**Institution:** University of Sussex

**Unit of Assessment:** 1 – Clinical Medicine

**Title of case study:** ARK-Hospital Programme: Improving the NHS initiative on good antimicrobial stewardship in NHS acute Trusts

**Period when the underpinning research was undertaken:** 2014 – 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: |
|---|---|---|
| Prof Martin Llewelyn | Professor of Infectious Diseases | 2004 – present |
| Dr Jasmin Islam | NIHR Clinical Lecturer in Infection | 2018 – 2020 |
| Dr Katy Fidler | Senior Lecturer in Paediatric Infectious Diseases | 2008 – present |

**Period when the claimed impact occurred:** 2015 – 2020

**Is this case study continued from a case study submitted in 2014?** N

## 1. Summary of the impact

Research evidence from the multi-centre Antibiotic Review Kit (ARK)-Hospital Programme led to the development of a set of four interventions to promote early review and revision of antibiotic prescriptions in hospitals (24-72 hours after initial prescription), with the aim of stopping unnecessary antibiotic use. Llewelyn led the feasibility study of the ARK-Hospital interventions at the Brighton and Sussex University Hospital Trust and showed that over the 12-week pilot, the Trust's antibiotic stop rate increased from 9% to 36% with no associated adverse outcomes. Subsequently, Llewelyn coordinated the network of 40 ARK participating Trusts (representing 25% of all NHS acute hospitals), which achieved a three-fold increase in prescribers' decisions to stop unnecessary antibiotic treatments. One of the four interventions, the decision aid tool, has since been included in [text removed for publication]. The ARK study findings led Dr Hopkins (PHE) and Dr Ridge (NHSE) to recommend the national scale-up of the ARK interventions from 2020/21 to the Antimicrobial Resistance Programme Board.

## 2. Underpinning research

Hospital prescribing accounts for approximately 65% of broad-spectrum antibiotic (AB) use; these ABs have the greatest potential to drive future resistance. To ensure patients' early access to AB at admission, while reducing unnecessary AB use, the Department of Health (DH) introduced an initiative called 'Start Smart then Focus' (SSTF) in 2011: early administration of AB followed by active 'review & revision' 24-72 hours later. However, a survey of NHS pharmacists, conducted by Prof Llewelyn and colleagues at the Brighton and Sussex Medical School (BSMS) in July-December 2013, found that although 100/105 responding Trusts included early AB review in their policy/guidelines, relatively few (<10%) prescription revisions were made [**R1**]. The ARK-Hospital NIHR-funded Programme sought to address this problem by developing and evaluating a set of training and behavioural interventions to increase prescribers' compliance with AB 'review & revise' strategies in hospitals.

The five-year Programme, co-led by Prof Peto and Prof Walker at the University of Oxford, was conducted in collaboration with Prof Llewelyn at BSMS and Prof Yardley at the University of Southampton [**G1**]. Peto and Walker led the Programme management, and Yardley led on the behavioural change/qualitative research aspects. Llewelyn led on clinical aspects of AB prescribing, established the national network of 40 NHS Trusts participating in the evaluation of the ARK interventions and led the work package assessing the impact of the interventions in a cluster-randomised trial.

As part of the ARK-Hospital Programme, Llewelyn and team contributed to key background studies on the perceived barriers to 'review & revise' compliance. With Dr Islam, Llewelyn conducted a national survey to understand perceptions in relation to the AMR-CQUIN – introduced in 2016 by NHS England as a financial incentive to improve AB use in secondary care [**R2**]. The survey, conducted between December 2016 and March 2017, revealed staff concerns regarding the quality of the review at 24-72 hours and a lack of confidence in stopping AB if someone else initiated the prescription; a phenomenon known as 'prescribing etiquette'.

