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Insights from the VICTORION-Spirit process evaluation

Interim report

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Authors

Wilson P, Elvey R, Mathieson A.

National Insitute for Health and Care Research (NIHR) Applied Research Collaboration Greater Manchester (ARC-GM) and The University of Manchester

Disclaimer

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1. Executive Summary

Identifying innovations that will benefit patients and ensuring their fast uptake in practice is a major global challenge. The cholesterol-lowering medication inclisiran▼ is one of the first products to be introduced through a population health approach to the NHS in England, in partnership with the NHS Accelerated Access Collaborative. In parallel, the VICTORION-Spirit study is taking a ground-breaking approach that harnesses implementation science to examine how best to deliver this novel treatment in primary care. So far, we have found:

- There is support from those delivering and receiving inclisiran that it should be available as a prescribing option in primary care for people when statins are not working.

- Patients generally found the process of arranging and attending appointments to be convenient and straightforward. There was a preference for receiving the injections at their local general practice, as opposed to travelling to another location.

- Delivery potentially entails some resource issues for practices. A lot of people are on statins, there will be challenges in identifying and then managing this population; all against a backdrop of significant workforce and workload pressures in primary care.

- Despite these, there was general consensus that primary care was 'the right place' for inclisiran prescribing and that delivery from here would be convenient for patients.

- Both patients and providers thought delivery could work as a practice nurse-led service and or could be incorporated as part of existing annual/ six monthly reviews.

- The costs of inclisiran were highlighted by participants and that their future prescribing will be guided by local Medicines Management Group decisions on local use. Many thought some form of incentive structure may be required to support prescribing in the longer term.

2. Context

Cardiovascular disease (CVD) is the leading cause of death in England, and is the largest cause of preventable death and disability in deprived areas. Reducing it is vital to improving people's health and meeting the NHS Long Term Plan goals. Secondary prevention of CVD has a crucial part to play and, effective lipid control is a vital part of any collective care approach to CVD prevention if wide-scale impact on outcomes is to be achieved.

Limiting health inequalities is also an NHS priority tackled by the Core20Plus5 initiative, where primary care can have a huge impact by preventing CVD.

To address this, the Academic Health Science Network (AHSN) is delivering a national lipids programme, which commenced in 2020/21, that will run for three years. The National Lipids Programme is part of the Collaborative Working population health agreement between NHS England (NHSE) and Novartis Pharmaceuticals UK and promotes use of lipid pathways in line with the NHS Accelerated Access Collaborative (AAC) NICE endorsed national guidance for lipid management.

The guidance was updated following publication of NICE TA 733, Inclisiran for treating primary hypercholesterolaemia or mixed dyslipidaemia. NICE recommends inclisiran as an option. As such, implementation of inclisiran as part of the national lipids programme uses eligiblity criteria that are different from the VICTORION-Spirit study inclusion criteria.

The programme aims to improve the management of cholesterol, increase the detection of those with familial hypercholesterolaemia and optimise the use of all medicines for patients on the cholesterol management pathway. The objectives are:

- Increase the number of people with measured cholesterol and to identify those with conditions that increase familial risk of hypercholesterolemia;
- Provide more treatment options to high-risk patients who remain at risk despite maximum tolerated statin therapy;
- Reduce health inequalities by ensuring a consistent, national approach to lipid management, using a NICE-endorsed clinical pathway;
- Reduce the risk of heart attacks and strokes occurring;
- Reduce the risk of admissions and re-admissions associated with CVD.

Most patients at high and very high risk of CVD are seen in primary care and barriers have been identified by the AHSN programme that are preventing implementation of the NICE-endorsed lipid pathways. Needs articulated by primary care organisations have highlighted that specialist resources are required to embed and implement the AAC NICE endorsed guidance. In response, clinical expert capacity is available and model pathways of care have been developed by the AHSNs to support conversations on pathway change and improvement. A patient search tool to support with case finding is available in GP systems, built in collaboration with NHS Digital.

