Public Health England

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NHS National Institute for Health Research

Study Protocol

Study Title: Schools Transmission Study

(COVID-19 and Scarlet Fever)

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Sponsor

Imperial College is the main research sponsor for this study. For further information regarding the sponsorship conditions, please contact the Research Governance Manager at:

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This protocol describes the investigation of group A strep and SARS-COV2 abundance and transmissibility during outbreaks and provides information about procedures for entering participants. Every care was taken in its drafting, but corrections or amendments may be necessary. If any, these will be circulated to investigators during the study. Problems relating to this study should be referred, in the first instance, to the Chief Investigator.

This study will adhere to the principles outlined in the NHS Research Governance Framework for Health and Social Care (2nd edition). It will be conducted in compliance with the protocol, the Data Protection Act (2018) and other regulatory requirements as appropriate.

1. Introduction

The purpose of this study is to gather much-needed information about the transmission of two notifiable infectious diseases in children within nursery and school settings. The two infections (scarlet fever and COVID-19) cause asymptomatic or mild infection in children, however if transmitted to a susceptible person can result in more serious disease.

Scarlet fever is a highly contagious paediatric infectious disease characterised by high fever, sore throat, and a red rash; it is a statutorily notifiable infection. Despite a sustained decline in scarlet fever notifications in the post-war period, since the spring of 2014 England & Wales have experienced an unprecedented annual marked upsurge in seasonal scarlet fever activity with over 15,000 cases in 2014, affecting predominantly children aged 4-6 years of age (1). Approximately 1 in 20 of these were admitted to hospital and, by 2016, the number of cases rose to over 19,000 (1, 2). Although fluctuations in scarlet fever activity are expected in an approximately four yearly cycle, the magnitude of increase is unprecedented. Reasons for the increase are unclear but may include changes in prescribing and testing for sore throat, altered patterns of childcare, climate or environment changes, prevalence of group A streptococcal (GAS) strains that have capacity to cause scarlet fever, and changes in population immunity. Our proposal seeks to reduce the considerable burden of the UK's scarlet fever surge on child health. In addition to possibly avoidable hospital admissions and the burden created by outbreaks in schools and nurseries, scarlet fever activity can be mirrored by surges in severe invasive GAS infections (iGAS). In 2016, cases of iGAS cases almost doubled during the scarlet fever surge compared with averaged rates in the previous 4 years and peaked at the same time (3). While scarlet fever primarily affects children aged 4-6y, increases in iGAS were seen in most age groups, however babies and young children were disproportionately affected: iGAS incidence increased by 78% in infants, (from 1.4 to 2.4 cases per 100,000) and by 47% in children under 4 (from 1.4 to 2 cases per 100,000) (3). Although a rare complication of iGAS, a British Paediatric Surveillance Unit study showed that 28% of children who have streptococcal toxic shock die (4).

Genome sequencing of strains from scarlet fever and iGAS confirms that the strains associated with iGAS infection are intermixed with (and in some cases identical to) those causing pharyngitis and scarlet fever (2, 5) suggesting that scarlet fever and other superficial GAS infections may act as a 'reservoir' for iGAS, spreading from infectious scarlet fever cases to cause invasive infection in those who are susceptible for example due to breaks in the skin from chicken pox, eczema, recent childbirth or reduced immunity. As such, there is an imperative to understand the factors that influence scarlet fever transmission, in order to identify interventions that might ultimately reduce iGAS.

Despite the link to iGAS, scarlet fever is nowadays considered a mild childhood exanthem without sinister outcome, albeit highly infectious. However the descriptions of scarlet fever are very much based on historical reports and the timing and sequence of symptoms and signs are poorly described, making guidelines on diagnosis challenging. Although antimicrobial treatment

is recommended, and a period of 24h exclusion recommended prior to return to school or nursery (6), the impact of treatment on duration of infectiousness or transmission is completely unknown. Indeed, the only data available to inform guidelines on scarlet fever management are general practice studies of sore throat treatment, which include a range of aetiologies, and show only modest benefit from antibiotic treatment (symptoms are reduced by less than one day) (7,8). The 10 day penicillin course has a basis in older 1950's studies related to rheumatic fever prevention; while effective in those studies, efficacy in the setting of a scarlet fever outbreak is unknown. The contribution of tonsillectomy to carriage rates is also uncertain in the modern era. In this study we will directly measure duration of infection and transmissibility in a small clinical observational study of children with scarlet fever who receive treatment, collecting simultaneous data on the types of treatment the children have received. These clinical data will be used to assess the validity of non clinical in vivo studies that compare four antibiotics.

We will also collect and archive the bacteria causing scarlet fever in this cohort (by taking swabs). This will be important because current NHS practice guidelines do not support the taking of diagnostic samples for microbiological culture; as such there is little evidence about the bacteria that are causing the scarlet fever upsurge. Indeed, evidence relating to GAS sore throat is routinely extended to the scarlet fever setting yet it is likely that the bacteria causing scarlet fever outbreaks may differ in response to certain interventions. These clinical data will be used to assess the validity of a non-clinical in vivo study that will experimentally compare transmission of leading strain types.

