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Child caries management: a randomized controlled trial in dental practice

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Abstract

This multi-centre, three-arm, parallel-group, patient-randomized controlled trial compared clinical effectiveness of three treatment strategies over three years for managing dental caries in primary teeth in UK primary dental care. Participants (3-7 years, with at least one primary molar with dentinal carious lesion) were randomized (1:1:1 via centrally-administered system using variable-length random permuted blocks) across three arms: C+P: conventional carious lesion management (complete carious tooth tissue removal; restoration placement) with prevention; B+P: biological management (sealing-in carious tooth tissue restoratively) with prevention and; PA: prevention alone (diet, plaque removal, fluorides and fissure sealants). Parents, children and dentists were not blind to allocated arm. Co-primary outcomes were: 1) the proportion of participants with at least one episode of dental pain and/or infection: 2) the number of episodes of dental pain and/or infection during follow-up (minimum: 23 months). 1144 participants randomized (C+P:386; B+P:381; and PA:377) by 72 general dental practitioners, of whom 1058 (C+P:352; B+P:352; PA:354) attended at least one study visit and were included in primary analysis. Median follow-up; 33.8 months (IQR 23.8, 36.7). Proportions of participants with at least one episode of dental pain and/or infection were: C+P:42%; B+P:40%; PA:45%. No evidence of a difference in incidence of dental pain and/or infection comparing B+P (adjusted Risk Difference (97.5% CI): -2% (-10%, 6%)) or PA 4% (-4%, 12%) to C+P. Mean number of episodes of dental pain and/or infection were: C+P: 0.62 (sd 0.95); B+P: 0.58 (0.87); PA: 0.72 (0.98). Superiority could not be concluded for number of episodes comparing B+P (adjusted Incident Rate Ratio (97.5%CI): 0.95 (0.75, 1.21)) or PA (1.18 (0.94, 1.48)) to C+P. In conclusion, there was no evidence of a difference between the three treatment approaches for incidence, or number of episodes, of dental pain and/or infection experienced by these high caries-risk participants with established disease. Trial registration: ISRCTN77044005.

Introduction

Dental caries, the most common childhood disease, has significant health and economic impact globally (Listl et al. 2015) and for the United Kingdom (UK) (Information Services Division 2014; Public Health Wales 2014; Royal College of Surgeons Faculty of Dental Surgery 2015; Vernazza et al. 2016).

In the UK, Dental Professionals (DPs) in primary dental care (non-specialist care in general practice or within the public health service) carry out most dental care for children. Two primary care studies questioned the success of conventional restorations in preventing pain and infection and challenged the value of operative treatment (Levine et al. 2002; Tickle et al. 2002) for primary teeth. Improved understanding of the dental biofilm in the establishment and progression of caries, and the effects of its manipulation, through modifying sugars in the diet, using topical fluoride, and sealing-in carious tooth tissue, have encouraged investigation of alternative approaches to caries management, including minimally-invasive techniques. Continuing uncertainty amongst DPs over how to most effectively manage carious lesions in primary teeth, together with growing evidence at a tooth level (Yengopal et al. 2009) for more successful minimally-invasive approaches, led the UK National Institute for Health Research to commission the FICTION (Filling Children's Teeth: Indicated Or Not?) trial, comparing the clinical- and cost-effectiveness of three strategies for the management of dental caries in primary teeth for children aged 3-7 years, in UK primary dental care.

This paper reports clinical effectiveness of these three strategies, using the co-primary outcomes of dental pain (incidence and number of episodes) and/or infection. The secondary outcomes (cost-effectiveness from a healthcare perspective; participants' oral health related quality of life; dental anxiety; caries incidence; and preferences, acceptability and experiences of participants, parents/carers, and DPs) are summarized here and reported in full elsewhere (Maguire et al. 2019).

Methods

The trial protocol has been published (Innes et al. 2013), an updated version is available at <http://www.nets.nihr.ac.uk/projects/hta/074403>. The University of Dundee sponsored the trial which was registered with the ISRCTN (ISRCTN77044005). East of Scotland Research Ethics Committee provided ethical approval (REC reference: 12/ES/0047).

Trial Design and Setting

FiCTION was a pragmatic, multi-centre, three-arm, parallel group, open, patient-randomized controlled trial with 1:1:1 allocation, set in NHS primary dental care. For training and administration, practices were grouped into five clinical centers in Scotland (1), England (3) and Wales (1).