3. VICTORION-Spirit

Challenges in getting proven innovations rapidly adopted into practice has long been a concern in health systems globally. The AAC has provided fresh impetus to tackling the barriers to real world adoption and provide faster access to novel technologies and products, ultimately to improve the health and care that people receive.

The cholesterol-lowering medication inclisiran is one of the first products to be implemented introduced through a population health approach by the NHS AAC. In parallel to the national implementation effort, VICTORION-Spirit (NCT04807400) is taking a ground-breaking approach that harnesses implementation science to examine how best to deliver this novel treatment in primary care. As the wider implementation of inclisiran is underway, this briefing presents interim findings from the process evaluation ahead of final study outcomes. Normally, the findings of a process evaluation are used to explain and contextualize the findings of the main study. Our aim here is to support decision making relating to the national implementation and to maximise the use of findings from the study as they emerge. A full analysis with outcomes will be presented as part of the main study final report which will be available in 2023.

VICTORION-Spirit has recruited 900 patients to assess the effect of nine months treatment with inclisiran with or without behavioural support, compared to usual care (existing lipid lowering therapy e.g. statin) with behavioural support. Patients included in the trial had elevated LDL-C or total cholesterol and had either pre-existing CVD or were at risk of atherosclerotic CVD. The trial is using what is known as a Type I Hybrid design where the focus is on testing an innovation in a pragmatic situation while gathering information on its 'implementability'. Type I hybrid designs are ideally suited to collecting data that can then be used to inform future implementation efforts, especially so in circumstances that may require new work flows or processes to be introduced.

As part of this study, researchers from the University of Manchester and the National Instiute for Health and Care Research (NIHR) Applied Research Collabration Greater Manchester (ARC-GM) have been undertaking the process evaluation element of the research. Process evaluations aim to provide a more detailed understanding of the delivery and effects of innovations within the real world conditions and populations. Undertaking a process evaluation can ensure that the drivers for implementation success are understood early so that efforts to implement more widely are evidence informed and that the chances of a sustained uptake are then maximised.

The VICTORION-Spirit process evaluation has focused on:

1. Exploring the views and experiences of those delivering and receiving Inclisiran.
2. Identifying barriers and enablers to integrating delivery within primary care.
3. Identifying 'core enabling ingredients' that can inform wider delivery across NHS.

4. Gathering insights

The VICTORION-Spirit process evaluation has gathered data from 97 interviews conducted with patients, relevant staff within participating GP practices, research nurses and with representatives from the AHSN network national lipids programme who have responsibility for the wider roll out of inclisiran in the NHS.

Interviews were conducted by two researchers using a semi-structured topic guide informed by the Consolidated Framework for Implementation Research (CFIR). CFIR is widely used in implementation research to guide the systematic assessment of barriers and enablers to adoption and spread. Using a determinants framework like CFIR provides a systematic basis for capturing and analysing patients', professionals' and commissioners' views on implementation processes. This can then be used to understand experience and the feasibility of different delivery models, and to inform decisions on their future use, in this case in primary care.

We interviewed a purposive sample of patients receiving inclisiran with or without behavioural support. Interviews included the patient's existing experience of managing high cholesterol; of taking part in the trial; of receiving the injection and attending the appointments; and where relevant, experience of the behavioural support programme. Provider interviews explored the structures, resources and processes required to embed inclisiran into routine general practice; any challenges to implementation; patients' response to inclisiran; and their views on future provision.

Interviews with representaties from a sample of four AHSNs covered their role in the national lipids management optimisation programme; their understanding of the role of inclisiran within the lipid management pathway; how the AHSN engages and supports stakeholders with regards to inclisiran; local drivers and barriers to the roll out of inclisiran; and views on the sustainability of current delivery models.

We conducted interviews between August 2021 and April 2022. All interviews were conducted via the telephone, audio-recorded and transcribed. Informed consent was obtained from all participants. This interim analysis utilises a rapid analysis approach developed specifically for this study. Compared to traditional qualitative methods, rapid analysis can be particularly useful within studies where there is a need to feedback to stakeholders and adjust implementation strategies accordingly in real time.

