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PROTOCOL

LOTUS PROJECT

FLuOridaTion for AdUltS

Version Number: 4.0
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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 2009 to 2019.
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 (2009-2019)
Sampling frame:	It is estimated that the records of 35.6 million individuals will be available for eligibility screening and matching
Sample size:	It is estimated that 6.4 million records will be included in the analysis
Duration of study:	Two years (1st Feb 2020 to 31st Jan 2022)

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
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.
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.
V3.0	2nd December 2019	Deborah Moore	Ethical approval received from Manchester University Research Ethics. Added to section 3. 'Approval of the Protocol' (p7)
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 2009-2019 (to exclude those practices who may have 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**

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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 application, 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 the need for 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

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 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 oral health inequalities in 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

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

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.

However, 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. **When this approval has been received it will be noted here**

3.2 Approval of protocol by independent Study Steering Committee

This protocol will be formally approved by the Study Steering Committee at their first meeting. The current version number (V3.0) will be amended to reflect any changes, and the date of approval by the SSC will be added here.

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 2009 to 2019

4.1 Summary of the prosed study (PECOST):

Population:	Adults attending NHS dental practices in England
Exposure:	10-year residence in a postcode area that has always been in receipt of fluoridated water
Comparison:	10-year residence in a postcode area that has never received fluoridated water
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 2009 to 2019.

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 between 2009 and 2019. The reason that we are limiting the period of observation to 10-years is that prior to 2009, 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.

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 35.6 million (Table 1, Row 5) (26,34–36).

Using this sampling frame (35.6 million), the following exclusion criteria will be applied:

2. 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 (2009-2019).
3. Individuals that lived in both fluoridated and non-fluoridated areas, (i.e. partial exposure) will be excluded from further analysis.
4. Individuals in the exposed group for whom no suitable match can be found within the un-exposed group will be excluded

Table 1 Estimated size of sampling frame available

		Receiving fluoridated water	**Not receiving fluoridated water**
1	**Total population (all ages)**	5,797,000 2012 Estimate. Source: (26)	51,809,700 2009 Mid-year population. Source: (34) Minus exposed population (26)
2	**Population aged over 12 years in 2009** 86%. Source: (34)	4,985,420	44,556,342
3	**Number estimated to use NHS dentistry** 85.1%. Source: (35)	4,237,607	37,872,890
4	**Number estimated to have attended dentist within ten years** 94% Source: (36)	3,983,350	35,600,516
5	**Final sampling frame**	**Exposed Group: 3,585,015**	**Unexposed Group: 32,040,464**

There is no existing data available on the proportion of the population who move between fluoridated areas and non-fluoridated areas within a ten-year period, but we would expect it to be minimal. The 2011 census reported that 12% of respondents had a different address 1 year previously, and the majority of migration is within the same local authority area (59%) (37).

If approximately 10% of the sampling frame are excluded, we can expect the final size of the exposed group to be approximately 3.2 million (see Participant Flow diagram). These exposed individuals will then be assigned a 'nearest neighbour' match from within the un-exposed group sampling frame, using propensity scores. We therefore estimate that around 6.4 million individuals will be included in the analysis of outcomes (see separate upload, 'Participant Flow Diagram').

4.3 Determination of water fluoridation exposure status

Water companies in England have a duty to monitor the fluoride concentration of public water supplies in the water supply zones (WSZs) they supply, and provide these monitoring data to the Drinking Water Inspectorate. Water supply zones are small area geographies that share a single point of water supply and provide coverage to a maximum of 100,000 people (38).

We will use postcode look-up tables supplied by water companies to match postcodes to water compliance zone (water supply) geography. These look-up tables will then be supplied to the NHS BSA to match to individual's addresses, and flag each address in receipt of fluoridated water. For the main analysis, complete 10-year residence in addresses which are all flagged as receiving fluoridated water, will be used to define the exposure group. Individuals who have lived in an address flagged as fluoridated and have also lived in one or more addresses that are not flagged as fluoridated will be excluded from the analysis (partial exposure). Individuals who have not lived at an address flagged as fluoridated will be allocated to the un-exposed, comparator group.

