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PROTOCOL

LOTUS PROJECT

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FLuOridaTion for AdUltS

Version Number: 5.3
28.01.2022

NIHR PHR Project Number: NIHR128533

Full Study Title:	How effective and cost-effective is water fluoridation for adults? A 10-year retrospective cohort study
Short study title:	The F**L**u**O**rida**T**ion for Ad**U**lt**S** study (LOTUS)
Investigator:	Professor Iain A. Pretty Professor of Public Health Dentistry Division of Dentistry Faculty of Medicine Biology and Health University of Manchester Williams House Lloyd Street North Manchester M15 6SE
Objective:	To compare the effect of 10-year exposure to fluoridated water with no exposure on the number of invasive dental treatments, including restorations, endodontics or extractions, received by adults attending NHS dental practices**.**
Participants:	Adolescents and adults (>12 years) attending NHS dental practices in England
Structure:	Retrospective cohort study using routinely collected NHS Dental data (NHS BSA FP17 data) from 20010 to 2020.
Number of centres:	N/A – England
Primary Outcome:	Number of invasive dental treatments (restorations, endodontics, extractions) received by adults attending NHS dental practices over ten years of observation (2010-2020)
Sampling frame:	It is estimated that the records of 35.6 million individuals will be available for eligibility screening and matching
Sample size: analysis	It is estimated that 6.4 million records will be included in the
Duration of study:	Two and a half years (1st Feb 2020 to 31st Jul 2022)

Plain English Summary:

Although fluoridation of tap water, that is adding fluoride to the public water supply, has been strongly promoted by dental professionals since the 1950's, only about 10% of the people in England and Wales receive water containing close to the government recommended fluoride level of 1 mg/Litre. The fact that fewer children now have dental caries, and more adults manage to keep their permanent teeth into old age, is put down to using fluoride-containing toothpastes. As a result, compared to the early 1970s when almost complete loss of permanent teeth to caries by late childhood was common, we now have dental problems from caries slowly progressing through to late adult age instead. For many people, this involves repeated dental surgery visits, tooth drilling, filling and extractions, and the final outcome may still be complete tooth loss, with periods in between when there can be varying levels of pain, anxiety and financial loss, making life miserable.

Wider use of water fluoridation across both countries is thought to be a practical, low cost public health measure that could offer further lifetime benefit in combating this new form of adult caries. As no firm evidence for or against this has been published, a study of anonymised NHS dental care patient data is proposed. The main aim of the study is to take advantage of the patchy use of fluoridation in different regions to determine whether or not 10 years of exposure to fluoridated water is associated with fewer invasive dental treatments (fillings, crowns, root canal treatment, extractions etc.) compared to no exposure to fluoridated water. It will examine possible dental health benefits, along with fluoridation costs, to find out if it is value for money. It will also explore whether there is evidence of any disadvantage from people's socio- economic background, or where they live, which could be addressed by policy makers, local authorities, and communities.

This study has been designed with public and patients' involvement and engagement (PPIE) and these groups are represented on both the project Steering Committee and the Operational Management Group.

Emily Lam, PPI member of the LOTUS Operational Management Group

Version Control

Minor changes
- Normally can be made by an authorised member of staff and do not need formal approval.
- Information relating to minor changes can be summarised when a new version is issued.
- Indicated by points, for example, V1.1 contains a minor change to V1.0.

Major revisions
- An appropriate authority (Study Steering Committee and NIHR) should usually approve major revisions.
- Each major revision should contain a summary of all the minor changes that it incorporates, in the version control table
- Whole numbers are used to indicate a revised version, for example, V2.0 is a revision of V1.0.

Version number	Date Issued	Author	Version / update information	Date version approved and name of approving body
V1.0	1st November 2019	Deborah Moore	Version submitted to NIHR in pre-contract period. Name of "Study Steering Group" changed to "Study Steering Committee" in line with NIHR Project Oversight Group Nomination Form. This version not yet approved by Study Steering Committee and University of Manchester Ethical Approval is still required.	N/A
V2.0	11th Nov 2019	Deborah Moore	Version same as above except for the start date; which has been changed to 1st Feb 2020. Duration still 24 months, so end date is now 31st Jan 2022. Change approved by Sue Pargeter at NIHR.	N/A
V3.0	2nd December 2019	Deborah Moore	Ethical approval received from Manchester University Research Ethics. Added to section 3. 'Approval of the Protocol' (p7)	2nd Dec 2019. University of Manchester Research Ethics Committee
V4.0	12th March 2020	Deborah Moore	• Exclusion criteria number 1 (p9 and Appendix 1 Participant Flow Diagram) deleted: 1. Dental practices will be excluded from further analysis if they did not submit claims data for every year of observation 2009-2020 (to exclude those practices who may have	30th March 2020. University of Manchester Research Ethics Committee

			converted from NHS to private dentistry during the period of observation) • Wording under 'Section 3: Approval of the Protocol' amended to reflect that NHS BSA have requested Confidentiality Advisory Group section 251 approval. This version was submitted as an amendment for UREC Proportionate Ethical Review and **approved on 30th March 2020**	
V4.1	29th April 2020	Deborah Moore	Advised by **Faculty Research Practice Governance Manager ,** Lynne Macrae that we need to seek NHS REC approval if we are seeking CAG approval. Deleted from Section 3: Approval of the Protocol (p9) "Studies using previously collected, non-identifiable information are generally excluded from NHS Research Ethics Committee (REC) review, provided that the patients or service users are not identifiable to the research team in carrying out the research. The data must be anonymised or pseudo anonymised (IRAS filter question 4 guidance). We will receive the data only once it has been fully anonymised by the NHS BSA." Inserted: "In line with the Governance Arrangements for Research Ethics Committees (GAfREC), as CAG approval is being sought, the study was also submitted for NHS REC review. New sub-headings added to section 3.2 to reflect the different approvals that are required: 3.1 Ethical Approval by the University of Manchester 3.2 Approval by NHS Confidentiality Advisory Group 3.3 NHS Research Ethics Committee Approval	This version approved by North East, Tyne & Wear South NHS Research Ethics Committee on 27th May 2020. (Subject to approval by the Confidentiality Advisory group of the HRA). This version approved by CAG on 7th July 2020

			3.2 Approval of protocol by independent Study Steering Committee Added: "IRAS ID: 274705 ISRCTN Registration:96479279" To document header. Added University of Manchester Logo	
V5		DM	**Changes to study design or analysis:** 1. Added inclusion criteria re: NHS number 2. Removed two exclusion criteria: 2. Individuals that lived in both fluoridated and non-fluoridated areas, (i.e. partial exposure) will be excluded from further analysis. 3. Individuals in the exposed group for whom no suitable match can be found within the un-exposed group will be excluded Study flow diagram updated to reflect changes to inclusion and exclusion criteria and classification of exposed / un-exposed groups in this version. (APPENDIX 1) 3. Amendments to '4.5 Analysis' section requested to SSC on 20.05.2020: a) Clarity on the use of propensity scores for matching areas rather than individuals: "A generalized linear model with clustering by local authority area will be used to analyse the primary outcome of number of invasive dental treatments received during the period of observation. This model will include the area level propensity score and individual level covariates." 4. Amendments to section 4.3.2 'Proposed approach to exposure	This version and Data Flow Diagram V7 was approved by CAG as a 'notification' on 14.09.20 and by NHS REC Tyne and Wear South as a substantial amendment on 17.09.20. Substantial amendment 1.