Participants

Children aged 3-7 years, with at least one primary molar tooth with a carious lesion extending into dentin, (defined according to the International Caries Detection and Assessment System (ICDAS) (Ismail et al 2007, Pitts 2004) for visual and/or radiographic diagnoses as extending into dentin and either cavitated or not) but with no associated pain or infection, were recruited by their dental practice. Children not accompanied by an adult with capacity to consent, with a medical condition requiring special dental consideration, currently involved in any other research, or moving from the area, were excluded.

Interventions

Participants were randomly allocated to one of three multi-component child-level treatment strategies. Throughout the trial these could be undertaken by any appropriately qualified DP, which might include a general dental practitioner (GDP), dental hygienist/therapist or dental nurse. DPs attended one day training in trial procedures and any clinical procedures self-identified as a training need. Although the detection of dental infection is a standard part of a dental clinical examination, given its importance as one of the primary outcomes, training specifically addressing this was included using photographs, radiographs and discussion. Training in clinical procedures was provided. Participants attended for dental care and review at intervals determined by their GDP, informed by national guidance relating to disease risk. In all three arms irreversible pulpitis, infection or pulpal exposure were treated with pulp therapy or extraction.

Best Practice Prevention Alone (PA) arm components (Public Health England 2014; Scottish Dental Clinical Effectiveness Programme 2018) were:

- Dietary investigation, analysis and intervention to reduce fermentable carbohydrate intake;
- Toothbrushing for plaque removal with a fluoridated toothpaste and, for over 7 year-olds, fluoride mouth-rinsing;
- Topical fluoride varnish (primary and permanent teeth); and
- Fissure sealants (permanent teeth).

Protocol dictated that within the PA arm there should be no rotary instrumentation to remove carious tissue, no sealing-in caries, and no restoration placement.

Conventional with Best Practice Prevention (C+P) arm protocol dictated local anaesthesia (LA) administration, complete mechanical removal of carious tooth tissue and placement of a restoration.

Biological with Best Practice Prevention (B+P) arm protocol dictated sealing-in carious tooth tissue with an adhesive restorative material or a preformed metal crown using the Hall Technique. Superficial carious tooth tissue could be removed to ensure the seal was complete but LA was not routinely required as protocol dictated that no affected dentin should be removed.

Co-primary outcomes

The original primary outcome – the proportion of participants with at least one episode of dental pain and/or infection (incidence) **over the study period** – was modified in May 2017 to include a co-primary outcome: the total number of episodes of dental pain and/or infection for each participant. Episodes were defined on a tooth-by-tooth basis; where there were two (or more) teeth with dental pain and/or infection at the same visit, this was recorded as one episode at that visit for that participant. If a participant had dental pain and/or infection on the same tooth at consecutive visits, this was considered a single episode, regardless of the time between visits. Full details of the definition of an episode of dental pain and/or infection are provided in Appendix 1.

Pain due to caries

Assessments for dental pain were carried out by the participant's dentists at each visit and recorded on a case report form (CRF). To differentiate between pain originating from caries rather than other causes (e.g. erupting or exfoliating teeth, mouth ulcers), the dentist formed a judgement based on patient/parent history and clinical evidence.

Dental infection

Clinical visual examination for dental infection, swelling, dental abscess or draining sinus, was specifically undertaken at every visit, and recorded on the CRF. Clinical examination was expected to be supplemented with radiographs (in line with FGDP guidelines (Pendlebury et al. 2004)) for signs of inter-radicular pathology. At the outset it was decided that if fewer than 80% of participants had radiographs within one year of entry to the trial, radiographs would not be used by the research team to supplement

clinical reports. We considered that if we found fewer than 80% of the children to have radiographs on entry to the trial (or within one year of entry) this would be too low (and not representative enough of the children across the trial) to be able to use the radiograph data to supplement the clinical data and we would rely on assessment of the clinical data alone for the outcome measure. Data were analysed using Stata V14 StataCorp. 2015. Stata Statistical Software: Release 14. College Station, TX, USA.

Secondary outcomes

The methods for assessing secondary outcomes are reported in full in Maguire et al. (2019). Cost-effectiveness from a healthcare perspective was assessed as incremental cost per incidence and incremental cost per episode of dental pain and/or infection avoided. Information on costs was collected via CRFs completed at every visit and costed using time/materials-based costing, which costs the quantity of each resource used to provide treatment (Drummond et al 2005). Participants' oral health related quality of life (COHRQOL) was measured at baseline and final visit using the 16 item Parental and Caregivers Perception Questionnaire (P-CPQ-16) (Thomson et al. 2013; Thomson et al. 2014). Dental anxiety was assessed at all visits using the Modified Child Dental Anxiety Scale (Howard and Freeman 2007) and additional single items assessing child and parent-reported anticipatory and treatment-related anxiety. Caries incidence was measured using the ICDAS at baseline and final visits. Qualitative methods evaluated preferences, acceptability and experiences of participants, parents/carers, and DPs.

