

OUT-TB Web

Ontario Universal Typing of Tuberculosis: Surveillance and Communication System

Dr. Frances Jamieson, Ontario Public Health Laboratories
November 30th, 2009

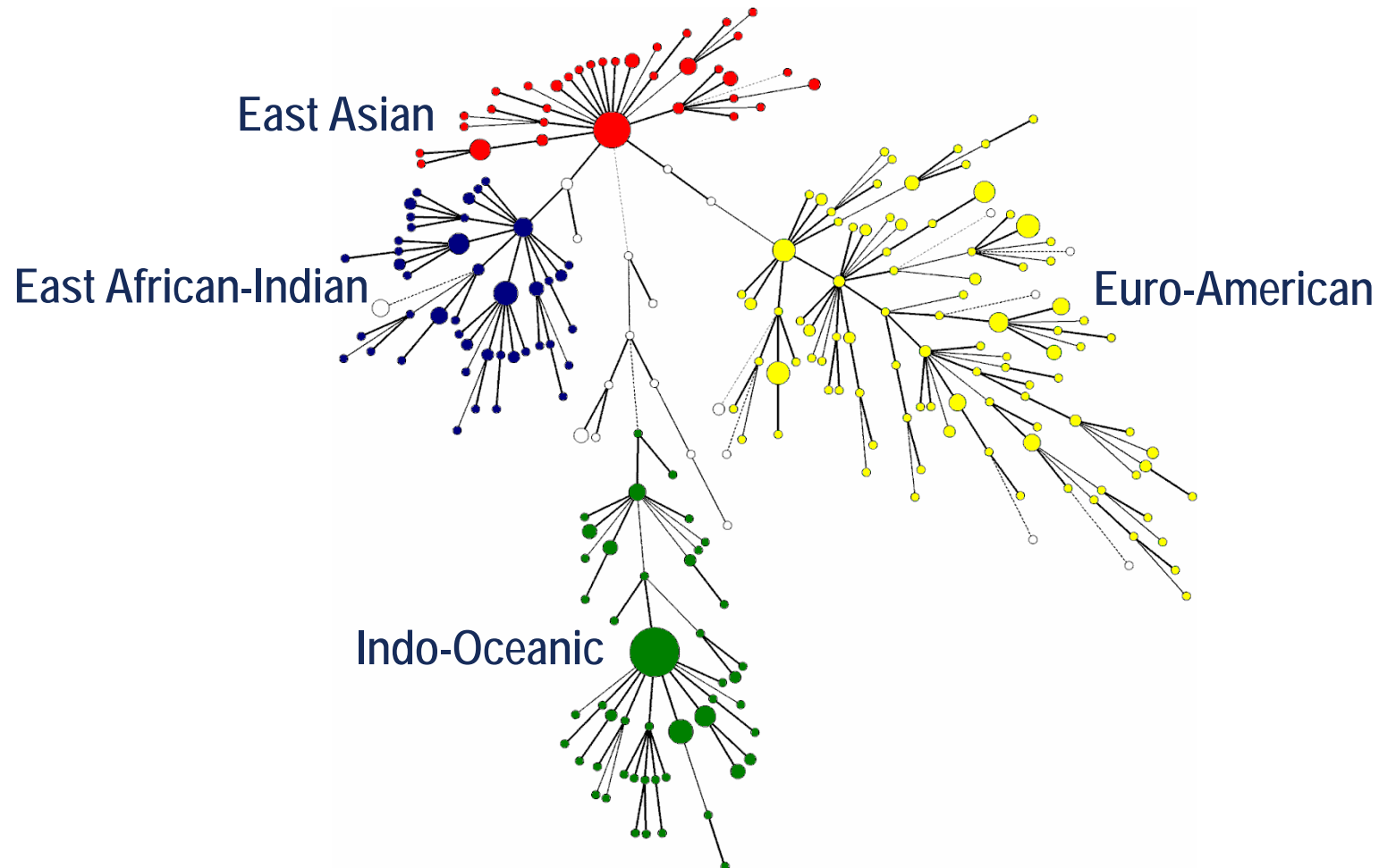
Tuberculosis : A Global Problem



WHO Estimates (2007 data):

- 9.2 million New Infections
- 1.8 million Deaths

Tuberculosis : A Provincial Problem



A small primer on TB genotyping...

Genotyping of *Mycobacterium tuberculosis*

All methods target unstable genomic features !

- Targets vary in number and/or position
- Changes occur within a short time span (e.g. a few generations/transmission events)

Restriction Fragment Length Polymorphism (RFLP)

- Monitor changes in the number and position of IS6110 transposon elements

Mycobacterial Intersperse Repetitive Unit - Variable Number of Tandem Repeat (MIRU-VNTR) Genotyping

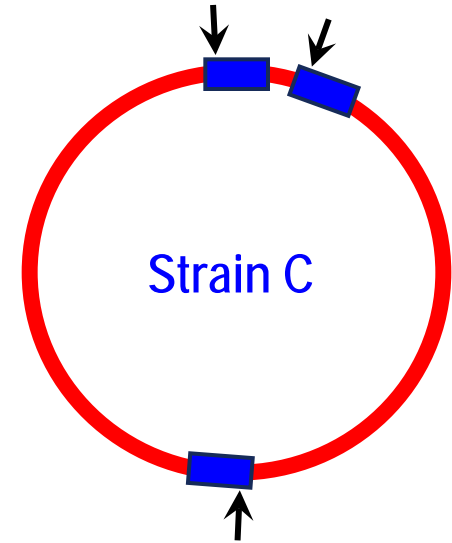
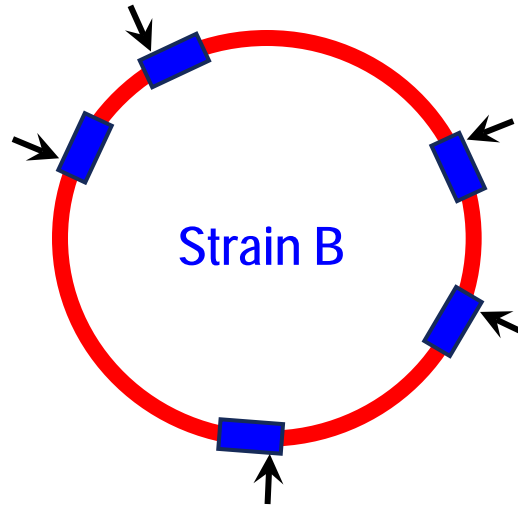
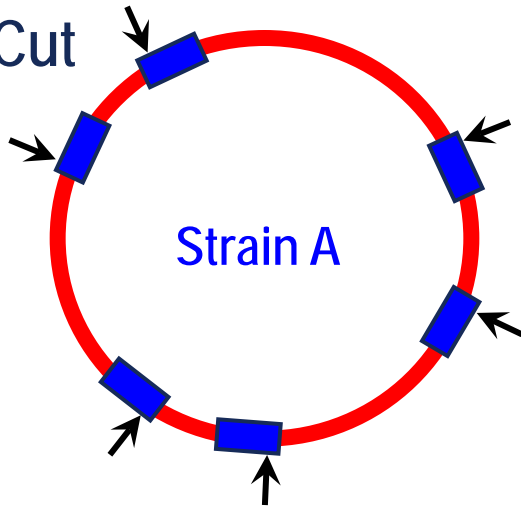
- Monitor changes in the number of repeat units found at specific genomic sites
- Resolution depends on the number of sites used (24 > 15 > 12)

Spacer Oligonucleotide Genotyping (Spoligotyping)

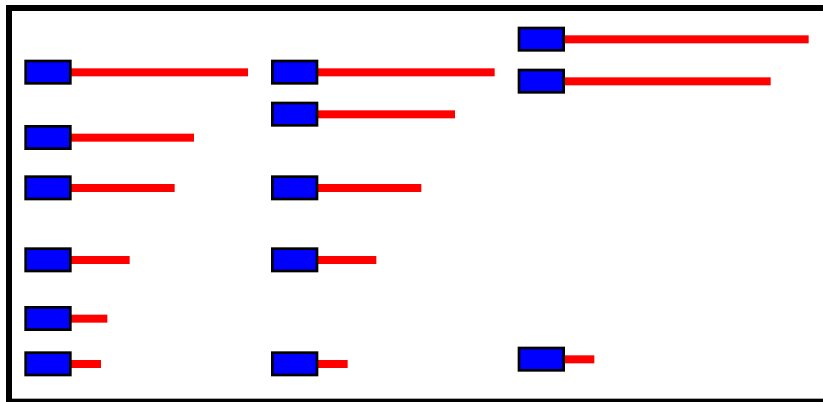
- Monitor changes in the presence/absence of 43 'spacers'
- All located at single conserved genomic site

