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Original Research Article

Identification of patients at risk of cardiovascular disease in Greater Manchester in the VICTORION-Spirit study

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ABSTRACT

Background: Inclisiran is a cholesterol-lowering small interfering RNA treatment licensed in the UK for lowering low-density lipoprotein cholesterol (LDL-C). VICTORION-Spirit (NCT04807400) is an implementation science study designed to provide evidence for inclisiran implementation within the National Health Service. The aim was to describe the process of patient identification employed in VICTORION-Spirit.
Methods: A Phase IIIb, multicentre, randomised controlled study, VICTORION-Spirit is evaluating inclisiran implementation in participants with atherosclerotic cardiovascular disease (ASCVD) or ASCVD-risk equivalents and elevated LDL-C. Feasibility Assessment and Recruitment System for Improving Trial Efficiency (FARSITE) software utilising natural language search functions identified patients who may benefit from inclisiran. FARSITE searches were performed within Salford, Manchester, Trafford and Bury Clinical Commissioning Groups to identify individuals with elevated LDL-C or total cholesterol and pre-existing cardiovascular disease (CVD) or at risk of ASCVD.
Results: FARSITE used 'total cholesterol >4 mmol/l' terminology rather than 'LDL-C'; the former yielded >3 times the number of eligible patients. The search for individuals with pre-existing CVD identified 24,196 people in a population of 560,969 (4.3%); including 'total cholesterol >4 mmol/l' identified 10,431 individuals with pre-existing CVD and elevated total cholesterol. Searches for individuals at risk of ASCVD identified 65,457 people, narrowing to 26,580 at risk of ASCVD plus elevated total cholesterol. The most discriminatory SNOMED concept codes and their prevalence within the dataset can inform national approaches to develop similar searches.
Conclusions: FARSITE searches employed in VICTORION-Spirit identified a population at risk of ASCVD in Greater Manchester, England, who may benefit from a cholesterol-lowering medication such as inclisiran.

Keywords: Inclisiran, Cardiovascular disease, Implementation science

INTRODUCTION

Cardiovascular disease (CVD) affects approximately 7 million people in the UK and is associated with 1 in 4 premature deaths.[1] It is a disease associated with significant health inequalities, with people in the most deprived 10% of the population almost twice as likely to die from CVD than those in the least deprived 10% of the population.[1]

Guidance for the primary prevention of CVD in the UK is provided by the lipid management pathway,[2] which advises that statin therapy should be considered in people without established CVD within five categories. These are: people aged ≤84 years and with QRISK ≥10% over the next 10 years; those with type 2 diabetes and with QRISK ≥10% over the next 10 years; those with type 1 diabetes, if they have ≥1 of the following: aged >40 years, have had diabetes for >10 years, have established nephropathy, have

other CVD risk factors; people with chronic kidney disease (CKD), estimated glomerular filtration rate [eGFR] <60 ml/min/1.73 m^2 and/or albuminuria; and people aged ≥85 years if appropriate, taking into consideration their comorbidities, frailty and life expectancy.

Inclisiran is a first-in-class, cholesterol-lowering small interfering RNA treatment that was approved in 2021 in the UK and licensed for lowering low-density lipoprotein cholesterol (LDL-C).[3,4] Inclisiran is indicated in adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia, as an adjunct to diet, and is intended for use either in combination with a statin or statin with other lipid-lowering therapies, or alone or in combination with other lipid-lowering therapies.[5] In clinical trials of patients at high risk for CVD with elevated LDL-C despite statin therapy at the maximum tolerated dose, inclisiran administered subcutaneously every 6 months was associated with reductions in LDL-C levels of approximately 50%.[6]

Primary care has a clear role within population health management strategies; people use primary care more than any other section of the healthcare system, allowing the sector unique access to data regarding the health of the population.[7] NHS England has chosen to implement such a population health management approach to target the large at-risk patient population with atherosclerotic cardiovascular disease (ASCVD).[8]

The VICTORION-Spirit study (NCT04807400) is a UK implementation science study designed to provide and assess evidence for the implementation of inclisiran within primary care in the NHS.[9] The study uses an established implementation science design (type 1 hybrid design)[10] and will focus on testing a clinical intervention in a real-world setting, that of primary care, while gathering evidence on its 'implementability'. It is anticipated that the delivery of inclisiran will be in primary care via general practitioners (GPs) working in collaboration with other healthcare professionals; therefore, patient identification and recruitment are an important component of the VICTORION-Spirit study design.