Sample Size

Based on evidence from studies on similar populations with no restorations (Levine et al. 2002), conventional restorations (Tickle et al. 2002) and the Hall Technique (Innes et al. 2007), infection rates of 20%, 10% and 3% were expected in the PA, C+P and B+P arms respectively. The original target sample size to detect the hypothesized effect sizes (incidence of infection of 20% vs 10% for PA vs C+P; 3% vs 10% for B+P vs C+P respectively) was 1460 children (90% power, 2.5% significance level to adjust for 2 comparisons, 2-sided tests), allowing for 25% loss to follow-up and including an inflation factor of 1.09 to allow for potential clustering of the treatment effect at practice level. The trial was extended by 12 months due to a lower than anticipated recruitment rate. Under the revised time frames for recruitment and follow-up, it was projected that 1113 children would be randomized and followed up for an average of 35.5 months (minimum 23 months). Assuming a linear incidence of dental pain and/or infection over the modified follow-up period, the revised sample size of 1113 resulted in 82% power to detect the hypothesized effect sizes, allowing for 25% loss to follow-up.

Randomization and Blinding

The unit of randomization was the child, with allocation to the three treatment strategies in a 1:1:1 ratio, using variable-length random permuted blocks, and stratified by practice. Randomization was via a secure web-based system administered centrally by Newcastle Clinical Trials Unit. Parents, participants and dentists were not blind to the allocated mode of caries management.

Statistical Methods

Analyses were completed blind and performed according to a pre-defined statistical analysis plan (Maguire et al. 2019) and on the basis of a modified intention-to-treat (mITT), defined as all randomized participants with at least one CRF. The original power calculation was based on a comparison of incidences and as such was the only powered analysis; an exploratory hypothesis test for the unpowered comparison of the mean number of episodes is therefore reported. Models were adjusted for age at randomization (years) and time in the trial (years). Differences between practices were included as a random effect. As the study was powered on a significance level of 2.5% we report 97.5% confidence intervals (CI). The primary analyses of the co-primary outcomes were:

- Logistic regression for incidence of dental pain and/or infection. The comparisons between treatment arms (PA vs C+P and B+P vs C+P) were expressed as adjusted Risk Differences (aRD).
- Negative binomial regression for the number of episodes of dental pain and/or dental infection with the comparisons between treatment arms expressed as adjusted Incidence Rate Ratios (aIRR).

Sensitivity analysis included only participants with at least 23 months' follow-up. A per-protocol (PP) analysis was conducted, excluding participants who were deemed likely to have had dental pain and/or infection at consent and/or who were defined as having a 'major' deviation (i.e. a major cross-arm tooth-level treatment undertaken outside of the allocated arm's treatment protocol) at more than 20% of their visits. Exploratory multivariable regression analysis investigated the relationship between incidence and age, ethnicity, practice-level tap water fluoride concentration, practice-level Index of Multiple Deprivation and number of **carious** teeth at baseline. Time to first episode of dental pain and/or infection was included as a secondary analysis of the primary outcome measure using Kaplan-Meier survival curves to estimate event rates and a Cox proportional hazards model was fitted to estimate treatment effects, expressed as adjusted Hazard Ratios (aHR).

Results

Practice recruitment and characteristics

Of the 93 practices receiving a site initiation visit, 21 did not randomize any participants, leaving 72 practices across the five clinical centres randomizing at least one participant. Ten practices subsequently withdrew but data collected until the practices' withdrawal date were included in the analysis. Practice characteristics for size (number of registered patients), deprivation index (quintiles) and tap-water fluoridation status (ppm F) are shown in Appendix 2.

Participant flow

Of 7699 children screened at review appointments, 6555 (85%) were ineligible, primarily due to not having dentin caries in a primary molar. Between October 2012 and June 2015, 1144 participants were randomized: C+P:386; B+P:381; and PA:377. Of these 1144 randomized participants, 86 (8%) did not attend any study visits. The remaining 1058 participants (C+P:352; B+P:352; PA:354) from 68 practices comprised the mITT analysis set (Figure 1).