We will conduct a parallel observational study to determine if existing public health advice on hygiene reduces the burden of *S. pyogenes* in the school/nursery outbreak environment and whether current guidance is adequate and appropriate by taking samples from unaffected children based in the same nursery or classroom and the environment. We are also interested to know if current guidance on treatment and hygiene is followed, and what the barriers to that might be, in order to provide better evidence to support guideline development. The necessary information can be collected via a survey administered or sent to the guardians of children with notified scarlet fever and a control group of households with children of the same age but without scarlet fever cases .

Data from this study so far have unequivocally shown asymptomatic dissemination of *S. pyogenes* from child to child within the classroom setting during scarlet fever outbreaks, resulting in acquisition of genetically identical strains by approximately 50% of children by week 2. The work has demonstrated asymptomatic shedding into the environment and unexpected airborne spread, explaining why outbreaks are hard to control. In March 2020, schools and nurseries were closed due to the COVID19 pandemic, associated with an abrupt decline in notifications of scarlet fever, likely related to a cessation of face to face GP consultations, coupled with the interruption of the scarlet fever transmission chain by social distancing and school closures. Unlike scarlet fever, the role of children in the transmission

chain of COVID19 is unknown, making modelling of public health interventions challenging. Questions remain as to whether asymptomatic children can transmit COVID19, and how long children might be infected. The re-opening of schools provides a much-needed opportunity to examine COVID19 transmission using the same successful approach to that used for monitoring spread of scarlet fever.

2.Study Objectives

Hypotheses underpinning the proposal We hypothesize that the overall burden of human infectious diseases including scarlet fever and COVID-19 can be reduced by interruption of transmission; this will reduce the reservoir of such infections in the community that might otherwise infect susceptible people leading to more serious COVID-19 or iGAS disease. Susceptibility to iGAS usually requires a portal of entry (9) including chicken pox, small cuts, eczema, or the respiratory tract, particularly when already primed by antecedent influenza. Susceptibility to serious COVID-19 is associated with comorbidities such as hypertension, cardiac illness and also advanced age; ethnicity and male sex also being important risk factors. Understanding the burden and transmission of COVID-19 in schools will inform community control measures and vaccination strategies going forward.

2.1. **Identify pathogen factors that influence transmission**. We will determine the importance of strain types to the level of infectiousness observed in this small clinical study of children exposed to cases of scarlet fever or COVID-19. The data will inform public health strategy, and reveal to what extent it is correct to consider all strains as similarly infectious. Any strains identified in this study will be sequenced and data related to clinical phenotype, including, for example, duration of carriage and extent of transmission.

2.2 **Identify treatment factors that influence transmission**. This small observational clinical study will provide much-needed evidence on the effect of antimicrobial treatment on the duration and infectivity of scarlet fever; this could influence public health guidelines on exclusion periods and potentially lead to a treatment trial. No treatments for COVID-19 are yet known to impact disease progression or transmission.

2.3 **Determine the impact of public health interventions on transmission**

This observational study will reveal whether current public health advice and strategies are sufficient to reduce the risk of transmission. Specifically, we will examine whether there is a change in contamination of the environment and of pathogen carriage by children in the same school or nursery who are asymptomatic contacts, and of carriage in household contacts (*S. pyogenes* only).

2.4 **Provide a more detailed description of these two diseases in children** . A questionnaire will be used to gather details of symptom onset and duration from each child who is a notified case.. In order to reach a larger number of cases, the questionnaire (in the form of a survey that

can be completed online or on paper) will be sent to the parents or guardians of each child notified to PHE with scarlet fever or COVID-19. This information will provide a clearer picture of symptomatology and also the burden of each disease on children, their families, and the health service. Such information is critical when planning interventions and vaccinations.

3 **Study Design**

The study will be a small prospective observational study of **cases** and the **contacts** with whom they are in contact with (at school and at home) that will commence upon notification of cases and outbreaks in the school or immediate community.

The study will not affect clinical treatment of any participants/patients.

The Study has two arms

- Scarlet Fever
- COVID-19

Confirmed Scarlet fever or COVID-19 Cases in a local community that trigger the study will be identified via voluntary or statutory notification to PHE, via local Health Protection Teams. For the purposes of this study, the notified case that triggers the study could be an adult member of staff or a child.

Eligible Contacts will be invited to participate based on their membership of a nursery or school affected by scarlet fever (2 cases within the same class) or by COVID-19 (1 case within the same school or 2 cases in the local community), or by membership of the same household as a case.

Cases who are recruited into the study will be school children aged 2y-11y (scarlet fever) or 2y-14y (COVID-19)

Contacts who are recruited into the study will be school children aged 2-11 (scarlet fever) or 2y-14y (COVID-19) attending the school affected by case(s) or school staff or members of Households (any age) affected by case(s).

