Institution: Imperial College London

Unit of Assessment: 01 Clinical Medicine

Title of case study: CovidNudge: an accurate, quick and easy-to-use diagnostic test for COVID-19 in the NHS.

Period when the underpinning research was undertaken: 2013 - 2020

Details of staff conducting the underpinning research from the submitting unit:

Name(s):	Role(s) (e.g. job title):	Period(s) employed by submitting HEI:
Christofer Toumazou	Regius Professor of Bioelectronics	1986 - present
Graham Cooke	Professor of Infectious Diseases	2006 - present
Graham Taylor	Professor of Human Retrovirology	1992 - present
Malick Gibani	Clinical Lecturer	2019 - present

Period when the claimed impact occurred: May 2020 - present

Is this case study continued from a case study submitted in 2014? No

1. Summary of the impact (indicative maximum 100 words)

Access to rapid diagnosis is key to the control and management of COVID-19 and this posed a major challenge at the start of the pandemic. The Imperial team developed a new diagnostic platform (CovidNudge) for rapid testing which, unlike other platforms, required no sample handling. This enabled a highly sensitive and specific test to be performed on the frontline, without the need for skilled operators, ensuring rapid results and clinical decision making. Following clinical validation and Medicines and Healthcare products Regulatory Agency (MHRA) approval, CovidNudge was included as part of Public Health England's testing strategy and deployed in eight hospitals. In October 2020, following a £161,000,000 government procurement, CovidNudge became more widely available with 320 machines operating at 87 sites across the NHS, and more than 62,000 tests performed as of 21 December 2021.

2. Underpinning research (indicative maximum 500 words)

COVID-19 has placed major strain on healthcare services throughout 2020. Early in the pandemic, access to rapid testing was limited by the lack of appropriate technology and inadequate supply chains of reagents for existing testing platforms.

In March 2020, in response to the SARS-CoV-2 pandemic, Regius Professor Chris Toumazou and his team within the Faculty of Engineering at Imperial College redesigned their commercial human DNA typing platform providing rapid and direct-from-specimen diagnostic sequencing from its previous commercial use in human DNA typing (1, 2) to CovidNudge, providing rapid and accurate, true sample-to-answer multiplex RT-PCR diagnosis of SARS-CoV-2 in just over an hour (2).

Prof Graham Cooke and team in the Department of Infectious Diseases at Imperial undertook the first clinical development and assessment of CovidNudge (3). Initially, using a range of SARS-CoV-2 isolates, they confirmed the ability of this test to detect the virus in nasopharyngeal swabs and established the lower limit of detection (LLOD).

A key advantage of the test is its ability to detect multiple targets within the viral genome: detection of a number of different genes within the SARS-CoV-2 virus allows improved sensitivity, and also allows future-proofing against mutated variants of concern, or additional detection of other viruses producing similar clinical symptoms.

The researchers then assessed clinical accuracy across three different clinical centres (Imperial College Healthcare Trust St Mary's Hospital, Chelsea and Westminster Hospital and the John Radcliffe Hospital in Oxford), where samples were collected from 386 people in three groups:

- Self-referred healthcare workers with suspected COVID-19 (Group 1, n=280/386; 73%)
- Patients attending the emergency department with suspected COVID-19 (Group 2, n=15/386; 4%)
- Hospital inpatient admissions with or without suspected COVID-19 (Group 3, n=91/386; 23%).

Of the 386 paired samples tested across all groups, 67 tested positive on the CovidNudge platform and 71 with standard laboratory RT-PCR. The sensitivity of the test varied by group (Group 1 93% [84-98%], Group 2 100% [48-100%] and Group 3 100% [29-100%], giving an average sensitivity of 94.4% (95% confidence interval 86-98%) and an overall specificity of 100% (95%CI 99-100%; Group 1 100% [98-100%]; Group 2 100% [69-100%] and Group 3 100% [96-100%]) (3).

This trial was the first to demonstrate the high sensitivity and specificity of a rapid point-of-care (POC) test for SARS-CoV-2 in a frontline clinical setting during the first peak of the COVID-19 pandemic.

3. References to the research (indicative maximum of six references)

(1) C. Toumazou, L.M. Shepherd, S.C. Reed, et al, "Simultaneous DNA amplification and detection using a pH-sensing semiconductor system", *Nature Methods*, (2013), 10, pp. 641646. DOI.

(2) C. Toumazou, S.B. Lowe, S.W. Green, P.S. Harding, G.H. Sanders, N.J. Wooder, N.A. Werdich, M.C. Twisk, R.H. Zander, J. Casey, H.V. Hare, "Method and apparatus for analysing a biological sample", US patent (filed 2016, granted 2018). https://patents.google.com/patent/US10093965B2

(3) M.M. Gibani, C. Toumazou, M. Sohabati, R. Sahoo, M. Karvela, T.-K. Hon, S. De Mateo, A. Burdett, K.Y.F. Leung, J. Barnett, A. Orbeladze, S. Luan, S. Pournias, J. Sun, B. Flower, J. Bedzo-Nutakor, M. Amran, R. Quinlan, K. Skolimowska, C. Herrera, A. Rowan, A. Badhan, R. Klaber, G. Davies, D. Muir, P. Randell, D. W. M. Crook, G. P. Taylor, W. Barclay, N. Mughal, L.S.P. Moore, K. Jeffery, G.S. Cooke. (2020). Assessing a novel, lab-free, point-of-care test for SARS-CoV-2 (CovidNudge): a diagnostic accuracy study. *The Lancet Microbe*; 1:e300-e307. DOI.