Baseline characteristics

There was balance between arms at baseline for demographic and clinical characteristics (Table 1).

Treatment provision and adherence to protocol

There were 7713 study visits. At least one component of prevention was delivered, primarily by GDPs, at 81% of all visits, with rates of delivery higher in PA (85%) but similar (at 79% each) in C+P and B+P. Operative care occurred at 34% of all visits (C+P 42%, B+P 42%, and PA 19%) and was also primarily undertaken by dentists (91% of all operative visits) (Appendix 3).

Less than half the participants (511/1058 (48%)) had a radiograph taken at any stage of the trial.

A major, cross-arm, deviation was recorded at 6% of the 7713 visits involving 263 participants of whom 46%, 39% and 15% were from C+P, PA, and B+P respectively. The main reasons given for cross-arm deviations were DP's clinical judgements (29%) and parent factors (28%) (Appendices 4 and 5). Most participants (89%) could be included in the PP analysis.

Co-primary outcomes

The co-primary outcome of incidence of dental pain and/or infection over a median (IQR) follow-up period of 33.8 (23.8, 36.7) months was 42% (148/352) in C+P, 40% (141/352) in B+P, and 45% (161/354) in PA (Table 2) with no evidence of a difference when comparing B+P (aRD (97.5% CI): -2% (-10%, 6%)) or PA (4% (-4%, 12%)) to C+P (Table 3). For the co-primary outcome of number of episodes of dental pain and/or infection, most participants, (910/1058 (86%)), had zero or one episode over the follow-up period (Table 2); the average number of episodes was 0.62 (sd 0.95), 0.58 (sd 0.87), and 0.72 (sd 0.98), in the C+P, B+P and PA arms respectively. Superiority could not be concluded when comparing B+P (aIRR (97.5%CI): 0.95 (0.75, 1.21)) or PA (aIRR (97.5% CI): 1.18 (0.94, 1.48)) to the C+P arm (Table 3). The sensitivity, PP, and exploratory analyses were consistent with the mITT analyses of the co-primary outcomes (Table 3, Appendices 6-10).

In the secondary analysis of the primary outcome measure, the estimated probabilities of having no dental pain and/or infection at 2 years post-randomization were 64% (97.5% CI: 58% to 69%), 65% (59% to 70%) and 56% (50% to 61%) (Table 2) in C+P, B+P and PA respectively; the overall Kaplan-Meier estimate of the median (97.5% CI) time to first episode of dental pain and/or infection was 3.1 (2.8, 3.6) years. There was no evidence of a difference in the time to first episode of dental pain and/or infection when comparing B+P (aHR (97.5% CI): 0.95 (0.73, 1.24)) or PA (aHR (97.5% CI): 1.19 (0.92, 1.53)) to C+P (Appendix 11).

Secondary Outcomes

Secondary outcomes are reported in Maguire et al. (2019) with a brief summary here to signpost relevant findings for context. On average, it cost £230 to manage dental caries in a child with at least one tooth with carious lesions into dentin over the follow-up period. PA was, on average, the least costly but the least effective for both co-primary outcomes; B+P and C+P would provide greater benefits, albeit at a higher cost. B+P had the highest probability of being considered cost-effective compared to PA and C+P at a willingness to pay threshold of £330 to avoid an incidence of dental pain and/or infection and £130 to avoid an episode of dental pain and/or infection. For dental anxiety (parent or child reported) and COHRQoL, there was no evidence of any statistically significant differences apart from parent-reported child anticipatory anxiety for PA vs C+P (6% lower in the PA arm; aRD -0.06 (97.5%CI: -0.11 to -0.003)) or clinically significant differences when comparing either B+P or PA to C+P for any outcomes. There was also no evidence of any differences between treatment arms for incidence of caries in primary teeth or first permanent molars. Qualitative interviews with participant/parent dyads indicated that all three

treatment arms were generally acceptable to them but trust in the DP played a significant role. Procedures, including LA and dental extractions, were generally viewed more negatively.

Discussion

This large, pragmatic multi-centre trial embedded in primary dental care recruited a representative sample of dental practices, a diverse selection of GDPs, and participants with cultural/ethnic diversity (Office for National Statistics et al. 2017) (Table 1). As such, this trial provides findings generalizable to the UK population of regularly attending high caries risk children in the primary or mixed dentition attending primary care. No other similarly-sized RCT has been undertaken with children in primary dental care and none have followed-up clinical outcomes at the level of the child (rather than a single tooth) for as long. Median (IQR) follow-up was good at 33.8 (23.8, 36.7) months and a major, cross-arm, deviation was recorded at only 6% of the dental visits. The pragmatic approach taken, observing what DPs did for participants in each of the arms when requested to follow caries lesion management protocols, is highly relevant to daily practice and akin to establishing what might happen if guidance or policy were put in place to direct clinical practice towards using one particular approach.