Based on the number of schools that can practically be investigated in any 3 month study period in any single region, we expect that approximately 4 schools will be investigated. This might represent 8 cases of suspected scarlet fever or 4 cases of COVID-19, who will each be recruited for intensive (daily or alternate daily), then weekly swabbing. Assuming an average class size of 25 (10-15 in current COVID-19 pandemic), and recruitment of children in 3 class groups, approximately 100-200 classroom contacts will be recruited for weekly swabbing in a 3 month period. No more than 20 household contacts will be recruited for weekly swabbing in a 3 month period.

Based on scarlet fever notifications, the number of households that will receive a postal invitation to participate in the scarlet fever online survey (London region only) is 400-600.

3.1 Study Steps: Items marked** are routinely undertaken processes and are not research

3.1** Outbreak or case of suspected scarlet fever/COVID19 in a nursery/school/community is notified to Health Protection Team, PHE by telephone or school notification form. Simultaneous notification of same cases may be received from physicians.

3.2** The HPT nurse/specialist will make contact with school or nursery to obtain more details about the children in the school or nursery. A risk assessment is undertaken and advice provided on recommended control measures. The nursery or school is directed to Government guidance about Scarlet Fever or COVID19 as appropriate which may include an FAQ for parents/guardians plus a template letter for parents/guardians.

Nursery or School

3.3 HPT nurse /specialist will inform the school or nursery about the study by telephone and ask if they are interested in assisting with participation in the study; this will be supplemented by an Information Leaflet about the Scarlet Fever/COVID19 Research study for Heads of Schools/Nurseries

Options

Attachment 1 Headteachers Information (Scarlet Fever) Leaflet V2.

Attachment 1A* Low Season Headteachers Information (Scarlet Fever) Leaflet

Attachment 1B Headteachers Information (COVID19) Leaflet

Staff and Children who are Classroom Contacts

3.4 If a school is interested, the HPT nurse/specialist will provide an additional Information Leaflet for Staff and Parents/Guardians of all Child Classroom Contacts to be sent home to all parents with children who are currently in school/nursery to invite their child to participate. The number of classes invited to participate will depend on school and class size and type of outbreak (usually 1-2 for scarlet fever and 3-4 for COVID-19). Parents/guardians should receive two copies of the information leaflet to enable them to retain a full copy of the leaflet with tear-off consent. Age-appropriate leaflets and assent forms will be provided for children to take home too. Only one copy is needed for children. For COVID-19 arm, adults who are staff in the affected school should receive one copy of the Adult/Young person leaflet. Email or hard copies will be available depending on school preference. Electronic returns of forms will be accepted.

Options

Scarlet Fever exposure

Attachment 2 Child Contact_Parent/Guardian Information Leaflet and Consent v3;

Attachment 3 Child Contact_Child Under 8 Information Leaflet and Assent v3;

Attachment 4 Child Contact_Child aged Over 8 Information Leaflet and Assent v3)

Scarlet Fever Low Season

Attachment 2A LowSeason Child Contact_Parent/Guardian Information Leaflet & Consent*

Attachment 3A LowSeason Child Contact_Child Under 8 Information Leaflet & Assent*

Attachment 4A LowSeason Child Contact_Child aged Over 8 Information Leaflet & Assent*

COVID19 exposure.

Attachment 2B COVID Child Contact_Parent/Guardian Information Leaflet & Consent

Attachment 3B COVID Child Contact_Child Under 8 Information Leaflet & Assent;

Attachment 4B COVID Child Contact_Child aged Over 8 Information Leaflet & Assent

3.5 Staff and Parents/Guardians of all Child Classroom Contacts will be encouraged to decide overnight whether to consent to study and to return signed form to school or nursery next working day with assent forms. Telephone and email contact of study nurse/specialist will be provided for questions. If parents cannot consent overnight but are able to consent the following working day, their child will be swabbed in week 2 rather than week 1.

3.6 HPT nurse/specialist will visit school or nursery next working day to answer further questions and collect completed consent and assent forms. Forms can be returned by email.

For scarlet fever outbreak, nurse/specialist will take throat and hand swabs and collect cough plates from all consenting children, at a time and place convenient for the school/nursery.

For COVID19 outbreak, nurse/specialist will visit school or nursery **or child isolating at home** to take throat, nose, hand and cheek swabs at a time and place convenient for the school/nursery. Nurse/specialist will collect saliva sample. Appropriate personal protective equipment will be used.

Swabs will not be taken from any child that refuses or is upset. In the case of children where parents wish to be present, time of swabbing will be by appointment. Each child will be assigned a unique study number (USN) and each swab labelled with USN and date.

3.7 HPT nurse/specialist/scientist will take environmental samples from classroom or nursery (prior to any cleaning undertaken) and for scarlet fever may place 'settle plates' in classroom or nursery (these do not pose a risk to health and will be placed out of reach of children). Air samples may be taken.

3.8 Nurse/specialist will visit school or nursery weekly thereafter for a maximum of 3 further consecutive weeks to collect the same samples from consenting children and from the environment. Where this is not possible, either due to practical difficulties or withdrawal of participants in some cases, a lesser number of visits and swabs or adjusted timings will be acceptable.