We are aware that due to equipment failures, unexpected weather events, and difficulty in obtaining the correct fluoridation chemicals, 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).

We will account for the effect of variation in achieved water fluoride concentrations in a planned sub-group analysis, separating out those individuals who have received optimally fluoridated water (annual mean concentration of fluoride greater than or equal to 0.7 Mg F/L in every year of observation), and those who have received sub-optimally fluoridated water (annual mean concentration of fluoride less than 0.7 Mg F /L in any year of observation). Using 0.7 Mg F/L to define 'optimally fluoridated' aligns with the approach that was used recently in the Public Health England Water Fluoridation Health Monitoring Report (39).

4.4 Outcomes

The choice of primary and secondary outcome measures has been informed by the patient and public engagement undertaken during the development of this application. Avoiding the discomfort and anxiety of dental treatment, as well as the costs due NHS patient charges were mentioned often as reasons why it was important to have good oral health. Patients also talked about good oral health meaning that they would keep their own teeth for as long as possible, so that they could continue to eat a range of foods, smile, socialise, and sing.

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 (2009-2019)

4.4.2 Secondary outcomes:

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

The number of **T**eeth which are **D**ecayed, **M**issing due to decay, or **F**illed (DMFT) has been included in the NHS dental data-set since 2017. DMFT is a cumulative measure of lifetime

decay experience which will be used to quantify differences in the number of remaining natural teeth, and the numbers of teeth affected by decay in individually-matched patients who have been resident in fluoridated or non-fluoridated regions since 2009. DMFT outcome data will be taken from the most recent dental visit (in 2019) where available, or whichever is the most recent recording (closest to 2020).

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 (40). 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 individuals, and at the analysis stage using adjusted regression models.

We will use propensity score matching to account for biases related to differences between individuals residing and not residing in areas receiving fluoridated water. 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). Covariate selection for the propensity score estimation will be undertaken according to the guidelines proposed by Lee and Little (2017) (41). The final selection of covariates will be informed by a full and explicit understanding of all causal relationships and confounding pathways of relevance to our research question, and how they interact (42–44). Covariates will be associated with both exposure and outcome, but not on the causal pathway.(42–44) The process of mapping out relevant causal pathways 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 how the potential confounders relate to both the exposure and the outcome.

Following the creation of balanced propensity scores the samples will be matched using nearest neighbour matching. Matched sets of individuals from the fluoridated and non-fluoridated areas will be formed, based on similar values of the estimated propensity score. A key advantage of using such a large dataset is that we anticipate that the propensity scores of a substantial number of residents of the fluoridated and non-fluoridated areas will overlap, and that consequently we will be successful in being able to match a large number of individuals on multiple characteristics. We anticipate that the number of individuals with available data in the fluoridated area will be around 3.6 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 32 million. The likelihood of finding a suitable match for each individual in the fluoridated group is therefore high, when there are so many individuals available in the non-fluoridated group. Any individuals within the exposed group for whom a suitable match cannot be found, will be excluded from further analysis. We estimate that that after exclusions and matching, the final size of each group will be around 3.2 million.

4.5.2 Effectiveness

A descriptive analysis will be undertaken to determine balance on the covariates has been achieved. Standardized differences will be used to explore covariate balance, in preference to statistical significance tests which can, in large datasets, be overly sensitive to observed differences. A generalized linear model will be used to analyse the primary outcome of number of invasive dental treatments (restorations, endodontics, extractions) received in the period of observation, including the covariates from the propensity score model. 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 between the groups will be defined 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 exemption (from patient charges) status. Deprivation will be primarily 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. 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

Cost-effectiveness will be based on the primary study outcome, assessed as the mean cost per episode of invasive dental treatments avoided, from a societal perspective by estimating (1) the incremental cost-effectiveness ratio (ICER) and (2) cost-effectiveness acceptability curve (CEAC). The ICER is measured by the difference in costs between fluoridated or non-fluoridated regions divided by the difference in outcomes between fluoridated or non-fluoridated regions. The CEAC is used to summarise uncertainty in the incremental costs and effects via nonparametric bootstrapping of the cost and effectiveness data to relate the ICER to subjective assessments of the value of health outcomes.