RFLP

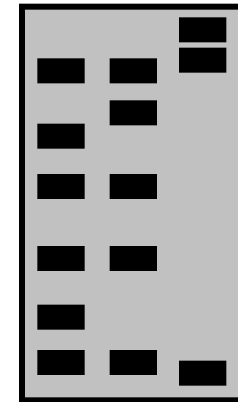
1. Cut



2. Separate by Size

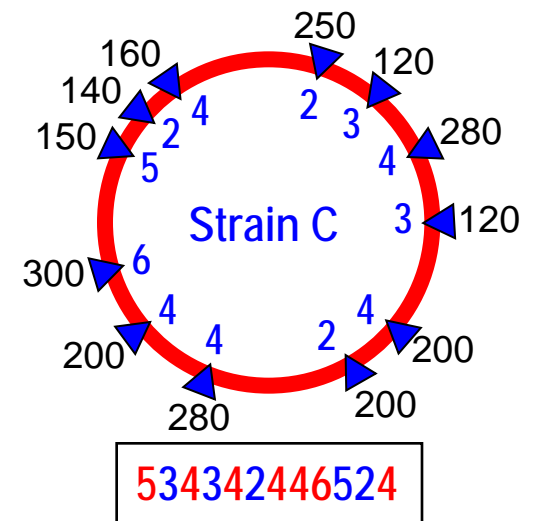
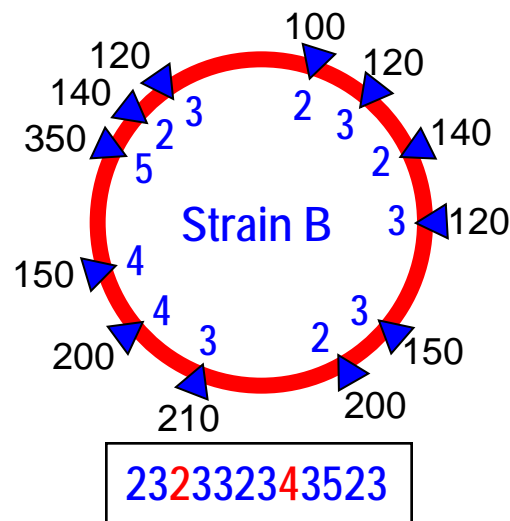
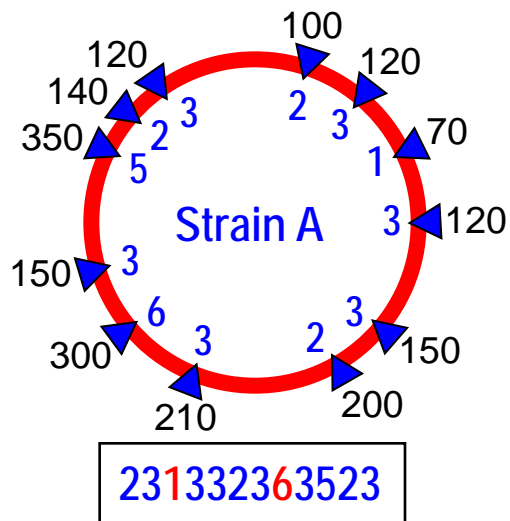


3. Probe



MIRU-VNTR Genotyping

1. Amplify repeat regions at 12, 15 or 24 MIRU-VNTR sites



2. Measure Size of Each Amplified Region

3. Calculate Number of Repeats at Each MIRU-VNTR Site

4. Generate 12, 15 or 24 Digit Code

OUT-TB Web:

Mission:

“Create a better system and process for the surveillance & monitoring of positive Tuberculosis cases. Provides the ability to communicate appropriate information to the right people, in the right place, at the right time.”

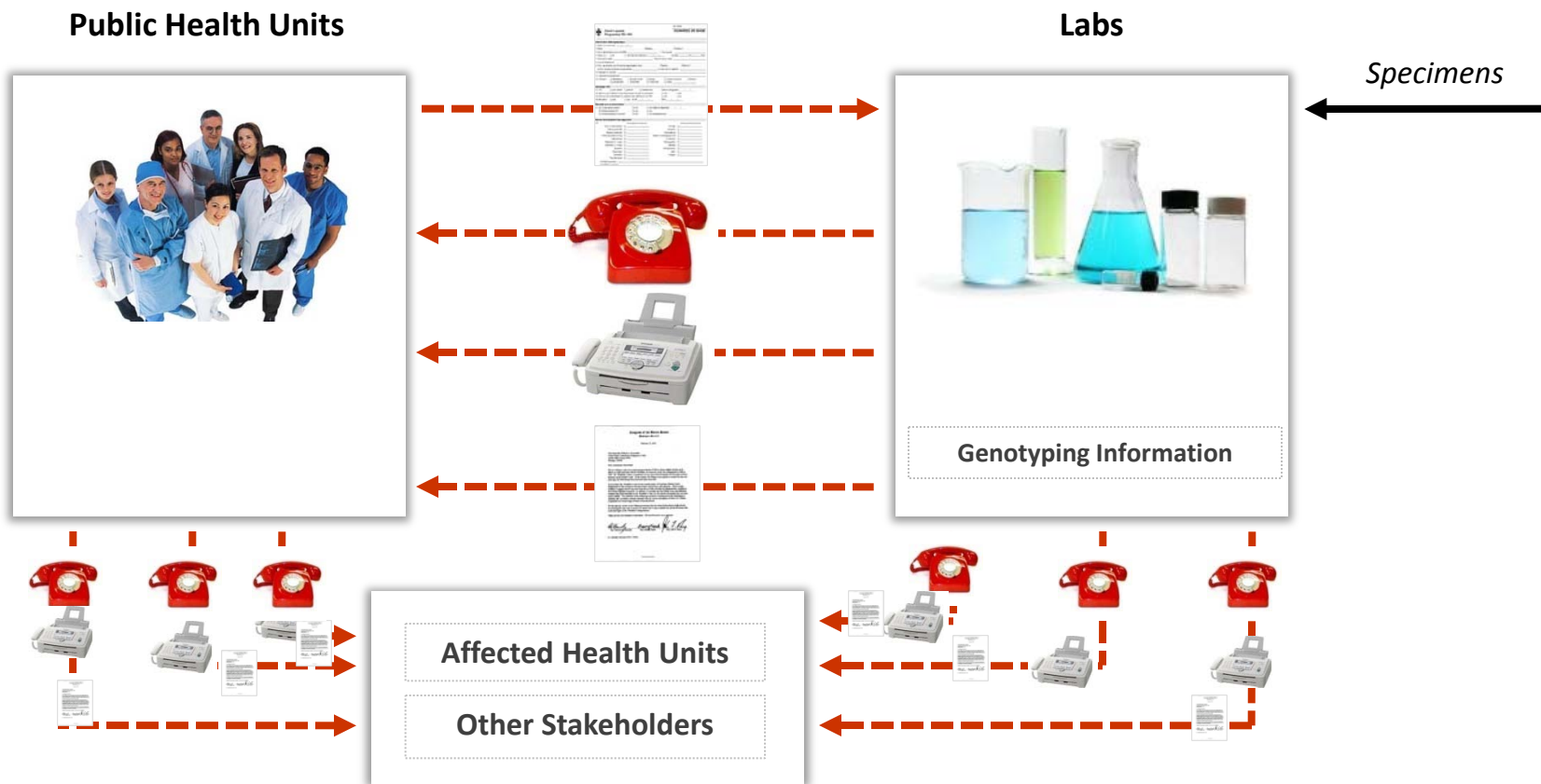
Goals:

- Enhanced TB Surveillance in Ontario:
- Make comprehensive genotype identification data actionable, in a usable & user friendly format
- Extend end-user/stakeholder’s proactive epidemiological capabilities

Increase Efficiency & Effectiveness:

- Improve information flow for reporting of TB genotyping information between Labs & Health Units
- Increase the Lab's ability to investigate & extend internal epidemiological capabilities
- Support control of TB by monitoring trends, supporting communication & outbreak investigation
- Provide additional information for planning & program evaluation
- Pilot successful local program to demonstrate success for a wider stakeholder group & across other disease types

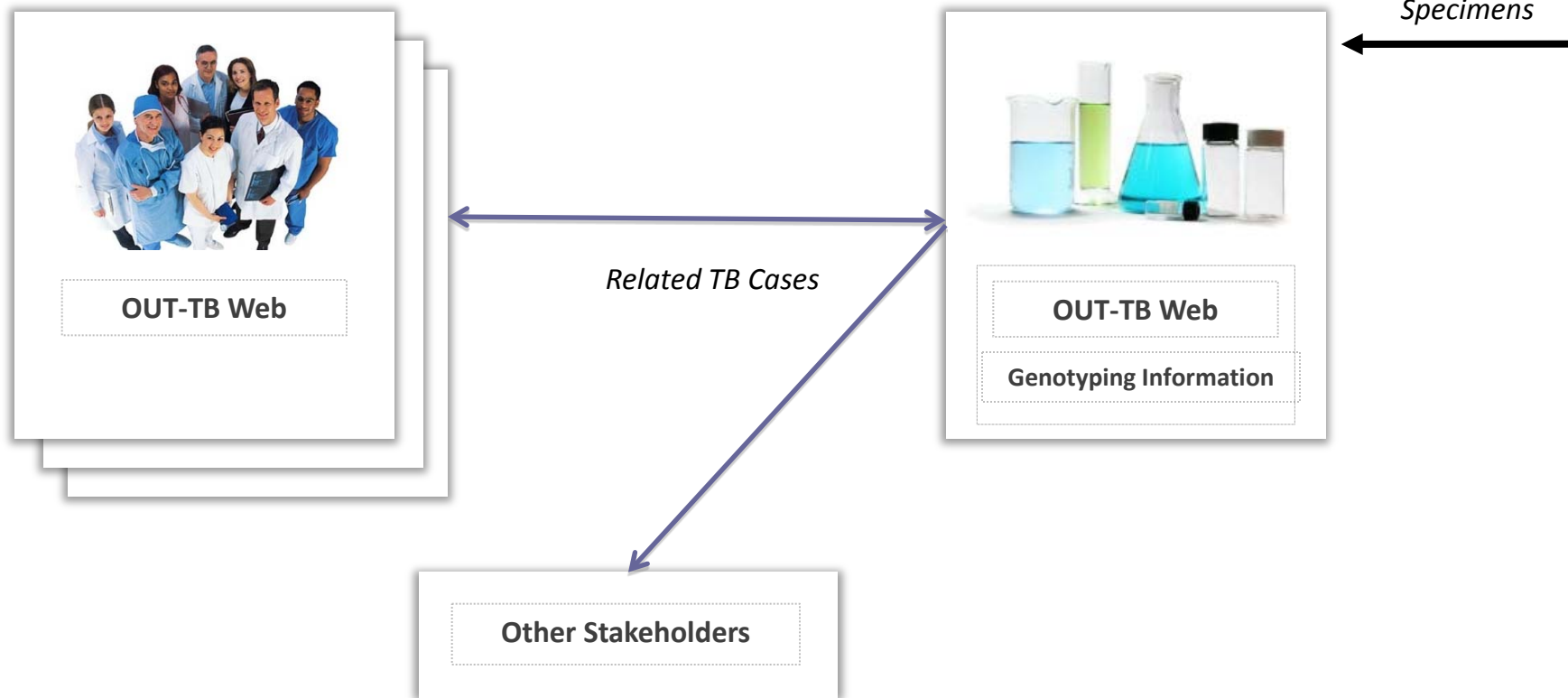
Current Process:



Future State:

Public Health Units

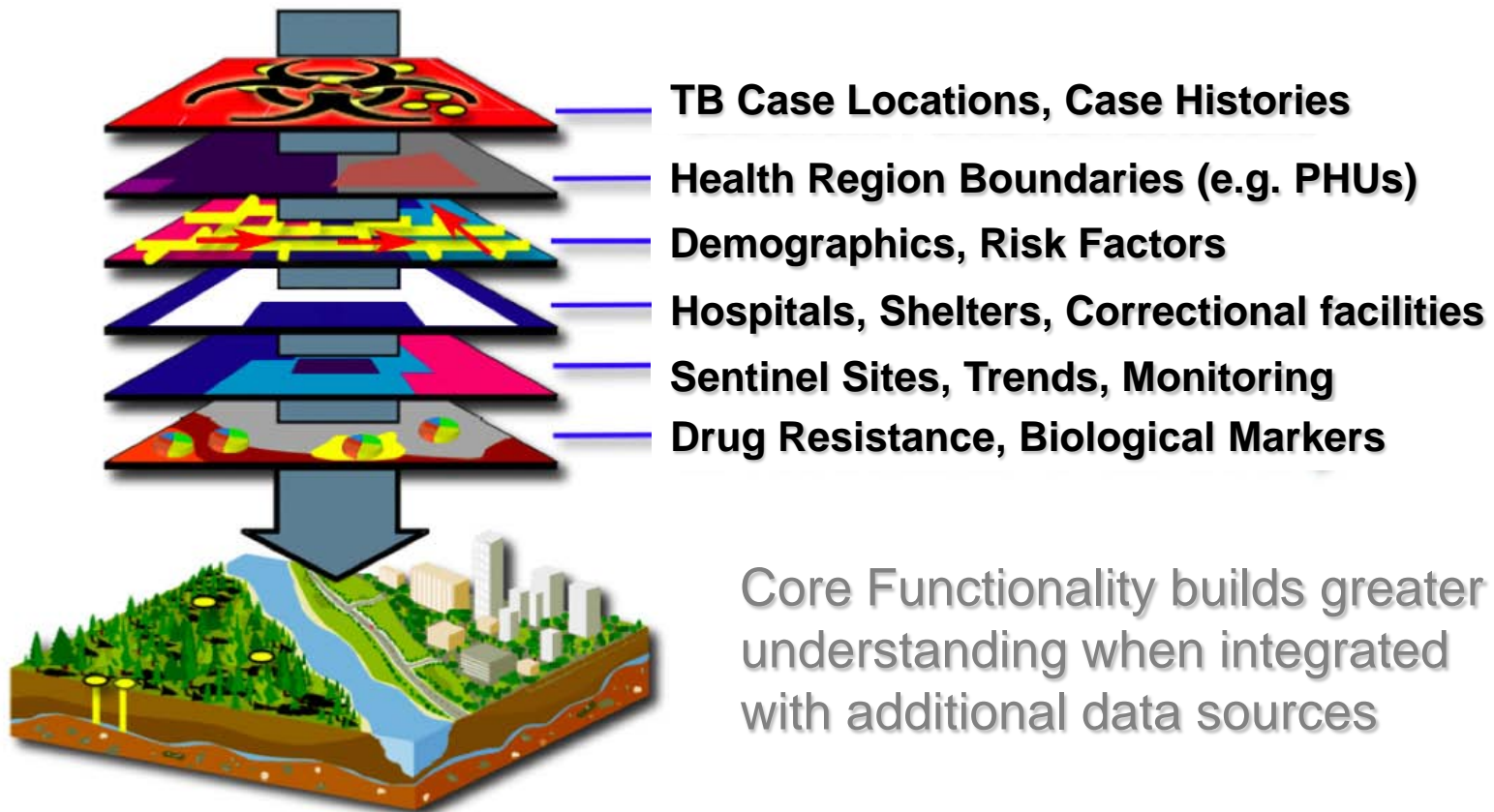
Labs



Vision for Improved System

- Expandable TB surveillance & communication system
- Improve genotyping, demographic, clinical & micro-biological information linkages on TB cases, e.g. drug resistance
- Monitor trends; support outbreak investigation, planning, implementation & evaluation of services
- Standardized minimum data set, typing & epidemiological results
- Rapid comparison of related cases & possible outbreaks at a local, health unit & Provincial level
- "Real time" ID of positive cases & strains– across multiple stakeholders

GIS & Disease Surveillance



Source: ESRI Canada

Advantages to GIS-based Approach

- Visualize affected areas, affected populations & historical location-based data for analysis
- Data & Alert Standards (CGDI + CAP COM)
- Extensible:
 - Spatial analysis (e.g. overlay population demographics, spatial statistics, cluster analysis)
 - Improved understanding of data and situational awareness
 - ‘Real-Time’ data capture from variety of data sources
 - Additional pathogen types

Core Functionality / Usage Scenarios

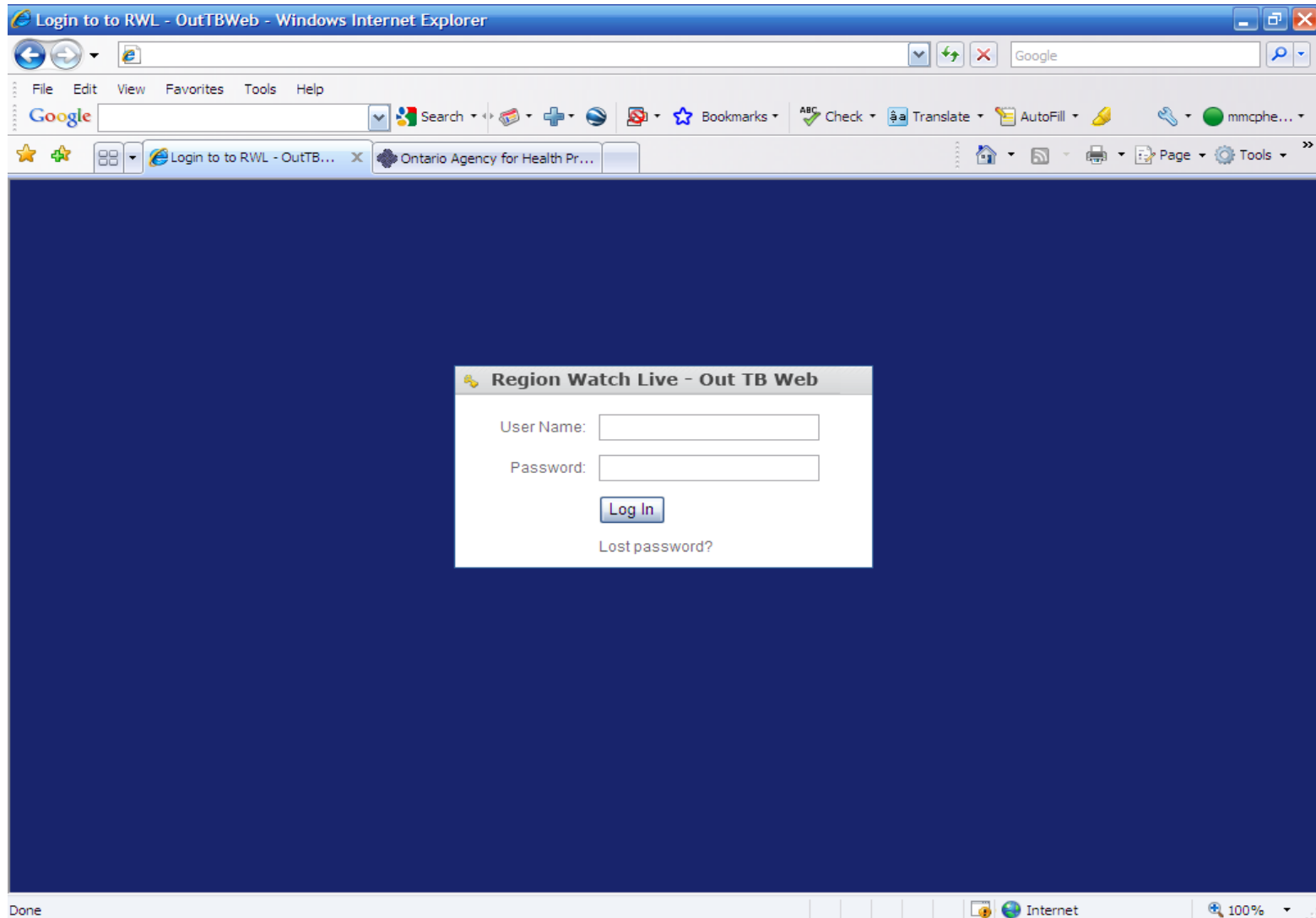
Scenario 1: Identify Genotypic Matches for a given case.

Scenario 2: Compare Two or More Cases

Scenario 3: Knowledge Discovery, Pattern Recognition & Analytics

Key considerations:

- TB surveillance is knowledge-intensive
- Logic required to identify related genotypic matches
- Risk factor integration is an important data element



OUTTBWEB - Windows Internet Explorer

Google

File Edit View Favorites Tools Help

Google Search

OUTTBWEB

Ontario Agency for Health Pr...