3.9 **Optional** If the 4th week of swabbing is delayed for operational reasons nurse/specialist will send Reminder letter (***Attachment 11A Scarlet Fever Reminder Letter v1 or 11B COVID Reminder Letter v1***) to staff and parents/guardians of consented participants one week before the final visit to conduct the 4th swab at a time convenient to the school or nursery concerned (likely to be shortly before end of term or shortly after start of term). Nurse/specialist will visit school at pre-arranged date to collect 4th swab from consented staff and children. The maximum number of swabs from any contact will not exceed 4.

Optional: For schools participating outside the scarlet fever season, only ONE swab will be taken from each child and the visits therefore limited to one week.

3.10 **If a positive result is identified**. For COVID-19 any positive result will be conveyed to parents/guardians of participant by the Health Protection Team, with a letter for the General Practitioner. Standard PHE advice regarding case and household isolation will be provided following current national guidance.

For Scarlet fever, results will not be provided since asymptomatic carriage of Strep A is not routinely treated or isolated.

Should a Child Contact be identified as a Case in the course of the study, they will be invited to re-join the study as a 'Case' rather than as a 'Contact'. Sampling of adult contacts recruited into the study who are identified as cases in the course of the study will not be altered.

3.11 Weekly follow up of each class remaining in school should continue to occur if a positive case is identified.

3.12 Weekly follow up of contacts from the same class as the case will be undertaken from home during the two week exclusion period via home visits wherever possible. If not possible, self or parent-administered nose and throat swabs will be collected; swab kits will be despatched to each child's home, (with instructions for use and helpline to study team) for return to designated laboratory.

Individuals who are cases

3.13** HPT provide standard information leaflet and FAQ for the parents/guardians of any child who is a suspected case of scarlet fever or COVID19.

3.14 HPT nurse or specialist will inform the parents/guardians of the suspected or proven case about the study by telephone, by email or in person and offer the Information Leaflet about the study. Note that some cases may be identified in the course of the Study as a Classroom Contact; these families will be aware of the Study.

Options

Attachment 5A *Scarlet Fever Case_Parent/guardian Information leaflet and consent v3*

Attachment 5B *COVID19 Case_Parent/guardian Information leaflet and consent*. V1

Parent/Guardian should receive <u>two</u> copies to enable the recipient to retain a full copy of the information leaflet and consent. Age appropriate information leaflets and assent will be provided to the affected child. Only <u>one</u> leaflet is required for children.

Options

Scarlet Fever case

Attachment 6 *Scarlet Fever Case_Child Under 8 Information leaflet and assent v3;*

Attachment 7 *Scarlet Fever Case_Child aged over 8 Information leaflet and assent v3.*

COVID-19 case

Attachment 6B *COVID19 Case_Child Under 8 Information leaflet and assent* ***v1***

Attachment 7B *COVID19 Case_Child aged over 8 Information leaflet and assent v1*

Note that Attachment 7 (for children aged >8) may not be required as Children with Scarlet Fever will be recruited from those identified within nursery or school clusters in the 2-8 year old age group. An information leaflet for those with suspected scarlet fever aged over 8 is retained in case of a class of 8-9 year olds.

3.15 HPT nurse or specialist will arrange to talk to parents/guardian of any child with scarlet fever or COVID-19 by phone, by videolink, or in person, if appropriate, to go through the Study Information Leaflet relating to a Child with Scarlet Fever or COVID-19. After discussion the nurse or specialist will request Consent for the child with suspected Scarlet Fever or COVID-19 to participate, and assent from the child. In the unlikely event that the parent or guardian lacks capacity the child will not be enrolled..The nurse or specialist will emphasise standard public health guidance. If consent is undertaken remotely, then consent and assent forms may be returned electronically.

3.16 Having gained consent, nurse or specialist will arrange for first samples to be taken

Options

Scarlet Fever Nurse or specialist will take a throat swab, a cheek swab, and a hand swab from the affected child. The child will be asked to cough directly onto a blood agar plate (swabs and plate will be immediately closed and sealed for transport). Samples will be labelled with the unique study number (USN) and date

COVID-19. Nurse or specialist will visit child and take a nose swab, throat swab, a cheek swab, and a hand swab from the affected child. Nurse/specialist will collect saliva sample. Nurse or

specialist will request stool sample from Case that can be collected at time of return visit. If household visit not possible, nurse or specialist will arrange for a postal kit to be delivered with instructions and PPE. The parent or guardian will be invited to take a nose swab, throat swab, a cheek swab, and a hand swab from the affected child and collect a saliva sample. Teachers who are cases will be invited to provide a nose swab, throat swab, a cheek swab, and a hand swab.

3.17 For scarlet fever only, having gained consent for administration of the questionnaire, the nurse or specialist will begin to complete the questionnaire with the parents/guardians and ask the parents or guardian to keep a symptom diary to facilitate completion of the survey.

Options ***Attachment 9 Scarlet Fever Questionnaire***

COVID19 cases will not complete a questionnaire as part of this research project as they will be subject to a routine PHE mandatory surveillance questionnaire for notified cases.