A primary principle of the VICTORION-Spirit study is that it is based on a population health approach using a primary care model of delivery, taking place in the setting in which inclisiran is intended to be implemented in clinical practice.[9] The patient population under study will be aligned with the licensed indication for inclisiran, intending to work with the population that will be affected by inclisiran in clinical practice and therefore likely to be of benefit to those patients. In this way, the study aims to address the significant health inequalities associated with CVD, which is aligned with the NHS England objective of levelling up.

The aim of the research described herein is to detail the process for identifying potential patients within the VICTORION-Spirit study, including the SNOMED Clinical Terms codes utilised, and to describe how this can inform clinical practice.

METHODS

Study design

VICTORION-Spirit (NCT04807400) is a pragmatic, type 1 hybrid effectiveness–implementation research study, designed to test and inform various implementation strategies. The Phase IIIb, multicentre, randomised controlled study, VICTORION-Spirit, will evaluate the implementation, patient experience and utility regarding inclisiran administration in people with ASCVD or ASCVD-risk equivalents and elevated LDL-C who are on established lipid-lowering medication or have been recommended lipid-lowering therapy but are unable to tolerate treatment. The primary objective of the trial is to demonstrate the superiority of inclisiran with or without behavioural support, compared with the standard of care (SOC) plus behavioural support, in a primary care setting, in the percentage reduction in LDL-C from baseline to day 270 in adults with elevated LDL-C. The study intends to randomise 900 eligible participants across 17 general practice centres in Greater Manchester, to 1 of 3 treatment groups (1:1:1 ratio) (Figure 1).[11] Participants in 'Group 1' will continue to receive lipid-lowering background therapy plus behavioural support; those in 'Group 2' will continue to receive lipid-lowering background therapy plus inclisiran; and participants in 'Group 3' will continue to receive lipid-lowering background therapy plus inclisiran plus behavioural support. This study is being conducted in accordance with the International Council for Harmonisation (ICH) Harmonised Tripartite Guidelines for Good Clinical Practice, with applicable local regulations, and the ethical principles set forth in the Declaration of Helsinki. An Independent Ethics Committee (South Central – Berkshire B Research Ethics Committee [21/SC/0040]) approved the study protocol, and all patients are required to provide written informed consent prior to participation in the study. The study period was from July 2021 (first patient first visit) to January 2023 (last patient last visit).

Overview of the FARSITE tool

The Feasibility Assessment and Recruitment System for Improving Trial Efficiency (FARSITE) tool is used to search and identify patients who may be eligible to participate in research opportunities while preserving patients' confidentiality. FARSITE was developed by NorthWest EHealth (NWEH) and is used by the local National Institute for Health and Care Research (NIHR) Clinical Research Network in Greater Manchester and by the Discover Now HDRUK hub in Northwest London. FARSITE software allows researchers to design and build trial protocols using anonymised data. The software is designed for use by clinicians and uses natural language search functions to provide an easy-to-use intuitive

interface (Figure 2). Once the study design has been finalised and all governance and ethical approvals are in place, the system can be used to alert participating primary care sites to identify patients within their practice who may be suitable to invite to participate in the trial. 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 under their care. Once the GP has reviewed the list of potentially eligible patients and excluded any at their discretion (e.g., rationale such as bereavement or infirmity), patients are sent a study invitation letter informing them that they may be eligible to enrol in the study. Telephone calls are then made to discuss participation and, for patients expressing an interest, appointments are made for patients to participate in interviews at the patient's GP practice. In this way, FARSITE protects patient confidentiality throughout the process.