Cost of dental treatments: In order to assess potential cost savings 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.
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.

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.

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 (45,46). 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.

9. References

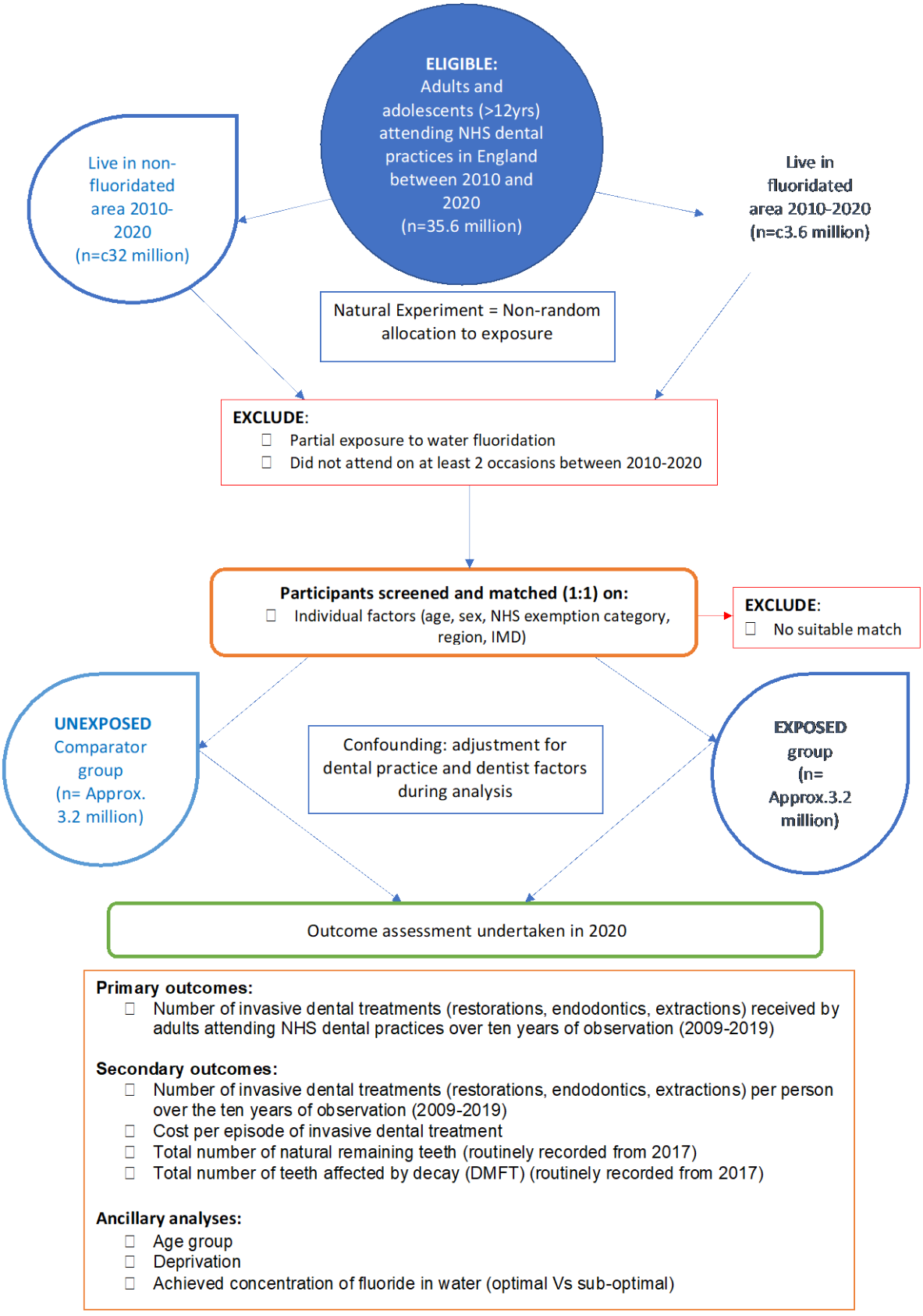
1. Abajobir AA, Abate KH, Abbafati C, Abbas KM, Abd-Allah F, Abdulkader RS, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet. 2017;390(10100):1211–59.
2. Steele J, Sullivan IO. 8 : Access and barriers to care - a report from the Adult Dental Health Survey 2009. 2011;1–52.
3. NHS England. Improving Dental Care and Oral Health – a Call To Action [Internet]. 2014 [cited 2018 Sep 17]. p. 1–34. Available from: https://www.england.nhs.uk/wp-content/uploads/2014/02/imp-dent-care.pdf
4. Broadbent JM, Foster Page LA, Thomson WM, Poulton R. Permanent dentition caries through the first half of life. Br Dent J [Internet]. 2013;215(7):1–6. Available from: http://dx.doi.org/10.1038/sj.bdj.2013.991
5. Steele J, Shen J, Tsakos G, Fuller E, Morris S, Watt R, et al. The Interplay between Socioeconomic Inequalities and Clinical Oral Health. J Dent Res [Internet]. 2015;94(1):19–26. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25344336
6. Bratthall D, Hänsel-Petersson G, Sundberg H. Reasons for the caries decline: what do the experts believe? Eur J Oral Sci [Internet]. 1996;104(4):416–22. Available from: http://doi.wiley.com/10.1111/j.1600-0722.1996.tb00104.x
7. Murray JJ, Vernazza CR, Holmes RD. Forty years of national surveys: An overview of children's dental health from 1973-2013. Br Dent Joural [Internet]. 2015;219(6):281–5. Available from: http://www.nature.com/doifinder/10.1038/sj.bdj.2015.723