4. Details of the impact (indicative maximum 750 words)

Since its emergence in late 2019, SARS-CoV-2 infection led to 4,144,577 confirmed cases of COVID-19 and 121,747 deaths in the UK alone, with worldwide cases over 83,000,000 and deaths over 1,800,000 by the end of 2020. Rapid and reliable testing is a key tool for controlling the pandemic. Initially this relied on existing testing resources in secondary care settings while centralised laboratories and lateral flow testing programmes were being commissioned. During the first peak of infections in the UK (March-April 2020) national viral PCR testing capacity was rapidly exceeded. Critically, conventional PCR testing requires samples to be sent to a central laboratory that often takes over 24 hours to return results.

These slow turnaround times delayed important clinical decisions, such as appropriate therapy and prioritisation for isolation facilities.

The collaboration between the research teams in the Faculty of Engineering and the Faculty of Medicine at Imperial led to the development of a rapid and accurate, true sample-to-answer multiplex RT-PCR diagnosis of SARS-CoV-2 in just over an hour, without the need for any laboratory facilities and trained personnel.

The clinical validation conducted with NHS partners demonstrated high sensitivity (94%) and specificity (100%). Following this trial, the MHRA approved CovidNudge for clinical use in April 2020 [**A**]. COVID-19 test machines ("Nudgeboxes") were first deployed for routine use in NHS settings in late April 2020 and were initially prioritised for cancer wards, A&E and maternity departments to protect those most at risk in eight London hospitals; St Mary's Hospital in Paddington, Charing Cross Hospital, West Middlesex University Hospital, Chelsea and Westminster Hospital, Royal Hospital Chelsea, Queen Charlotte's and Chelsea Maternity Hospital, the Renal Transplant Centre at Hammersmith Hospital, and the Tower Hamlets Centre for Mental Health at Mile End Hospital.

From 27 April 2020, the NHS required PCR based testing for all unscheduled admissions to hospital [**B**] and the CovidNudge testing platform was able to provide this. The primary impact was in supporting the management of patients in busy acute hospitals, with Chelsea and Westminster Hospital performing up to 200 test per day [**C**]. However, an important additional role was the testing of patients admitted by psychiatric services preventing any unnecessary isolation that may exacerbate a patient's illness. In addition to directly benefitting patients admitted to hospital, rapid CovidNudge testing allowed relatives access to hospitals (e.g. partners of women going into labour were able to attend following a negative test) [**C**].

At the beginning of July 2020, the device obtained a CE Mark enabling its additional use in non-clinical locations including care homes and other public emergency services where access to PCR remained limited [**D**]. DnaNudge Ltd was indicated on the list of approved coronavirus test providers [**E**] and an application for FDA approval began in November 2020. In August 2020 the UK Government placed a £161,000,000 order for DNA Nudgeboxes, to roll out the test UK-wide in urgent NHS patient care and elective surgery settings, plus out-of-hospital locations [**F**] at a time when there was very limited availability of rapid viral detection diagnostics.

The lab-free sample-to-answer RT-PCR CovidNudge test, provided the medical community with the means to rapidly diagnose, monitor, and treat disease with high confidence and at a low cost. The rapid deployment of the test continued during the 4th quarter of 2020, with increasing volumes month on month as more sites adopted the technology with 12,339 point-of-care tests performed in December 2020.

As of the end of December 2020, the system was in use at 87 sites, with over 320 machines deployed and more than 62,000 tests run, complementing other programmes focussed on community settings. The test was designed to detect the emergent B.1.1.7 variant and with the second wave of hospitalised infections, positivity rates rose from 1.1% in September 2020 to 13.7% in December 2020. In December 2020 alone the test identified over 1,600 positive cases allowing rapid and accurate point-of-care clinical decision making.

5. Sources to corroborate the impact (indicative maximum of 10 references)

[**A**] MHRA approval: https://www.reuters.com/article/us-health-coronavirus-britain-test-idUKKBN22Z0PI. Archived here.

[**B**] Letter to NHS Trusts:

https://www.england.nhs.uk/coronavirus/wp-content/uploads/sites/52/2020/04/C0420-Patient-testing-letter.pdf. Archived here.

[**C**] Letter from the Chief Executive of Chelsea and Westminster Hospital NHS Trust

[**D**] https://www.dnanudge.com/en/COVID-Nudge. Archived here.

[**E**] List of Approved coronavirus test providers. Archived here.

[**F**] https://www.gov.uk/government/news/roll-out-of-2-new-rapid-coronavirus-tests-ahead-of-winter. Archived here.