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Can cross sectional imaging contribute to the investigation of unexplained child deaths? A literature review

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Abstract

Background

This review examines the factors that can influence an investigation into the unexpected death of a child before considering if using imaging techniques could be of benefit.

Method

A systematic search strategy was adopted to search databases using keywords, these results were then subjected to inclusion and exclusion criteria to filter and refine the evidence base further.

Discussion

More research is published on the use of MRI in comparison with other modalities. There is evidence in the case of MRI in particular that its use could be of benefit in identifying and ruling out potential causes of death in children.

Conclusion

More research is needed on the use of CT but the routine use of MRI in child death investigation could now be considered. Ethical considerations appear to be a barrier to research in this area and discussions as to how such considerations can be overcome is necessary.

Keywords: CT; MRI; Imaging; Autopsy; Post mortem; Medico-legal

Introduction

The purpose of this review is to identify and critically appraise the evidence that could support the increased use of cross sectional imaging in the investigation of child deaths that are initially unexplained. Should the evidence be sufficient, the routine introduction of imaging into autopsies on children could result in greater accuracy, speedier establishment of cause of death and a less invasive overall procedure.

Epidemiology

The death of a child remains a tragic but thankfully rare event. The Department of Education (2010) reports an estimated 5000 child deaths per year in the UK. This figure incorporates a significant proportion of neonatal deaths and 65% of child deaths in 2009–2010 were under one year of age. The Office of National Statistics identified 254 unexplained deaths of infants accounting for 8% of overall infant deaths in 2010. This figure incorporates sudden infant deaths (SIDS) and cases where cause of death is reported as unascertained, such as deaths involving fire. Creighton and Tissier (2003) report an average of 79 child homicides per year.

The overwhelming majority of child deaths can have a cause attributed to them. However the statistics are significant in terms of unexplained deaths and homicide as a high number are still regarded as "unexplained". Both in cases where cause of death can be attributed and those cases where it cannot, high level investigations are required to ensure causes of death are ascertained. In addition, the investigation must make sure that the burden of proof as to a person's guilt or innocence is reached and when possible, that closure is brought to surviving relatives. For many years, the autopsy or post mortem has remained the cornerstone of medico-legal practices but there is growing evidence that forensic radiology could be of considerable benefit to any investigation into an unexplained death of a child. The work of numerous centres, notably the Virtopsy™ project in Switzerland has seen the evidence base for the use of forensic radiology grow dramatically.
Investigating the unexplained death of a child

“Sudden infant death syndrome” (SIDS) became a registerable cause of death in the UK in 1971 and the rather non-specific term “cot death” has been in use since the 1950s. Considerable conjecture still exists around these terms. In essence, SIDS is a diagnosis of exclusion, when no other cause of death can be identified. However, ruling out homicide as a cause of death remains a highly important step. A multi-disciplinary approach is necessary to ensure no important evidence in the investigation of an unexplained death is missed. The involvement of different disciplines in an investigation is of paramount importance with the legal principle of beyond reasonable doubt being of great significance. The greater amount of evidence that involvement of imaging may provide could represent the difference between that standard being made or not.

The acronym SUDI or Sudden Unexplained Death of an Infant is used in some countries as an umbrella term that encapsulates not just those that die of SIDS but other unexplained deaths.

Table 1 from Busuttil and Keeling (2009) demonstrates factors that would cause concern in an investigation of an unexplained death of a child:

Table 1 Factors in the history causing concern in SUDI (Sudden Unexplained Death of an Infant).

<table>
<thead>
<tr>
<th>Factor</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Many GP/accident and emergency attendances without clear evidence of illness</td>
<td></td>
</tr>
<tr>
<td>Apparent life threatening events (ALTEs), especially if more than one and starting at less than 4 weeks of age and un-witnessed or if the same person finds the baby each time.</td>
<td></td>
</tr>
<tr>
<td>Age under 1 year</td>
<td></td>
</tr>
<tr>
<td>Epistaxis</td>
<td></td>
</tr>
<tr>
<td>Seizures - especially unexplained</td>
<td></td>
</tr>
<tr>
<td>Death occurs during the day when the baby was apparently well earlier</td>
<td></td>
</tr>
<tr>
<td>ALTE in siblings</td>
<td></td>
</tr>
<tr>
<td>Previous SUDI in sibling</td>
<td></td>
</tr>
<tr>
<td>Death on anniversary of previous SUDI</td>
<td></td>
</tr>
<tr>
<td>Parental involvement with the media after child's death</td>
<td></td>
</tr>
</tbody>
</table>