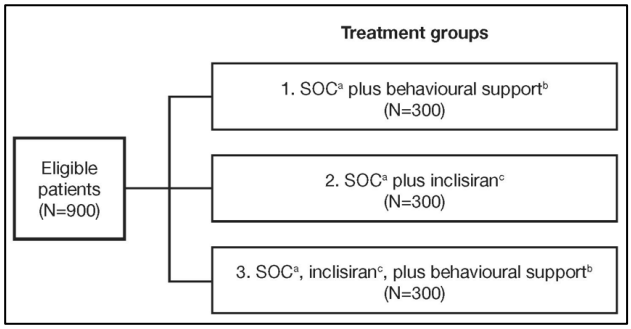


Figure 1: The VICTORION-Spirit study design.[11]

[a]Patients will receive SOC (statin and/or other lipid-lowering therapies) as background therapy; [b]the behavioural support service provided to patients will consist of a monthly telephone-based, lifestyle intervention to motivate and support patients to make effective choices for improving self-management through behaviour change, goal setting and empowerment; [c]subcutaneous inclisiran sodium 300 mg; SOC, standard of care

FARSITE searches

In order to recruit a pragmatic sample of potentially eligible people within the study geography, two separate FARSITE searches were conducted to identify all eligible patients, one to identify those individuals with pre-existing CVD and elevated LDL-C or total cholesterol, and a second to identify all individuals at risk of ASCVD and with elevated LDL-C or total cholesterol. These groups are mutually exclusive and are summed to provide the total number of potential eligible patients in the study region. Regarding CVD, individuals with codes for peripheral arterial disease were not included, as previously this coding provided an over-representation of significant disease. Searches were conducted on general practices who had signed up to FARSITE within the Salford, Manchester, Trafford and Bury Clinical Commissioning Groups, with a total population of 560,969.

Statin prescription was pragmatically assumed to be an indicator of high risk in the primary prevention group, because it should not have been offered by healthcare professionals otherwise. Previous trials of cholesterol-lowering therapies such as inclisiran have used LDL-C as a study endpoint,[6] since LDL-C correlates most closely with subsequent reduction in CVD risk. Therefore, inclusion criteria for the VICTORION-Spirit study were originally based on LDL-C criteria. However, prior research has shown that total cholesterol is requested far more frequently in primary care than a full lipid profile that includes a calculated LDL-C measurement; therefore, searches comparing LDL-C >2.6 mmol/l or total cholesterol >4 mmol/l were performed (described in the Results section). No formal statistical analysis was performed for this study; the analyses reported are descriptive.

RESULTS

Comparison of coding prevalence of total cholesterol and LDL-C

As noted above, searches comparing the use of total cholesterol and LDL-C coding were conducted, because, while previous studies have examined LDL-C as a study endpoint,[6] total cholesterol is requested more frequently in primary care.

Of a total population of 560,969 people, FARSITE searches using pre-existing CVD inclusion criteria returned 24,196 people. Adding the coding term LDL-C returned 3302 eligible patients, while adding the term 'total cholesterol >4 mmol/l' returned 10,431 eligible patients. Therefore, use of total cholesterol yielded more than 3 times the number of eligible patients compared with LDL-C, demonstrating that total cholesterol coding is much more prevalent than LDL-C within the general practice dataset. If these data reflect the national prevalence of CVD within England, this equates to ~1 million people based on total cholesterol and ~320,000 based on LDL-C.

FARSITE searches using an ASCVD equivalent inclusion criteria (type 2 diabetes AND/OR QRISK CVD 10-year risk score >20 AND/OR a currently prescribed statin) returned 65,457 people. Adding the term LDL-C returned 10,232 people, which after removing those with pre-existing CVD returned 8490 eligible patients. By comparison, adding 'total cholesterol >4 mmol/l' returned 33,671 people, and after removing those with pre-existing CVD returned 26,580 eligible patients. As for pre-existing CVD above, these searches demonstrated that use of total cholesterol coding within the general practice dataset is >3 times more prevalent than use of LDL-C; therefore, subsequent searches were performed using total cholesterol coding.

Study population identified by FARSITE searches

FARSITE searches identified 24,196 people with pre-existing CVD (Figure 3), in a population of 560,969

(4.3%). This is representative of 4313 patients per 100,000 across the total Salford, Manchester, Trafford and Bury Clinical Commissioning Groups. Across all age groups, men identified by these searches were most commonly aged 65–74 years (17.2%), while women were most commonly aged 75–84 years (12.6%) (Table 1). Narrowing the search to identify individuals with total cholesterol >4 mmol/l yielded a population of 10,431 patients with pre-existing CVD and elevated total cholesterol.