3.18 If it is reported that a swab was previously taken by another healthcare provider, the nurse or specialist will contact the relevant diagnostic laboratory to ask that any pathogen identified is forwarded to the main PHE reference laboratory. This will be labelled with the USN and sample date for collation with other samples from the same child.

3.19 Samples from the case will be requested daily or alternate days for a maximum of 5 days in the 2 week period following initial positive diagnosis of the case (Ideally, days 1, 3, 5, 7, 14) . Where this is not possible, either due to practical difficulties or withdrawal of participants, a lesser number of visits and swabs will be acceptable. If the child returns to school during this time the nurse/specialist will arrange to take the daily swabs at school at a time agreed with the school and parent/guardian.

3.20 Visits will then be requested weekly thereafter for a further 2 weeks (day 21 and 28) to collect the same samples from the Child with Scarlet Fever or COVID-19. Where this is not possible, either due to practical difficulties or withdrawal of participants, a lesser number of visits and swabs or adjusted timings will be acceptable. The total number of samples will not exceed the maximum. If the child returns to school during this time the nurse/specialist will arrange to take the swabs at school at a time agreed with the school and parent/guardian. For cases who are teachers, swabs will be taken once a week for a total of 4 weeks. They will be taken by the nurse/specialist, and when not possible to do so, they will be self-administered.

3.21 The nurse/specialist will complete the questionnaire with the parents/guardians at one of the weekly visits.

Household Contacts of Children who are Cases

3.22 Nurse or specialist will inform the carer and any other household members about the Study and provide the Information Leaflets for Contacts who may be children or adults. Adults will be asked to consent to participate as contacts and will also be asked to consent on behalf of dependent children. Two copies of leaflets will be provided to adults and young people over 14 to enable the recipient to retain a copy of the consent as well as the information leaflet.

Options

Scarlet Fever

Attachment 2 *Child Contact_Parent/Guardian Information Leaflet and Consent;*

Attachment 8 *Household contact Adult/Young person aged 14-18 Information Leaflet and Consent*

COVID19

Attachment 2B *COVID Child Contact_Parent/Guardian Information Leaflet and Consent;*

Attachment 8B *COVID Adult/Young person Household or Teacher Contact Info leaflet & Consent*

Children in the household who are contacts will be provided with one copy of an age appropriate information leaflet and detachable assent form.

Options

Scarlet fever

Attachment 3 *Child Contact_Child Under 8 Information Leaflet and Assent;*

Attachment 4 *Child Contact_Child aged over 8 Information Leaflet and Assent*

COVID19

Attachment 3B *Child Contact COVID19 _Child Under 8 Information Leaflet and Assent;*

Attachment 4B *Child Contact_COVID19 Child aged over 8 Information Leaflet and Assent*

It will be acceptable for household contacts to provide nose and throat swabs only

3.23 Nurse or specialist will seek consent from carer and any other household members to participate. Each participant will have a unique consent form. Older children aged 14-18 who have capacity to consent will be invited to do so, although with the support of a parent or guardian. Parents or guardians of children aged under 14 will be asked to consent on their behalf however all children will be invited to assent. Adults who lack capacity will not be included.

3.24 Having gained consent, nurse or specialist will arrange for samples to be taken

Options

Scarlet Fever Nurse or specialist will take a throat swab. Each participant will be assigned a unique USN and each sample will be labelled with this. Swabs will be sealed for transport to laboratory.

COVID19. Nurse or specialist will visit household to collect nose & throat and hand swabs from consenting household members as well as cheek swabs and saliva samples in some cases. If not possible, they will arrange for a postal kit to be delivered with instructions and PPE. The household contact(s) will be invited to take a nose, and throat swab and saliva sample. Each participant will be assigned a unique USN and each sample will be labelled with this. Swabs will be returned by post or courier to laboratory.

3.25 Having gained consent, the nurse or specialist will arrange for the household to provide samples weekly thereafter for a maximum of 3 further weeks.. Where this is not possible, either due to practical difficulties or withdrawal of participants in some cases, a lesser number of visits and swabs or altered timings will be acceptable. The maximum number of swabs from any individual household contact will not exceed 4.

Household Environmental Samples

3.26 If parent/guardian agreeable, swabs will be taken from frequent–contact surfaces such as door handles and keyboards.

3.27 If parent/guardian consents, air samples will be collected from room in which Case is seated or playing. Samples will be taken with Case talking, singing, or shouting. Samples will be taken at fixed distances from Case

……..

Scarlet Fever Questionnaire ONLY – Other Children notified to PHE as Cases of Scarlet Fever

3.28 Nurse/research team at PHE will send letters addressed to parents/guardians of children notified as cases inviting them to participate anonymously in the questionnaire on line. Participants without access to the internet or requiring a translation or help will be invited to contact the team by post or telephone and an appropriate paper copy sent out for postal return (postage paid). Cases of COVID-19 aged under 16y are being invited to participate in a separate on line PHE-led survey.