Our approach comprised: creating a summary template based on the five CFIR domains, with space for other observations or unexpected findings and 'key quotations'; test-driving, refining and finalising the summary template; completing the template soon after each interview using field notes; discussing analysis as a research team; transferring summaries to a matrix; and then using the summary matrix to inform the interim report. The following section summarises findings from interviews with those delivering and receiving Inclisiran as part of the VICTORION-Spirit study.

5. Early insights

5.1 Patient experiences

5.1.1 Living with high cholesterol and existing treatment

Patients were aware that they had high cholesterol, although this usually wasn't having an obvious impact on their day to day life and had typically been identified through blood tests during routine health checks or reviews, or at a time when they had experienced some other health problem which prompted diagnostic tests to be run. Some interviewees said they gave high cholesterol little thought as it was having no impact on their day to day life. Others felt concerned, aware of its potential to lead to CVD, or spoke about family histories of heart disease, their fears of this repeating and desire to stay as healthy as possible.

Most patients had been taking a statin for some time but their cholesterol was still raised. Several had been prescribed a statin and experienced side effects and swapped to another (a few had tried several different statins). Some generalised concerns about statins were mentioned – one had stopped taking statins for a while due to 'bad press', another had them prescribed but did not take them as he 'heard they were not good for him'. No side effects with current statins were mentioned. One patient disliked taking tablets in general. A few said they did sometimes forget to take their statin.

5.1.2 Receiving the injection

Participants generally found the process of arranging and attending the appointments straightforward. The booking process was 'easy', 'straightforward' and everything 'ran smoothly'. Appointments mostly matched expectations. General practice was a convenient location for all participants. They all found it easy to travel to and several mentioned that they preferred to receive the injections here, as opposed to travelling to another location, such as a hospital clinic. As injections were administered by GPs/nurses from the practices, patients often knew the person giving them the injection.

5.1.3 Receiving behavioural support

The behavioural support service was delivered by an established service based at Salford Royal Hospital (part of Northern Care Alliance NHS Fundation Trust). The service is a monthly telephone-based, lifestyle intervention delivered by non-clinical health advisors trained in motivational interviewing techniques. It aims to motivate and support patients to make effective choices for improving self-management through behaviour change, goal setting and empowerment. Advice about diet, exercise, and medication will be provided and where necessary about glucose management and smoking cessation.

This form of lifestyle coaching was a new type of intervention for most patients. The closest similarities in terms of past interventions that participants had experience of, was weight loss groups (weight watchers or similar). All were happy with receiving this component remotely, via the telephone, a few commented that they felt particularly comfortable with this, as opposed to having the conversations face to face, and thought it helped them to be

more open. For most patients, this intervention focussed on a plan for some weight loss and a few participants expressed that it would be nice to have 'weigh ins' in person – perhaps at the GP practice, as this would provide some external validation that they do not get when weighing themselves at home.

Participants generally expressed that they were already familiar with the overall subject matter of the behavioural support programme, that is, high cholesterol and the effect that diet and other lifestyle factors can have on this. However most had not participated in coaching in this area (or any other health related area) and several had been concerned it might be overly prescriptive or delivered in a judgemental way. In terms of the content of the sessions, some participants commented that there had been a lot of information, but generally agreed that it was communicated in a way that was easily understandable. In terms of the goal setting, they thought the goals were manageable and that having a longer term goal, broken down into smaller short term goals provided a workable structure.

Participants mentioned the social skills of the health advisors, saying they had been able to quickly build a rapport with them, that it was 'like talking to a friend'. Participants seemed to appreciate the combination of the 'informative' and 'motivational' elements – the printed materials were useful and the health advisors were knowledgeable, and patients also welcomed the moral support and chance to 'talk it through'. Some felt that information was not always tailored to the individual, sometimes resulting in disengagement.

5.1.4 Views on future provision

Most patients were keen to keep receiving inclisiran beyond the trial. In later interviews with participants, several who had their day 90 appointment had seen a reduction in LDL-C, which might explain this concordance.