The second search, to identify all individuals at risk of ASCVD, returned 65,457 people with type 2 diabetes and/or QRISK CVD 10-year risk score >20 and/or a currently prescribed statin (Figure 3). Examining the demographic breakdown of this population, both men and women were most commonly within the 65–74 years age group (17.2% and 13.0% respectively) (Table 1). After narrowing the search to identify people with total cholesterol >4 mmol/l and exclude those with pre-existing CVD, this yielded a population of 26,580 patients at risk of ASCVD and with elevated total cholesterol.

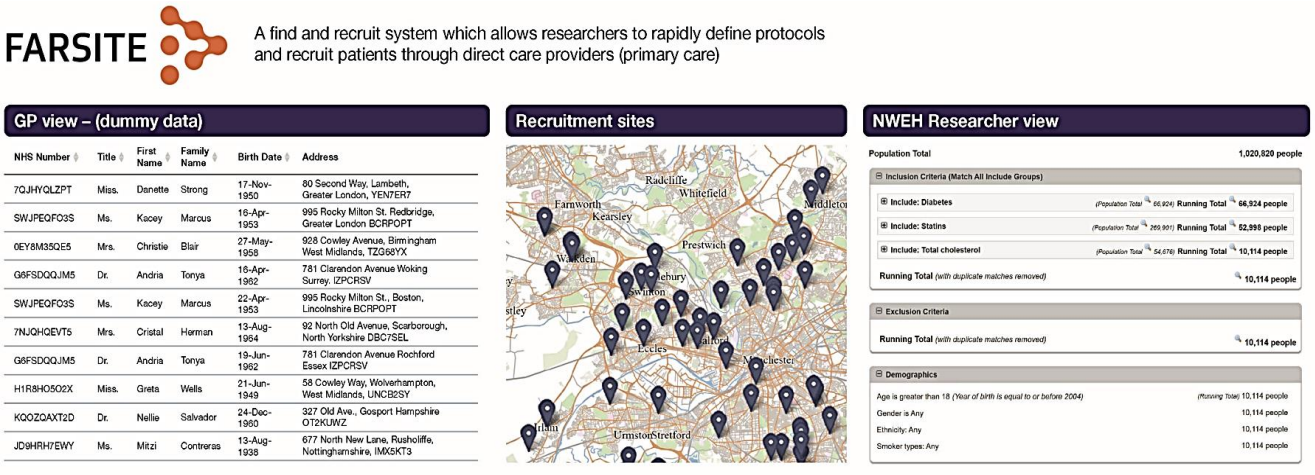
The most discriminatory codes and their prevalence with the data are provided in Table 2 and can be used to inform the national approach to develop searches for people at risk of ASCVD. Some codes had very high frequency within the data, such as 'coronary artery bypass graft' (89.2%). Other searches included SNOMED concept codes with greater variation in frequencies, such as cerebrovascular disease, represented in the data mainly by the codes 'transient cerebral ischaemia' (36.9%); 'stroke' (29.6%) and 'cerebrovascular disease' (11.8%).

The number of patients per practice who met the inclusion criteria for being at risk of ASCVD, with total cholesterol >4 mmol/l and excluding those with pre-existing CVD was calculated. The estimated average number of patients potentially eligible for recruitment across all 67 practices with results returned in the search is 397 patients. Of the top 30 general practices, this number ranged from 388 to 1506 patients.

Table 1: Demographic breakdown of people identified by FARSITE searches for: (a) pre-existing CVD; and (b) high risk of ASCVD.

Age group, years	Male, n (%)	Female, n (%)
(a) Pre-existing CVD		
0–4	<5 (0.00)	<5 (0.00)
5–16	16 (0.07)	12 (0.05)
17–24	11 (0.05)	10 (0.04)
25–34	55 (0.23)	47 (0.19)
35–44	206 (0.85)	143 (0.59)
45–54	958 (3.96)	548 (2.26)
55–64	2873 (11.87)	1444 (5.97)
65–74	4165 (17.21)	2379 (9.83)
75–84	3968 (16.40)	3051 (12.61)
85–89	1302 (5.38)	1246 (5.15)
90+	710 (2.93)	1044 (4.31)
Total	14,268 (58.97)	9928 (41.03)
(b) High risk of ASCVD		
0–4	<5 (0.00)	<5 (0.00)
5–16	17 (0.03)	8 (0.01)
17–24	24 (0.04)	33 (0.05)
25–34	212 (0.32)	199 (0.30)
35–44	1046 (1.60)	744 (1.14)
45–54	3919 (5.99)	2307 (3.52)
55–64	8695 (13.28)	5545 (8.47)
65–74	11,254 (17.19)	8482 (12.96)
75–84	8445 (12.90)	8278 (12.65)
85–89	1994 (3.05)	2310 (3.53)
90+	725 (1.11)	1217 (1.86)
Total	36,332 (55.51)	29,125 (44.49)

