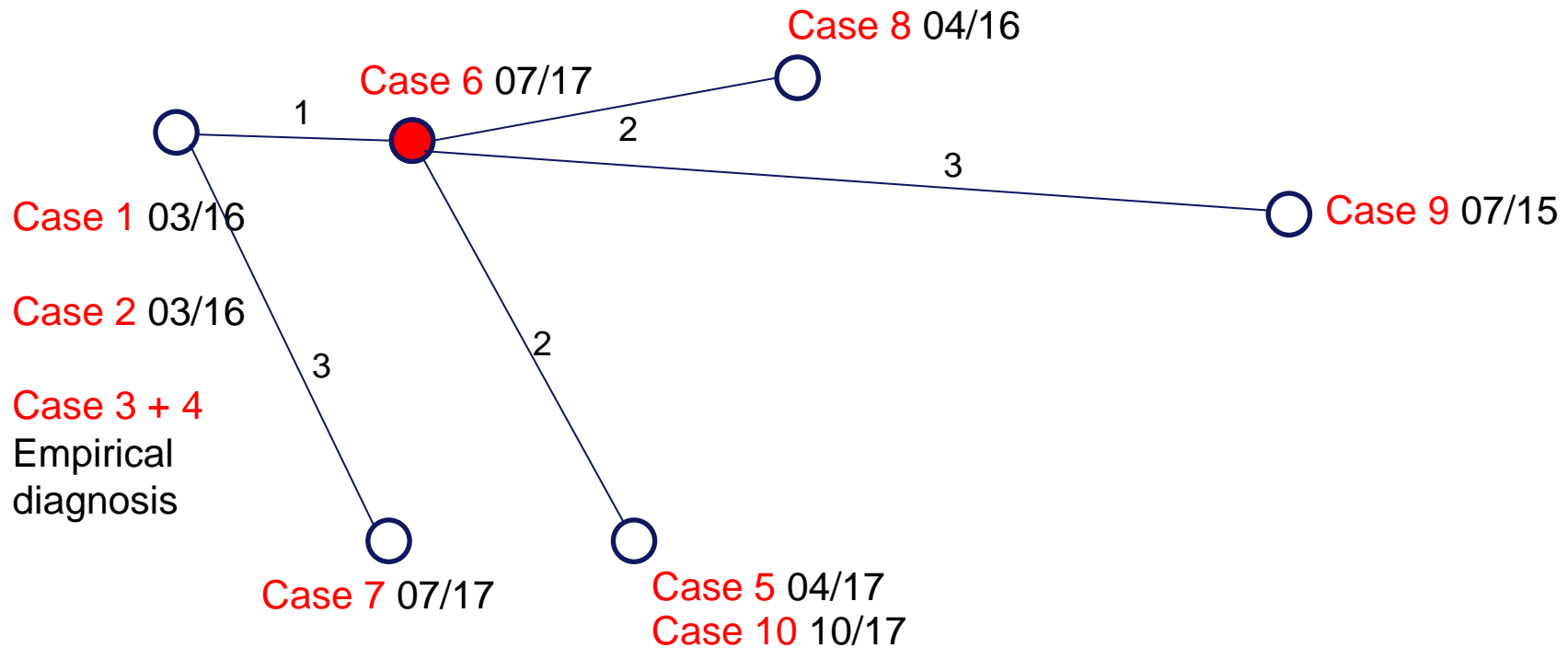
Cluster 1: GM MDR (AA726-2_B1006)