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Ontario OUT-TB Web

Agency for Health Protection and Promotion

New Cases in Past 30 Days

Show cases with matches only


IPHISnum	Matches	RecDate
1326903	1	10/29/2009 10:2

Match Finder

Layers

Display Options

Map Reports Administration Help News Feeds



ESRI

Internet 100%

OUTTBWEB - Windows Internet Explorer

Google

File Edit View Favorites Tools Help

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Map Reports Administration Help News Feeds

Ontario
Agency for Health Protection and Promotion

OUT-TB Web

New Cases in Past 30 Days

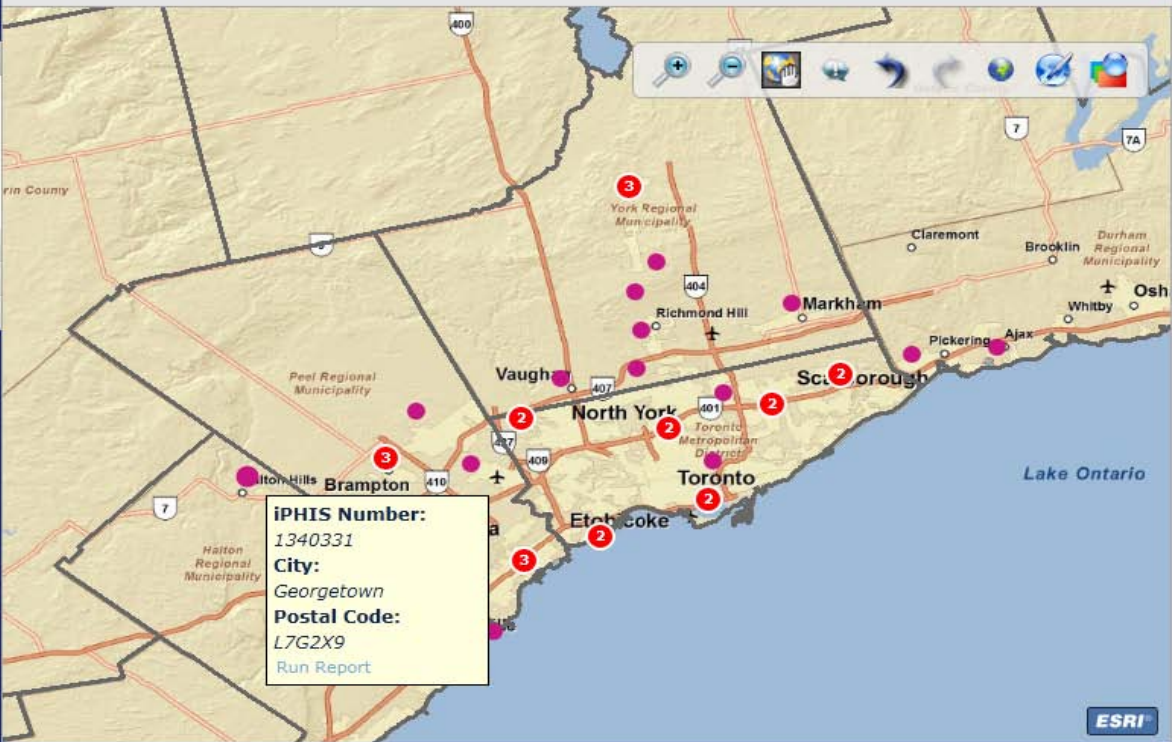
Show cases with matches only

IPHISnum	Matches	RecDate
1326903	1	10/29/2009 10:2

Match Finder

Layers

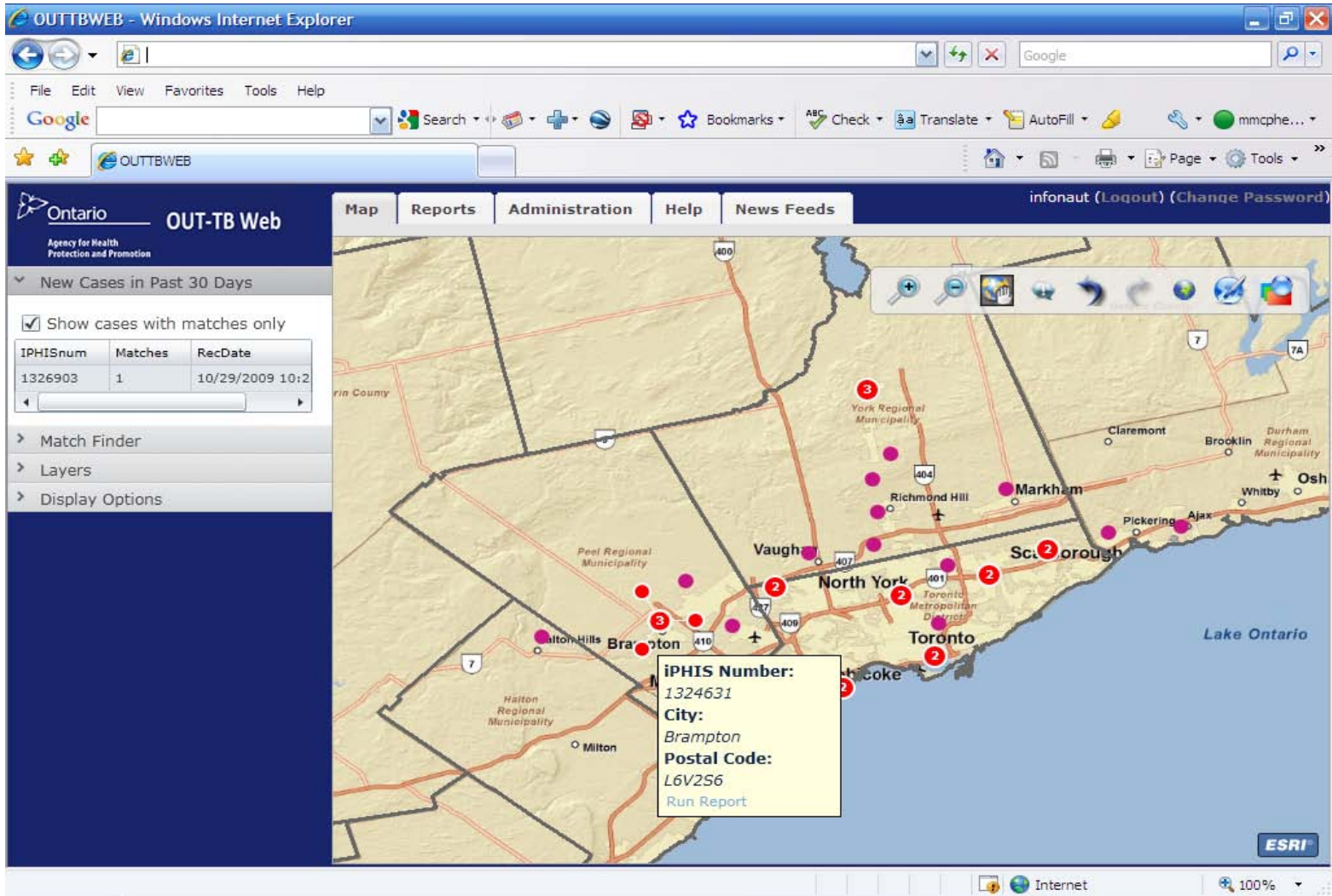
Display Options



Map

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OUTTBWEB - Windows Internet Explorer

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OUTTBWEB

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Agency for Health Protection and Promotion

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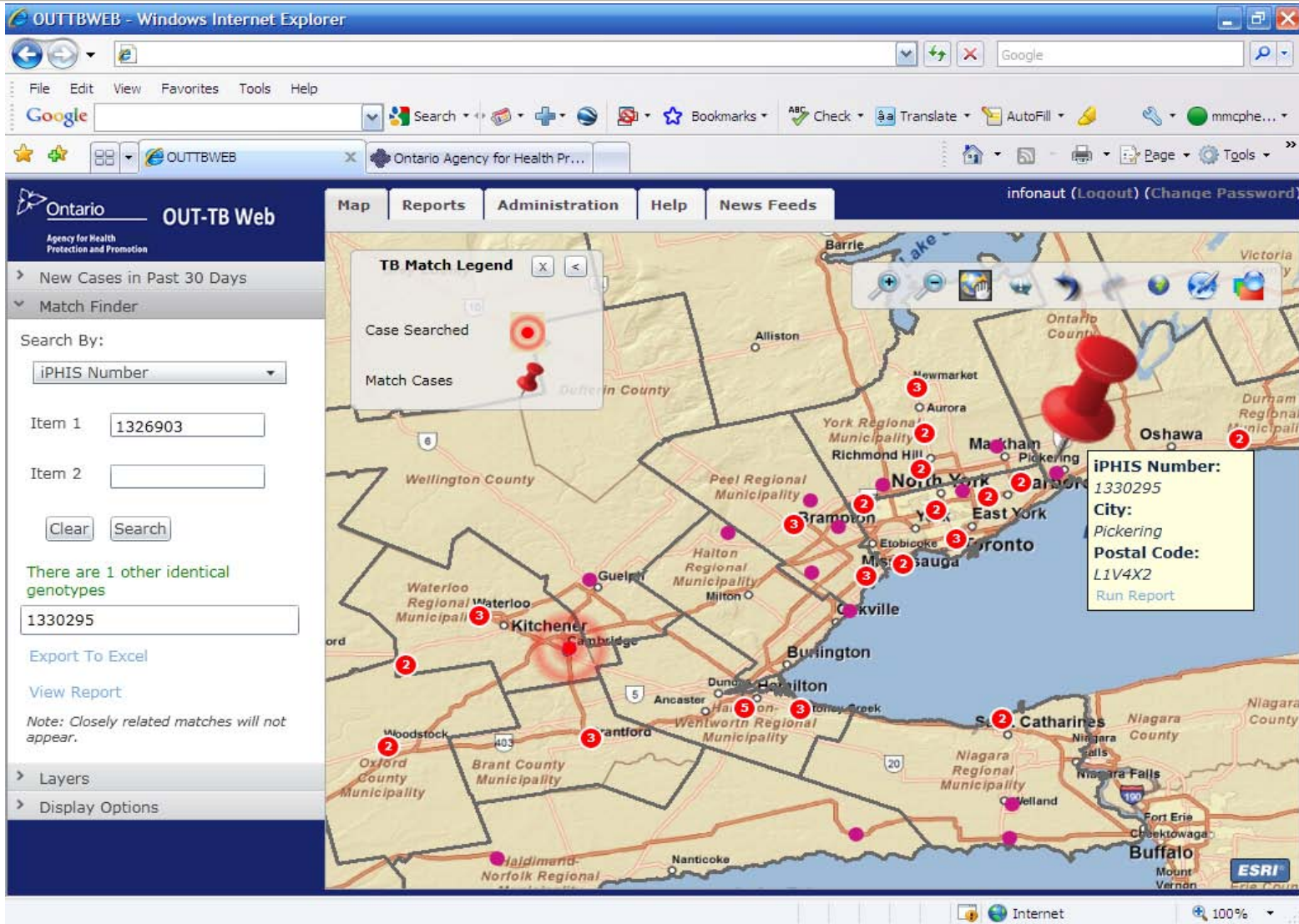
iPHISnum	Matches	RecDate
1326903	1	10/29/2009 10:2

Match Finder
Layers
Display Options

iPHIS Number:
1324631
City:
Brampton
Postal Code:
L6V2S6
[Run Report](#)

ESRI

Internet 100%



The screenshot displays the 'OUT-TB Web' application interface within a Windows Internet Explorer browser. The browser's address bar shows the URL 'http://www.ontario.ca/outtbweb/'. The application header includes the Ontario logo and navigation tabs for 'Map', 'Reports', 'Administration', 'Help', and 'News Feeds'. A user profile 'infonaut (Logout) (Change Password)' is visible in the top right.