			classification' requested by Study Steering Committee on 20.05.20: a) Threshold for exposed group changed to a period average of 0.7 mg f/l (removed 'in each year' specification). Final choice of mean or median for average will depend on distribution of data. b) Clarified that exposed group will include 'natural' and 'artificial' as long as water fluoride concentration is greater than or equal to 0.7 mg f/l for the observation period **Changes to protocol document:** 1. Added date of NHS REC favorable opinion to section 3 'Approval of the Protocol' 2. Added date of CAG fully supported approval to section 3 Approval of the Protocol' 3. Added new section 4.3.1 'Challenges and insight from recent studies'. Discussion of the issues related to mapping water fluoride exposure and how previous studies have addressed this. More detail provided in section 4. Added more detail to '4.4.1 Primary Outcome' on the rationale for choosing this measure 5. General amendments requested by Study Steering Committee on 20.05.2020: a) Observation period dates changed from 2009-2019 to T - 10 years to reflect that the data will cover the period of ten years prior to the day of data download by the NHS BSA. b) Clarified that we are using an individual measure of deprivation (NHS Dental charges exemption category)	

			as well as area-based IMD. (section 4.5.3) 6. Health economics amendments requested by the Study Steering committee on 20.05.2020: a) Health economics section updated to include return on investment calculations previously not mentioned b) Clarity that a societal perspective cannot be taken given the focus on routine data c) Clarity on the use of only the primary outcome for calculating ICER d) Clarity on sensitivity analyses regarding characteristics of the population and water fluoridation scheme e) Clarity on the use of a discount rate of 1.5% with additional sensitively analysis using 3.5% f) Clarity that decision analytic modelling is not covered by this protocol 7. Added a Plain English Summary authored by PPI study team member E. Lam, to p2 8) Section 4.2 'Population and Sampling' - Deleted: "The reason that we are limiting the period of observation to 10-years is that prior to 2010, the routine NHS dental data set did not include the number and types of dental treatment provided, only which 'Band' of treatment was claimed for by dentists." and added: "The exact dates for the cohort period will depend on the date that the NHS BSA undertakes the data download from within their systems. The NHS BSA hold identifiable data for a maximum of ten years. For this reason, the time period for the cohort will be referred to a T-10 years (T= the date	

			that the NHS BSA undertake the data download)." 9) Changes to wording of aim and objectives for clarity 2.1 Aim: To pragmatically assess the clinical and cost-effectiveness of water fluoridation for preventing dental treatment and improving oral health and in a contemporary population of adults, using a natural experiment design. 2.2 Primary Objective: • To compare the effect of 10-year exposure to fluoridated water with no exposure, on the number of invasive dental treatments, including restorations (fillings), endodontics or extractions, received by adults attending NHS dental practices over the same 10-year period 2.3 Secondary Objectives: • To evaluate the cost-effectiveness of water fluoridation in reducing the amount of invasive dental treatment in an adult population with 10-year exposure to fluoridated water when compared to a population with no exposure taking a patient, NHS and Local Authority public sector perspective • To measure the impact of 10-year exposure to water fluoridation on social inequalities in the oral health inequalities of adults attending NHS dentists.	
V5.1	20.01.21	DM	Added that protocol V5 has now been formally approved by the Study Steering Committee (Section 3.2)	

V5.2	18.05.2021	DM	Updated the wording of the PECOST summary (section 4.1) to reflect the changes to exposure classification that were approved by SSC (v5).	
V5.3	28.01.22	DM	Study end date changed on P1 to reflect six-month extension. Amendment to ethical approval (for the extension only) section 3.3. added	Amendment classed as non-notifiable.

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1. Introduction

1.1 Background

As the most common disease affecting humanity,(1) tooth decay is a major public health problem with significant costs for both the individual and society. Untreated decay can cause pain, sleepless nights, sepsis, overuse of antibiotics, embarrassment and the loss of productive workdays. As the disease claims progressively more tooth tissue throughout life its effects are cumulative and can lead to complete tooth loss; one of the leading causes of years lost to disability (1). Treatment can provoke severe anxiety for some, and is an uncomfortable experience for many others. Thirty per cent of UK adults report that having a tooth drilled would make them very or extremely anxious, and 27% would feel the same about a dental local anaesthetic injection (2). It is also very costly; the NHS in England spends around £3.4 billion per year on dental services, and patients contribute a further £653 million as 'out of pocket' expenses.(3) A significant proportion of this spend will be related to the treatment and repair of tooth decay, with more than 9 in 10 adults affected by their mid-thirties.(4) As with many chronic diseases, health inequalities exist and the number of teeth affected by decay is strongly associated with low income and deprivation.(5)

Despite almost universal experience of tooth decay by adulthood, oral health has improved greatly in the last forty years. This is considered to be due to the widespread use of fluoride toothpastes, which became available in the mid-1970s (6). Fluoride can now be applied in mouthwashes, gels, and varnishes; all of which are effective in preventing decay. As a result of increased exposure to fluoride, the proportion of 15-year-olds affected by decay has more than halved; from 97% in 1973 to 42% in 2013.(7) Correspondingly, in 1968 37% of all adults had no remaining natural teeth; in 2009, that figure was just 6%.(8) Increased fluoride exposure has significantly improved oral health in both adults and children, but it is now becoming accepted that fluoride slows down the decay process, rather than eliminates it.(9) Tooth decay has evolved from a rapidly progressing disease of childhood resulting in tooth extractions, to a slowly progressing disease with the majority of the burden experienced by adults. There is now a major evidence gap around the effectiveness of interventions to improve oral health and reduce tooth loss in adults, as the majority of studies to date have focused on prevention of caries in children.

The maintenance of teeth into old age should be celebrated, but it does bring new challenges. Reduced salivary flow, brought on by multiple medications, reduced dexterity, and cognitive decline can all drastically increase susceptibility of older people to decay. Furthermore, after a lifetime of repair, the teeth of older people are often heavily filled and fragile. Restoring new cavities or replacing old crumbling fillings in such teeth can be technically demanding and hence, costlier. With the number of people aged over 75 projected to double in the next 30 years (10), this changing pattern of dental disease has significant implications, both for the population, the NHS and care providers. A recent Healthwatch survey found that 8% of care home managers in one local authority had taken a resident to A&E because of dental problems (11). Community water fluoridation is the only dental health programme that has the potential to offer preventive benefits for all age groups. This presents a significant advantage over targeted fluoride programmes which are delivered to children through schools and nurseries or practice-based interventions delivered by dentists which are costly and available only to regular dental attenders. However, decision makers and the public are faced with a paucity of contemporary evidence on its clinical and cost-effectiveness particularly in adults.

1.2 Review of Existing Literature

The majority of studies on the effectiveness of water fluoridation have been conducted in children. This is in part because recruitment of adults poses greater challenges than for children, who can be accessed relatively easily through schools. A Cochrane systematic review '*Water Fluoridation for the Prevention of Dental Caries'* was published in 2015 and although the review inclusion criteria included studies with adults, none were found which met the inclusion criteria for study design. (12) This was limited to controlled before-after studies where the fluoridation status was the same at baseline and subsequently changed.(12) This inclusion criterion has been criticised as unrealistic for determining the effects in adults, because to assess the impact of life-time exposure to fluoridated water for 50-year-olds would require an interval of 50 years between baseline and outcome measurement.(13) Adequately controlled cohort studies or cross-sectional studies have been suggested as more appropriate study designs.(13,14) These designs would allow evaluation of lengthy exposure to fluoridated water in adults, without necessitating a life-time of prospective follow-up. They are also in line with the MRCs guidance on using natural experiments, or non-random allocation to intervention, to evaluate population health interventions.(15)

To inform this, a systematic literature search was undertaken to identify relevant studies in adults, using the broad search terms "*Water Fluoridation" AND "Adults*". The databases searched included: Medline, Dentistry & Oral Sciences Source, Web of Science, Cochrane Database, Google Scholar and WHO International Clinical Trials Registry. A systematic review and meta-analysis of studies investigating the effects of water fluoridation on adults was found, which suggested that the number of teeth affected by decay was reduced by 34.6% (95%CI: 12.6% to 51.0%) when including all studies, and by 27.2% (95% CI: 19.4% to 34.3%) when including only those studies published after 1975.(16) However, there was significant heterogeneity of study designs and the majority of included studies were cross-sectional, rather than longitudinal and did not adequately account for known confounding factors.

Several more recent studies from the US(17,18) and Australia (14,19–23) have taken a natural experiment approach to studying the effect of water fluoridation in adults. Exposure to the intervention has been allocated in a non-random way, for example by the participant living in fluoridated regions for a varying percentage of their lifetimes,(14,19–23) or by varied start dates and coverage of water fluoridation programmes.(17,18) Information on place of residence and dental outcomes has been collected using cross-sectional or longitudinal surveys.(14,19–23) A limitation of several of these studies is that they evaluate effects on a highly selective population,(17,19,20) experience substantial loss to follow-up,(23) or exclude large numbers of participants due to incomplete information on residential history.(14,21,22) Only one US study included information on dental treatment costs, and this was not relevant to the UK context because of the US health insurance system.(17) Additionally, as with many of the other studies, there was no consideration of factors which may be linked to both area of residence and tooth decay outcomes such as socio-economic status, ethnicity, sex, and frequency of dental attendance.(17) There are no on-going UK studies examining the effects of water fluoridation in adult populations.