Running an RCT in the relatively research-naïve environment of NHS primary dental care was challenging. Slow recruitment rates increased the length of time practices were involved in the trial, necessitating the update of existing, and training of new, practice staff (clinical and administrative) in trial procedures, and resulting in some research fatigue. Data collection towards the end of the trial required high levels of motivational input from research staff and practice teams, especially as some secondary outcomes were only measured at baseline and scheduled final visits. Practices also had to contend with requests from the trial team to verify any questionable or missing data. However, the resulting high quality of the data collected and the analyses conducted minimized potential for bias.

Although there was no evidence of a difference in the proportion of participants with at least one episode of dental pain and/or infection between arms, the incidence was higher than anticipated (C+P: 42%; B+P: 40%; PA: 45%) and consequently the associated CIs were also wider. **This level of incidence of dental pain and/or infection is of some concern especially when observed in a developed country with comprehensive dental health services, although the rate of experience of dental pain ever during the trial (overall 36%) was higher than dental infection (25%) and may reflect differences between reported versus clinically observed outcomes.** As the co-primary outcomes were measured at child (mouth) level, the incidence

was higher than in studies reporting on single tooth treatments. It is difficult to directly equate the findings of single tooth studies using single treatment strategies with those of FiCTION, a child-level trial with multi-component interventions (with up to 20 teeth involved per participant). The overall levels of dental pain and/or infection are probably comparable to single tooth studies and possibly even lower in FiCTION participants (de Amorim et al. 2018; Dorri et al. 2017; Innes et al. 2015; Santos et al. 2016; Yengopal et al. 2009). Nonetheless, the trajectory of dental caries, once established (Hall-Scullin et al. 2017; Warren et al. 2017), means that these high risk children require a high level of care. It is possible that low use of radiographic diagnosis may have affected clinicians' diagnostic thresholds, leading to undetected carious lesions and misdiagnosis of the lesions' extensiveness. This may have increased the potential for non- or late-management of lesions contributing to occurrences of dental pain and infection, although a counter-argument is that unnecessarily invasive treatment was avoided (Bader et al. 2001; Schwendicke et al. 2015; Wenzel 2004). The general practice primary dental care environment differs from secondary dental care where additional resources, with respect to time and expertise, lead to more favourable outcomes (BaniHani et al. 2019; Chadwick et al. 2001) and these factors may also have contributed to the rates of dental pain and/or infection seen. However, the FiCTION trial was designed to compare three treatment approaches within primary dental care and fulfilled this objective. The trial was sufficiently powered to detect any true differences between arms, particularly with regard to the incidence of dental infection events, as they formed the basis of the original power calculation. Possible explanations for finding no evidence of clinical superiority between the three caries treatment approaches are the combination of: i) the inevitability in the co-primary outcomes being observed in all arms since the participants began the trial with established dentinal lesions; ii) since radiographs were used infrequently, some initially undetected lesions progressed without being managed; iii) the co-primary outcomes being measured at child- rather than tooth-level meant the possibility of observing dental pain and/or infection from teeth treated prior to FiCTION, and iv) the pragmatic nature of the trial may have meant that DPs reverted to treatments most familiar to them rather than strictly following the evidence-based protocols. Future work could explore the possibility of looking at individual tooth outcomes in the FiCTION.

As with the co-primary outcomes, there was no evidence of a difference in caries incidence, COHRQoL or dental anxiety between the three caries management strategies, and all were generally acceptable to participants, parents and DPs without provoking anxiety. PA was, on average, the least costly and least effective treatment strategy for both of the co-primary outcomes. B+P has the potential to provide more oral health benefits; however this comes with additional costs and a judgement is required as to what value should be placed on the avoidance of dental pain and/or infection in primary teeth.

When dentin caries is present, the biological approach could be the most likely strategy to be considered cost-effective if society is willing to pay a minimum of £130 to avoid dental pain and/or infection in a primary tooth. The importance of trust in the DP was highlighted in the qualitative studies, with a conversation between child, parent, and DP to agree the best options for the individual child being key.

