No better than picking results out the blue - Clinical diagnosis of flu

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BACKGROUND

Funding was obtained in 2016 to conduct a pilot of on-site laboratory-based influenza PCR testing, using the Cepheid GeneXpert platform. The aim of the pilot was to assess the clinical impact of a faster result turnaround time.

Prior to this pilot, all influenza testing for NHS Ayrshire & Arran was undertaken by a reference laboratory, whose turnaround times were between 2 and 10 days. With the Cepheid GeneXpert platform, reliable results could be provided in under 2 hours from sample receipt.

Between January and May 2017, on-site testing was made available to the Combined Assessment Unit at University Hospital Crosshouse. Over this time period 209 patients were tested, of which 63 patients tested positive for influenza.

METHOD

All samples were sent to the reference laboratory for ongoing quality assurance (no false positive or false negative results occurred).

Only patients who were clinically assessed as having possible influenza were tested. Collection kits, comprising a flocked swab and 3ml vial of transport medium, were provided for testing. Staff were given training on how to use these kits to obtain a combined nose and throat sample. Once samples were obtained, they were then sent to the laboratory for on-site PCR testing.

Clinicians completed an audit form with each request, which included the following information :

- Clinical suspicion of influenza, on a scale from 1 to 10
- Symptoms present

Further data was collected, the results of which we plan to publish in the near future.

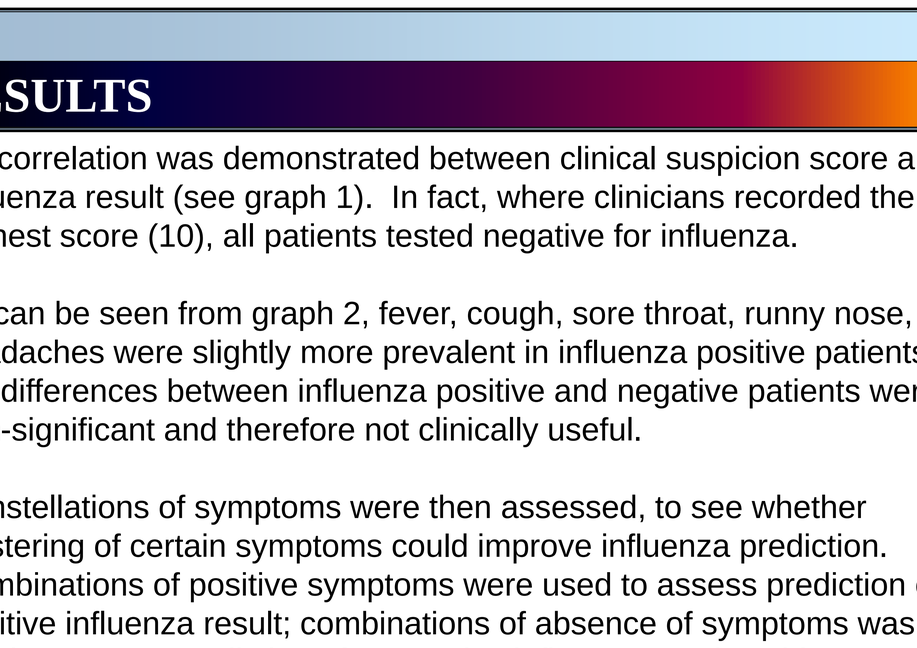
RESULTS

No correlation was demonstrated between clinical suspicion score and influenza result (see graph 1). In fact, where clinicians recorded the highest score (10), all patients tested negative for influenza.

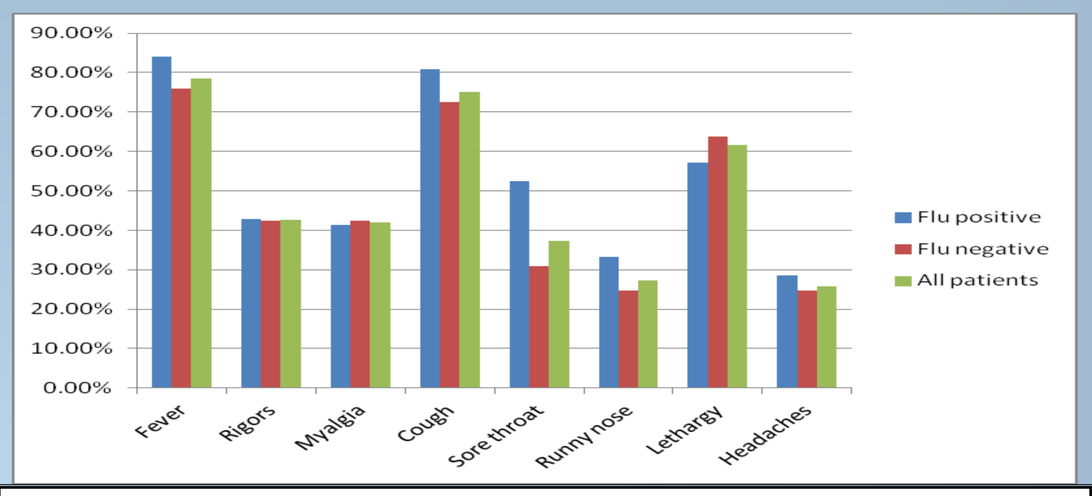
As can be seen from graph 2, fever, cough, sore throat, runny nose, and headaches were slightly more prevalent in influenza positive patients, but differences between influenza positive and negative patients were non-significant and therefore not clinically useful.