The proposed study has been designed to meet the needs of decision-makers by taking a pragmatic, natural experiment approach but avoiding the pitfalls of the previous studies by using readily available routine data held by the NHS Business Services Authority (NHS BSA), in the form of dental records. (14,17–23) Individual exposure to water fluoridation will be identified by reference to home postcode held in the dental records. Using routine data has several advantages over designs using clinical examinations to assess outcomes. Firstly, recruiting adults to a clinical examination survey would require significant input in terms of recruitment, clinical facilities and clinician time, the costs of which would be prohibitive,

especially if the effects on different age groups are to be evaluated. Secondly, to answer the question of whether water fluoridation is cost-effective requires real world information on treatment decisions and use of resources, which are available in NHS dental datasets. Thirdly, as has been observed in previous studies, loss to follow-up,(23) selection bias, (14,21,22) and lack of generalisability(17,19,20) are common problems in prospective cohort studies. Finally, routine datasets often contain substantial amounts of data over a long period of time. Analysis of comprehensive datasets can facilitate the production of timely information for decision-makers.

1.3 Rationale for current study

Informing public health strategies to improve oral health: Several areas of the country are currently considering investing in water fluoridation to improve the dental health of their populations.(24,25) Cost-effectiveness is a key piece of information for policy-makers who are balancing competing priorities within limited budgets. In England, the decision on whether to implement a community water fluoridation scheme rests with local government.(26) To aid decision-makers, Public Health England have produced a Return on Investment (ROI) calculator for the top five recommended community oral health improvement programs. Water fluoridation currently comes out as the most cost-effective intervention, with a return of £21.98 predicted for every £1 invested after ten years. However, this ROI calculator uses the summary effect size from a Cochrane systematic review, where 70% of the studies were conducted prior to 1975 before the widespread adoption of fluoride toothpastes; and none of these studies included adults.(12) The size of the preventive effect, and therefore the cost-effectiveness of this intervention, is unknown in the current context.

Informing current and future provision of NHS dental services in England: The current NHS Dental Contract was introduced in 2006 in England and Wales. General Dental Practitioners (GDPs) are paid according to activity categorised into three broad Bands using a contractual currency known as 'Units of Dental Activity (UDAs)'. Practices are paid an agreed price per UDA provided (national average is approximately £25 per UDA) and have an annual UDA activity target to hit. A Band 1 course of treatment is worth one UDA and includes an examination, radiographs and a simple scale and polish. Band 2 courses of treatment are worth 3 UDAs and include restorations (fillings), extractions and root canal treatments, whilst more complex crowns, bridges and dentures attract twelve UDAs as a Band 3 course of treatment. Patient charges are tied to each Band of treatment: £21.60 for Band 1, £59.10 for Band 2, and £256.50 for Band 3.

Currently all four of the UK home countries are considering and evaluating reform of NHS dental contracts (27). TICKLE and WALSH have been co-applicants on a recently completed NIHR HS&DR study (HS&DR - 14/19/12) evaluating the impact on activity and costs of a move from Fee for Service remuneration model to a Capitation-based model (28). In all four of the home countries new approaches to NHS dental contract reform all seek to focus on prevention, expand access, reduce inequalities and contain costs. Studies by our research group show that the type and volume of activity provided by dentists is very sensitive to the way they are paid (29–32). The approach in England has been one of slow evolution with piloting of new contracts in a small number of selected practices over the last 5-6 years. However apart from these small number of practices the NHS system of remuneration for dentists has been stable over the last 10 years. The findings of this study and CATFISH will be fed into discussions on development of policy on contract reform, providing an understanding of the role that water fluoridation can play in achieving the policy objectives of

prevention, expanding access (through reducing the need for dental treatment), reducing inequalities and containing costs.

2. Research Objectives

2.1 Aim:

To pragmatically assess the clinical and cost-effectiveness of water fluoridation for preventing dental treatment and improving oral health and in a contemporary population of adults, using a natural experiment design.

2.2 Primary Objective:

- To compare the effect of 10-year exposure to fluoridated water with no exposure, on the number of invasive dental treatments, including restorations (fillings), endodontics or extractions, received by adults attending NHS dental practices, over the same 10-year-period.

2.3 Secondary Objectives:

- To evaluate the cost-effectiveness of water fluoridation in reducing the amount of invasive dental treatment in an adult population with 10-year exposure to fluoridated water when compared to a population with no exposure taking a public sector perspective

- To compare the impact of 10-year exposure to community water fluoridation with no exposure on the oral health (number of remaining natural teeth and decay experience) of adults attending NHS dental practices.

- To measure the impact of 10-year exposure to water fluoridation on social inequalities in the oral health of adults attending NHS dentists.

For the purposes of this application, ‘adults’ includes adults and adolescents who have their adult, permanent teeth. This occurs from 12 years of age (33).

3. Approval of the Protocol

3.1 Ethical Approval by the University of Manchester

This study was reviewed and approved by the University of Manchester Research ethics committee by proportionate review on the 2nd of December 2019.
Ref: 2019-8391-12289 02/12/2019

3.2 Approval by NHS Confidentiality Advisory Group

Because we are asking NHS BSA to carry out multiple data linkages (within their secure systems), prior to de-identification and subsequent transfer to UoM, NHS BSA have requested that we seek Confidentiality Advisory Group Section 251 approval.

The 'Fully supported outcome' approval letter was received from the Health Research Authority Confidentiality Advisory Group (CAG) on 07.06.2020.

CAG Reference: **20/CAG/0072**

Notification of substantial amendment 1 (V5) was approved on 14.09.20.

3.3 NHS Research Ethics Committee Approval

In line with the Governance Arrangements for Research Ethics Committees (GAfREC), as CAG approval is being sought, the study was also submitted for NHS REC review. A favourable ethical opinion was received from NHS HRA North East – Tyne and Wear South REC on the 27.05.2020, subject to approval by Confidentiality Advisory Group (CAG).

REC reference: 20/NE/0144.

Substantial amendment 1 (V5) approved on 17.09.20

Amendment 2 (extension only) classed as 'non-notifiable' by the HRA's study amendment tool on 28.01.22.

3.2 Approval of protocol by independent Study Steering Committee

Protocol V5 approved by the five SSC members present at the SSC meeting on 27.07.20, and approval by SSC member Mohsan Ahmed given 13.08.20 via email (to be quorate 6 members were required).

4. Study Design

The study is a retrospective cohort study using the routinely collected electronic records (NHS BSA data) of individuals receiving NHS dental care between the periods 2010 to 2020

4.1 Summary of the prosed study (PECOST):

Population:	Adults attending NHS dental practices in England
Exposure:	Individuals who have lived in LSOAs with an average fluoride concentration of greater than or equal to 0.7 mg f/l.
Comparison:	Individuals who have lived in LSOAs with an average fluoride concentration of less than 0.7 mg f/l.
Outcomes:	Dental treatments received, number of remaining natural teeth and caries experience (DMFT), cost-effectiveness, and impact on health inequalities.

Setting: Dental treatment data will be obtained from NHS BSA electronic dental health records
Timing: The period of observation is 2010 to 2020 (exact dates are T -10 years)

See Appendix 1 for participant Flow diagram.

4.2 Population and sampling:

The sampling frame for the data set will be all adolescents and adults aged over 12 years who attended an NHS dental practice in England within the last ten years. The exact dates for the cohort period will depend on the date that the NHS BSA undertakes the data download from within their systems. The NHS BSA hold identifiable data for a maximum of ten years. For this reason, the time period for the cohort will be referred to a T -10 years (T= the date that the NHS BSA undertake the data download).

The data sources and assumptions that we have used to derive estimates for the number of individuals that will form the sampling frame are outlined in Table 1. We estimate that the total number of unique individuals with dental data eligible for inclusion will be 34.8 million (Table 1, Row 4) (26,34–36).