Of the estimated 500 child deaths per year, a large proportion occur in hospital, particularly in the neonatal period. The significance of this is that these children are more likely to have been under medical observations in the immediate pre-death period. A large proportion of these will be those born prematurely and/or in respiratory distress, those with known intra-uterine pathology and those who have had a traumatic birth that result in admission to a special care baby unit or similar unit. Being present at such a unit means their vital signs will be monitored immediately prior to death meaning a cause of death can potentially be more easily attributed and the child would be expected to be under close observation, thus reducing the likelihood of external interference. The 2008 CMACE study gave the most common causes of neonatal deaths to be as a result of respiratory disorders (37.7%), major congenital abnormality (21%) and neurological disorders (14.2%). Unexplained deaths accounted for 2% of the population from this study that reflects the neonatal period only (Tables 2 and 3).

Table 2 Characteristic imaging findings in non-accidental trauma.

<table>
<thead>
<tr>
<th>Finding</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metaphyseal corner (“bucket handle”) fractures</td>
<td></td>
</tr>
<tr>
<td>Fractures in different stages of healing/periosteal reaction</td>
<td></td>
</tr>
<tr>
<td>Spiral fractures in infants and toddlers</td>
<td></td>
</tr>
<tr>
<td>Fractures caused by unusual mechanisms (such as to the posterior ribs)</td>
<td></td>
</tr>
<tr>
<td>Fractures in unusual locations (such as to the thoracic spinous process)</td>
<td></td>
</tr>
<tr>
<td>Multiple skull fractures</td>
<td></td>
</tr>
</tbody>
</table>

Table 3 Pathological findings causing concern.

<table>
<thead>
<tr>
<th>Finding</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Petechial haemorrhages on face or neck</td>
<td></td>
</tr>
</tbody>
</table>
Potential causes of sudden death of a child

Most instantaneous deaths will be cardiovascular in origin and are likely to be related to congenital heart disease (CHD). Pathologists are likely to be alerted to the presence of CHD by cardiomegaly visualised at post mortem. A genetic metabolic disease and bacterial and viral infection also represents common causes of child death. Within the neonatal period, hypoxia at birth and acute intestinal obstruction are considered more common causes of death.\(^5\)

Imaging with autopsy

Until the 1970's, the X-ray examination was the only imaging readily available. Since that time, other imaging techniques have been developed to the clinical benefit of patients globally. In forensic practice, use of imaging incorporates chiefly X-rays, CT and MRI scanning. Whilst the former has been in use for many decades,\(^4\) the use of CT and MRI scanning in forensic medicine is a more recent phenomenon with particular progress since the advent of MDCT (multi-detector computed tomography). Levy and Harcke (2011) regard cross sectional imaging as making radiology's contribution to autopsy more effective, potentially increasing accuracy and speed.\(^6\) McPhillips in Busuttil and Keeling (2009) identifies that post mortem imaging in paediatric deaths is rarely used but does bring potential benefits.\(^7\) These benefits are given as high resolution volumetric scans being obtained in a short time but do acknowledge the time taken to report such images. Anecdotal evidence suggests that limited access to the scanners may preclude the use of cross-sectional imaging.

Radiological signs raising suspicion of homicide in children

In living patients under two years of age, skeletal surveys are undertaken to demonstrate any potential sign of mistreatment. The 2008 report from the Royal College of Radiologists and Royal Society of Paediatrics and Child Health gave firm guidance as to the imaging techniques to be used in cases of suspected non accidental injury (NAI). Such guidance is based upon specific injuries that could be regarded as suspicious, particularly in the absence of coherent clinical history. This skeletal imaging has been the historical method of examining children and this 2008 guidance does begin to introduce other imaging techniques into the examination.\(^9\) Blickman et al. (2009) listed the following skeletal injuries as characteristic of non accidental trauma:

Given that the musculoskeletal system changes little in the period immediately after death, these characteristic signs could still be visualised on a post mortem skeletal survey. Blickman et al. (2009) also identify parieto-occipital subdural haematoma, hepatic or splenic tears, duodenal haematomas and pancreatic injury as suspicious injuries that can be identified by computed tomography.\(^9\) However, questions may remain about the reliability of post mortem soft tissue imaging given the physiological changes that would occur and how they may manifest themselves.