8. Steele JG, Treasure ET, O'Sullivan I, Morris J, Murray JJ. Adult Dental Health Survey 2009: transformations in British oral health 1968-2009. Br Dent J [Internet]. 2012;213(10):523–7. Available from: http://dx.doi.org/10.1038/sj.bdj.2012.1067
9. Bernabé E, Sheiham A. Extent of differences in dental caries in permanent teeth between childhood and adulthood in 26 countries. Int Dent J. 2014;64(5):241–5.
10. Office for National Statistics. One third of babies born in 2013 are expected to live to 100 [Internet]. 2015. Available from: http://www.ons.gov.uk/ons/rel/lifetables/historic-and-projected-data-from-the-period-and-cohort-life-tables/2012-based/sty-babies-living-to-100.html
11. Healthwatch Bolton, Healthwatch Kirklees. Oral health in care homes. Evidence from Bolton and Kirklees [Internet]. 2014. Available from: http://healthwatchbolton.co.uk/wp-content/uploads/Final-Healthwatch-Bolton-and-Healthwatch-Kirklees-Report-on-Dentistry-in-Care-Homes-20150202.pdf
12. Iheozor-Ejiofor Z, Worthington H, Walsh T, O'Malley T, Clarkson J, Macey R, et al. Water fluoridation for the prevention of dental caries. Cochrane Database Syst Rev. 2015;(6).
13. Rugg-Gunn AJ, Spencer AJ, Whelton HP, Jones C, Beal JF, Castle P, et al. Critique of the review of "Water fluoridation for the prevention of dental caries" published by the Cochrane Collaboration in 2015. Bdj [Internet]. 2016;220(7):335–40. Available from: http://www.nature.com/doifinder/10.1038/sj.bdj.2016.257
14. Slade GD, Sanders AE, Do L, Roberts-Thomson K, Spencer AJ. Effects of fluoridated drinking water on dental caries in Australian adults. J Dent Res. 2013;92(4):376–82.