The study also analysed the Public Health England AB prescription surveillance data over the survey period. It showed that across all Trusts in England, only 8% of prescribed AB had a documented stop decision. These findings on AB usage in hospitals, and perceived barriers to 'review & revise' identified through qualitative research of health professionals (Yardley and team at Southampton), were used to develop a set of interventions to promote AB 'review & revise' [**R3; G1**]. Peto, Walker, Yardley and Llewelyn contributed equally to the development of the four ARK interventions. The design of the ARK interventions and their optimisation was completed through an iterative process of stakeholder engagement and piloting, involving the ARK-Hospital research team, patients and front-line hospital staff. The outcomes of these consultations were [**R3; G1**]:

- a brief online education module for health professionals which provided a rationale for 'review and revise' and addressed one of its key barriers – the belief about the need to 'complete the antibiotic course', challenged by Llewelyn and colleagues' British Medical Journal analysis 'The antibiotic course has had its day' [**R4**]
- a decision aid to support AB prescribing, the ARK decision aid, with compulsory requirement to record the degree of certainty surrounding the initial prescription and its review at 72 hours
- a structure for AB use audit and feedback sessions
- a patient leaflet.

Llewelyn and team led on the assessment of the feasibility and acceptability of introducing the four components of the ARK at BSUHT [**R5; G1**]. During the 12-week assessment period, the uptake of the ARK online tool, adoption of the decision aid into prescribing practice, and rates of decisions to stop AB at review by staff were measured. This feasibility study showed that the implementation of ARK was associated with a substantial and sustained increase in AB stop rates over the 12-week period, from 9% pre-implementation to 36% post-implementation.

A nationwide stepped-wedge randomised controlled trial is currently underway in 39 additional NHS Trusts to establish the impact of the ARK interventions on AB consumption and patient outcome [**R6; G1**]. Final data from the intervention evaluation will be available in summer 2021.

## 3. References to the research


**R1**. **Llewelyn, M. J.**, Hand, K., Hopkins, S., & Walker, A. S. (2015). Antibiotic policies in acute English NHS trusts: Implementation of 'Start Smart—Then Focus' and relationship with Clostridium difficile infection rates. *Journal of Antimicrobial Chemotherapy*, *70*(4), 1230–1235. https://doi.org/10.1093/jac/dku515

**R2**. **Islam, J.**, Ashiru-Oredope, D., Budd, E., Howard, P., Walker, A. S., Hopkins, S., & **Llewelyn, M. J.** (2018). A national quality incentive scheme to reduce antibiotic overuse in hospitals: Evaluation of perceptions and impact. *Journal of Antimicrobial Chemotherapy*, *73*(6), 1708–1713. https://doi.org/10.1093/jac/dky041

**R3**. Santillo, M., Sivyer, K., Krusche, A., Mowbray, F., Jones, N., Peto, T. E. A., Walker, A. S., **Llewelyn, M. J.**, Yardley, L., & ARK-Hospital. (2019). Intervention planning for Antibiotic Review Kit (ARK): A digital and behavioural intervention to safely review and reduce antibiotic prescriptions in acute and general medicine. *Journal of Antimicrobial Chemotherapy*, *74*(11), 3362–3370. https://doi.org/10.1093/jac/dkz333

**R4**. **Llewelyn, M. J.**, Fitzpatrick, J. M., Darwin, E., Sarah Tonkin-Crine, Gorton, C., Paul, J., Peto, T. E. A., Yardley, L., Hopkins, S., & Walker, A. S. (2017). The antibiotic course has had its day. *BMJ*, *358*, j3418. https://doi.org/10.1136/bmj.j3418

**R5**. Cross, E. L. A., Sivyer, K., Islam, J., Santillo, M., Mowbray, F., Peto, T. E. A., Walker, A. S., Yardley, L., & **Llewelyn, M. J.** (2019). Adaptation and implementation of the ARK (Antibiotic Review Kit) intervention to safely and substantially reduce antibiotic use in hospitals: A feasibility study. *Journal of Hospital Infection*, *103*(3), 268–275. https://doi.org/10.1016/j.jhin.2019.07.017