Table 1 Estimated size of sampling frame available

1		**Receiving fluoridated water (11.5%)** (26)	**Not receiving fluoridated water (88.6%)** (26)	**Total**
2	**Population aged over 12 years on 1st Jan 2010** (34)	5,102,932	39,464,168	44,567,100
3	**Number who report they prefer NHS dentistry** 83.1% (35)	5,102,932 * 0.831= 4,240,536	39, 464,168 * 0.831= 32,794,723	37 035,259
4	**Number estimated to have attended dentist within last ten years** 94% (36)	4,240,536 * 0.94= **3,986,103**	32,794,723 * 0.94= **30,827,039**	**34,813,142**

Using this sampling frame (estimated to be 34.8 million), the following inclusion and exclusion criteria will be applied by the NHS BSA to select the study cohort:

Inclusion:

1. Dental records that can be assigned to a unique individual using the combination of NHS BSA Identifier (initial, surname, gender, D.O.B) and NHS number

Exclusion:

1. Individuals will be excluded from further analysis if they do not have at least two episodes of dental attendance, within the ten-year observation period (T – 10-years).

Preliminary scoping work undertaken by NHS BSA, suggests that approximately 18 million unique individuals will meet the study inclusion and exclusion criteria.

4.3 Determination of water fluoridation exposure status

4.3.1 Challenges and insights from recent studies

Water fluoridation is an intervention delivered on a geographical level, which makes assigning exposure status to individuals challenging and vulnerable to miss-classification. Any method must consider where the individual resides, alongside some knowledge of the geographic coverage of the fluoridated water supply. Even for studies involving children, where the recall periods are relatively short, obtaining accurate residential histories can be difficult. For adults, the recall periods are potentially much longer. Matching addresses to the coverage of fluoridated water is an additional challenge, because the geographical units used to describe a water of a "similar nature and treatment" (water supply zones) do not align with any other administrative geographies (37,38). Furthermore, names and boundaries of water supply zones (WSZ) may change over time (37,38). Regulations specify that water companies must review their WSZs annually, to ensure they contain water that is relatively uniform, from one source, and that the population covered does not exceed 100,000 (37,38). Any zones that no longer meet these requirements must be split into new zones or merged.

UK legislation specifies that the health effects of water fluoridation programmes in England must be reported on every four years from 2014. There have been two monitoring reports published to date, in 2014 and 2018. These reports have taken an ecological approach, but the methods used to categorise fluoridation exposure offer valuable insights for the present study. Both monitoring reports have approximated WSZs onto standard national geographies (lower super output areas, or LSOAs) using Geographic Information System (GIS) mapping (39,40). The reports state that the maps, along with details on which WSZs were included in a fluoridation programme, were supplied by the U.K. water regulator, the Drinking Water Inspectorate (DWI) (39,40). WSZs were then were approximated to LSOAs by using the most heavily populated point of the LSOA (the population-weighted centroid) as the matching point. Population-weighted centroid files for LSOAs are supplied by the Office for National Statistics, using population data from the 2011 census (41). In the 2014 report, lower-tier local authorities were classified as 'fluoridated' if more than 50% of their component LSOAs were situated within a WSZ that was flagged as being part of fluoridation scheme, i.e. the exposure variable was binary (40).

In the 2018 report, a more sophisticated method of measuring exposure was used. Instead of assigning water fluoridation as a binary variable, the water fluoride concentration (annual mean milligrams of fluoride per litre (mg f/l)) was taken-into-account, using annual water quality sampling records, taken from within each WSZ, supplied by the DWI (39). Additionally, in the 2018 report, a defined exposure period was specified for each outcome. For example, the exposure period for caries in five-year-olds (measured in 2014-5) was 2009-2014. The

annual water fluoride concentration for each exposure period for each WSZ was condensed into a grand-mean (mg f/l). The grand means of fluoride concentration for the exposure period were then applied to LSOAs, using the population-weighted centroid method (41). For analysis at larger administrative geographies, for example, lower tier local authorities, the grand means of the constituent LSOAs were combined and weighted according to proportion of population they contained. The grand means (mg f/l) for each geography were then collapsed into five categories: 0.0-<0.1mg/l, 0.1-<0.2mg/l, 0.2-<0.4mg/l, 0.4-<0.7mg/l, ≥0.7mg/l. For the main a-priori analysis of the effect of water fluoridation on dental caries, the exposed group was defined as LSOAs with 'public water supplies with a concentration of fluoride of at least 0.7mg/l, where fluoride was adjusted as part of a fluoridation scheme'. The non-exposed group were defined as any LSOAs where the concentration of fluoride was <0.2 mg/l (even if the LSOA was intended to be part of a water fluoridation programme).

The advantage of using the more detailed approach to exposure classification that was used in the 2018 report is that variation in water fluoride dose control, over time and across areas, can be examined. Achieved fluoride concentration at the consumer's tap (within the WSZ) is important, because there are some water fluoridation plants which have had periods of inactivity, or have been producing water which is sub-optimally fluoridated, some for a number of years (39,42). This may be due to equipment failures, difficulties in sourcing fluoride chemicals, or extreme weather events. It could also be due to mixing of water supplies in the network, i.e. some WSZs may receive a mixture of water that is supplied by both fluoridated and non-fluoridated treatment plants; this may be dependent on re-routing of water supplies during periods of drought.

To illustrate the magnitude of this variation, Table 8 in the 2018 report shows that between 2005 and 2015, of the 6.4 million people living in an LSOA that was approximated to a WSZ flagged as being part of a fluoridation programme, 1.4 million (22%) were receiving water that contained sub-optimal fluoride levels for caries prevention (0.2-<0.7 mg f/l) (39). The impact of this variation was examined in post-hoc analyses. The authors identified an overall (though not smoothly linear) trend, whereby the crude odds of caries experience decreased with increasing fluoride concentration (39). This trend was evident even when moving from the lowest concentration category (0.0-<0.1mg/l) to the next lowest (0.1-<0.2mg/l), i.e. there was no 'threshold' effect identified. However, even with this more detailed methodology, there will still be miss-classification of exposure for those in the population who reside on the borders of LSOAs that straddle two WSZs, because of the approximation involved in matching WSZs to LSOAs.

The approach used in the 2014 monitoring report, of classifying lower-tier local authorities as fluoridated if >50% of their constituent LSOAs were intended to be in receipt of fluoridated water, is at even greater risk of miss-classification, due to geographical approximation, sub-optimal operation of fluoridated water dosing systems, and mixing of fluoridated and non-fluoridated water supplies. Greater miss-classification of exposure would have the effect of blurring the difference that water fluoridation makes, resulting in a smaller difference between groups. Furthermore, with any analysis at the ecological level, there must also be an acceptance that individuals who contributed to the outcomes measured may not have been resident in the area for the defined exposure period, thus having a different exposure profile. Recent studies in Australia that have examined both exposure and outcomes on an individual basis have combined detailed knowledge of annual water fluoride concentrations with residential histories (14,19–22,43,44). However, in most of these studies, incomplete

residential histories have resulted in the exclusion of relatively large proportions of participants (15-30%)(14,21,22,43,44).

4.3.2 Proposed approach to exposure classification

We propose to quantify exposure to water fluoridation for individuals, for a defined 10-year exposure period (T – 10-years). It is accepted that we do not know where the participants have lived prior to the ten-year period, and what their exposure to water fluoridation has been historically. In view of the main method of action of fluoride now being understood to be topical (45), and the fact that caries has been estimated to progresses at a rate of around 0.8-1.2 new surfaces per year in adults (4,46,47), we would expect to see some difference in the number of dental treatments received due to new caries over a period of ten years, even for those who moved into the fluoridated region at the start of the observation period. Of course, there will be a proportion of participants who have been resident for much longer than 10 years in either a fluoridated or non-fluoridated region. This means any observed differences in outcomes may be a result of longer exposure times (anything from ten years up to lifetime), which we will need to reflect in the write up of our results. The advantage of this pragmatic approach is that we do not need to restrict our sample to participants who have lived in fluoridated or non-fluoridated regions since childhood. Such a criterion would make any study extremely difficult to recruit to, resulting in a small sample size (48) and would also result in a skewed sample that is unlikely to be generalisable to the wider population.