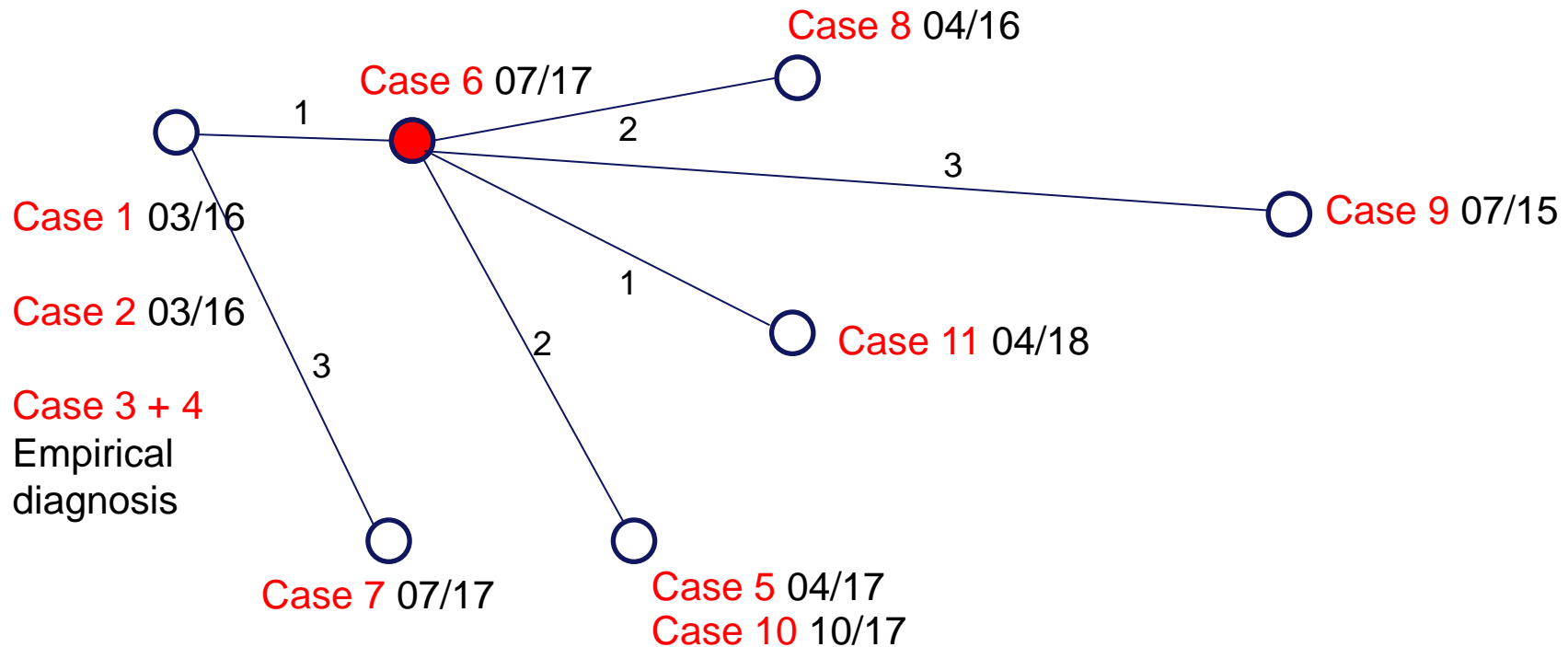
Cluster 1: GM MDR (AA726-2_B1006)



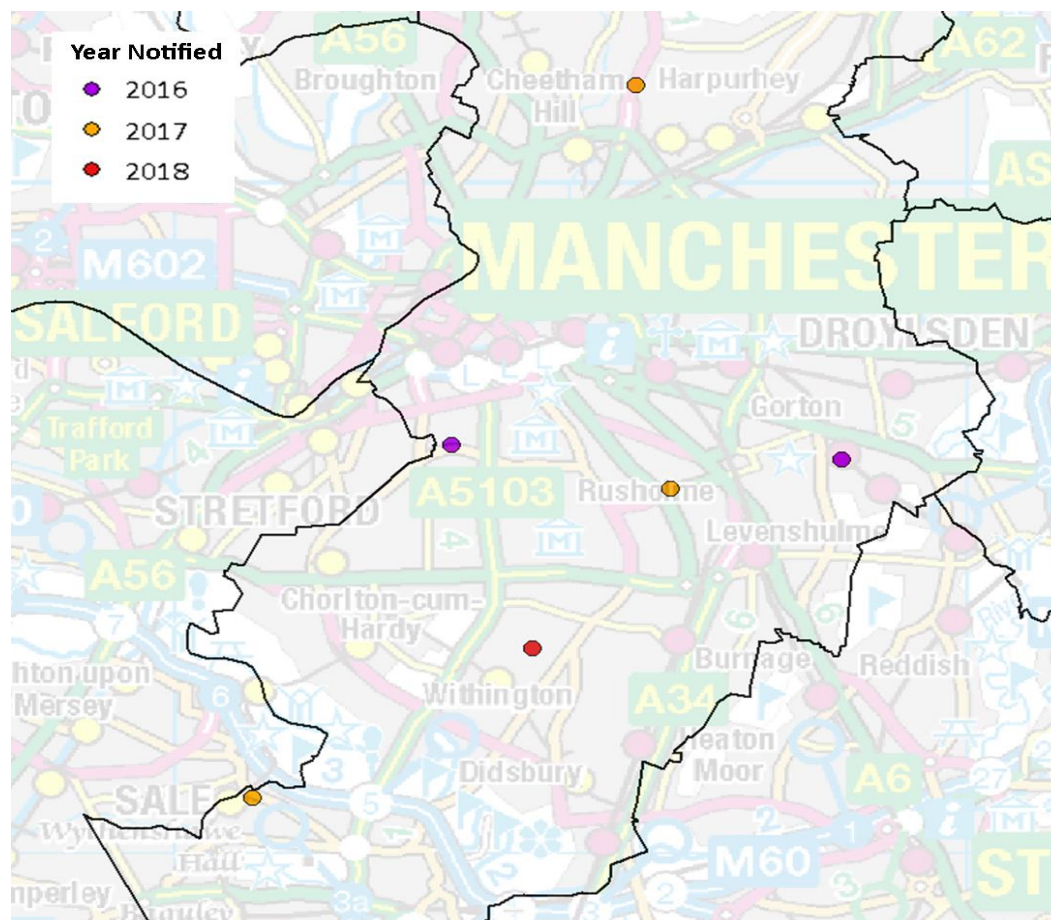
Cluster 1: GM MDR (AA726-2_B1006)