**R6**. Walker, A. S., Budgell, E., Laskawiec-Szkonter, M., Sivyer, K., Wordsworth, S., Quaddy, J., Santillo, M., Krusche, A., Roope, L. S. J., Bright, N., Mowbray, F., Jones, N., Hand, K., Rahman, N., Dobson, M., Hedley, E., Crook, D., Sharland, M., Roseveare, C., **Llewelyn, M.J.**, on behalf of the ARK trial team. (2019). Antibiotic Review Kit for Hospitals (ARK-

Hospital): Study protocol for a stepped-wedge cluster-randomised controlled trial. *Trials*, *20*(1), 421. https://doi.org/10.1186/s13063-019-3497-y

**Key Research Grants**

**G1**. Llewelyn, M.J. [Co-I]. (2016-2021). Antibiotic Reduction and Conservation in Hospitals (ARK-Hospital). [RP-PG-0514-20015] NIHR Programme Grants for Applied Research. Sussex Total £298,869; Total Award £2,649,834.

## 4. Details of the impact

The Antibiotic Review Kit (ARK)-Hospital Programme has provided the research-based evidence to develop a set of four interventions promoting and supporting hospital health professionals' adherence to the Department of Health 'review & revise' guidance, outcomes of which are described below. This contribution was recognised by Deputy Director of Public Health England (PHE), Healthcare Associated Infections and AMR, Dr Susan Hopkins:

> "The approach that ARK has developed to making finalised antibiotic prescribing decisions of "stop unless you can justify continue" incorporated in digital prescribing […] supported by prescriber education around antibiotic "review and revise" decisions […], supports the delivery of Dame Sally [Davies]'s vision [i.e. for a digital AB prescribing in hospitals]". [**S1**]

**Informing PHE's strategy on the implementation of the NHS 'Start Smart then Focus' to improve AB Stewardship in hospitals**

In June 2015, Dr Diane Ashiru-Oredope at PHE directly referred to Prof Llewelyn's research [**R1**] in her expert commentary in the NICE 'Eyes on Evidence' newsletter, which contextualises key new evidence that could signal a change in clinical practice. The research was specifically used to highlight the need for implementing and monitoring the 'focus' element of NHS 'Start smart then focus' to reduce unnecessary use of AB in NHS Trusts [**S2**]. In addition, the detailed overview of the AMR-CQUIN evaluation [**R2**] directly underpinned the conclusions of PHE's English Surveillance Programme on Antimicrobial Use and Resistance 2017 report, i.e. to explore changes in AB prescribing in acute Trusts, and develop resources and tools for hospital engagement with the AMR-CQUIN [**S1, S3**].

In a proposal put forward to the AMR Programme Board in December 2019, co-authored with Prof Llewelyn, Dr Susan Hopkins and Dr Keith Ridge (NHS England Chief Pharmaceutical Officer) used the findings of the ARK-Hospital Programme to recommend the roll-out of the ARK interventions across all NHS Trusts in England [**S1 & S4**]. This request was made in addition to the agreed decision by the AMR Programme Board in September 2019 for feedback letters addressed to acute Trusts CEOs, to include the requirements to use the ARK interventions as support for the 'Start smart then focus' initiative [**S1 & S4**].

Several factors led to Dr Hopkins and Dr Ridge's recommendation to the AMR Programme Board [**S1 & S4**]:

- the significant demand from ARK participating Trusts for national leadership to sustain the remarkable impact of the ARK interventions at their Trusts
- the ARK interventions directly addressing the UK AMR Strategy in relation to workforce development, by educating prescribers and non-prescribers involved in AB use about safe effective AB prescribing in hospitals, and how to put 'Start smart then focus' into practice
- its support of the relevant NICE Guidance (NICE NG15, Antimicrobial stewardship: systems and processes for effective antimicrobial medicine use) and Quality Statements (NICE QS121 Antimicrobial stewardship) for secondary care.

The COVID-19 situation has delayed the decision of the AMR Board in response to this application, but Dr Hopkins has confirmed (January 2021) that "work is continuing to ensure this is implemented over the next 12 months." [**S1**].