ASCVD, atherosclerotic cardiovascular disease; CVD, cardiovascular disease



NHS Number	Title	First Name	Family Name	Birth Date	Address
7QJHYQLZPT	Miss.	Danette	Strong	17-Nov-1950	80 Second Way, Lambeth, Greater London, YEN7ER7
SWJPEQFO3S	Ms.	Kacey	Marcus	16-Apr-1953	995 Rocky Milton St. Redbridge, Greater London BCRPOPT
0EY6M35QE5	Mrs.	Christie	Blair	27-May-1958	928 Cowley Avenue, Birmingham West Midlands, TZG68YX
G6FSDQQJM5	Dr.	Andria	Tonya	16-Apr-1962	781 Clarendon Avenue Woking Surrey. IZPCRSV
SWJPEQFO3S	Ms.	Kacey	Marcus	22-Apr-1953	995 Rocky Milton St., Boston, Lincolnshire BCRPOPT
7NJQHQEVT5	Mrs.	Cristal	Herman	13-Aug-1964	92 North Old Avenue, Scarborough, North Yorkshire DBC7SEL
G6FSDQQJM5	Dr.	Andria	Tonya	19-Jun-1962	781 Clarendon Avenue Rochford Essex IZPCRSV
H1R8HO5O2X	Miss.	Greta	Wells	21-Jun-1949	58 Cowley Way, Wolverhampton, West Midlands, UNCB2SY
KQOZQAXT2D	Dr.	Nellie	Salvador	24-Dec-1960	327 Old Ave., Gosport Hampshire OT2KUWZ
JD9HRH7EWY	Ms.	Mitzi	Contreras	13-Aug-1938	677 North New Lane, Rusholiffe, Nottinghamshire, IMX5KT3

Figure 2: Example of the FARSITE tool in use.

Table 2: Listing of common SNOMED concept codes (≥5%) and their prevalence in the FARSITE searches.

Concept ID	Name	Frequency, %
Common codes associated with pre-existing CVD		
Coronary artery bypass graft		
232717009	Coronary artery bypass graft	89.24
3546002	Aortocoronary artery bypass graft with saphenous vein graft	6.31
Stroke		
230690007	Stroke	82.29
230691006	CVA – cerebrovascular accident due to cerebral artery occlusion	7.07
Myocardial infarction		
57054005	Acute myocardial infarction	54.26
401314000	Acute non-ST segment elevation myocardial infarction	25.84
401303003	Acute ST segment elevation myocardial infarction	11.55
Coronary angioplasty		
11101003	Percutaneous transluminal coronary angioplasty	64.33
429639007	Percutaneous transluminal balloon angioplasty with insertion of stent into coronary artery	17.43
14201006	Coronary angioplasty by open chest approach	9.89
Ischaemic heart disease		
414545008	Ischaemic heart disease	51.51
194828000	Angina pectoris	18.82
57054005	Acute myocardial infarction	13.46
401314000	Acute non-ST segment elevation myocardial infarction	6.41
Cerebrovascular disease		
266257000	Transient cerebral ischaemia	36.89
230690007	Stroke	29.60
62914000	Cerebrovascular disease	11.78
Coronary arteriosclerosis		
53741008	Coronary arteriosclerosis	58.88
443502000	Coronary atherosclerosis	16.44
233817007	Triple vessel disease of the heart	11.73
194842008	Single coronary vessel disease	7.23
Common codes associated with ASCVD equivalent		
Type 2 diabetes mellitus		
44054006	Type 2 diabetes mellitus	98.96
QRISK cardiovascular disease 10-year risk calculator score		
763244005	QRISK cardiovascular disease 10-year risk calculator score	100.00
HMG-CoA reductase inhibitor		
320000009	Simvastatin 40mg tablets	29.79
320030001	Atorvastatin 20mg tablets	16.20
319997009	Simvastatin 20mg tablets	12.90
320031002	Atorvastatin 40mg tablets	12.03
320029006	Atorvastatin 10mg tablets	8.62
134489001	Atorvastatin 80mg tablets	6.22
Common codes associated with total cholesterol		
121868005	Total cholesterol measurement	98.89
Serum total cholesterol level		
994351000000103	Serum total cholesterol level	100.00
Serum cholesterol level		
1005671000000105	Serum cholesterol level	99.92
Common codes associated with LDL cholesterol		
Serum low-density lipoprotein cholesterol level		
1022191000000100	Serum low density lipoprotein cholesterol level	99.74
Low-density lipoprotein cholesterol measurement		
113079009	Low density lipoprotein cholesterol measurement	100.00
Calculated LDL (low-density lipoprotein) cholesterol level		
1014501000000104	Calculated LDL (low density lipoprotein) cholesterol level	100.00