The social gradient in health inequity (Marmot 2005), with the poorest shouldering the highest burden, is reflected in the socio-economic distribution of dental caries. Children who experience caries in their primary dentition carry a greater burden of dental caries and its consequences into later life (Hall-Scullin et al. 2017). There was no evidence of a difference in clinical effectiveness between arms in children with established dentin caries when managed in primary dental care; consequently this study highlights that the primary prevention of disease is paramount and emphasises the importance of early prevention for young children to avoid dental caries altogether rather than trying to manage multiple dentinal carious lesions. DPs' willingness and abilities to deliver effective strategies and individual items of care should be carefully considered in any implementation strategies for policy, teaching and practice.

Author Contributions

Trial conception: NI, JC, GD, EM. Trial design: NI, AM, JC, GD, CD, ZM, EM, RH, RF, BC, FW. Trial conduct: NI, AM, JC, GD, ZM, LV, MR, BC, FW, EM. Data acquisition: NI, AM, GD, CD, ZM, MR, AA, RH, BC, FW. Data analysis: NI, JC, VR, TH, LV, ZM, NW, RH, AM, GD. Data interpretation: NI, AM, JC, GD, CD, VR, TH, LV, ZM, EM, NW, MR, RH, RF, BC, FW. Drafted manuscript; NI, AM, JC, VR, EM, NW, TH, MR. Critically revised the manuscript: all authors.

All authors gave final approval and agree to be accountable for all aspects of this work.

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The supplemental appendix for this article is available online.

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Figure and Table Legends

Figure 1: CONSORT flow diagram of participant journey through trial

Table 1. Participant characteristics at baseline, by randomized treatment arm [mITT analysis set, n=1058].

Table 2. Summary statistics for Incidence, Number of episodes and Probability of having no dental pain and/or infection at 2 years post-randomization (mITT analysis set, n=1058).

Table 3. Estimates of the Risk Difference and Incident Rate Ratio over the follow-up period in dental pain and/or infection between randomized treatment arms; models are adjusted for age in years, time in study in years and a random effect for practice.

Table 3. Participant characteristics at baseline, by randomized treatment arm [mITT analysis set, n=1058].

| Participant characteristic | n | C+P | n | B+P | n | PA | n | Total n= 1058 |
|--|-----|--|-----|---|-----|------------------------------|------|------------------|
| | | (conventional carious lesion management with prevention) n= 352 | | (biological management with prevention) n= 352 | | (prevention alone) n= 354 | | |
| Age (years) Mean (sd) | 352 | 6.0 (1.3) | 351 | 6.0 (1.3) | 354 | 5.9 (1.2) | 1057 | 6.0 (1.3) |
| Sex n (% female) | 349 | 175 (50.1) | 349 | 181 (51.9) | 349 | 180 (51.6) | 1047 | 536 (51.2) |
| Ethnicity¹ n (%) | | | | | | | | |
| White | | 236 (75.4) | | 248 (77.0) | | 243 (75.9) | | 727 (76.1) |
| Black | 313 | 9 (2.9) | 322 | 11 (3.4) | 320 | 10 (3.1) | 955 | 30 (3.1) |
| Indian, Pakistani or Bangladeshi | | 37 (11.8) | | 38 (11.8) | | 36 (11.3) | | 111 (11.6) |
| Chinese | | 5 (1.6) | | 3 (0.9) | | 3 (0.9) | | 11 (1.2) |
| Mixed race | | 11 (3.5) | | 13 (4.0) | | 13 (4.1) | | 39 (4.1) |
| Other | | 15 (4.8) | | 9 (2.8) | | 15 (4.7) | | 37 (3.9) |
| d₃mft² mean (sd) | 339 | 2.8 (2.7) | 333 | 2.8 (2.8) | 334 | 2.6(2.6) | 1006 | 2.7 (2.7) |
| P-CPQ16³ Mean (sd) | 300 | 8.9 (6.7) | 314 | 8.0 (6.3) | 309 | 8.3 (6.2) | 923 | 8.4 (6.4) |
| MCDASf⁴ Mean (sd) | 336 | 13.8 (4.9) | 324 | 14.2 (5.3) | 329 | 14.3 (5.3) | 989 | 14.1 (5.1) |

¹ Representing ethnic/ cultural variation was one of the strengths of the trial with the non-white population of the UK at 8.17 million (12.9% of the overall UK population) Office for National Statistics, National Records of Scotland and Northern Ireland Statistics, Research Agency (2017) 2011 Census Aggregate Data, UK Data Service., 24% of FICTION children were non-white.