**Providing a sustainable and adaptable approach to implementing 'review & revise' in clinical practice**

By clarifying the conditions of the initial prescription, the ARK decision aid toolkit gave the reviewing team (often different from the team initiating the AB treatment) increased confidence in their decision to stop or continue the AB course at the 24-72 hours review point. The success of

the toolkit's implementation is illustrated by the feedback provided by participating NHS sites to the [text removed for publication] [**S5**].

In light of this overwhelming support, [text removed for publication] the ARK decision aid toolkit into its existing e-Prescribing system managed by WellSky, who control 60% of the pharmacy secondary care marketplace for medicines management e-platforms [**S6**]. Key elements of the research – the timing of data recording, their nature, auditing and reporting requirements – informed the majority of the new system design and operation, which now supports the ARK-informed behavioural shift from "continue unless there is evidence to stop" to "stop unless there is evidence to continue" [**S6**]. The updated system will be provided free of charge in all 50 large NHS Trusts currently using the WellSky e-Prescribing system [**S6**]. WellSky anticipates that the remaining 40% of the pharmacy secondary market will likely soon engage with their system in one form or another, notably due to the predicted NHS mandate to follow the ARK principles in terms of AB prescribing [**S6**].

**Enhancing prescribers' knowledge on shorter AB course duration and risks of AB overprescribing**

Between April 2017 and July 2019, a total of 7,444 Healthcare Professionals (HCPs) involved in AB use completed the online module at the 40 participating NHS sites [**S7**]. Out of the 40 sites, 8 (i.e. 5% of all acute Trusts) have now included the ARK online module in their e-learning platform, demonstrating their sustained commitment to this element of the ARK interventions as part of their standard practice [**S8**]. Since May 2019, the ARK brief online training module is provided free of charge to the NHS via two main platforms: the e-learning platform of NHS Health Education England and the British Society for Antibiotic Chemotherapy (BSAC). A total of 8,596 individuals completed the module between May 2019 and November 2020 [**S8**]. Feedback comments demonstrate the key role played by the course in increasing HCPs' knowledge about good AB stewardship and enabling them to re-think their current AB prescribing practice: "Evidence based, sensible, useful. Will change my practice" and "The course has increased my knowledge regarding antibiotic prescribing. It has equipped me to monitor antibiotic use in the patients I care for" [**S8**]. Dr Neil Powell, Consultant Antimicrobial Stewardship at the Royal Cornwall Hospital, and one of the ARK trial Champions, acknowledges that the online module is one of the main elements in the ARK interventions for promoting good AMR Stewardship to all HCPs involved in AB prescribing [**S9**]. As of November 2020, the module online package has been incorporated in 31 healthcare organisations' e-learning platforms, including 1 NHS Trust in Wales, 2 NHS Trusts in Northern Ireland, and 10 in Zambia, with the University Teaching Hospital in Zambia and the Ministry of Health among others [**S8**].

**Improving Antibiotic Stop Rate in all 40 NHS Trusts implementing the ARK interventions**

In the first NHS Trust to implement the ARK interventions, the Brighton and Sussex NHS Hospital Trust, AB stop rates (i.e. decisions to safely discontinue the initial AB prescription following its review at 72 hours) increased from 9% to 36% in hospitalised patients without any harmful effect [**R5**]. The Trust management adopted the interventions across the whole organisation following which AB consumption fell quarter on quarter for two years. In North Middlesex University Hospital – one of the 40 implementing sites and 6$^{th}$ highest consumer of AB out of the 153 NHS Acute Trusts – compliance with 72-hour reviews went from 63% at the start of ARK interventions implementation in May 2019 to 90% at the end of the 12-week evaluation [**S10**]. Stop rates at 72 hours rose from 10% to 20% within the same period. The Trust has projected savings of £35,000/year in drugs costs alone just through the increase in stop rates [**S10**]. Similarly, the stop rate at the Royal Cornwall Hospital went from 5-9% at the start of the ARK interventions implementation to 20% at the end of the 12-week period. This rate steadily increased to 24% in November 2019 [**S9**]. For both Trusts, the ARK audit tools and feedback sessions were key in driving this change in AB prescribing by HCPs, as it allowed them to assess in real time the effectiveness of the interventions and thus provide targeted support where required. This view is best illustrated in a quote from one of the ARK Champions at another participating NHS site:

> "[ARK] was a helpful tool and resources to enable us to do what we needed to do, in terms of antimicrobial stewardship. It's the activities that we wanted and needed to do, but ARK provided us with a framework for that." [**S11**]

Across the 39 other acute NHS Trusts that implemented ARK, AB stop rates increased by a median of 8% and up to 25% depending on how robustly the interventions were implemented. The participating Trusts have extended use of the ARK interventions beyond Acute Medicine and into clinical areas such as surgery, and to other Trust sites not involved in the original evaluation [**S1**].

**Informing change to national and international Antibiotic Awareness Campaign strategies and raising public awareness to AMR**

In its survey study of World Antibiotic Awareness Campaigns (WAAC), the WHO – referring to Prof Llewelyn's BMJ analysis [**R4**] – acknowledges:

> "The validity and usefulness of the 'Complete the course' message has, for instance, been questioned, since antibiotics are often prescribed unnecessarily and for too long, and the evidence for the impact of duration of treatment on AMR is weak." [**S12**]

Given these concerns, since 2017, the WHO has eliminated this message from WAA Week [**S12**]. The ARK findings, and successful implementation in all 40 participating sites, were especially fitting for the 2020 PHE World Antimicrobial Awareness Week and European Antibiotic Awareness Day in England, which focussed on avoiding inappropriate AB prescribing while working together to prevent serious infections – including COVID-19 [**S1**]. As a result, in its set of suggested actions to healthcare professionals, PHE recommended to "visit the Antibiotic Review Kit (ARK) website to engage with a range of resources designed to help all healthcare professionals to reduce antibiotic overuse in hospitals" [**S13**].

**5. Sources to corroborate the impact**

**S1**. Testimonial statement from Dr Hopkins Deputy Director of Public Health England leading on Healthcare Associated Infections and AMR
**S2**. NICE Eyes on the evidence, expert commentary authored by Dr Diane Ashiru-Oredope (PHE) June 2015
**S3**. PHE ESPAUR 2017 Report
**S4**. Proposal to the AMR Board made by Dr Hopkins (PHE) and Dr Ridge (NHS England) for the implementation of the ARK Intervention across all NHSE Trusts – December 2019
**S5**. Testimonial statement from [text removed for publication]
**S6**. Testimonial statement from Mr Steve Reggione, Head of Operations at WellSky
**S7**. ARK Hospital Programme Trial data on uptake of the online educational module at the 40 implementing sites (Prof. Llewelyn's data)
**S8**. BSAC ARK online educational module stats and quotes from learners. Sept-Nov 2020. (Excel format; available from HEI for audit)
**S9**. Testimonial statement from Neil Powell, Consultant Antimicrobial Pharmacist, Royal Cornwall Hospitals NHS Trust, and ARK Champion at the Trust.
**S10**. Testimonial statement from Mariyam Mirfenderesky, Consultant Microbiologist, North Middlesex University NHS Trust, London, and ARK Champion at the Trust.
**S11**. ARK Champions quotes from Prof Llewelyn's presentation at the UK Clinical Pharmacy Infection Network workshop (11 Oct 2019)
**S12**. Huttner B, *et al*. *BMJ Glob Health* 2019;4:e001239. doi:10.1136/bmjgh-2018-001239 Article showing the change in the WHO WAAC based on Llewelyn's BMJ 2017 analysis
**S13**. PDF of the PHE WAAC and EAAD toolkit for Healthcare Practitioners in England listing ARK toolkit as one of its supported initiatives to reduce AMR.