To create a 10-year water fluoridation exposure variable for each individual, we will need to combine information on residential history with information on water fluoridation coverage. The NHS BSA dental record contains the patient's address at every course of treatment, which avoids the difficulties of relying on participant recall that previous studies have encountered (14,21,22,43,44). The NHS BSA will link each recorded address to LSOA using publicly available lookup files supplied by the Office for National Statistics (ONS). We will assume that the patient has remained living in the same LSOA for each year, until a new home address LSOA is recorded in the BSA dataset. Miss-classification of place of residence could occur if patients move into a fluoridated or non-fluoridated area for a period but do not attend for dental treatment (thereby updating their address in the dental record). However, there is no reason to suppose that incorrect recording of place of residence will be linked to receipt of water fluoridation, so any miss-classification in exposure arising in this way would be non-differential, i.e. the same in both groups.

In terms of quantifying water fluoridation coverage over the ten-year exposure period, we would prefer to take the most detailed approach possible, calculating a 10-year water fluoride concentration variable for each participant, using water fluoride concentration data (mg f/l) for each Water Supply Zone (WSZ) in England. Preliminary enquiries have revealed that the Drinking Water Inspectorate (DWI) is not able to supply these centrally for the whole of England (as they did for the 2014 and 2018 statutory water fluoridation health monitoring reports (39,40)). The DWI have also advised that they do not hold information on which WSZs in England are 'flagged' as receiving fluoridated water as was described in the 2014 and 2018 PHE water fluoridation health monitoring reports (39,40). Therefore, we will need to approach each of the 25 water companies in England separately for the annual water fluoride concentration data that they hold for each WSZ, and the GIS maps of the WSZs. The Environmental Information Regulations (EIR) 2004 (SI 2004 No. 3391) provides a statutory right of access to environmental information held by UK public authorities. We intend to make requests to the water companies under these regulations.

We plan to match annual water fluoride concentrations for each WSZ to LSOA geographies, using the same population-weighted centroid method that was used in the 2014 and 2018 statutory water fluoridation health monitoring reports (39,40). After we have approximated the geographies, we will create a ten-year exposure profile (mg f/l) for each individual, based on how many years they lived within each LSOA, and what the annual water fluoride concentration was for that LSOA during that time period.

Depending on the distribution of these data, we will either summarise the average 10-year water fluoridation exposure variable using 10-year mean and standard deviation, or 10-year median and IQR.

For main analysis, we will group individual participants according to their personal residential water fluoride concentration over the ten-year period (T – 10-years):

- **The exposed group:** Individuals who have lived in LSOAs with an average fluoride concentration of greater than or equal to 0.7 mg f/l. This is estimated to be ~10% of English population (39).

- **The un-exposed group:** Individuals who have lived in LSOAs with an average fluoride concentration of less than 0.7 mg f/l. This is estimated to be ~90% of English population (39)).

This approach to exposure classification will not differentiate between fluoride that is in the water as a result of geology (naturally fluoridated), or as a result of a public health programme (artificially fluoridated). However, variability in implementation of water fluoridation programmes and the effect of achieved fluoride concentration is important and will be considered in ancillary analyses.

4.4 Outcomes

Our choice of outcome measures has been informed by the patient and public engagement undertaken during the development of this application, and the Medical Research Council (MRC) recommendation in 2002 that researchers must consider:

> *"Economic impacts and the effects of fluoridation on health and wellbeing beyond the usual measures of decayed, missing and filled teeth"* (49).

Avoiding the discomfort and anxiety of dental treatment, as well as out-of-pocket expenses due NHS dental patient charges were mentioned often as reasons why it was important to have good oral health during the patient and public engagement to develop this protocol. Furthermore, any cost-effectiveness analysis of the health effects of water fluoridation must consider real-life information on dental resources use.

We recognise that a proportion of dental care in the UK is carried out privately, and we will not be able to account for this treatment as it is not included in the NHS BSA database. The G.P. patient survey reports that the proportion of respondents who prefer to use private dentistry varies by area, ranging from 7.8% in the North east, to 14.6% in London (35). However, we will still be able to draw conclusions regarding the effect of water fluoridation on resource use in NHS dental services, consistent with the public sector perspective of our health economic approach.

4.4.1 Primary outcome:

- Number of invasive dental treatments (restorations, endodontics, extractions) received by adults attending NHS dental practices over ten years of observation (T-10 years)

Using 'number of invasive dental treatments' as our primary outcome measure has the benefit that it is that it is sensitive to the long-term progression and consequences of dental caries in a way that the traditional epidemiological caries measures (DMFT/S) are not. Caries is usually measured by counting the number of Decayed, Missing, and Filled Teeth (DMFT), or Surfaces (DMFS) that a person has. A mean DMFT or DMFS can then be created for groups. Disease progression can be recorded in how the count or mean increases over time. These measures have mainly been used in studies which include children.

However, in older adults, DMFT/S have been shown to be insensitive where new caries lesions occur on teeth or surfaces that have previously been affected and treated (and therefore have already contributed to the DMFT/S count) (22). This is termed the 'saturation' or 'ceiling effect'. This effect was observed in a recent study of the effects of water fluoridation in older adults in Australia, where the authors found a protective effect in the younger age groups, but not in those over the age of 45, which they attributed to saturation in the DMFS outcome measure (22).

Furthermore, a large proportion of invasive dental treatments are not due to *new* caries but are necessary to repair old fillings and cracked teeth that have been weakened by previous caries and fillings. Repeated repairs of failed fillings are a long-term consequence of dental caries that add to the burden of interventions that patients wish to avoid. Lifetime repairs also need to be accounted for in in economic models. Traditional epidemiological measures (DMFT/S) do not capture this important real-life consequence of caries.

We accept that some invasive dental treatments such as extractions are due to other pathologies, such as periodontitis (gum disease). Some fillings are a result of erosive tooth wear, teeth grinding and dental trauma. However, we would expect that these non-caries reasons for dental treatment will be similarly distributed in all exposure categories (after control of confounding factors), so that we should still be able to identify any differences associated with water fluoridation.

Participants who have lived in areas receiving optimally fluoridated water for longer than the 10-year exposure monitoring period may have a lower past caries experience and correspondingly, fewer fillings on entry to the study observation period (2010). This could mean they may have a lower potential need for repairs and re-treatments over the ten-years. As described in section 4.3.2 this is not necessarily a study limitation, but it will need to be considered when interpreting the potential benefit from living in an optimally fluoridated area for 10 years (as many study participants are likely to have lived in the same region for longer than 10 years).

4.4.2 Secondary outcomes:

- Mean cost per episode of invasive dental treatment avoided
- Total number of natural remaining teeth (routinely recorded in BSA dataset from 2017)
- Total number of teeth affected by decay (DMFT) (routinely recorded in BSA dataset from 2017)

The DMFT of NHS dental patients has been included in the NHS dental dataset since 2017. DMFT outcome data will be taken from the most recent dental visit (in 2020) where available, or whichever is the most recent recording.

4.5 Analysis

4.5.1 Creation of balanced comparator groups:

Propensity score analysis has been widely used to assess causal effects in observational studies (51). A propensity score analysis will be used to minimise the effects of selection bias, controlling for potential confounders at the design stage using propensity score estimation and matching of local authority areas (50) and at the analysis stage using adjusted regression models.

A key consideration in the design of this study is the selection of appropriate control areas to minimise bias and to strengthen causal inference. Previous studies have often opportunistically chosen control areas, perhaps using neighbouring local authority areas or other, broadly comparable areas, with no lack of formal guiding methodology. Using relevant information from local authority areas, we propose to use propensity scores to formally select local authority areas with the most similar area characteristics to the fluoridated local authority areas across a number of key variables. Propensity scores will be estimated using data from within the NHS BSA dataset, and through data linkage, using data from external datasets such as; the English Indices of Deprivation (Index of Multiple Deprivation), NHS Dental Statistics for England (dentist: population ratio by Clinical Commissioning Group) and local authority level data from the UK Office of National Statistics. The process of identifying relevant inputs will be carried out in partnership with key stakeholders, through a workshop where clinicians, public health specialists, statisticians and policymakers will be invited to consider potential matching variables and individual level covariates.