Constellations of symptoms were then assessed, to see whether clustering of certain symptoms could improve influenza prediction. Combinations of positive symptoms were used to assess prediction of a positive influenza result; combinations of absence of symptoms was used to assess prediction of a negative influenza result. Tables 1 and 2 illustrate the specificity/sensitivity for a variety of symptom groupings.

No constellation of symptoms demonstrated a clinically useful sensitivity and specificity, either for influenza presence or influenza absence.



Graph 1 – Clinical suspicion of influenza pre-test. The percentage of influenza positive results (green) are shown against the percentage of influenza negative results (red) for each score. 1 was the lowest level of suspicion recorded and 10 was the highest.



Graph 2 – The percentage of patients with each symptom; blue bars indicate the percentage of influenza positive patients with each symptom, red bars indicate the percentage of influenza negative patients with each symptom, and green bars indicate the percentage of all patients (regardless of result) with each symptom.

	ST+F+RN+C+H	ST+F+RN+C	ST+F+RN	ST+F+C	ST+F	ST+RN	ST+C	F+RN	F+C	RN+C
Flu pos & all Sx present	5	12	12	25	29	14	29	18	44	18
Flu pos & not all Sx present	58	51	51	38	34	49	34	45	19	45
Flu neg & all Sx present	7	9	15	20	31	22	33	25	78	25
Flu neg & not all Sx present	139	137	131	126	115	124	113	121	68	121
Specificity for pos flu result	41.67%	57.14%	44.44%	55.56%	48.33%	38.89%	46.77%	41.86%	36.07%	41.86%
Sensitivity for pos flu result	79.37%	19.05%	19.05%	39.68%	46.03%	22.22%	46.03%	28.57%	69.84%	28.57%

Table 1 – Positive symptom constellations, and specificity/sensitivity for a positive influenza result. ST = sore throat, F = fever, RN = runny nose, C = cough, H = headache

	ST+F+RN+C+H	ST+F+RN+C	ST+F+RN	ST+F+C	ST+F	ST+RN	ST+C	F+RN	F+C	RN+C
Flu pos & all Sx absent	2	2	5	3	6	23	8	7	3	9
Flu pos & not all Sx absent	61	61	58	60	57	40	55	56	60	54
Flu neg & all Sx absent	3	3	16	5	20	86	27	23	6	28
Flu neg & all Sx not absent	143	143	130	141	126	60	119	123	140	118
Specificity for neg flu result	60%	60%	76.19%	62.50%	76.92%	78.90%	77.14%	76.67%	66.67%	75.68%
Sensitivity for neg flu result	2.05%	2.05%	10.96%	3.42%	13.70%	58.90%	18.49%	15.75%	4.11%	19.18%

Table 2 – Negative symptom constellations, and specificity/sensitivity for a negative influenza result. ST = sore throat, F = fever, RN = runny nose, C = cough, H = headache

CONCLUSIONS

Findings from this pilot suggest that it is <u>impossible</u> to diagnose influenza clinically.

Currently used clinical definitions of influenza, such as the PHE/ECDC definition of influenza-like-illness, are sensitive but not especially specific.

A rapid and reliable laboratory test is therefore essential, and is particularly useful in newly admitted patients, before they are transferred to other parts of the hospital.

Rapid results will:

- Improve individual patient management
- Assist with safer and more efficient use of side rooms
- Reduce risk of influenza outbreaks and associated bay/ward closures
- Reduce risk of influenza transmission to patients, visitors, and health care workers

OTHER BENEFITS HIGHLIGHTED BY PILOT

Appropriate use of droplet precautions and antiviral medications dramatically improved following provision of a laboratory result.

Faster test turnaround time also appeared to reduce length of hospital stay. During this pilot, the median length of stay for an influenza positive patient was 46 hours, versus 98 hours for an influenza negative patient (equating to an approximate total cost saving of £45,000). Furthermore, a significantly larger proportion of influenza positive patients (28.6%) were discharged home within 24 hours of admission, compared to influenza negative patients (11.7%). This is highly suggestive that a faster positive influenza result aided earlier discharge.