Overall, there was a general consensus that general practice is the ideal place for delivery, that a nurse led (or health care assistant) service would be acceptable and that it would best fit as part of their existing annual/ six monthly reviews.

Most barriers highlighted related to the conduct of the trial rather than intervention itself. These included consent processes, the wait for and length of appointments and the number of people in the room. As this is a pragmatic study with eligibility criteria, a few patients were uncertain about whether they would be able to continue receiving inclisiran after the trial ended. Some also cited media representations of the potential cost to the NHS leading to a few to question whether this would affect future access generally.

5.2 Provider experiences

5.2.1 Existing management of high cholesterol

Supporting patients with high cholesterol was a regular part of the day to day work of all GPs. High cholesterol is often identified by blood tests done as part of routine care, such as

health checks, reviews for other long term conditions, or during searches/reviews of records.

Most patients with high cholesterol are managed in-house at general practices and statins are the main treatment prescribed. Several of the GPs mentioned that they had interests in relevant areas, such as preventative medicine, lipids, diabetes. GPs had some interaction with lipids clinics but this was limited; one found that although guidance recommended referring certain patients to lipid clinics, when he did the referrals were often declined and he was advised to prescribe statins himself.

Some GPs mentioned that lifestyle factors, in particular diet, were also important and some described a desire to encourage patients to make lifestyle changes, as far as possible, before prescribing medicines. However, finding time to discuss these with patients was difficult within the constraints of GP appointments.

Several GPs mentioned non-compliance with, resistance to and intolerance to statins as ongoing problems. The 'bad press' and 'misinformation' around statins and the difficulty of differentiating side effects from other problems contribute to an often negative public image. They had experienced patients' reluctance to take a medicine for a problem they can't see, or other 'strong' feelings; some of these patients had been persuaded to take stains 'after several consultations over several years'. One reported that in their own experience patients aged 80 and over were particularly resistant to being prescribed statins, and linked this to the relative lack of evidence on effectiveness in this age group.

5.2.2 Identifying and recruiting patients

In the study, the FARSITE software tool was used to search, identify and contact potentially eligible patients while preserving confidentiality . In FARSITE, which is compatible with all the major GP clinical systems, GPs don't run the searches as these are run centrally saving time and effort. Only the GP providing direct care to the patient is able to access the identifiable patient data and to decide whether or not to invite individual patients to participate in the study.

All GPs reported that they reviewed the list of potentially eligible patients generated by North West EHealth (NWEH) in FARSITE. GPs removed patients who were not suitable, for reasons not picked up by coding, such as being housebound, having memory problems, awaiting a cancer diagnosis, receiving palliative care, or who have a severe mental illness. Those patients whose GPs considered not to have a sufficient level of English to enable them to consent to participate in the study were also excluded at this stage. A GP at one of the larger practices was surprised when they did not meet their initial study enrolment targets after the first search and had to have it re-run. Another commented that the screening method meant that patients with an out of date LDL-C score in their records would be excluded by the FARSITE screen when they would actually have become eligible since their last blood test. This is suggestive of incomplete coded data at the general practice level.

5.2.3 Views on delivery

The requirement for anyone administering the injection was that they had to be Good Clinical Practice trained and compliant. This meant that at most practices, GP time had had to be made available for administration purposes. Despite this, inclisiran was generally seen as a useful addition to existing prescribing options. Several GPs mentioned that it may be best to deliver in conjunction with support for other health/lifestyle factors and that patients should try to address these, not just rely on a medicine.

Overall, GPs viewed the injection as familiar, simple, effective and well tolerated – and with a good evidence base. Most GPs had had direct experience of delivering the inclisiran injections, as part of ORION trial(s), and this helped with competence and confidence. As one GP described it, the VICTORION-Spirit trial was a 'natural progression'. GPs agreed that the injection was simple and straightforward to administer. One commented that the volume of fluid was slightly more than she had expected, but no problems were reported. All GPs felt comfortable with their patients receiving inclisiran as part of the trial, all agreed that it was effective and well tolerated (did not cause side effects). eductions in LDL-C at day 90 were helping to reinforce this view.