15. Medical Research Council. Using natural experiments to evaluate population health interventions : guidance for producers and users of evidence. Guidance for producers and users of evidence. 2011.
16. Griffin SO, Regnier E, Griffin PM, Huntley V. Effectiveness of Fluoride in Preventing Caries in Adults. J Dent Res. 2007;86(5):410–5.
17. Maupomé G, Gullion CM, Peters D, Little SJ. A comparison of dental treatment utilization and costs by HMO members living in fluoridated and nonfluoridated areas. J Public Health Dent. 2007;67(4):224–33.
18. Neidell M, Herzog K, Glied S. The association between community water fluoridation and adult tooth loss. Am J Public Health. 2010;100(10):1980–5.
19. Mahoney G, Slade GD, Kitchener S, Barnett A. Lifetime fluoridation exposure and dental caries experience in a military population. Community Dent Oral Epidemiol. 2008;36(6):485–92.
20. Hopcraft MS, Yapp KE, Mahoney G, Morgan M V. Dental caries experience in young Australian Army recruits 2008. Aust Dent J. 2009;54(4):316–22.
21. Crocombe LA, Brennan DS, Slade GD, Stewart JF, Spencer AJ. The effect of lifetime fluoridation exposure on dental caries experience of younger rural adults. Aust Dent J. 2015;60(1):30–7.
22. Do L, Ha D, Peres M, Skinner J, Byun R, Spencer AJ. Effectiveness of water fluoridation in the prevention of dental caries across adult age groups. Community Dent Oral Epidemiol [Internet]. 2017;(September 2016). Available from: http://doi.wiley.com/10.1111/cdoe.12280
23. Spencer AJ, Liu P, Armfield JM, Do LG. Preventive benefit of access to fluoridated water for young adults. J Public Health Dent. 2017;77(3):263–71.
24. Hull City Council. Community Water Fluoridation [Internet]. 2018 [cited 2018 Aug 8]. Available from: http://www.hull.gov.uk/resident/healthy-living/community-water-fluoridation
25. Durham County Council. Report of Amanda Healy, Director of Public Health County Durham, Adult and health Services, Durham County Council [Internet]. Oral Health Update. 2017 [cited 2018 Aug 8]. Available from: https://democracy.durham.gov.uk/documents/s83873/Agenda Item 13 - Oral Health Update.pdf
26. British Fluoridation Society. The extent of water fluoridation. One in a million: the facts about water fluoridation [Internet]. 2012. Available from: http://www.bfsweb.org/onemillion/09 One in a Million - The Extent of Fluoridation.pdf
27. British Dental Asscoiation. Dental contract reform [Internet]. 2019 [cited 2019 Apr 2]. Available from: https://bda.org/contractreform
28. NIHR. Impact of a change to remuneration on the technical efficiency of dental practices: evaluation of the pilots of a new NHS Dental Contract in Northern Ireland [Internet]. Journals Library. 2019 [cited 2019 Apr 4]. Available from: https://www.journalslibrary.nihr.ac.uk/programmes/hsdr/141912/#/
29. Hill H, Birch S, Tickle M, McDonald R, Donaldson M, O'Carolan D, et al. Does capitation affect the delivery of oral healthcare and access to services? Evidence from a pilot contact in Northern Ireland. BMC Health Serv Res. 2017;17(1):1–10.
30. Brocklehurst P, Tickle M, Birch S, Glenny A-M, Mertz E, Grytten J. The effect of

