Matthew Bowden

Transformation Fellow 2020-21

Why fellowship? Benefits to date?

Personal and professional development

Interest in developing systems in which I work, supporting others, team working, improving outcomes for patients (individual and population level)

I'm an aspiring future leader in primary care - open to participation at any level

Future GP partnership

Insight to and working with current leaders, as well as exposure to different levels of management

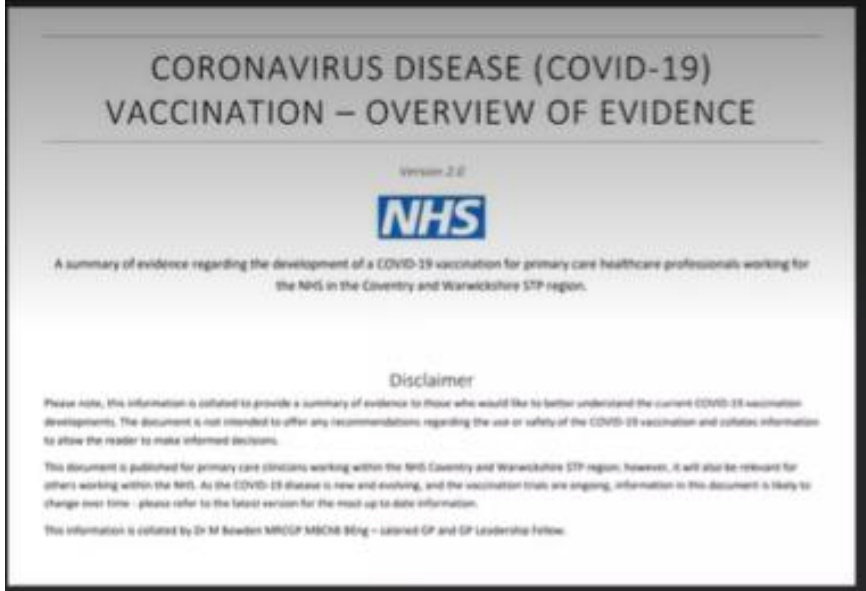
Teaching / mentoring to develop skills

Opportunities to lead on projects whilst having support

Networking

Summary of activities/projects

Project	- GP resilience workforce pool
Course	- Introduction to Leadership and Management in Healthcare Contexts (Uni of Warwick)
Project	- COVID-19 Vaccine Overview of Evidence *
Course	- Building Future of General Practice (RCGP)
Collaboration	- Public health, CCG, First5, training hub
Course	- New to Practice Programme (Uni of Warwick/Coventry)
Personal Development	- NHS coaching course and monthly mentor input
Mentoring others	- Mentoring of WMS students on Leadership Programme
Course	- A Fresh Approach to General Practice (RCGP)
Project	- New to Practice Fellowship (Clinical Lead)*
Participation	- Attended VTS sessions, PCN meetings, CCG meetings, NHSE regional meetings
Course	- RCGP Annual Conference (RCGP)
Networking / review	- AL Fellowship Forum and as well as informal networking with peers



CORONAVIRUS DISEASE (COVID-19)
VACCINATION – OVERVIEW OF EVIDENCE

Version 2.0

NHS

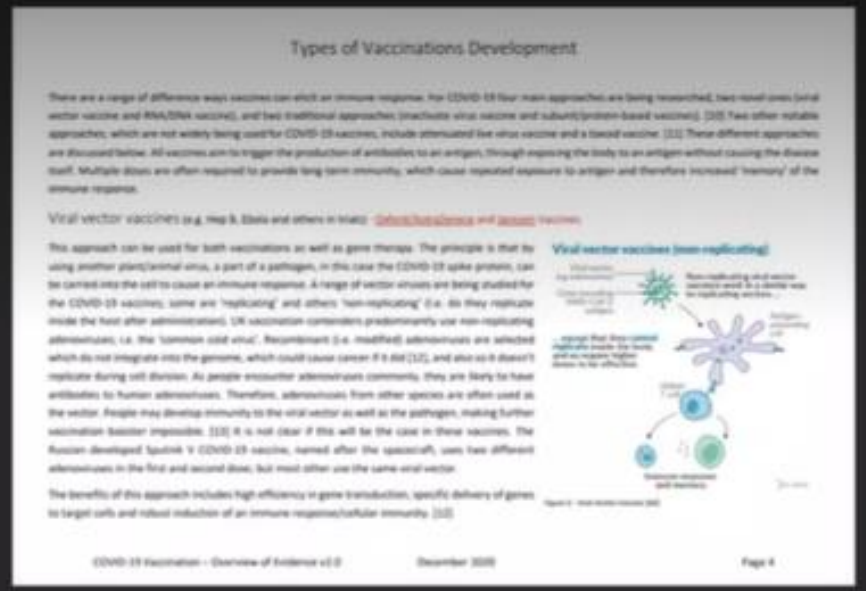
A summary of evidence regarding the development of a COVID-19 vaccination for primary care healthcare professionals working for the NHS in the Coventry and Warwickshire STP region.