The main content area features a map of Ontario with various municipalities labeled. A 'TB Match Legend' window is open, showing a red circle for 'Case Searched' and a red pushpin for 'Match Cases'. A large red pushpin is placed on the map over Pickering, Ontario. A tooltip for this location displays the following information:

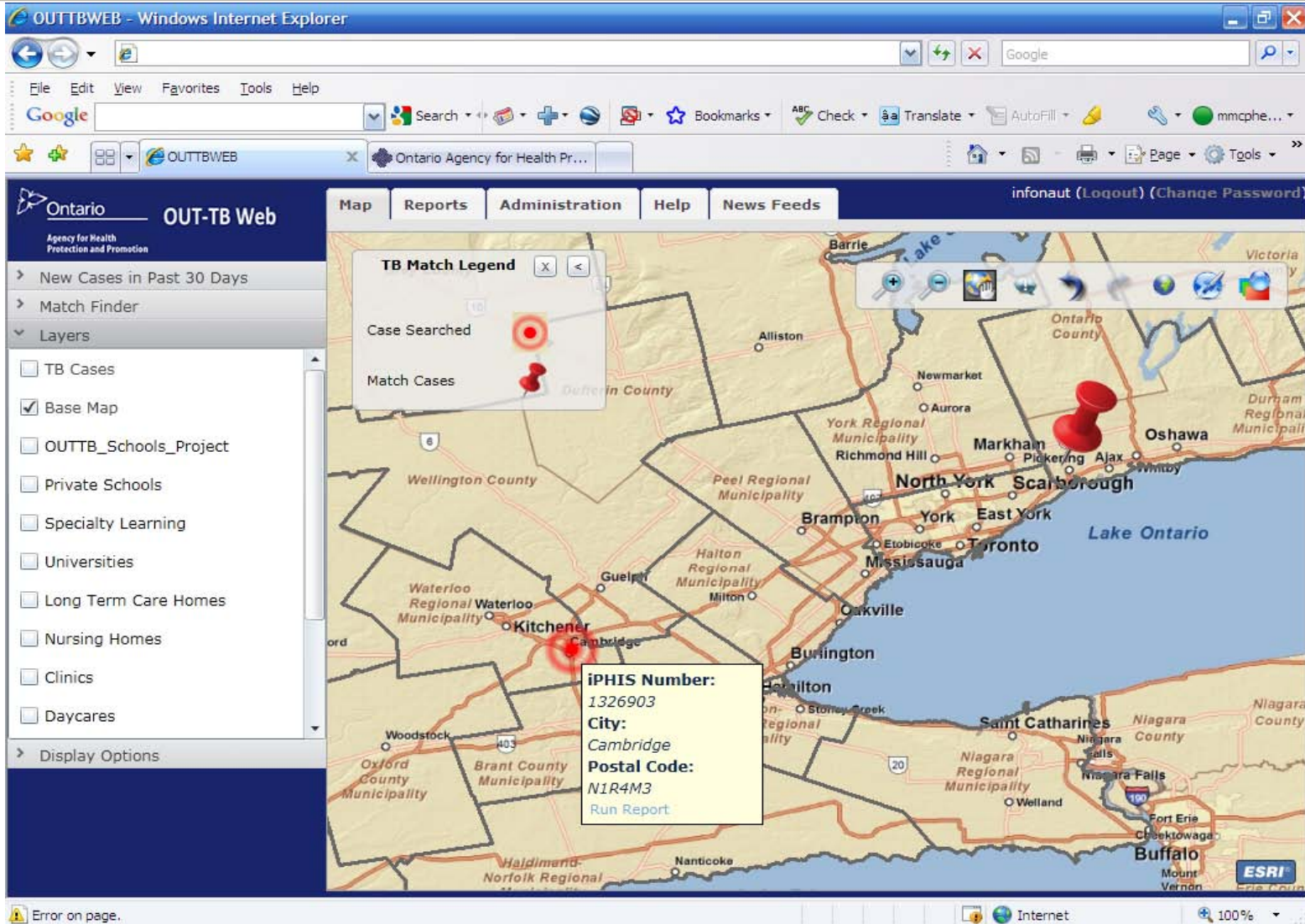
- iPHIS Number: 1330295
- City: Pickering
- Postal Code: L1V4X2
- Run Report

On the left side, the 'Match Finder' section allows searching by 'iPHIS Number'. The search criteria are:

- Item 1: 1326903
- Item 2: (empty)

The search results show 'There are 1 other identical genotypes' with the iPHIS number 1330295. Below the search results are links for 'Export To Excel' and 'View Report'. A note states: 'Note: Closely related matches will not appear.'

At the bottom of the browser window, the status bar shows 'Internet' and a zoom level of '100%'.



OUT-TB Web

Map Reports Administration Help News Feeds

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Case Searched

Match Cases

iPHIS Number:
1326903
City:
Cambridge
Postal Code:
N1R4M3
[Run Report](#)

Error on page.

OUTTBWEB - Windows Internet Explorer

OUT-TB Web Mapping - Windows Internet Explorer

Report Date: Sep. 15, 2009 6:46:52AM

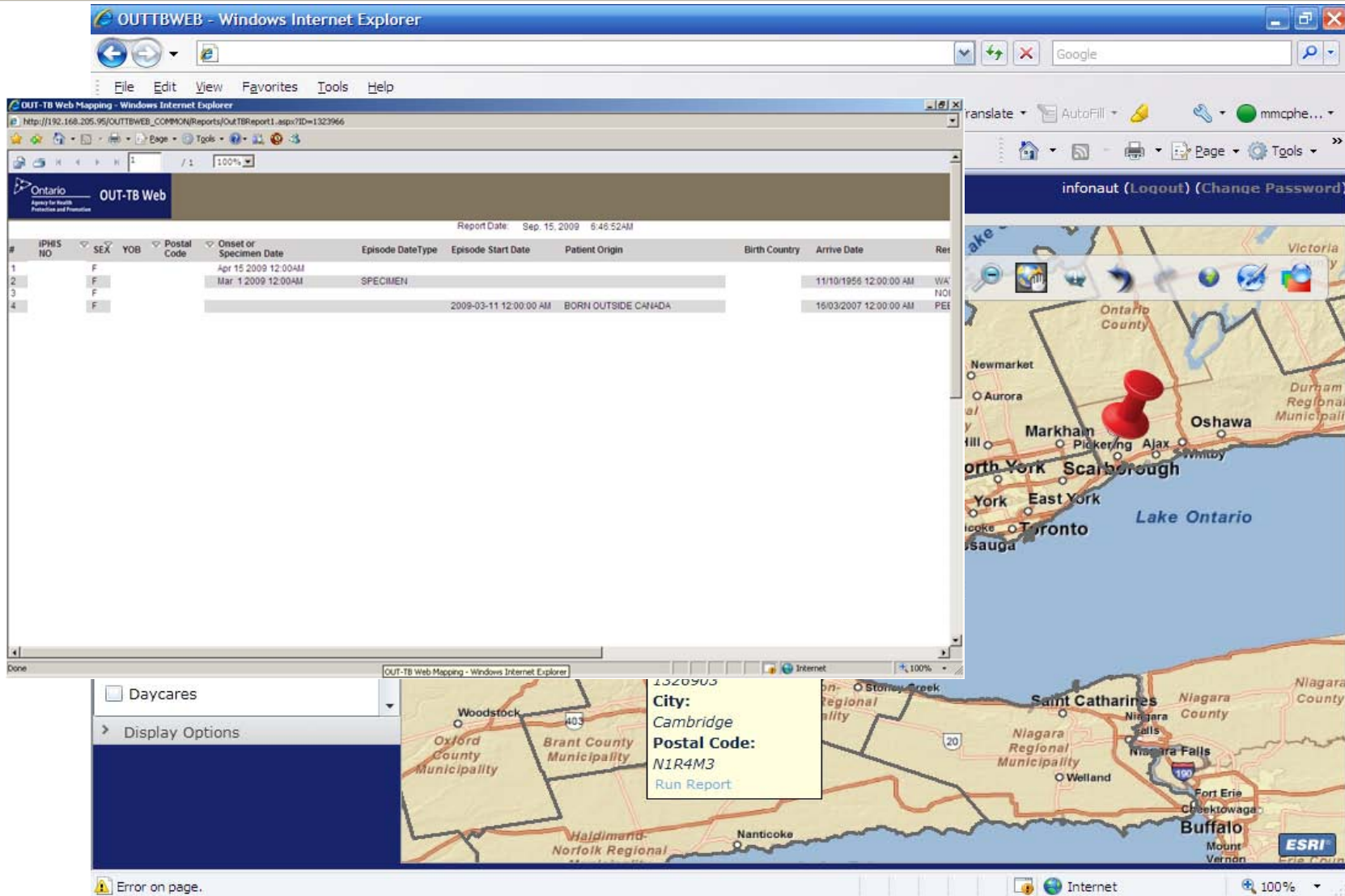
#	IPHS NO	SEX	YOB	Postal Code	Onset or Specimen Date	Episode Date/Type	Episode Start Date	Patient Origin	Birth Country	Arrive Date	Ret
1		F			Apr 15 2009 12:00AM						
2		F			Mar 1 2009 12:00AM	SPECIMEN				11/10/1956 12:00:00 AM	WA NOI
3		F									
4		F					2009-03-11 12:00:00 AM	BORN OUTSIDE CANADA		16/03/2007 12:00:00 AM	PEI