ASCVD, atherosclerotic cardiovascular disease; CVA, cerebrovascular accident; CVD, cardiovascular disease; LDL, low-density lipoprotein

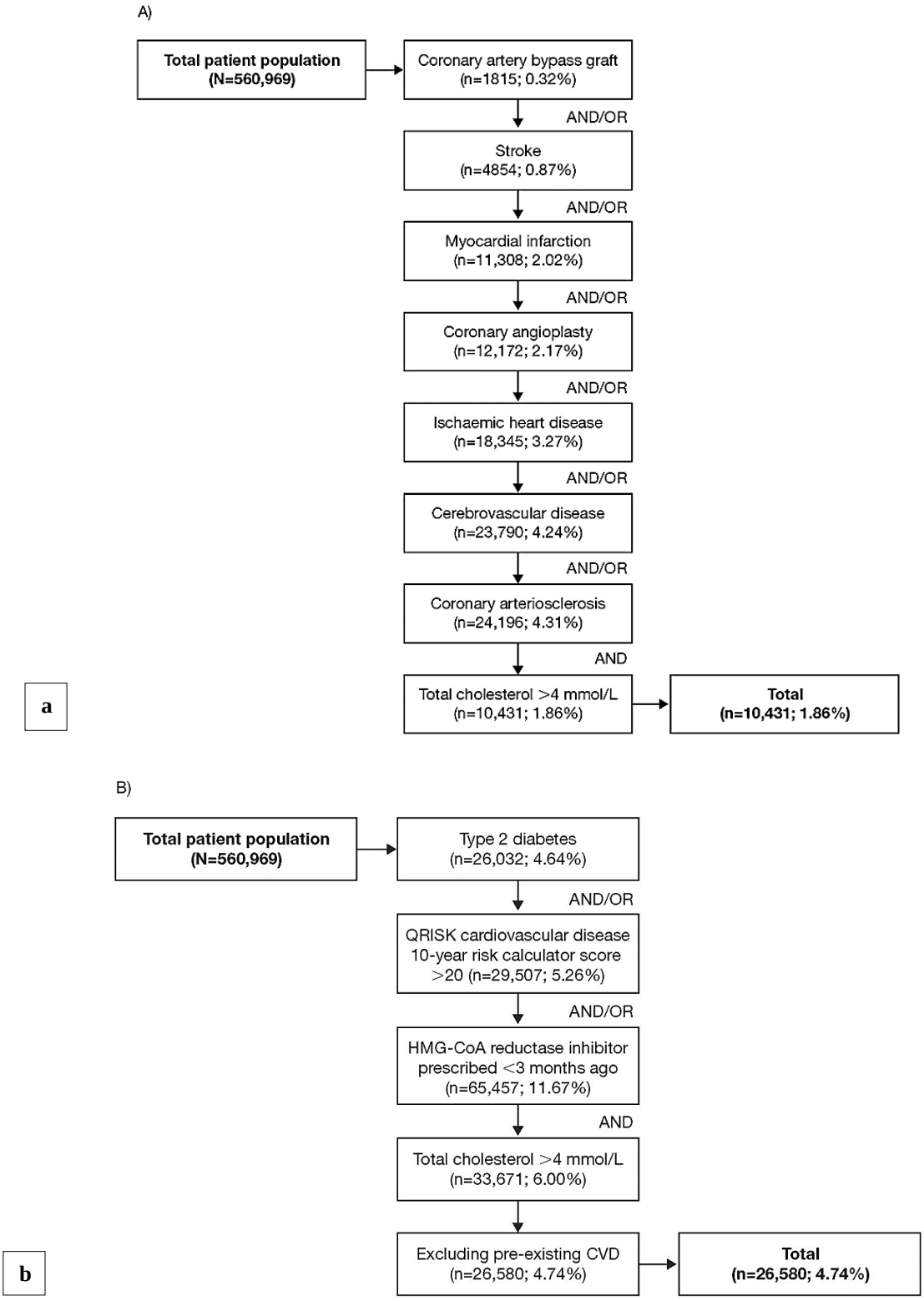


Figure 3: Flowchart of FARSITE search results for: (a) patients with pre-existing CVD; and (b) patients at high risk of ASCVD.

ASCVD: atherosclerotic cardiovascular disease; CVD: cardiovascular disease; HMG-CoA, 3-hydroxy-3-methylglutaryl coenzyme-A.

DISCUSSION

The VICTORION-Spirit study was designed to evaluate the implementation, patient experience and utility regarding inclisiran administration in participants with ASCVD or ASCVD-risk equivalents and elevated LDL-C. Additionally, the trial also aims to inform NHS England regarding appropriate patient identification strategies that

may be used to identify and treat patients in England with established ASCVD and elevated LDL-C who could benefit from inclisiran therapy. FARSITE software was developed by NWEH and was used to search and identity patients as part of the VICTORION-Spirit study. As detailed in the Methods and Results sections, the searches were conducted using total cholesterol as a surrogate for LDL-C because total cholesterol is more commonly requested in primary care. FARSITE searches conducted on general practices within the Salford, Manchester, Trafford and Bury Clinical Commissioning Groups of the Northwest of England identified 24,196 people with pre-existing CVD, within a population of 560,969 (4.3%). This figure closely matches the national recorded rate of CVD of 4%, lending support to the accuracy of the FARSITE tool in identifying individuals with CVD. A second search in the same population, aiming to identify all those individuals at high risk of ASCVD, identified 65,457 people with type 2 diabetes and/or QRISK CVD 10-year risk score >20 and/or a currently prescribed statin. This population is similar to the primary prevention population highlighted in the NHS lipid management pathway[2] who could potentially benefit from inclisiran therapy.

In order to achieve a positive impact on national cholesterol management, inclisiran initiation and management should be performed in primary care, where the patient population is predominantly located.[8,9] However, identifying those patients within the population who are at risk of ASCVD is associated with various challenges. One of these is variation in the consistency of query generation: general practice systems are capable of creating queries based on coded information within the system, and there are four general practice system suppliers in the UK. Although queries can be generated at a system-wide level, they are more commonly generated at a local or federation level, and there is no guarantee of consistency across these levels. Additionally, there is the possibility of incomplete coded data at the general practice level: previous research conducted by NWEH and The Medicines Company found that a significant number of events for patients with ASCVD that occurred in secondary care were not coded in primary care (personal communication/unpublished data). Finally, it can be challenging to access and engage with patients who resist intervention and are likely to be most in need of a cholesterol-lowering medication, and to gain the most benefit. While FARSITE can be used to easily identify appropriate patients, gaining their active participation in a clinical trial may be more difficult to achieve. An engagement strategy to encourage wide engagement across the community can be of great benefit in ensuring the success of a population health management approach.[9] Therefore, it will be of utmost importance to overcome these challenges in order to identify the population at risk of ASCVD, and likely to benefit from inclisiran treatment, as a route to reducing the health inequalities that exist in CVD.