Disclaimer

Please note, this information is collated to provide a summary of evidence to those who would like to better understand the current COVID-19 vaccination developments. The document is not intended to offer any recommendations regarding the use or safety of the COVID-19 vaccination and collates information to allow the reader to make informed decisions.

This document is published for primary care clinicians working within the NHS Coventry and Warwickshire STP region; however, it will also be relevant for others working within the NHS. As the COVID-19 disease is new and evolving, and the vaccination trials are ongoing, information in this document is likely to change over time - please refer to the latest version for the most up to date information.

This information is collated by Dr M Bowden MRCGP MBChB BEng – salaried GP and GP Leadership Fellow.



Types of Vaccinations Development

There are a range of different ways vaccines can elicit an immune response. For COVID-19 four main approaches are being researched, two novel ones (viral vector vaccine and RNA/DNA vaccine), and two traditional approaches (inactivate virus vaccine and subunit/protein-based vaccines). [10] Two other notable approaches, which are not widely being used for COVID-19 vaccines, include attenuated live virus vaccine and a toxoid vaccine. [11] These different approaches are discussed below. All vaccines aim to trigger the production of antibodies to an antigen, through exposing the body to an antigen without causing the disease itself. Multiple doses are often required to provide long-term immunity, which cause repeated exposure to antigen and therefore increased 'memory' of the immune response.

Viral vector vaccines (e.g. Hep B, Ebola and others in trials) - Oxford/AstraZeneca and Sputnik V vaccines

This approach can be used for both vaccinations as well as gene therapy. The principle is that by using another plant/animal virus, a part of a pathogen, in this case the COVID-19 spike protein, can be carried into the cell to cause an immune response. A range of vector viruses are being studied for the COVID-19 vaccines; some are 'replicating' and others 'non-replicating' (i.e. do they replicate inside the host after administration). UK vaccination contenders predominantly use non-replicating adenoviruses; i.e. the 'common cold virus'. Recombinant (i.e. modified) adenoviruses are selected which do not integrate into the genome, which could cause cancer if it did [12], and also so it doesn't replicate during cell division. As people encounter adenoviruses commonly, they are likely to have antibodies to human adenoviruses. Therefore, adenoviruses from other species are often used as the vector. People may develop immunity to the viral vector as well as the pathogen, making further vaccination booster impossible. [13] It is not clear if this will be the case in these vaccines. The Russian developed Sputnik V COVID-19 vaccine, named after the spacecraft, uses two different adenoviruses in the first and second dose, but most other use the same viral vector.

The benefits of this approach includes high efficiency in gene transduction, specific delivery of genes to target cells and robust induction of an immune response/cellular immunity. [10]

Viral vector vaccines (non-replicating)

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BioNTech/Pfizer - BNT162b2 [mRNA vaccine]

Summary: In combined phase I/II trials (43,998 participants), 95% effective overall (>94% in over 65s), no serious adverse effects recorded. Temporary approval gained in December 2020. First vaccine to be used in mass vaccination in the world. It needs to be stored at -70c until ready to be given.

Data Source: MHRA and Pfizer's interim results

Vaccine characteristics

BioNTech/Fosun Pharma/Pfizer has developed an RNA vaccine, using lipid nanoparticle to carry the COVID-19 mRNA into a host cell. The vaccine BNT162b2 encodes a 'membrane anchored' SARS-CoV-2 full-length spike. [16] The RNA naturally degrades after a few days within the body.

The BNT162b2 vaccine is animal-product free, latex free and contains no preservatives. The ingredients includes RNA protein, ALC-0315, ALC-0159, 1,2-distearoyl-sn-glycero-3-phosphocholine, cholesterol, potassium chloride, potassium dihydrogen phosphate, sodium chloride, disodium hydrogen phosphate dihydrate, sucrose and water for injection. [48] The vaccine contains 30mg of potassium and 23mg of sodium, and is essentially potassium / sodium free.