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Cluster 2: Manchester Uni (AC372-2)

- 2 cases of INH resistant TB at Uni in 1st years
- Request for WGS (London labs) – 1 SNP apart
- Index was smear positive pulmonary TB, symptomatic for 4 months before diagnosis
 - Household 3/3 screened positive, started on LTBI treatment
- Second case – pleural TB
 - Household – no evidence of transmission
- Cluster questionnaires/initial discussion with cases (both out of area)
 - Shared halls of residence campus (but not same building)
 - No other epi links
 - Did not know each other

Cluster 2: Manchester Uni (AC372-2)

- Screening for index:
 - **Round 1: Close social circle** 4/6 diagnosed LTBI (66%)
 - **Round 2: extended social circle** 24 identified, 19 screened and 7 diagnosed with LTBI (37%)
 - **Round 2: Tutor group (students and tutors)** 63 identified, 41 screened, 1 positive (2%)
- Risk assessment after round 2:
 - Limited transmission at uni course – no need for further screening
 - Social circle highest risk of transmission
 - No other named individuals
 - A number of friends self-presenting
 - Likely transmission to someone who the case doesn't know, only occasionally shares dining hall

Cluster 2: Manchester Uni (AC372-2)

- Enhanced questionnaire completed with each of the extended social contacts
 - Halls of residence clear potential next screening round
 - Limited other useful information – lots of bars/clubs

	Identified	Screened	Positive	Negative	Attack rate in those screened	Total rooms
Green Court (halls of index case)	8	8	6	2	75%	119
Little Court	4	4	2	2	50%	146
Tree Court	3	3	1	2	33%	316
Tower	1	1	0	1	0%	396
Oak House (various)	7	6	1	5	17%	
Unknown	5	2	1	1	50%	
Totals	28	24	11	13	46%	

- Agreed to screen Green Court and Little Court as share dining hall (case 2 also confirmed that does attend there occasionally)