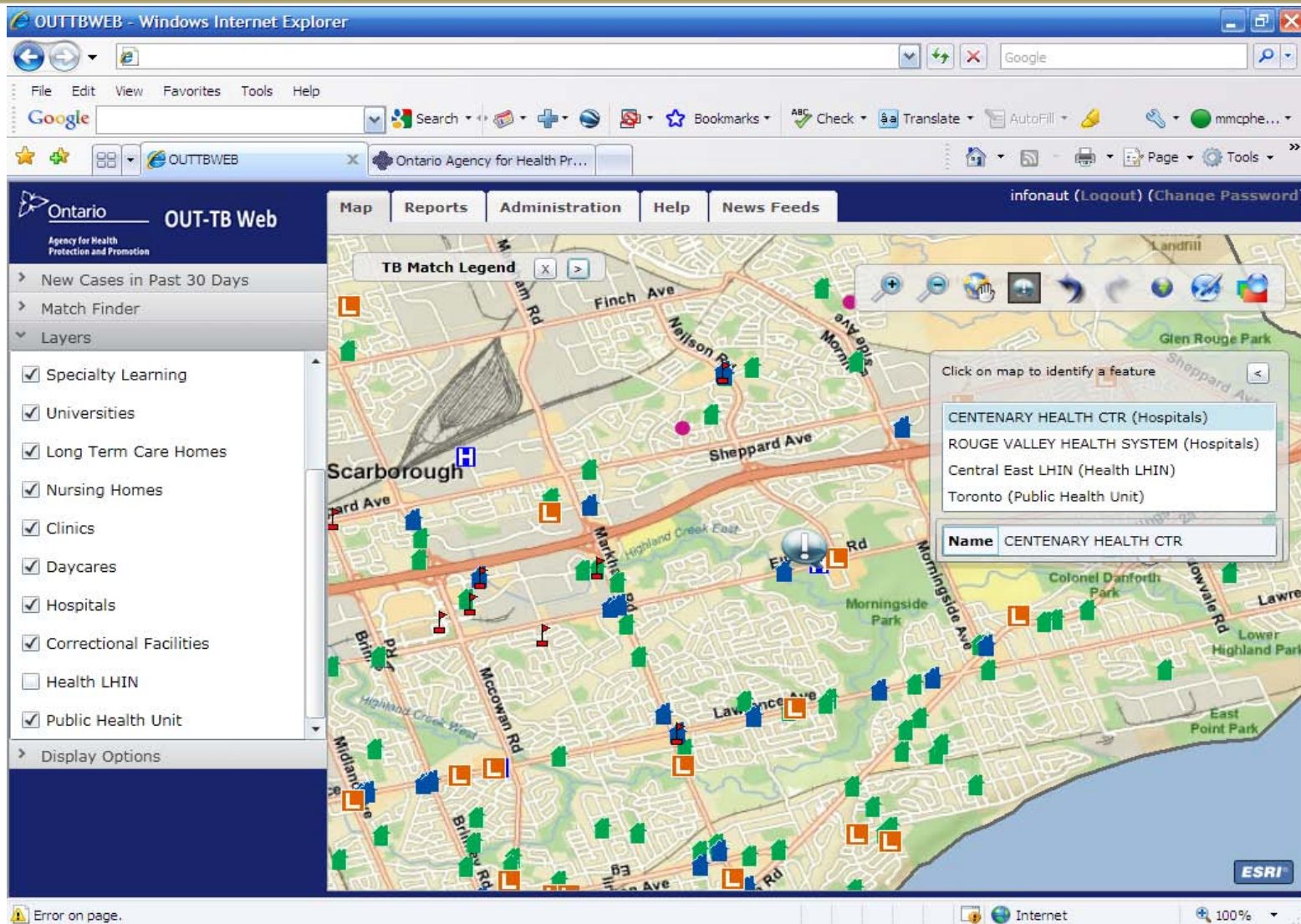
Daycares

Display Options

City: Cambridge
Postal Code: N1R4M3
Run Report

Error on page.





The screenshot shows the OUTTBWEB application running in a Windows Internet Explorer browser. The browser's address bar shows the URL "OUTTBWEB" and the page title is "Ontario Agency for Health Pr...". The application interface includes a navigation menu with "Map", "Reports", "Administration", "Help", and "News Feeds". A sidebar on the left lists various layers for the map, including "Specialty Learning", "Universities", "Long Term Care Homes", "Nursing Homes", "Clinics", "Daycares", "Hospitals", "Correctional Facilities", "Health LHIN", and "Public Health Unit". The main map area displays a street map of Scarborough, Ontario, with various colored markers (green, blue, orange) indicating TB Match locations. A "TB Match Legend" window is open, and a pop-up window identifies a feature as "CENTENARY HEALTH CTR (Hospitals)".

Map Reports Administration Help News Feeds infonaut (Logout) (Change Password)

Ontario OUT-TB Web
Agency for Health Protection and Promotion

- New Cases in Past 30 Days
- Match Finder
- Layers
 - Specialty Learning
 - Universities
 - Long Term Care Homes
 - Nursing Homes
 - Clinics
 - Daycares
 - Hospitals
 - Correctional Facilities
 - Health LHIN
 - Public Health Unit
- Display Options

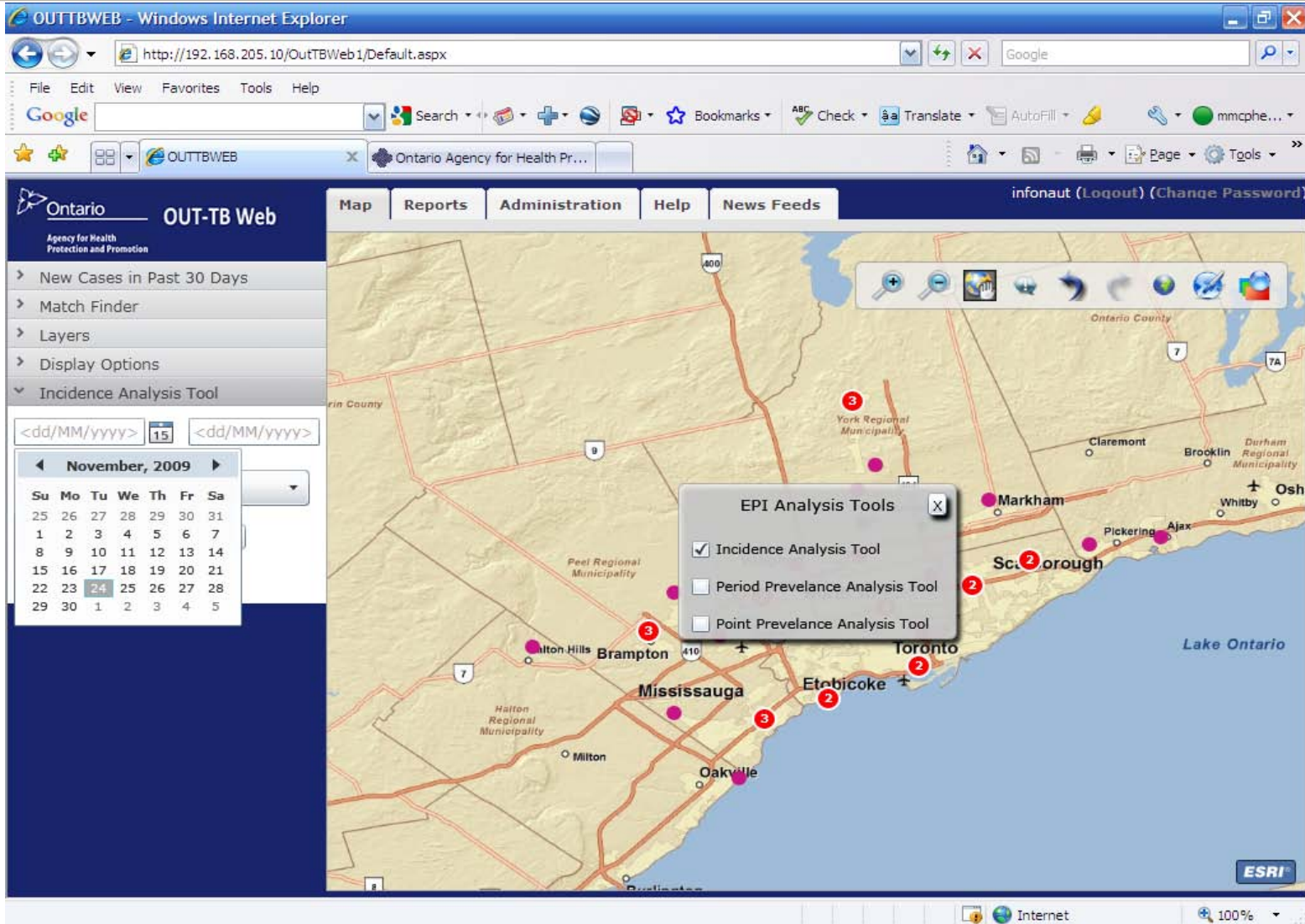
Click on map to identify a feature

- CENTENARY HEALTH CTR (Hospitals)
- ROUGE VALLEY HEALTH SYSTEM (Hospitals)
- Central East LHIN (Health LHIN)
- Toronto (Public Health Unit)