Following the creation of balanced propensity scores, the intervention local authority areas will be matched to the control local authority areas using nearest neighbour matching or ‘greedy’ matching using the ‘MatchIt’ package in R (51,52). Matched sets of local authority areas will be formed using one to many matching (with a ratio of no more than 1:5 of intervention local authority units to controls), based on similar values of the estimated propensity score.

From our initial scoping exercise we anticipate that the number of individuals with available data in the fluoridated areas will be around 3.9 million (see section ‘3.6 Sampling frame and availability of data’), whilst the number of individuals in the non-fluoridated areas with available data is estimated to be 30.8 million. We estimate that that after exclusions and matching on local authority area that the final sample size of the study will be around 6.4 million.

4.5.2 Effectiveness

A descriptive analysis will be undertaken to determine whether balance at the local authority level has been achieved. Average standardized absolute mean differences will be calculated as a global measure of successful matching. This approach is preferable to statistical significance tests which can, in large datasets, be overly sensitive to observed differences. Expert knowledge of local areas will also be used to qualitatively assess success. A generalized linear model with clustering by local authority area will be used to analyse the

primary outcome of number of invasive dental treatments received during the period of observation. This model will include the area level propensity score and individual level covariates. Given the large number of observations, clinical importance of the magnitude of the treatment effect will be preferred over statistical significance. Thresholds for minimally important differences will be defined a priori in partnership with key stakeholders including decision-makers, public health professionals, patients, clinicians, and the public.

4.5.3 Health inequalities

It is well established that inequalities in dental health are significant. We will examine if the effect of fluoridation on dental health (number of remaining natural teeth and number affected by decay) differs according to area level measures of deprivation and by individual NHS dental charge exemption (from patient charges) category. Area-based deprivation will be measured using the Index of Multiple Deprivation generated by the Department for Communities and Local Government. This area level measure will be attributed to individual patients via their home postcode at the start and the end of the study observation period (first and last dental visit). NHS Dental charge exemption category will give us an individual level measure of income-deprivation. All 'potential' identifiers, (such as postcode, dental practice postcode) to be removed from the data set before it leaves the NHS BSA and is available for analysis by the University of Manchester.

4.5.4 Health economics

The economic evaluation of water fluoridation will focus on an assessment of cost-effectiveness and calculating the return on investment.

Cost-effectiveness will be based on the primary study outcome, assessed as the mean cost per episode of invasive dental treatments avoided, from a Public Sector perspective by estimating the incremental cost-effectiveness ratio (ICER). The ICER is measured by the difference in water fluoridation costs between fluoridated and non-fluoridated regions (incremental costs), divided by the difference in the number of invasive dental treatments between fluoridated or non-fluoridated regions (incremental effects). Reductions in dental service costs are not factored in to the incremental costs of fluoridation (numerator in the ICER) because the reduction in treatment episodes is used as the measure of effects (denominator in the ICER). Deduction the costs of reduced dental treatments from the costs of water fluoridation would involve 'double counting' this change in treatment episodes and these effects on costs are instead considered in an estimation of the financial return on investment (see below). Sensitively analysis will determine if cost-effectiveness is impacted by characteristics of the population or water fluoridation scheme.

To provide valuable information to Public Health England and Local Authorities, we will calculate the public sector financial return on investment in water fluoridation. The investments will be captured by the costs of providing water fluoridation, while the returns will be captured by changes in NHS costs relating to reductions in dental service utilisation.

Cost of dental treatments: In order to assess the financial return on investment associated with fewer dental treatments in fluoridated areas we will measure the following:

1. **NHS Costs:** The average cost of 1 UDA to the NHS in England is £25.00. A Band 1 course of treatment (examination, prevention, radiographs) attracts 1 UDA (for which the NHS pays £25.00). A Band 2 course of treatment (restoration, endodontics,

extractions) attracts 3 UDAs (for which the NHS pays £75.00). A Band 3 course of treatment (crowns, dentures) attracts 12 UDAs (for which the NHS pays £300.00).

2. **Patient Costs:** Where patients are not exempt from NHS charges, they pay a portion of the above total NHS costs. The proportion of the full NHS cost that is paid by patients has increased in recent years. At present, the patient charges for each band is as follows: Band 1 (£21.60), Band 1 Urgent (£21.60), Band 2 (£59.10), and Band 3 (£256.50). Patient costs will be allocated using the true costs for the year in question. Patient costs relating to the time and travel required for dental treatments cannot be measured using data available for this study.
3. **Cost per item of treatment:** Payment bands will also be disaggregated to extract a more precise costs of the treatment provided within each band. This will involve assigning a unit cost per item of treatment. NHS dental costs are still assigned in this way in Scotland based on the estimated mean time taken to provide different items of service, so we will utilise Scottish dental treatment costs data as a more 'resource-based' approach to costing.

Patient costs will be deducted from NHS costs to reflect that patient charges are recovered by the NHS and are a source of income. Each costing approach will be applied to the patient level data for patients living in fluoridated and non-fluoridated regions.

The wider, societal costs associated with oral health problems and their treatment, such as absenteeism and presenteeism with relation to work or school, cannot be measured from the routine data available in this study. However, it is not expected that the relationship between treatments and these costs will differ between fluoridated and non-fluoridated regions.

The costs of dental treatments and the number of treatments avoided will be discounted at 1.5% which is the NICE recommended discount rate for public health interventions. Sensitively analysis will apply the 3.5% discount rate common for health care interventions.

Cost of fluoridation: Costs of water fluoridation involve capital expenditure for equipment, and ongoing revenue costs, which include; maintenance, training of operators, the time taken by water company staff, and the fluoride chemical supply. Public Health England, on behalf of the Secretary of State, fund capital costs. Revenue costs are paid by Public Health England and subsequently recharged to Local Authorities. Capital costs will also need to consider the estimated lifetime of the plant and any major refurbishments required. Capital and revenue costs of fluoridation will be obtained by liaising with Public Health England and the appropriate water companies. Fluoridation costs will be allocated appropriately to the whole population in each fluoridated region to calculate the per capita cost. As costs do not vary by patient characteristics, the per capita cost will be applied to our patient population. We will determine the degree to which the cost of water fluoridation is driven by fixed costs and variable cost, the latter varying with the size of the population served. The team has already collected the equivalent costs for specific areas in the North of England for the ongoing CATFISH study.

Our current study will provide estimates of the costs and effects of water fluoridation. If appropriate (that is, if we detect an effect), these estimates could be used to inform the design of a future Cost- Benefit Analysis including eliciting the preferences of the public and/or local authorities (via willingness-to-pay) regarding water fluoridation. Such a WTP study would also require the effectiveness estimates for children (coming from CATFISH) to fully inform the public and / or Local Authorities. We will seek additional funding for this future CBA study if an effect is detected.

Study data will be available for use in decision analytic models if fluoridation is effective over the 10-year study period. Such modelling is not covered by this protocol.

5. Data Handling

5.1 Data Protection

We have requested fully anonymised data from the NHS BSA. To allow this to happen, any linking that requires the use of the patient's or their dental practice's postcodes (for example, water fluoridation status, area-based deprivation measure (IMD), Government Office Region, dentist: population ratio at CCG level) will be completed prior to data transfer. We will prepare the water fluoridation postcode look-up tables to send to the BSA to allow them to carry out the linkage within their own secure systems.

When the data linkage has been completed within the BSA, any personal data (name, address, previous surname etc) and any 'potential identifiers' (home postcode, dental practice address and postcode) will be removed prior to transfer. The information will then be fully anonymised. BSA apply data suppression at the level of Lower Super Output Area (LSOA) for 5 or less patients to further prevent inadvertent patient identification.

Despite the anonymity of the data we take data security seriously and will apply the same governance requirements as those we would use for patient identifiable data. The source files will be located within the University of Manchester's Safe Haven data store. This store is held within a private subnet only accessible to nominated users with appropriate role-based access. Data will be encrypted at rest and hence will be fully compliant with GDPR requirements. Access to the data will be restricted to research team members only and all queries will be fully recorded in an access log and will be available for audit. We are currently planning on a secure data courier to transport the data to the Manchester University site – this is to ensure prompt delivery. However, depending on the final file size, we may utilise a secure file transfer protocol.

