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The Respiratory Specimen Collection Trial (ReSpeCT): a randomized controlled trial comparing quality and timeliness of respiratory sample collection in the home by a parent or healthcare worker in children aged <2-years.

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Keywords: acute respiratory infections, nasal swabs, children, specimen collection, parent

Running title: Respiratory Specimen Collection Trial

Supplementary data

METHODS

Recruitment

Children were recruited through local childcare centres and general practitioners using mail-outs; contact with eligible families identified from a database held by the Department of Emergency Medicine at the Brisbane Royal Children's Hospital; and via an email to the staff at the same hospital. Eligible responding parents received detailed study information and an initial home visit by a study nurse.

Randomized controlled trial (RCT) study component

Children were randomized into a parent-collected (P-group) or healthcare worker-collected group (HCW-group) in a 1:1 ratio, using computer-generated, random allocation codes, placed in sequentially numbered opaque envelopes. Envelopes were prepared by a staff member not involved in the trial prior to study commencement. Due to the nature of the study, once assigned, concealment of group allocation from either parents or staff was not possible.

Parents were trained in all aspects of the study at the enrolment visit. This education consisted of reviewing the simple written instructions left with parents and reviewing the completion of trial paperwork; training in the identification of a new acute respiratory infection (ARI); training in specimen collection, handling, and return (P-group RCT specimen; HCW-group: nested diagnostic study specimen). An initial study visit took between 60 to 90-minutes, including initial collection of informed consent.

Completed symptom diaries were returned monthly by mail. At enrolment, sociodemographic and health-related data, including household and socioeconomic variables (income categories

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were based on Australian Bureau of Statistics income quartiles [1]), vaccination status, childcare attendance, breast-feeding, and tobacco smoke exposure were recorded using a standard questionnaire.

Parents in the P-group were taught to collect an anterior nasal swab using a plastic-shaft, rayon-budded swab, which comes with a transport tube with a foam pad reservoir soaked with viral transport medium containing chloramphenicol and amphotericin (Virocult MW950; Medical Wire & Equipment, Wiltshire, UK). Parents were instructed to insert the swab into the anterior cavity of the nose and rub around the internal walls of the nares. Parents were asked to target swabbing nasal discharge if present. Parents were not given specific guidance about the duration of swabbing. Parents were asked to collect specimens at the occurrence of a new ARI and to mail them to the research laboratory as soon as possible after collection. These specimens were mailed as single swabs through the standard post, without an ice brick or coolant, subjected to ambient temperature for the duration of transit. The HCW-collected nasopharyngeal swab was placed in universal transport media (Flocked swabs with UTM, 305C; Copan, Brescia, Italy) and returned by the HCW directly to the laboratory in a small polystyrene transport container with an ice brick.

Parents were asked to collect a single specimen at the point in time where the child had symptoms that meet the definition of an ARI. Where multiple specimens were collected, only the first specimen was analyzed by the laboratory.

Nested diagnostic study component

Parents collected a dry anterior nasal swab (Tubed Sterile Dryswab™ Rayon MW1021; Medical Wire & Equipment, Wiltshire, UK) from the HCW-group children during the HCW home visit. A visit envelope contained random allocation into one of four groups providing

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collector order and location (HCW or parent first, right or left nostril first) in a 1:1:1:1 allocation ratio. The nasopharyngeal swab collected by the HCW was returned directly to the laboratory and the parent-collected nasal swab was placed in a post box by the HCW for mailing back to the laboratory.

Laboratory testing

As detailed elsewhere [2-4], stored specimens were thawed and tested by polymerase chain reaction assays for sample quality using ERV3, as well as for 17 respiratory viruses (rhinovirus; respiratory syncytial virus A and B; influenza virus A and B; parainfluenza viruses I, II, III; human metapneumovirus; human coronaviruses OC43, 229E, NL63, and HKU1; adenoviruses; human bocavirus-1; human polyomaviruses KIV and WUV), and three bacteria (*Streptococcus pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis*).

Data analyses

In producing values for positive and negative agreement (PA and NA respectively), asymptotic 95% CIs were produced using standard errors (SEs) calculated using the formulae given by Mackinnon 2000 [5]. SEs were calculated using the following formulae:

$$SE(PA) = \sqrt{4a(c+b)(a+c+b)} / (2a+b+c)^2$$

$$SE(NA) = \sqrt{4d(c+b)(d+c+b)} / (2d+b+c)^2$$

Asymptotic confidence limits for PA and NA were then derived using the formulae; where CL and CU are the lower and upper confidence limits:

$$CL(PA) = PA - SE(PA) \times 1.96$$

$$CU(PA) = PA + SE(PA) \times 1.96$$

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$$CL(NA) = NA - SE(NA) \times 1.96$$

$$CU(NA) = NA + SE(NA) \times 1.96$$

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