²Decayed into dentin, missing and filled primary teeth

³ Parental-Caregiver Perceptions Questionnaire (16 item version)

⁴ Modified Child Dental Anxiety Scale (faces)

Table 2. Summary statistics for Incidence, Number of episodes and Probability of having no dental pain and/or infection at 2 years post-randomization (mITT analysis set, n=1058)

| Outcome | C+P (conventional carious lesion management with prevention) n=352 | B+P (biological management with prevention) n=352 | PA (prevention alone) n=354 | Total n=1058 |
|---|--|---|---|-------------------------------|
| Incidence of dental pain and/or infection | | | | |
| Dental pain ever ⁵ (%) | 126 (35.8) | 113 (32.1) | 140 (39.5) | 379 (35.8) |
| Dental infection ever ¹ (%) | 90 (25.8) | 87 (24.7) | 91 (25.7) | 268 (25.3) |
| Dental pain and/or infection ever ¹ (%) | 148 (42.0) | 141 (40.1) | 161 (45.5) | 450 (42.5) |
| Number of episodes of dental pain and/or dental infection | | | | |
| Min | 0 | 0 | 0 | 0 |
| Median (IQR) | 0 (0,1) | 0 (0,1) | 0 (0,1) | 0 (0,1) |
| Mean (sd) | 0.62 (0.95) | 0.58 (0.87) | 0.72 (0.98) | 0.64 (0.94) |
| Max | 7 | 6 | 5 | 7 |
| Number (%) | | | | |
| 0 | 204 (58.0) | 211 (59.9) | 193 (54.5) | 608 (57.5) |
| 1 | 106 (30.1) | 97 (27.6) | 99 (28.0) | 302 (28.5) |
| 2 | 23 (6.5) | 29 (8.2) | 40 (11.3) | 92 (8.7) |
| 3 | 15 (4.3) | 13 (3.7) | 15 (4.2) | 43 (4.1) |
| 4 | 2 (0.6) | 1 (0.3) | 5 (1.4) | 8 (0.76) |
| 5 | 0 (0.0) | 0 (0.0) | 2 (0.6) | 2 (0.2) |
| 6 | 1 (0.3) | 1 (0.3) | 0 (0.0) | 2 (0.2) |
| 7 | 1 (0.3) | 0 (0.0) | 0 (0.0) | 1 (0.1) |
| Probability of having no dental pain and/or infection at 2 years post-randomization (97.5% CI) | 64% (58%, 69%) | 65% (59%, 70%) | 56% (50%, 61%) | 62% (38%, 48%) |

⁵ during the follow-up period of the trial

Table 3. Estimates of the Risk Difference and Incident Rate Ratio over the follow-up period in dental pain and/or infection between randomized treatment arms; models are adjusted for age in years, time in study in years and a random effect for practice.

| | Incidence | | Number of episodes | |
|--|--|---------------------------|--|-------------------------------|
| | Adjusted ⁶ Risk Difference ⁷ (97.5% Confidence interval [CI]) | | Adjusted ¹ Incident Rate Ratio (97.5% Confidence Interval [CI]) | |
| Analysis set | B+P ⁸ vs C+P ⁹ | PA ¹⁰ vs C+P | B+P vs C+P | PA vs C+P |
| Intention to Treat (mITT) (n=1057) | -2% (-10%, 6%) P=0.6 | 4% (-4%, 12%) P=0.2 | 0.95 (0.75,1.32) P=0.6 | 1.18 (0.94,1.64) P=0.1 |
| At least 23 months in study (n=797) | 1% (-9%, 10%) P=0.9 | 5 (-4%, 14%) P=0.2 | 1.02 (0.78,1.32) P=0.9 | 1.26 (0.98,1.50) P=0.04 |
| Per Protocol (PP) (n=939) | -1% (-9%, 8%) P=0.9 | 2% (-6%, 11%) P=0.5 | 1.03 (0.80,1.34) P=0.8 | 1.17 (0.90,1.51) P=0.2 |