6. Project Management

6.1 Research Governance

6.2 Study Steering Committee (SSC)

We plan to create an independent Study Steering Committee (SSC), which will be chaired by a senior independent public health academic, and in addition to the joint lead applicants, will also include an independent Director of Public Health and Health & Wellbeing Board member, an independent senior dental clinician, an independent senior biostatistician and an independent lay specialist advisor (PPI member). The SSC will provide independent oversight of research integrity, study management and the quality of the data and provide advice and comment on conclusions drawn and development of our dissemination strategy. Formal minutes will be taken during each meeting, to be signed off by the chair and shared with NIHR PHR.

6.3 Operational management Group (OMG)

Operational management of the project will be overseen by the Operational Management Group (OMG) – chaired by WALSH and made up of the co-applicants plus one PPI lay specialist. The OMG will meet regularly to ensure progress is maintained according to the milestones set out in the Gantt Chart, provide required reports to HTA and SSG and produce the final report of the project and oversee dissemination activities. A record will be taken of each meeting. Financial oversight will be the responsibility of the University of Manchester as contract holder. Annual financial summaries of expenditure will be produced by the University finance team and made available to NIHR as required. A final financial report will produced at the end of the project.

7. Patient and Public Involvement

Patient and public involvement has already been a key part of this research proposal and we intend to involve patients and the public throughout the study. During the engagement that we undertook to inform the development of this proposal, some members of the public stated that if they were aware of the expected benefits of water fluoridation, in terms they understood (i.e. saving money, avoiding unpleasant dental treatments), then they would become advocates for water fluoridation by writing to their MP or local councillors.

We will recruit a lay specialist to be a member of both the Operational Management Group and Study Steering Group, to ensure that the results of the study will be explained in a way that is accessible and understandable to members of the public. It is anticipated the PPI members will directly contribute towards the content and design of the infographic and video animation, as well as the analysis plan and dissemination strategy. Producing information in an accessible way means that it could be used as part of future public consultations on water fluoridation proposals.

A range of channels will be used to advertise the lay specialist roles, including the NIHR INVOLVE ‘People in Research’ website, local Council and CCG public engagement forums, Healthwatch, community and voluntary organisations, the University of Manchester Facebook page, Twitter account and blogs. The budget includes allocation for the lay specialist advisors to receive training, and prepare for and attend meetings, including travel and childcare costs. Costs have been calculated using the INVOLVE costs calculator.

8. Dissemination and Knowledge Transfer

A comprehensive dissemination strategy will be developed in partnership with key stakeholders. We intend to leverage relationships with key stakeholder groups that will have already been developed as part of the CATFISH project (NIHR PHR project number 12/3000/40). CATFISH will establish a “Water Fluoridation Evidence to Impact Group”. This group will include:

- Chair: To be determined
- Joint Cis of proposed study and CATFISH, plus appropriate members of the academic team
- LA representation - one Director of Public Health from a fluoridated locality and one from a locality interested in exploring implementation of fluoridation
- Director of Dental Public Health at Public Health England

- Senior Representation from NICE
- Dental leadership in NHSE (Chief Dental Officer)
- Dental leadership in PHE
- British Dental Association Representative
- Senior Leader Cochrane Oral Health Group
- PPI representative

We will utilise this existing network and relationships to support the further dissemination of the results of this study.

In addition to statutory bodies with decision-making powers, we recognise the key role played by professional and public opinion-leaders and the media. Legislation prescribes that Local Authorities must undertake a 3-month public consultation as part of the water fluoridation decision-making process. Whilst the local authority holds the final decision on the implementation or withdrawal of water fluoridation, local Councilors, MPs, and Health and Wellbeing Board members will be influenced by the views of their constituents and respected local clinicians (53,54). We will ensure that the results of our study are understandable and have impact with the public through their trusted sources of health information, counteracting any sensationalist or political spin from the media.

We will produce plain-language summaries, an infographic and a PPI-inspired animated video. The development of the non-academic dissemination products will be led by the PPI members of the study team. We will seek input and feedback on the products from key stakeholder representatives during their development. The animated video and infographic will be made available as a resource for Local Authorities to use in possible future water fluoridation consultations. These will be hosted on the Manchester University website, but we will also contact key stakeholders to ask them to link to our site and / or share the results through their social media existing channels.

We will issue press releases coordinated with PHE and CDO's office as well as holding webinars for the UK public health community, promoted via links with the Faculty of Public Health and NIHR. We will distribute the briefing materials, infographic and animated video through NHS England regional offices and Clinical Commissioning Groups for distribution to their individual dental and medical contract holders via newsletters, meeting notes or webpages. We will also share our dissemination products through social media channels that are context-sensitive and relevant for that particular target group, for example, the popular members-only Facebook group "For Dentists, By Dentists", which has 14,000 General Dental Council registered members. We will also seek to publish briefings in primary care focused magazine-style publications with high circulation figures, for example; "*Dental Update*", "*Community Practitioner*", and "*Pulse Magazine*".

A full stakeholder engagement plan outlining the range of stakeholders to be engaged with and the most appropriate methods to do so, will be developed iteratively by the Operational Management Groups of the proposed project and CATFISH and will be reviewed by the CATFISH "Water Fluoridation Evidence to Impact Group". However, it is envisaged that the key targets for tailored dissemination products will include: Parliamentarians and local government leaders, evidence producing institutions, commissioning organisations, professional societies and associations, primary care medical and dental clinicians and community practitioners, and community and voluntary sector organisations.

From an international perspective we will seek to mobilise the knowledge produced from the two projects (this study and CATFISH) by feeding the outputs into an update of the Cochrane

systematic review of water fluoridation and work with the Cochrane Oral Health Group Global Alliance to provide tailored summaries of the outputs of the research to WHO, Executive Board of FDI's Chief Dental Officers section and to governments and agencies of countries with high coverage of water fluoridation notably, United States, Australia, Canada, Israel, Republic of Ireland.

The results will be presented nationally and internationally, at PHE Integrated Academic Network events, and at conferences held by the Faculty of Public Health, the British Association for the Study of Community Dentistry, and the International Association for Dental Research. We have also planned in a 'policy implications workshop', where we will share the findings of the current research, and invite key stakeholders to consider the implications of the totality of the contemporary water fluoridation evidence base for their organisations and their partners.