Inclisiran is licensed for use in adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia, as an adjunct to diet.[5] The patient inclusion criteria of the VICTORION-Spirit study are aligned with this broad inclisiran indication to ensure that the study is as pragmatic as possible. The aim of such inclusion criteria was to recruit a population that will be affected by the intervention in clinical practice, rather than to select those patients most suitable for a standard clinical trial.[9]

The National Institute of Clinical Excellence (NICE) technology appraisal guidance (TAG) population is a subset of the population covered by the licensed indication of inclisiran.[12] Specifically, the NICE TAG states that inclisiran is recommended only in patients with a history of any of the following cardiovascular events: acute coronary syndrome (such as myocardial infarction or unstable angina needing hospitalisation), coronary or other arterial revascularisation procedures, coronary heart disease, ischaemic stroke, or peripheral arterial disease. Additionally, patients must have LDL-C concentrations persistently ≥2.6 mmol/l, despite maximum tolerated lipid-lowering therapy.[12] Guidance aligned to the NHS partnership is available via the Academic Health Science Networks (AHSN) networks[13,14] to aid identification of patients within primary care systems who may require lipid optimisation. The inclusion criteria and SNOMED concept codes within such an approach may be used to appropriately identify patients, as per the NICE TAG, whereby eligible patients should meet the following criteria: identify patients with a known history of any of the following cardiovascular events: acute coronary syndrome (e.g., myocardial infarction or unstable angina needing hospitalisation), coronary or other arterial revascularisation procedures, coronary heart disease, ischaemic stroke, or peripheral arterial disease; and identify patients from those found by these criteria who have LDL-C concentrations persistently ≥2.6 mmol/l despite maximum tolerated lipid-lowering therapy, ie, maximum tolerated statins with or without other lipid-lowering therapies, or other lipid-lowering therapies when statins are not tolerated or contraindicated.

The methodology employed to identify patients in the VICTORION-Spirit study has both strengths and limitations. A major strength is that the SNOMED concept codes identified by FARSITE software can readily be applied in future studies. The frequency and utility of these codes can facilitate wider implementation of the FARSITE tool, by utilising the most discriminatory codes with the highest frequency in the data and avoiding those with limited value. In this way, the tool can easily be implemented in other regions of the country to identify patients with pre-existing CVD or who are at risk of ASCVD. Notably, patient recruitment to the VICTORION-Spirit study has now completed and was achieved in a time frame of approximately 6 months, which lends considerable support to the utility of the

FARSITE patient identification system. A further strength is the geographic region in which the study was undertaken, as the Greater Manchester area is an ideal population in which to perform an implementation research study with a population health approach utilising primary care. Reasons for this include the existence of established primary care networks, the cohesion of the primary and secondary electronic medical record, and the established use of implementation research approaches in the Greater Manchester region.[9] While some may consider it a limitation that the study was based on only one geographic area, the applicability of this population to England overall has been demonstrated in prior research such as the Salford Lung Study in chronic obstructive pulmonary disease (COPD) by Pate et al.[15] That study found that the trial cohort was broadly comparable to the cohort of patients with COPD across England, with similarities in sex, comorbidities and previous COPD exacerbations.[15] Furthermore, the Greater Manchester population is known to be comparable to the wider population in terms of characteristics including ethnicity, age distribution, sex and the prevalence of chronic diseases.[16-18]

As noted earlier, limitations of the patient identification process include potential inconsistencies in the quality and coding of data in the primary care record. Furthermore, there can be a disconnect between the identification of an eligible patient population and achieving those patients' active participation in a clinical trial, as mentioned above.

CONCLUSION

To conclude, the FARSITE searches employed in the VICTORION-Spirit study have identified a population of people at risk of ASCVD in the Greater Manchester region of England who will potentially benefit from a cholesterol-lowering medication such as inclisiran. Such methodology can be used to inform the wider healthcare system regarding appropriate patient identification approaches, including coding, system search criteria and the proportion of patients meeting such criteria.[9] The information from the VICTORION-Spirit study will be used to inform the implementation of inclisiran into primary care, in addition to future implementation efforts.[9]

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Conflict of interest: JMG is the Chief Medical Officer for NorthWest EHealth and is Co-Clinical Director of the Greater Manchester NIHR Clinical Research Network. NorthWest EHealth received funding from Novartis for conducting the study. JM and CW are employees of NorthWest EHealth. PMW and PB are employees of The University of Manchester and are in receipt of funding from the National Institute for Health Research Applied Research Collaboration Greater Manchester (NIHR ARC-GM); The University of Manchester and NIHR ARC-GM received funding from Novartis via NorthWest EHealth for the work conducted as part of the VICTORION-Spirit study. SD is an employee of and owns shares in Novartis.
Ethical approval: The study was approved by the Institutional Ethics Committee

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