Options

Attachment 10 Invitation to Scarlet Fever online Questionnaire V2

4. Participant Entry

Eligible schools will be identified via notification of confirmed cases within the school (Scarlet Fever: at least 2 cases; COVID-19 Single case) or notification of >2 cases in local community.
For Scarlet Fever arm, primary schools only are included. Triggering cases may be in children or adults.

Eligible CONTACTS (in the nursery/school setting) for the main study will be invited to participate based on their membership of a specific class or year group. These will be aged 2-11 (for scarlet fever arm), or 2-14 (COVID-19 arm) or adult staff members.

Eligible children who are suspected CASES within a school will be identified via notification to the local Health Protection Team at PHE or will be identified in the course of this study. Eligible children will be aged 2-11 (for scarlet fever arm), or 2-14 (COVID-19 arm).

Eligible contacts in the household setting for the main study will be invited to participate based on membership of (living in/sleeping in) the same household as a CASE. These will be adults or children of any age.

Eligible children for the Scarlet Fever Questionnaire study will be all those aged 16 or under who are a notified case; a letter will be sent to include a link to the online survey.

5. Regulatory Issues

a. Ethical Approval

The Chief Investigator is applying for approval from the Research Ethics Committee and the HRA.

b. Consent

For school/nursery outbreaks, invited participants will be given an Information Sheet to read at home along with an opportunity to ask questions of the research nurse/specialist by telephone or in person at the school or nursery prior to consent being provided the next day. For cases of scarlet fever or COVID-19, the information sheet will be discussed in person with the parent or guardian of each affected child in person, at home prior to consent being gained.

For the online Questionnaire only part of the Study (where participants are invited to participate anonymously) (Scarlet Fever arm only) consent will not be sought as participation is indication of voluntary consent.

If a participant/guardian lacks the capacity to consent to the study, we will not include them/their child in the study. Participants will be reminded that they can withdraw consent at any time during the study.

c. Confidentiality

All true identifiers relating to cases of notified scarlet fever, or COVID-19 including name, address, DOB, NHS number, will only be retained within PHE as routine for notifiable infections, and will not leave PHE. Only the Principal Investigator and PHE Data Custodian will have access to this record. Each participant including cases of scarlet fever or COVID-19 as well as classroom and household contacts will be allocated a Unique Study Number (USN). The USN will be used on each questionnaire (scarlet fever arm only) and on each bacteriological sample hence no part of the research material is identifiable. All PHE/NHS research staff will have full information governance training and will be familiar with and comply with the Data Protection Act (2018) and Regulation (EU) 2016/679 General Data Protection Regulation (GDPR). All identifiable records will be kept on an encrypted PHE computer with a secure login and password. All identifiable paper records such as consent forms and questionnaires will be retained at the Study site securely in a locked cabinet in a secure area to which only authorised PHE staff have access.

To retrieve isolates that were identified in samples previously submitted to routine NHS diagnostic laboratories prior to the study beginning, NHS laboratories will be asked (by the PHE Health Protection Team) to forward the relevant samples if available using the USN assigned to the subject to the Study Research laboratory. If for whatever local reason this is not possible then the diagnostic laboratory will be asked to forward the isolate to the PHE reference laboratory, where the USN can be applied to the sample prior to sending it to the Study laboratory; this can then be assimilated with other study samples that are labelled only with USNs. The Study Research laboratory will only handle material that is anonymised using the USN.

We intend to only use anonymised data in our research. USNs of children from a nursery will be alphanumerically linked to codes for individual nurseries and household contacts linked to codes for scarlet fever or COVID-19 cases. All identifiers will be deleted before loading up onto the research database. Only authorised research staff will have access to the database, via secure logon and password. Online questionnaires will not contain any identifiable material and cannot be traced or linked to individuals however will carry a unique study number USN to ensure that the correct individuals are completing the responses.

Imperial College London holds negligent harm and non-negligent harm insurance policies which apply to this study.

d. Sponsor

Imperial College London will act as the main sponsor for this study. Delegated responsibilities will be assigned to the Health Protection Teams (PHE) taking part in this study and the participating NHS laboratory.

e. Funding

Action Medical Research funded the study with additional support from the NIHR Health Protection Unit in AMR and HCAI. New funding is being sought

f. Audits

The study may be subject to inspection and audit by Imperial College London under their remit as sponsor and other regulatory bodies to ensure adherence to GCP and the NHS Research Governance Framework for Health and Social Care (2nd edition).

6. Data Management and Analysis

Biological samples (plates and swabs) will be analysed in a designated study Microbiology Research Laboratory. Patient identifiable data will only be attached to samples within an NHS or PHE laboratory but will not be attached to samples submitted to a Research laboratory. Many of the samples will be negative. Where samples are positive, these will be submitted for confirmatory testing and where appropriate antimicrobial resistance testing, viral culture, and pathogen genome sequencing. All strains identified from the study will be frozen, linked to the USN.

Data will be analysed using a standard statistical package such as Stata or Graph Pad Prism as appropriate. Microbiological data (both presence/absence of pathogen as well as quantity of pathogen) will be analysed against parameters such as time, duration of antimicrobial treatment, type of antimicrobial treatment.