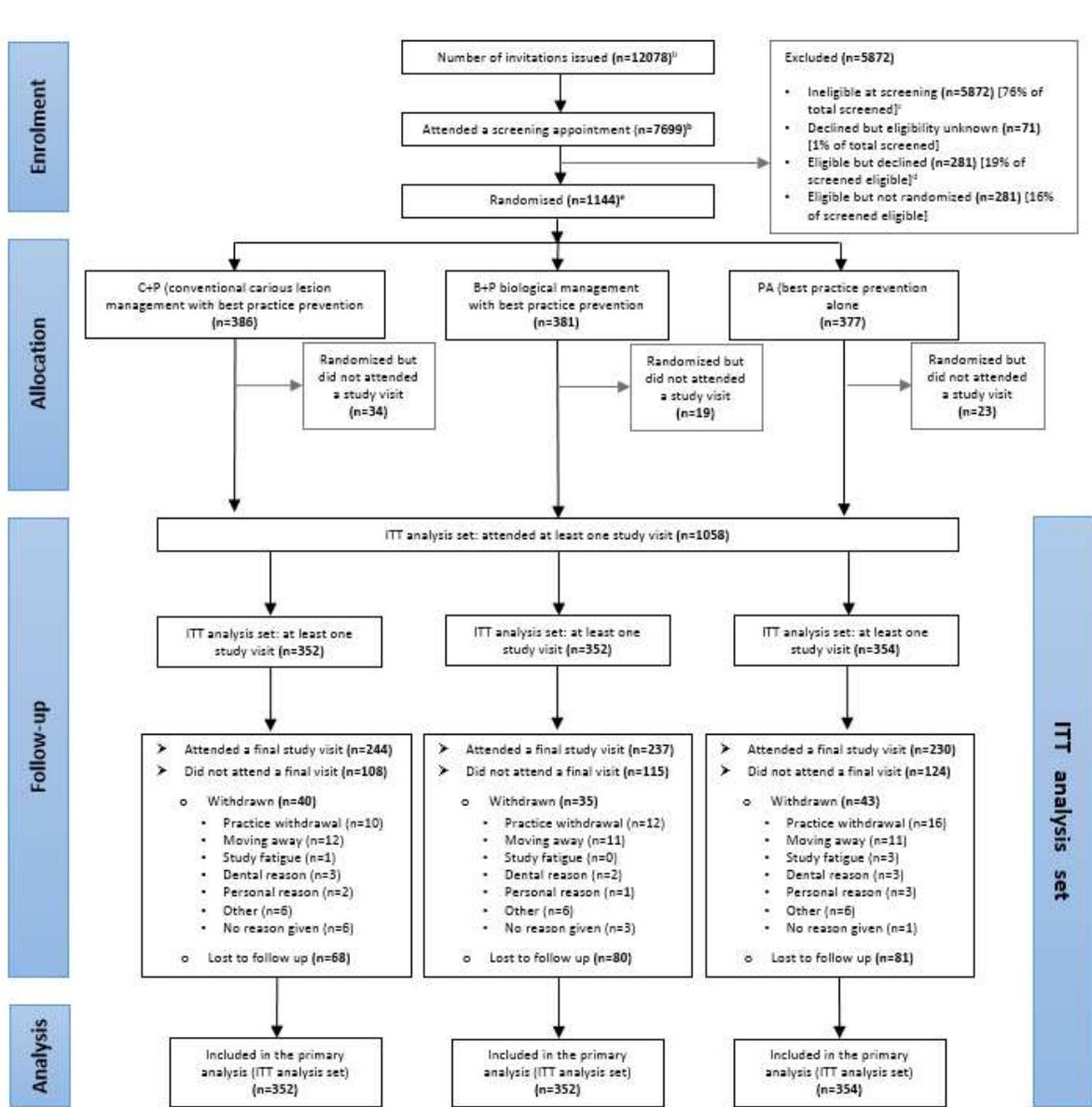
⁶ Estimates of the Risk Difference and Incident Rate Ratio are over the follow-up period and models are adjusted for age in years, time in study in years and a random effect for practice.

⁷ A risk difference less than zero indicates a lower incidence of dental pain and/or dental infection compared to C+P

⁸ Biological management with best practice prevention

⁹ Conventional carious lesion management with best practice prevention

¹⁰ Best practice prevention alone



^a Prior to the start of the study, it was estimated that 18,717 children would be invited.

^b Prior to the start of the study, it was estimated that 65% of children invited would attend a screening appointment; 64% attended.

^c Prior to the start of the study, it was estimated that 85% of children screened would be ineligible; 76% were ineligible and 1% declined screening.

^d Prior to the start of the study, it was estimated that 20% of children screened and found eligible would decline to take part in the trial; 19% of those eligible declined.

^e Prior to the start of the study it was estimated that 12% of children screened would be randomised; 15% of those screened were randomised.

Figure 1. CONSORT flow diagram of participant journey through the trial