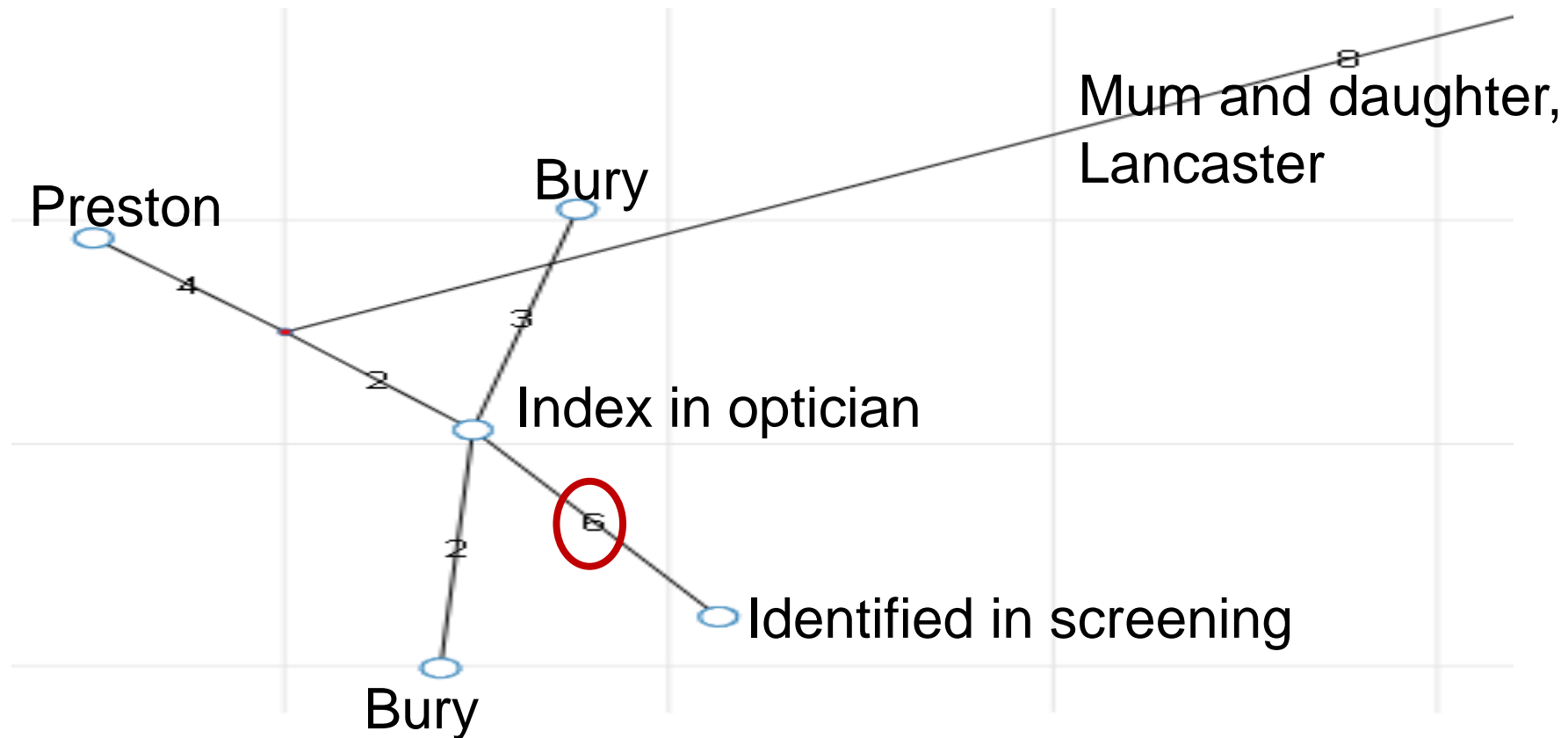
Cluster 2: Manchester Uni (AC372-2)

- Screening ongoing in halls, but no evidence of transmission
- Case 3 notified in May 2018
 - Not identified on screening lists for index
 - 1 SNP from index, 0 SNPs from case 2
 - Out of area case
 - Questionnaire did not reveal any links to uni courses, halls or social settings named in previous questionnaires

Cluster 2: Manchester Uni (AC372-2)

- Exhausted screening options for this situation
- WGS supported need for further screening, and increased levels of suspicion
- However, likely that we will see further cases linked to this cluster

Cluster 3: Bolton optician (AB869-4 E1394)



Lessons learnt

WGS is helpful to identify TB clusters and suggest or exclude transmission between cases

However, challenging some of our understanding of TB transmission

- socially and epidemiologically disparate cases linked on WGS
- Epi linked cases a larger number of SNPs apart than would expect

Need to continue to review this and consider how this will change practice in future

Looking to collate learning from around England

Many thanks

WGS cluster investigation is only possible through collaboration between staff working in TB surveillance and microbiology at national and subnational levels in PHE, to whom we extend our thanks. We also gratefully acknowledge all those who contribute information on TB cases in England, including physicians, nurses, microbiologists, scientists and administrative staff

Thanks to all those involved in investigating and managing these clusters

NW task group - Grainne Nixon, Alison Waldrum, Andy Burkitt, Diane Fiefield, Evdokia Dardamissis, Katherine Platt, Grahame Moore, Stefanie Davies, Mark McGivern, Dan Todkill, Paul Cleary