Name CENTENARY HEALTH CTR

ESRI

Error on page. Internet 100%



OUT-TB Web

Agency for Health Protection and Promotion

Map Reports Administration Help News Feeds

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> New Cases in Past 30 Days
> Match Finder
> Layers
> Display Options
v Incidence Analysis Tool

<dd/MM/yyyy> 15 <dd/MM/yyyy>

November, 2009

Su	Mo	Tu	We	Th	Fr	Sa
25	26	27	28	29	30	31
1	2	3	4	5	6	7
8	9	10	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28
29	30	1	2	3	4	5

EPI Analysis Tools

- Incidence Analysis Tool
- Period Prevalence Analysis Tool
- Point Prevalence Analysis Tool

ESRI

Region Watch Live - OUTTB-Web - Windows Internet Explorer

http://192.168.205.95/OUTTBWEB_COMMON/RSS.aspx

Region Watch Live - OUTTB-Web

Map Reports Administration Help News Feeds phuser (Logout) (Change Password)

Ontario OUT-TB Web
Agency for Health Protection and Promotion

TB Feeds

Google Maps >>

Documents

Title	Date	Description
CU study reveals germs lurking in US showerheads - Denver Post	Tue, 15 Sep 2009 07:02:36 GMT+00:00	<p>CU study reveals germs lurking in US showerheads Denver Post</p> <p>Symptoms of <i>M. avium</i> infection are similar to those of tuberculosis: a chronic shallow cough, fever, fatigue and weight loss. <i>M. avium</i> infections are on the ...</p> <p>and more »</p>
Tuberculosis spreads through coughing, sneezing - Henderson Gleaner	Mon, 14 Sep 2009 13:06:39 GMT+00:00	<p>Tuberculosis spreads through coughing, sneezing Henderson Gleaner</p> <p>Although most of us have never been exposed to a case of tuberculosis, we live in a global community where the next big infectious outbreak is only a plane ...</p> <p>and more »</p>
New tool to fight syphilis? Wal-Mart gift cards - msnbc.com	Mon, 14 Sep 2009 12:20:56 GMT+00:00	<p>New tool to fight syphilis? Wal-Mart gift cards msnbc.com</p> <p>Monroe says he's also seen an uptick in infectious diseases such as HIV and tuberculosis. The rising number of syphilis cases is worrisome on several counts ...</p>
Who gets the antibiotics? - Philadelphia Inquirer	Mon, 14 Sep 2009 07:03:06 GMT+00:00	<p>Who gets the antibiotics? Philadelphia Inquirer</p> <p>Resistant infections include not only MRSA, but also pneumonia, food poisoning, and tuberculosis. Microbes can develop resistance any time antibiotics are ...</p> <p>and more »</p>

What have we
found so far.....?

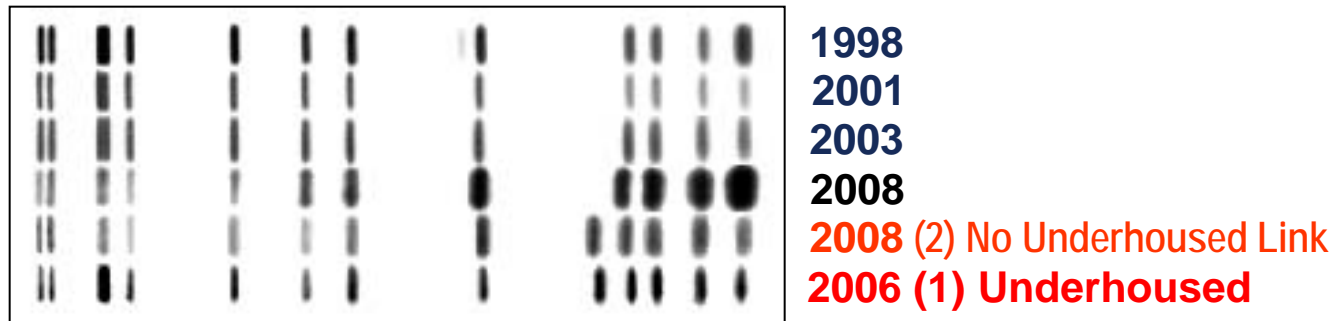
OUT-TB Complements Traditional Contact Tracing

Universal Genotyping permits:

- ✓ Validation of **Suspected** transmission events
- ✓ Identification of **Unexpected** transmission events
- ✓ Detection of transmission across Health Unit boundaries
- ✓ Monitoring for laboratory cross-contamination
- ✓ Surveillance of changing disease trends/patterns
 - Prevalence of various *M.tb* lineages
 - Incidence of specific strains/patterns
 - Distribution in different communities

Transmission of Toronto's 'Underhoused' Strains

- ✓ Four *M.tb* strains are endemic to Toronto's 'underhoused' population
- ✓ Largest cluster: **Strain A** >40 cases over the past 12 years
- ✓ Most common among shelter users and shelter workers
but OUT-TB reveals spread of **Strain A** to general population

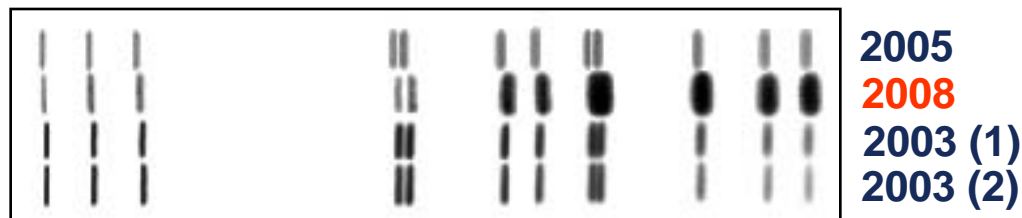


24-MIRU: 452233444212719252212523

Spoligo: 740000007760731

Transmission of Toronto's 'Underhoused' Strains

- ✓ **Strain D** is an emerging 'underhoused' strain
- ✓ Responsible for 4 cases dating back to 2005
- ✓ OUT-TB revealed case in small town Ontario with **Strain D** genotype
- ✓ Subsequent public health investigation revealed:
 - Epidemiological link to Toronto's underhoused community
 - Additional **Strain D** cases dating back to 2003

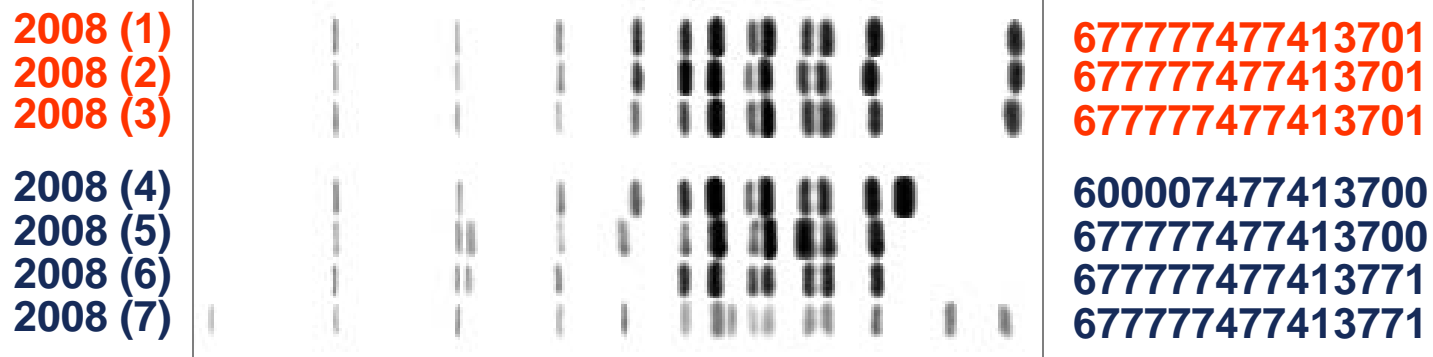


24-MIRU: 261645424234237253213423

Spoligo: 700377740003771

Prevalence of Indo-Oceanic (Manila) Lineage

- ✓ MIRU-VNTR genotyping revealed large cluster of identical patterns
- ✓ Spoligotyping and IS6110 RFLP allowed resolution of 'pseudo-cluster' but some cases still identical by all three genotyping methods!
- ✓ No local connection found between cases but all individuals were immigrants from same island (Luzon) of Philippines



24-MIRU : 5224341442218A7263223363

Challenges.....

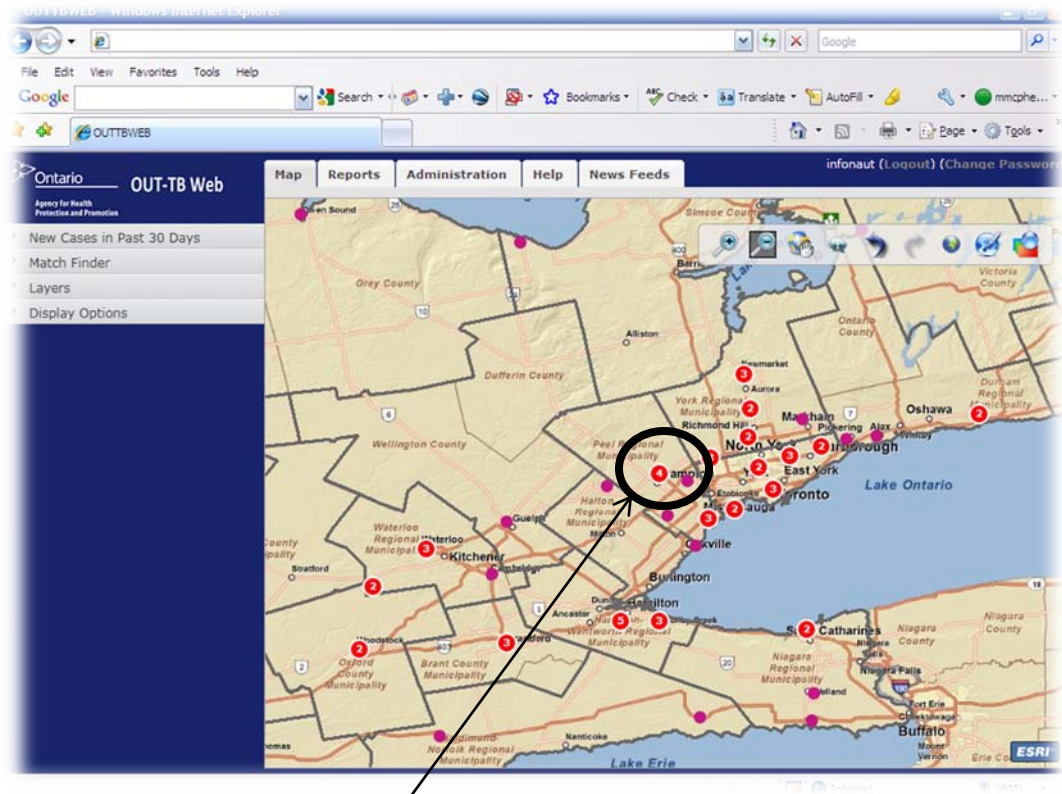
Under-housed / Undocumented Patients

Causes

- Marginalized populations are at high risk for TB
- Most TB cases are not acquired in Canada