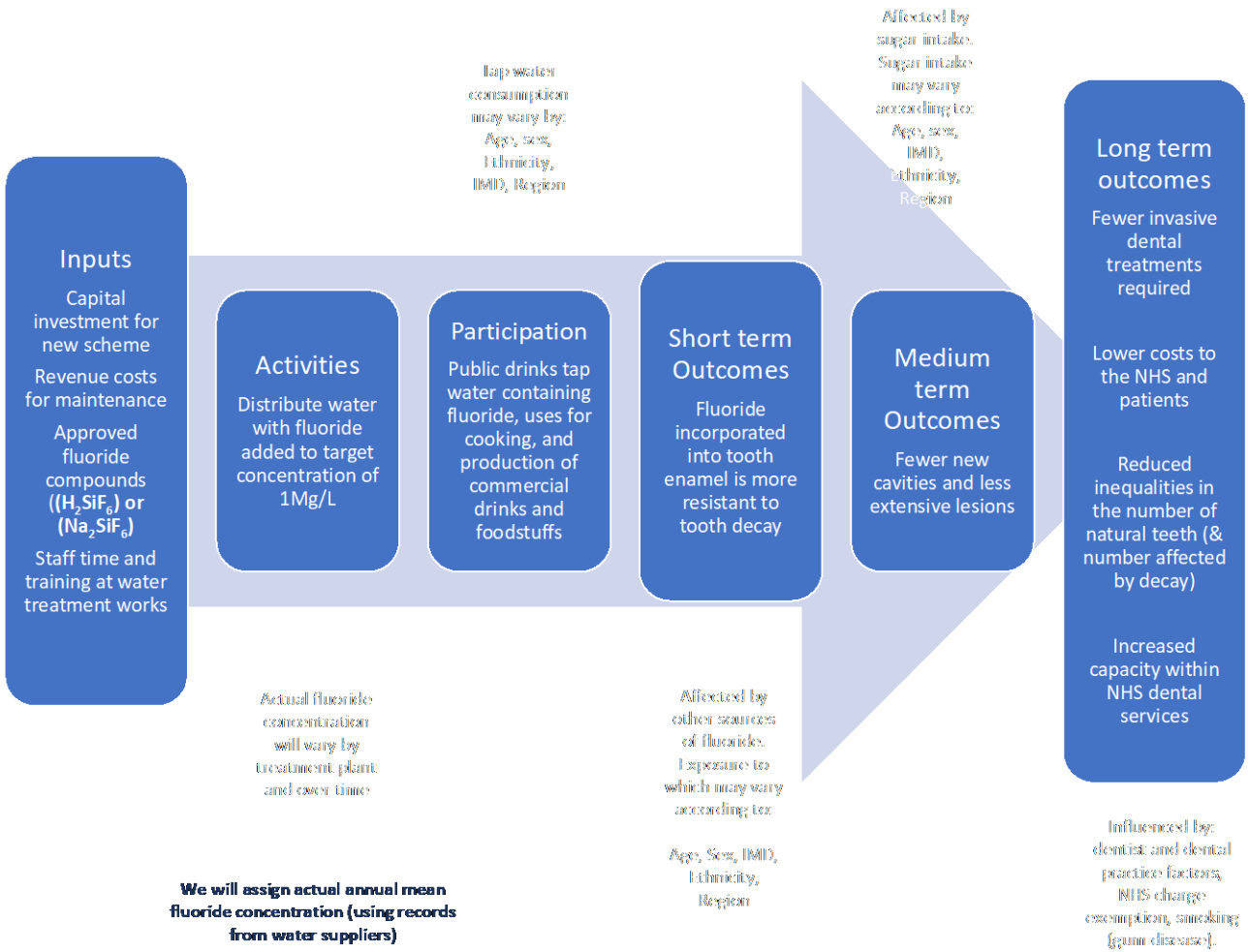
different methods of remuneration on the behaviour of primary care dentists. Cochrane Database Syst Rev. 2012;(11):1–38.
31. McDonald R, Cheraghi-Sohi S, Sanders C, Tickle M. Changes to financial incentives in English dentistry 2006-2009: A qualitative study. Community Dent Oral Epidemiol. 2012;40(5):468–73.
32. Tickle M, McDonald R, Franklin J, Aggarwal VR, Milsom K, Reeves D. Paying for the wrong kind of performance? Financial incentives and behaviour changes in National Health Service dentistry 1992-2009. Community Dent Oral Epidemiol. 2011;39(5):465–73.
33. AlQahtani SJ. Atlas of Tooth Development [Internet]. Barts and London School of Medicine and Dentistry. London; 2009. Available from: https://www.atlas.dentistry.qmul.ac.uk/content/english/atlas_of_tooth_development_in_English.pdf
34. Office for National Statistics. Dataset: Estimates of the population for the UK, England and Wales, Scotland and Northern Ireland. Mid 2009: Superseded. 2019.
35. NHS England. Summary of the Dental Results from the GP Patient Survey - January to March 2018 [Internet]. 2018. Available from: https://www.england.nhs.uk/statistics/wp-content/uploads/sites/2/2018/08/GP-Survey-Dental-Results-Summary-PDF-842KB-1.pdf
36. The information centre for health and social care. 8 : Access and barriers to care - a report from the Adult Dental Health Survey 2009. 2011.
37. UK Office for National Statistics. 2011 census: Internal and international migration for the united Kingdom in the year prior to the 2011 census. 2014.
38. Drinking Water Inspectorate. Guidance on the implementation of the Water Supply (Water Quality) Regulations 2016 (as amended) in England and the Water Supply (Water Quality) Regulations (Wales) 2018 [Internet]. 2018 [cited 2019 Feb 12]. p. 2016–9. Available from: http://www.dwi.gov.uk/stakeholders/guidance-and-codes-of-practice/wswq/02-zones.pdf