At the end of the study, an encrypted version of the anonymised dataset will be archived according to College Policy, and held for a full 10 years. After 3 years, at the end of the research project, the dataset within PHE will be extracted into encrypted data drives, and deleted from the PHE database. The encrypted data drives will be kept in the PHE secured archive for a minimum of 10 years after which the data archive will be destroyed, unless an extension to the project is granted. Paper consent forms and questionnaires and any other raw study data will be retained securely for 10 years.

7. Study Management

The management of the study will be directed by Professor Shiranee Sriskandan and Dr. Rebecca Cordery (day-to-day clinical management). Coordination of the study will be by Head of Operations, NIHR Health Protection Research Unit, Section of Infectious Diseases, Imperial College London, Du Cane Road, London W12 0NN.

Email head.ops@imperial.ac.uk

8. Publication Policy

No identifiable personal data will be held or released to any third parties and non PHE or non-NHS staff. We will follow Office for National Statistics guidance on the dissemination of health statistics to ensure that there is no risk of general attributes disclosure for outputs at aggregate level. This will ensure that someone who has information about a statistical unit could not, with the help of data from the table, discover details that were previously not known to them (See National Statistics: Review of the Dissemination of Health Statistics: Confidentiality Guidance 2006).

9. References

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4. Adalat S, Dawson T, Hackett SJ, Clark JE. Toxic shock syndrome surveillance in UK children. Arch Dis Child. 2014;99(12):1078-82
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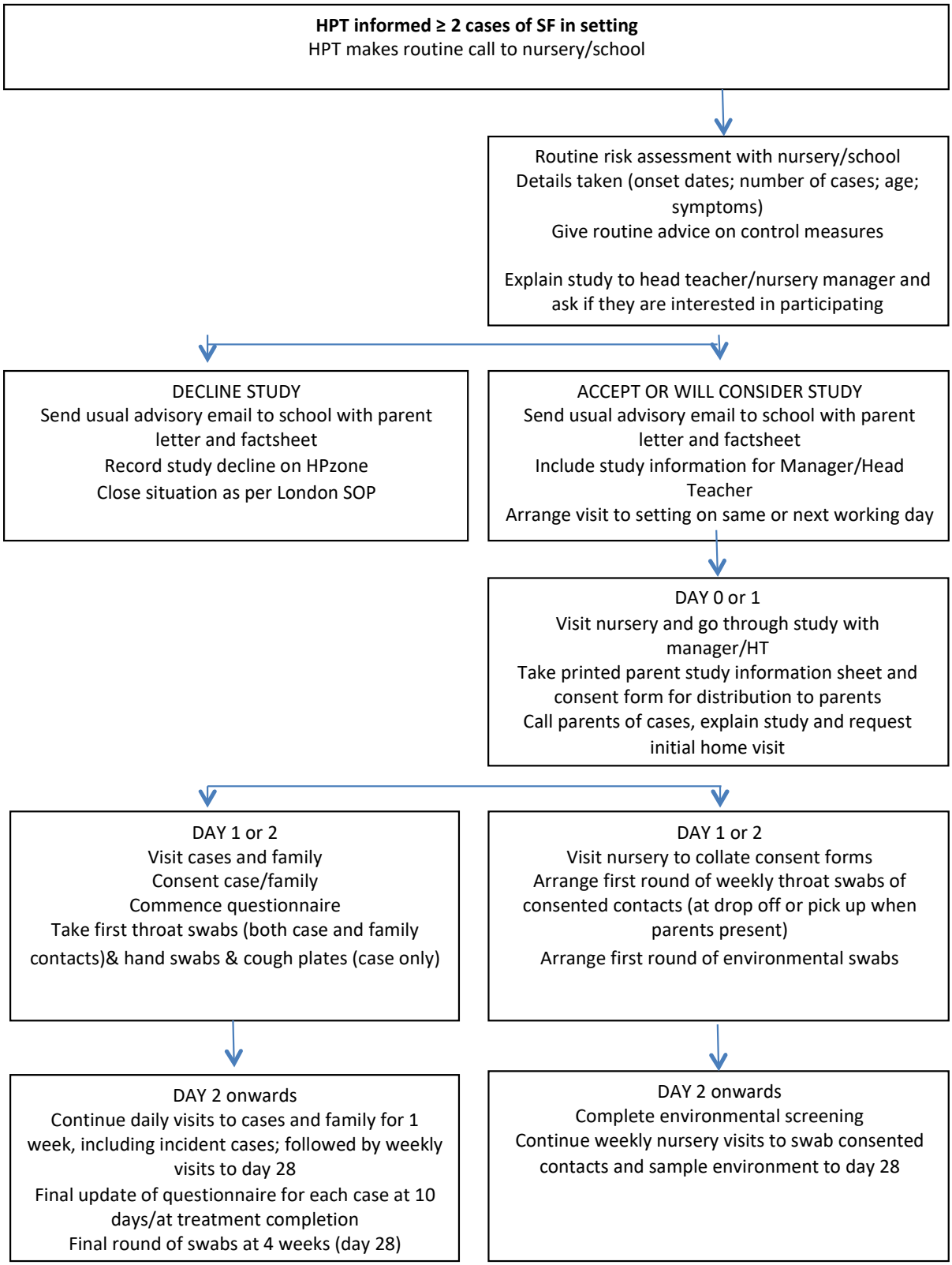
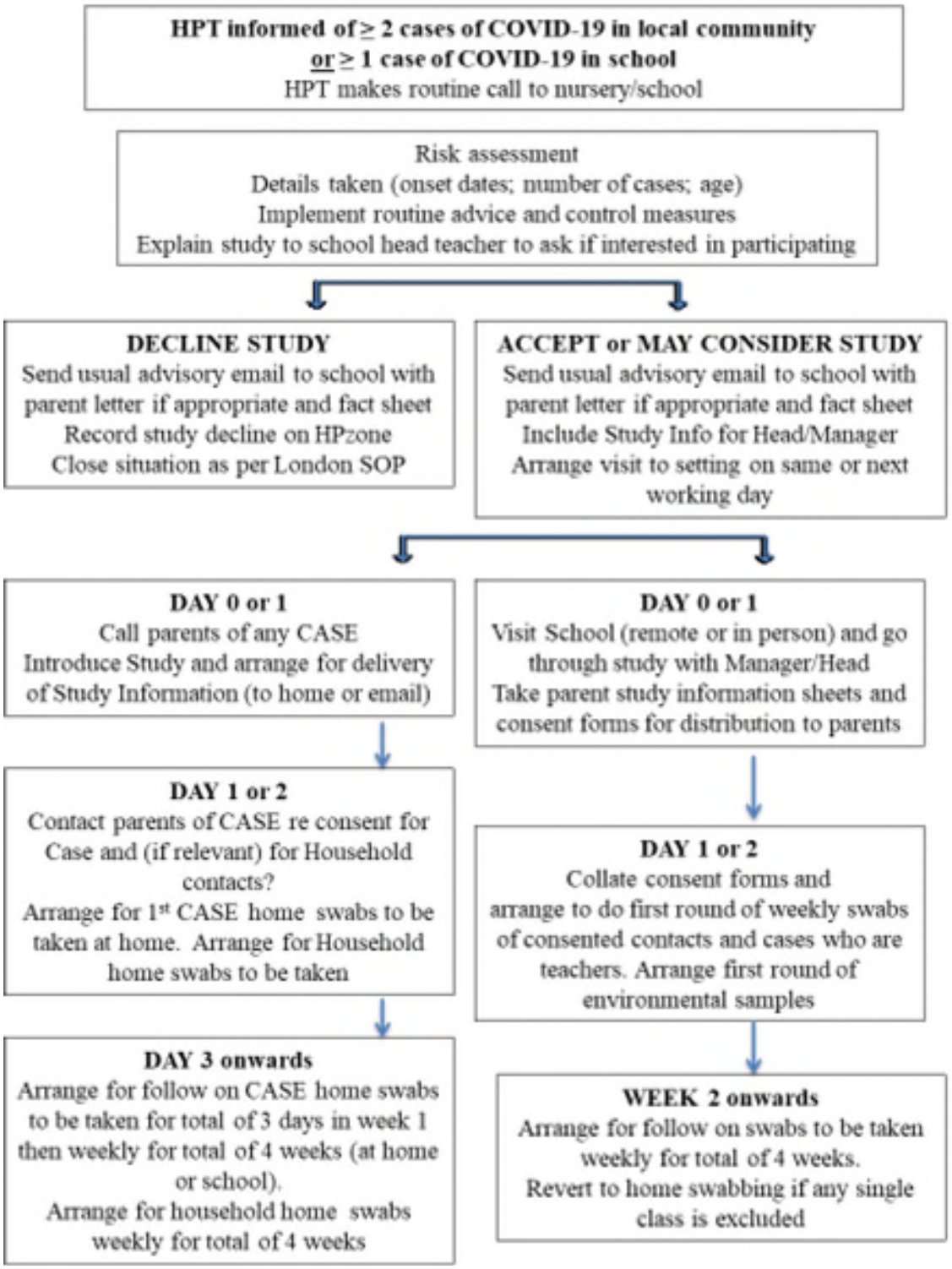
8. Little P, Stuart B, Hobbs R (2014). Antibiotic strategies for acute sore throat: a prospective observational cohort study. Lancet Infectious Diseases, 2014;14(3):213-9.

10. Appendices

Appendix 1 Flow Chart of Actions for tracking scarlet fever



Appendix 2 Flow Chart of Actions for tracking COVID19



Samples from ‘Cases’ will include separate throat, nose, hand and cheek swabs, plus saliva and faeces.

Household home swabs to include surfaces and air samples,

‘Contacts’ who are found to be SARS-CoV2 positive will be consented as ‘Cases’. Advisory information to school and any health protection action as per current London Covid-19 schools SOP to be given.