Absence of any radiological signs of NAI may be reassuring but would not definitively rule out abuse. Follow up imaging should also be considered in some cases.

Pathological appearances raising suspicion of abuse

Busuttil and Keeling (2009) listed the findings seen at post mortem that may raise suspicion of an un-natural cause of death.

Direct examination as part of a post mortem will identify the overwhelming majority of the listed clinical signs. However, the notion of "any other injury" could be further explored by the use of imaging techniques. Blickman et al.,'s previous reference to parieto-occipital subdural haematoma or indeed other brain or visceral injury being potentially identified by cross-sectional imaging is not referred to in the above list which may indicate they have not fully considered the significance of head injury to possible NAI.\(^10\)

Carty and Pierce (2002) in their retrospective analysis discussed the mortality within a cohort. 8% of the 467 children under suspicion of NAI had died with 78% of deaths caused by head injury, with or without shaking, Table 4.
Carty and Pierce (2002) in their retrospective analysis discussed the mortality within a cohort. 8% of the 467 children under suspicion of NAI had died with 78% of deaths caused by head injury, with or without shaking.

Table 4 represents the causes of death identified.11

<table>
<thead>
<tr>
<th>Cause of death</th>
<th>Total (n=37)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head injury: shaking (with or without impact)</td>
<td>26</td>
</tr>
<tr>
<td>Head injury (no shaking)</td>
<td>3 (Total head injury (n=29)</td>
</tr>
<tr>
<td>Unknown cause of death (no post mortem information)</td>
<td>3</td>
</tr>
<tr>
<td>Suffocation^</td>
<td>2</td>
</tr>
<tr>
<td>Septicaemia</td>
<td>1</td>
</tr>
<tr>
<td>Inhalation of vomit</td>
<td>1</td>
</tr>
<tr>
<td>Hypoxic ischaemic encephalopathy (not NAI)</td>
<td>1</td>
</tr>
</tbody>
</table>

\(^{\text{a}}\) Thought to be cause of death due to pattern of bruising. Both had old rib fractures.

Given that there is growing evidence\(^\text{4-6}\) that imaging can be a useful adjunct to autopsy in conjunction with other studies demonstrating the frequent causes of death associated with NAI (and indeed the case where NAI was not the cause which is particularly significant) a literature review was undertaken to analyse the evidence that imaging can be a significant addition to the current level of investigation. Performing a literature review in this area could demonstrate the potential impact of the involvement of cross-sectional imaging in these investigations, leading to a more accurate and robust cause of death being established.

**Current practice**

Weber et al.\(^\text{'s} 2008\) study into post mortems of SUDI highlighted that the cause of death was not established in 63% of cases in deaths of children under one year of age. This was despite the fact that the post mortems were carried out by specialist paediatric pathologists. The authors also comment that this represented an improvement from a previous study completed 10 years earlier. There is no evidence that imaging was involved in these post mortems.\(^\text{12}\) Given the relatively high figure of 63% and the lack of evidence of the role of imaging, the involvement of imaging could lead to a reduction in the number of cases that cause cannot be established.

**Method**

The method underpinning the review is under the guidance produced by the Centre for Review and Dissemination (CRD). Search terms and inclusion and exclusion criteria were formulated. The search terms were applied to appropriate databases to identify relevant literature. The databases should not simply confirm to a traditional “medical” model but take into account the forensic science element that is strongly relevant in this case. The searches included one of the Cochrane library.

In addition to the databases, the reference lists of relevant literature were also searched to ensure the literature review was sufficiently robust.

**Inclusion and exclusion criteria**

Exclusion criteria were applied to exclude non cross-sectional imaging related studies and studies that were of living patients. Studies before 2000 were excluded due to advances in technology. Studies that were written from a purely legal standpoint were excluded as they did not evaluate the contribution of imaging.

The studies that concerned themselves only with fetal death were excluded as they had limited significance in terms of suspicious deaths. Case reports provide only limited evidence of the contribution of an intervention and were excluded.

Studies not written in the English language were excluded on the grounds of time and lack of translation facilities available.

