Improving HIV drug resistance test turnaround times at The Cambridge Clinical and Public Health Laboratory

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Impact:

- Recent changes to laboratory work flow have led to an overall improvement in HIV resistance test laboratory turnaround times.
- Improved time-to-result availability enables earlier treatment decisions to be made, for the benefit of patients and clinicians.
- The majority of samples with total turnaround times in excess of 21 days are received from external centres, suggesting that the pathway for external sample submission needs refining.
- There remains room for improvement to bring total and laboratory turnaround times for both internally and externally submitted samples in line with BHIVA's Standards of Care for People Living with HIV.

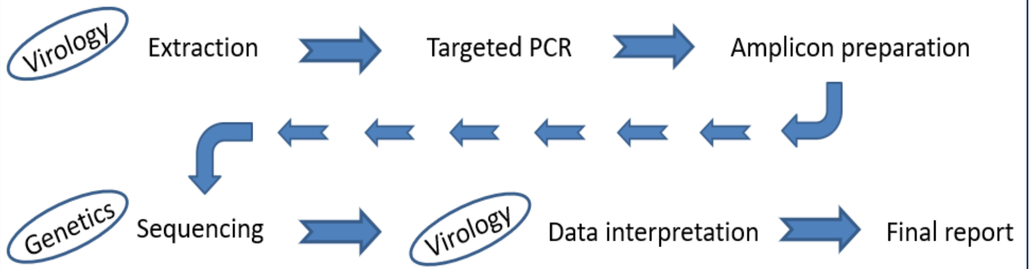
Background:

Drug resistance testing forms an important component of the management of HIV infection, allowing better tailored antiretroviral therapy. Prompt processing of samples and reporting of results is necessary to allow treatment decisions to be made in a timely manner. The British HIV Association's (BHIVA) 2013 *Standards of Care for People Living with HIV* suggest a desired turnaround time (TAT) of 2 weeks from the time of specimen collection for HIV resistance testing. In view of the number and complexity of steps involved in the laboratory process, the Cambridge Clinical and Public Health Laboratory (CMPHL) service contract details more realistic target turnaround times of 14-21 days.

Methods:

Following an audit of HIV resistance testing at CMPHL in June 2016, which demonstrated laboratory TAT of ≤21 days in 93% (90/97) of HIV resistance tests performed over a six month period, but laboratory TAT of ≤14 days in only 41% (40/97), the timetable of pre-sequencing laboratory work flow was altered in an attempt to reduce TATs as best possible. Where previously samples had been taken to the clinical genetics department for sequencing on the first Friday after completion of preliminary work, and sequencing data returned the following Thursday, collection for sequencing is now undertaken each Monday and data returned 3-4 days later, allowing more samples received in the week prior to sequencing to be included in each run.

Adaptations to laboratory workflow



Laboratory work flow prior to change

Monday	Preliminary work
Tuesday	Preliminary work
Wednesday	Preliminary work
Thursday	Preliminary work
Friday	Amplicons submitted to molecular genetics
Saturday	
Sunday	
Monday	
Tuesday	
Wednesday	
Thursday	Receive sequences, compare with Stamford database
Friday	Final report issued

Laboratory work flow after change

Monday	Preliminary work
Tuesday	Preliminary work
Wednesday	Preliminary work
Thursday	Preliminary work
Friday	Preliminary work
Saturday	Preliminary work
Sunday	Preliminary work
Monday	Amplicons submitted to molecular genetics
Tuesday	
Wednesday	
Thursday	Receive sequences, compare with Stamford database
Friday	Final report issued

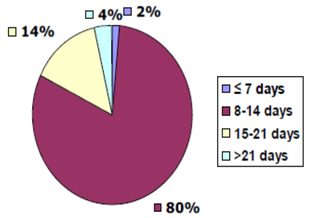
= Cut-off for RNA extraction

To assess the effect of this change, we re-audited the TATs of all HIV resistance tests undertaken at CMPHL between 1st July and 31st December 2016, recording both laboratory TAT (time from sample booking in to final report being issued) and total TAT (time from recorded sample collection to final report being issued).

Results:

Re-audit revealed a laboratory TAT of ≤21 days in 96% (54/56) of tests, and laboratory TAT of ≤14 days in 82% (46/56). For samples with laboratory TAT >21 days, inability to amplify the virus for sequencing despite several attempts was identified as a reason for delay in result reporting. When laboratory TATs were compared with total TATs, it became apparent

Turnaround time from recorded time of sample receipt (or time request was retrospectively added to HIV PCR sample) to time of final report:



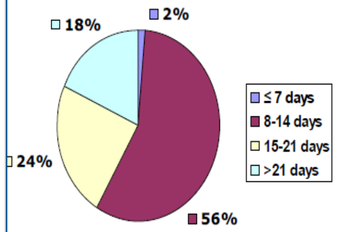
Percentage of samples reported within 21 days: **96%**

Median turnaround time: **10.2 days**

Interquartile range: **4.9 days**

- 1/56 test reported in ≤ 7 days
- 45/56 tests reported in 8-14 days
- 8/56 tests reported in 15-21days
- 2/56 tests reported in >21 days

Turnaround time from recorded time of sample collection (or time request was retrospectively added to HIV PCR sample) to time of final report:



Percentage of samples reported within 21 days: **82%**

Median turnaround time: **13.1 days**

Interquartile range: **8.1 days**

- 1/55 test reported in ≤ 7 days
- 31/55 tests reported in 8-14 days
- 13/55 tests reported in 15-21days
- 10/55 tests reported in >21 days

that handling of samples prior to arrival at the laboratory is a significant cause of additional delay in the testing process; only 82% (45/55) of samples had a total TAT of ≤21 days, and 58% (32/55) had TAT of ≤14 days. Of note, 90% of samples with total TAT >21 days were submitted by external centres, including Grantham (4/10), Grimsby (2/10), Peterborough (1/10), Newcastle (1/10), and Colchester (1/10).

Recommendations:

We now aim to collaborate with external service users to streamline the process of sample submission, in an attempt to bring total test TATs in line with BHIVA's recommendations. We will also issue an interim report for each failed sequencing attempt on all samples, to enable repeat sampling if urgent results are required.

Cambridge University Hospitals NHS Foundation Trust

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