Administration

The vaccine is administered intramuscularly, and requires 2 doses (0.3ml / 30µg), at least 21 days apart. [7] Dose may be given at 28 days apart for organisational reasons, to facilitate a consistent approach with other two dose vaccines for the UK market. Protection is achieved 7 days after the second dose. [47]

It requires storage at -70°c, where it will remain stable for 6 months. Once thawed, it is stable for 5 days when stored between 2-8°c, and 2 hours at room temperature. There are 5 doses per vial and is supplied in 195 vial packs. Each vial needs to be prepared by adding 1.8ml 0.9% sodium chloride for injection when ready for administration [25], and will last for 6 hours refrigerated once reconstituted.

Trial Developments

Trial information is from company-own press releases and confirmed in publications by MHRA.

During phase I trials, 195 healthy adults (18-55 and 65-85 years old) were randomised to either placebo or BNT162b1/BNT162b2 (of varying doses: 10 µg, 20 µg, 30 µg, and 100 µg), with the primary outcome being safety. All groups had two doses at 21 days apart, except the 100 µg of BNT162b1 group which had a single dose only. BNT162b2, which encodes the spike protein, had less incidence and severity of systemic reactions than BNT162b1, which encodes the receptor-

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Who should be vaccinated?

The Joint Committee on Vaccination and Immunisation (JCVI) recommends that priority of vaccination should be given to those at increased risk of serious disease/death from COVID-19 (stratified by age/risk factors) and frontline health and social care workers (who may be reservoirs of transmission). [49] It is deemed that an age-based programme will likely result in faster delivery, better uptake in those at the highest risk as well as protecting the NHS capacity. This is based on epidemiological, microbiological and clinical considerations as well as disease incidence, hospitalisation / mortality data and mathematical modelling of different strategies. It is recognised such a method means unequal access across a population, and thus has implications for health inequalities. These should therefore be addressed during implementation, whilst being aware of unintentional consequences of targeting any particular population group. [3]

The ranking of prioritisation in the first phase is set out below. [50] Subsequent phases are under review.

Ranking of prioritisation:	
	1. Residents in a care home for older adults and their carers
	2. all those 80 years of age and over and frontline health and social care workers
	3. all those 75 years of age and over
	4. all those 70 years of age and over and clinically extremely vulnerable individuals*
	5. all those 65 years of age and over
	6. 16 to 64 years old with underlying health conditions which put them at higher risk of serious disease/mortality
	7. all those 60 years of age and over
	8. all those 55 years of age and over
	9. all those 50 years of age and over

* This does not include women who are pregnant or those under 16

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Project – COVID-19 Vaccine: Overview of Evidence

- 30-page, fully referenced, review of all leading vaccinations in development at the time, with background to vaccine development.
- Early collection of resources for healthcare professional.
- Set key principles prior to undertaking project (impartial, EBM, relevant to vaccine options)
- Recognition of legal aspect, ethics and not wanting to conflict with emerging guidelines
- Updated regularly. Support from specialists and PH colleagues. Hosted online. Circulated to other CCGs. Sources: Gov, NHS, Vaccine developers, publications.
- Eventually superseded by NHSE/I training packages, national guidance/Greenbook

Project – New to Practice Fellowship

- Role: Development, roll out and management as Clinical Lead on the locally delivered, national initative, GP Fellowship.
- Project: 2-year programme of support, personal development, and PCN project working for newly qualified GPs and GPNs
- Collaboration: Working with project facilitator, training hub, lead mentor, GPN lead, University Warwick/Coventry, PCNs, Practice Managers, NHSE/I, CCG finance team
- Activities: Oversight of activities of the fellowship, collaborating in development of policies/protocols and documentation, executive decision making, drafting/reviewing promotional material, promoting programme to PCN, future fellows and other clinical leaders, hosting Q&A webinars, delivering induction, attending regional meetings, being an advocate for fellows.

In summary (what's next?)

- Unique and privilege opportunity to develop, refine and practise leadership skills
- Introduction to and networking with current and future leaders
- Great supervision and content from inspiring leaders – massive thank you to all that have helped us in our journeys (especially Dr Cat Roberts and Joanna Ladlow)

- Legacy – handing over projects, supporting next Fellows, promoting the programme
- Continue to take on leadership / supervisory roles. Working in new wider network
- Seek more senior leadership positions