39. Public Health England. Water fluoridation: Health monitoring report for England 2018 [Internet]. 2018. Available from: https://www.gov.uk/government/publications/water-fluoridation-health-monitoring-report-for-england-2018
40. Rosenbaum PR, Rubin DB. The central role of the propensity score in observational studies for causal effects. Biometrika. 1983;70(1):41–55.
41. Lee J, Little TD. A practical guide to propensity score analysis for applied clinical research. Behav Res Ther [Internet]. 2017;98:76–90. Available from: http://dx.doi.org/10.1016/j.brat.2017.01.005
42. Greenland S, Pearl J, Robins JM. Causal diagrams for epideimiologic research. Epidemiology. 1999;10:37–48.
43. Shrier I, Platt RW. Reducing bias through directed acyclic graphs. BMC Med Res Methodol [Internet]. 2008 Jan [cited 2015 Feb 16];8:70. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2601045&tool=pmcentrez&rendertype=abstract
44. Williams TC, Bach CC, Matthiesen NB, Henriksen TB, Gagliardi L. Directed acyclic graphs: a tool for causal studies in paediatrics. Pediatr Res [Internet]. 2018;84(4):487–93. Available from: http://dx.doi.org/10.1038/s41390-018-0071-3

45. Sivaneswaran S, Chong G. Investing in professional advocacy: a case study of a successful fluoridation campaign in rural New South Wales, Australia. Community Dent Health. 2011;28(1):243–7.
46. Allukian M, Carter-Pokras OD, Gooch BF, Horowitz AM, Lida H, Jacob M, et al. Science, Politics, and Communication: The Case of Community Water Fluoridation in the US. Ann Epidemiol [Internet]. 2018;28(6):401–10. Available from: https://doi.org/10.1016/j.annepidem.2017.05.014

APPENDIX 1: Study Flow Diagram



APPENDIX 2: Logic Model



APPENDIX 3: Gantt Chart