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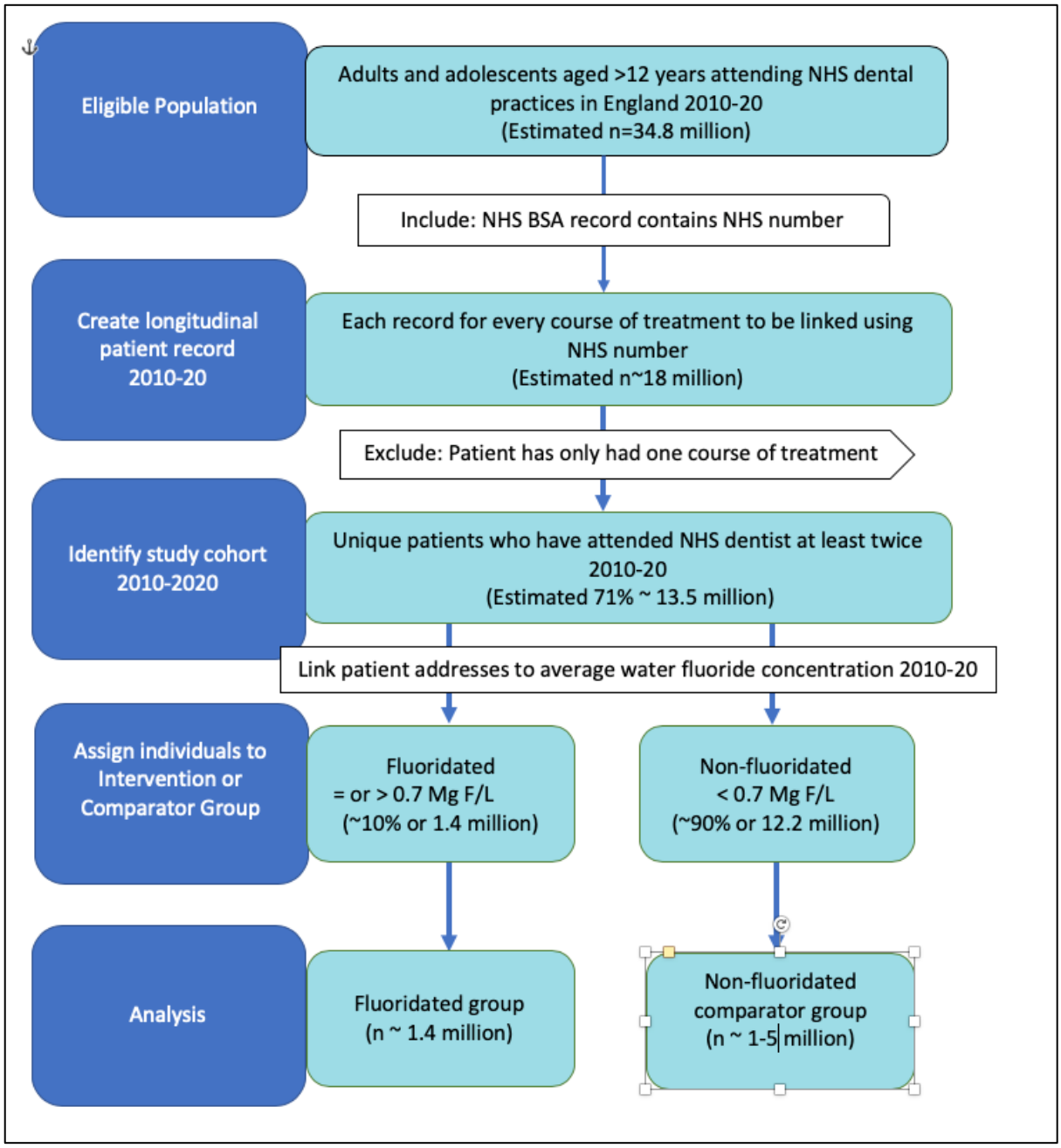
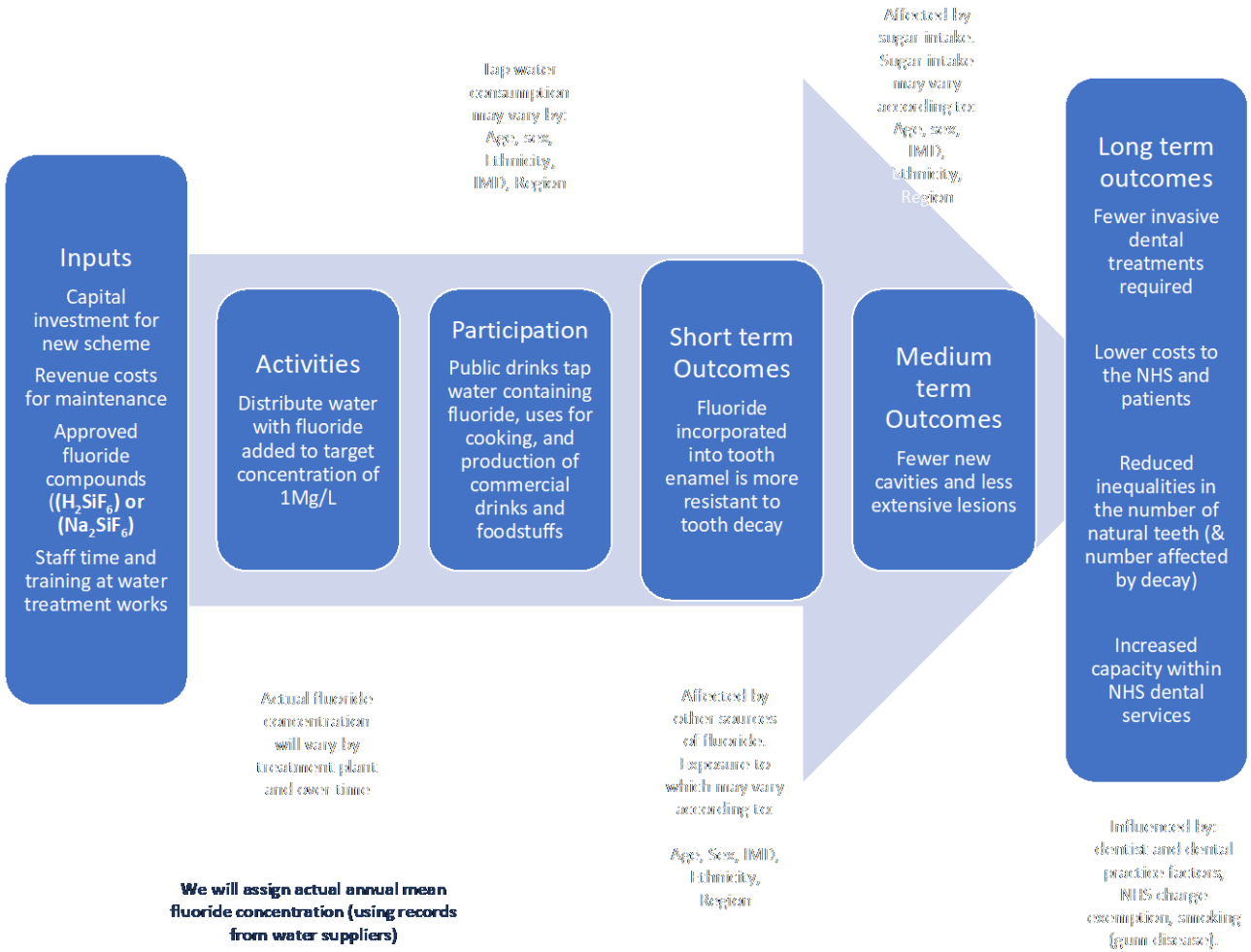
APPENDIX 1: Study Flow Diagram



APPENDIX 2: Logic Model



APPENDIX 3: Gantt Chart

Milestones	Preparation			2020												2021											
	O	N	D	J	F	M	A	M	J	J	A	S	O	N	D	J	F	M	A	M	J	J	A	S	O	N	D
Project month	-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	
STUDY SET-UP																											
Advertise and recruit project manager																											
Advertise and recruit for PPI lay specialist roles																											
Training needs analysis for PPI roles																											
Commission study website																											
Submit Publication 1: Study protocol including statistical plan																											
WP:1 RETROSPECTIVE COHORT STUDY DENTAL CLAIMS DATA																											
Complete NHS Digital Data Access Request Process																											
Finalise data sharing and IG plan with NHS BSA and UoM																											
If necessary, apply to University of manchester Research Ethics Committee																											
Key stakeholder workshop on confounders, to inform statistical analysis and matching																											
Prepare look-up tables linking WF exposure and other covariates to postcode areas																											
NHS BSA to identify data and link necessary variables																											
Remove 'potential identifiers' and transfer from BSA to UoM using secure data transfer																											
Individual matching using propensity scores																											
Analyse effect of WF on treatment received, numbers of natural teeth, teeth affected by decay and inequalities																											
Write-up health outcomes																											
Submit Publication 2: Effectiveness of water fluoridation in adults																											
WP:2 HEALTH ECONOMICS ANALYSIS																											
Identify which societal costs and benefits are to be included																											
Seek actual costs of water fluoridation from PHE, local authorities and water companies																											
Assign costs of water fluoridation to population																											
Cost benefit analysis including sensitivity																											
Write up health economic outcomes																											
Submit Publication 3: Cost-effectiveness of water fluoridation in adults																											
DISSEMINATION																											
Website updates																											
PHE Integrated Academic Network presentations																											
Publication 1: Protocol																											
Publication 2: Effectiveness of water fluoridation for adults																											
Publication 3: Cost-effectiveness of water fluoridation for adults																											
Conferences																											
Commission and develop infographic																											
Commission and develop video animation																											
Policy implications workshop																											
GOVERNANCE																											
PPI attendance at OMG (+/- SSG) includes 1 hour lay specialist pre-meeting																											
Operational Management Group meetings																											
Study Steering Group (SSG) meetings																											
Financial oversight																											

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