An amendment to the trial protocol was made allowing the injection to be given in the arm or thigh instead of the abdomen. Whilst the abdomen remained the preferred injection site, the arm or thigh was considered to be more familiar to patients and a choice should be given. GPs noted that having the injection in the arm was considered most familiar to participants and often preferable as most patients had recently had their COVID-19 vaccine and flu jab administered there. Some mentioned that administering the injection in the patient's arm also meant they did not have to adjust clothing, which some patients were not comfortable doing.

5.2.4 Views on sustainability

When asked about the future of inclisiran, beyond the trial, interviewees agreed that there were still large numbers of people with raised LDL-C that needed more treatment, and that inclisiran had the potential to address some of this need.

The resource implications for implementation beyond the trial were raised – whilst the intervention had run successfully at practices within the trial, this was limited to relatively small numbers of patients. GPs thought that higher numbers of patients eligible for inclisiran might be identified in the future and that this potentially higher throughput could affect the feasibility of delivery. Whilst the drug still had black triangle status, there would be a need to discuss the drug in detail with patients, that some of this discussion would need to be with a doctor (not a nurse) and that they would not have time for this. Limited and stretched resource in general practice was mentioned, in particular the issue of how to make space for the appointments. As one GP described it 'anything new that is introduced is at the expense of something else'.

Beyond the trial, some GPs said they would be comfortable to prescribe it for their patients, however they thought that other GPs, who were less familiar with it, would not be. Training

and education were suggested as necessary to raise GPs' knowledge of and confidence in using the medicine and this should include advice (and support) from lipidologists.

Despite this, there was general consensus that primary care was 'the right place' for inclisiran prescribing and delivery. An inclisiran service was seen as one that could fit or 'gel' well within general practice and that delivery from here would be convenient for patients. Interviewees offered various ideas and suggestions about how this might work in practice. In terms of delivery models, there was consensus that to be sustainable, inclisiran would not be delivered by GPs – and therefore not in the same way as it had been for most of the trial.

Several GPs mentioned that it would work well as a service led by nurses, health care assistants or assistant practitioners - nurses currently administer more injections than GPs and, would be more time efficient. Opinions differed however, regarding what this would look like in practice. Some thought there could be dedicated nurse-led clinics, whereas others thought it would work best if incorporated into patients' annual reviews. The latter would mean practices would only need to offer one extra appointment per patient per year, saving time. One interviewee argued that GPs would need to initiate the treatment but subsequent doses could then be administered by nurses. One GP cautioned that practice nurses were already 'overworked and under paid'.

The prescribing costs of inclisiran were mentioned by several GPs, with several noting that it was currently much more expensive than statins. Several GPs mentioned that they will be guided by local Medicines Management Group decisions on future local use. AHSN interviews highlight medicines optimisation leads as the key decision makers with regard to local uptake and highlight getting inclisiran on to formularies (green lit) has been challenging. Most interviewees thought that future prescribing would also need to be supported via a monetary incentive, Direct Enhanced Service or Local Enhanced Service. Despite this, a common view amongst participants was "prevention is better than cure" and that use of inclisiran may save spending in the long run.

Finally, it was highlighted that the eligibility criteria for the trial were broader than the NICE guideline recommendations, and that there remained a lack of long-term data on cardiovascular outcomes. There would be a need therefore, to narrow future practice prescribing in line with the population parameters recommended and supported by NICE.

6. Next steps

The VICTORION-Spirit study is due to complete in January 2023 with a full report combining trial outcomes and process evaluation findings available soon after. The NIHR ARC-GM are conducting a follow on study that will systematically document the implementation efforts by the AHSN network. Findings from this work will be available in 2023.

For more information on the VICTORION-Spirit study, please email: paul.wilson@manchester.ac.uk

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The information in this report is correct at the time of publication.