Challenges

- Cannot represent no address
- Reliance on proxy addresses (e.g. PHU, treatment facility, shelter...)
- Can skew visual interpretation & spatial analysis



Coding cases to geographic centre of municipality can skew visual & spatial analysis

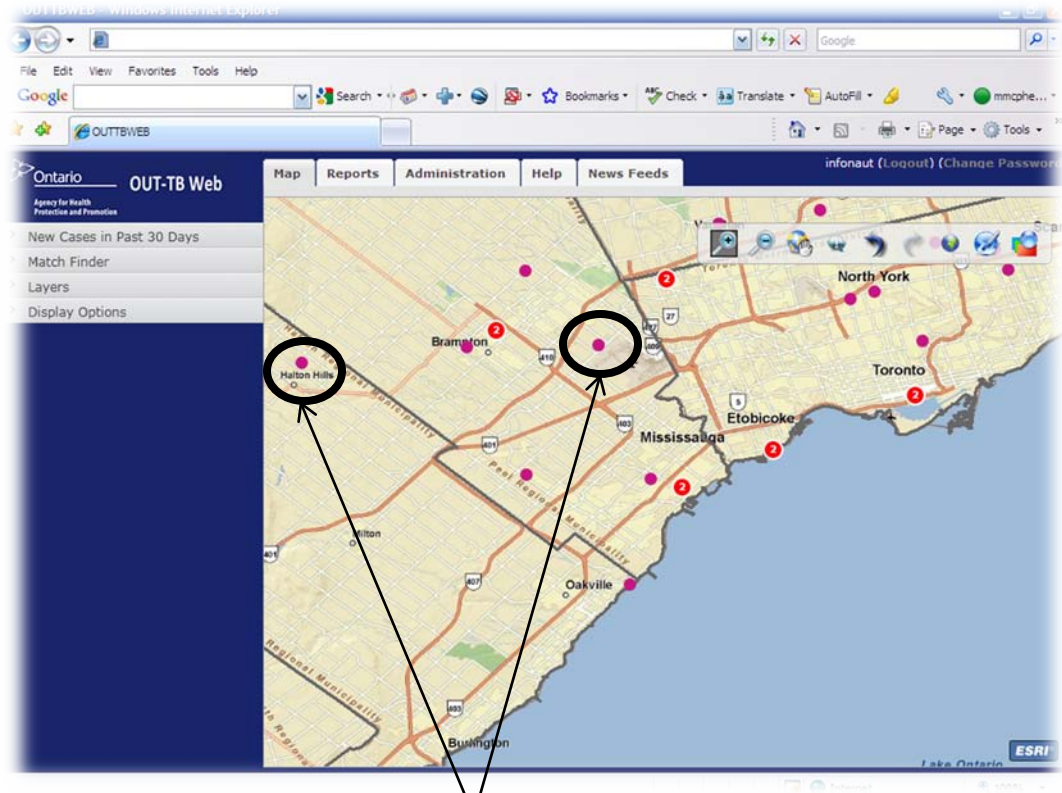
Duplicate Records for a Patient

Causes

- Under-housed / Undocumented Patients
- Multiple lab tests over time
- Re-infected individuals

Challenges

- How to spot duplicates?
- Phantom matches
- May be time-consuming to resolve



Exact match or duplicate record?

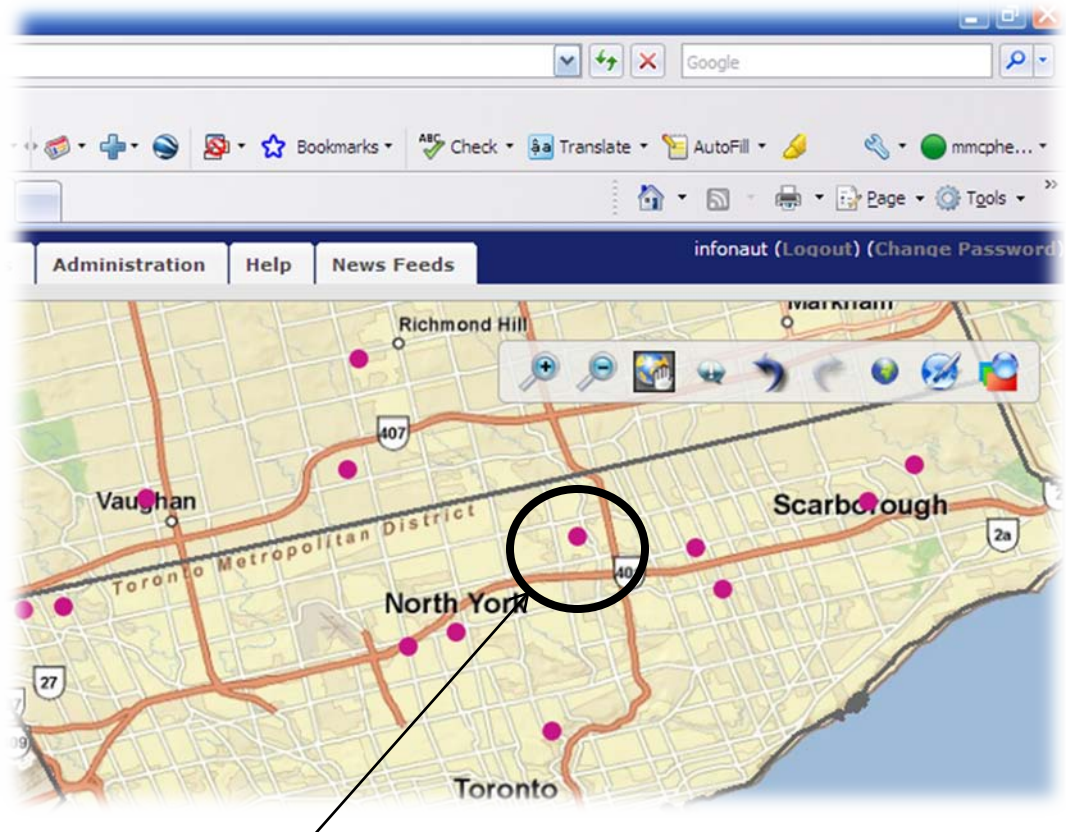
Currency of Addresses

Causes

- Long latency of TB
- Many patients are highly transient e.g. under-housed
- Patients move cities / health units

Challenges

- Years can pass between matching cases presenting
- Older addresses may be unreliable



Patient may have moved from this location

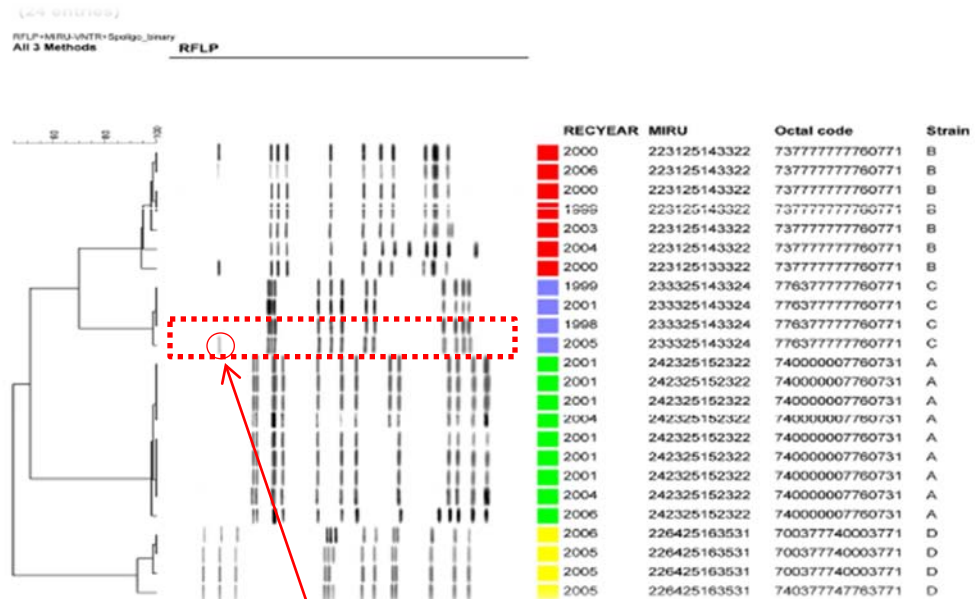
Exact Genotypic Match vs. 'Close' Match

Causes

- Active disease occurs long after original infection (strain mutations occur over time)
- Transmission cases may not be an **exact** genotypic match

Challenges

- Some 'close' matches are plausibly related, but some may not be
- Automation of 'close matches' are difficult



Some variations between these bands plausibly result from mutation, others indicate that strains are **not** related