**Search terms**

The process of review requires the formation of search terms. Table 5 details the specific search terms used in this review in addition to the Boolean algebra application. By producing an extensive list of search terms, the review intends to be as comprehensive as possible to increase external validity.
**Results**

The searches produced 15 results by using the search terms and Boolean algebra. The studies comprising these results were filtered down to 6 results by applying inclusion and exclusion criteria. The articles were also examined to assess if any additional studies had been missed by the original search.

**Discussion**

Within the UK, the National Institute of Clinical Excellence in their 2007 guidance (reviewed in 2011) on head injuries states the use of CT is essential in the assessment of head injury in the living patient including children. Given the extensive amount of research that has informed this guidance, it is perhaps surprising that most published literature in the assessment of post mortem injuries in children is MRI based and not CT. Within the abstracts of the reviewed articles, six specifically referred to MRI and only two to CT. One possible explanation for this is that the small number of centres publishing literature in this area have a stronger background in MRI.

In 2010 a systematic review was published by Thayyil et al., detailing MRI in children, fetuses and adults which gave a 28% sensitivity and 63% specificity in identifying the final cause of death in children and adults. The authors acknowledge that the available data is small and that the quality of published literature is limited. An important omission was the exclusion of all trauma and homicide cases giving the reason that reviews had already been reported and that the method of autopsy was different in suspicious deaths and the grouping of children and adults together. Given this, the sensitivity and specificities provided would exclude those deaths which were considered at the time as unexplained or suspicious. A similar team from the same centre published an evidence based approach in the same year, more significantly this publication highlighted evidence that MRI missed subdural and subarachnoid bleeds which would be of concern given the high incidents of head injuries in traumatic infant deaths. In addition, the authors found the image contrast of post mortem CT in the visceral organs of children extremely poor. The authors are at pains to state that interprofessional collaboration between radiology and pathology is important and that more research is needed before CT or MRI can be used routinely. However, a 2013 study again by a similar team from the same centre reports a similar accuracy of minimally invasive autopsy to conventional autopsy for detection of cause of death or major pathological abnormality. There was a lower concordance with children then with fetuses which the authors put down to undetected pneumonia and myocarditis. They report a sensitivity and specificity of greater than 95% for detection of intracranial and non-infective pathological abnormality which is of particular significance in unexplained deaths. The key to the differences appears to be the use of MRI as part of a minimally invasive autopsy as opposed to its use in isolation. This team's 2012 publication linked post mortem MRI with endoscopic investigation that reduced the cosmetic effects on the deceased seen with a conventional post mortem further extolled the virtues of the “minimally invasive autopsy”.

Oyake et al.,’s study from Japan in 2006 detailed the use of CT in the investigation of infant death but, as with some of the previous studies, they excluded known traumatic patients which reduces its applicability to this review. However, the authors did comment that no indication of child abuse could be identified if any of their fifteen documented cases. The conclusion stated that CT alone could not definitively find a cause of death but using CT in conjunction with other techniques could give a higher rate of detection. Notable was the undertaking of CT scanning within two hours of certification of death. Given the origin of the study, this can be equated as equivalent to within two hours of confirmation of death.

A possible cause of the historical notion of “cot death” was that of airway occlusion whilst sleeping. A factor that has dramatically reduced the incidence of sudden infant death syndrome in the UK is a recommendation to ensure babies sleep on their backs, an intervention that stretches back to the mid 1990s. Rambaoud and Guilleminault's 2004 study detailed the use of CT scanning to investigate SUDIs, identifying airway occlusion at the base of the tongue in

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**Table 5 Search strategy.**

<table>
<thead>
<tr>
<th>Population</th>
<th>Intervention</th>
<th>Comparison</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paediatrics</td>
<td>CT</td>
<td>Post mortem</td>
<td>Diagnosis of Non accidental injury</td>
</tr>
<tr>
<td>OR</td>
<td>OR</td>
<td>OR</td>
<td>OR</td>
</tr>
<tr>
<td>Child</td>
<td>MRI</td>
<td>Diagnosis of Sudden Infant Death Syndrome</td>
<td></td>
</tr>
<tr>
<td>OR</td>
<td>OR</td>
<td>OR</td>
<td>OR</td>
</tr>
<tr>
<td>Infant</td>
<td>Diagnosis of Sudden Unexpected Death of an Infant</td>
<td></td>
<td></td>
</tr>
<tr>
<td>OR</td>
<td>OR</td>
<td>Diagnosis of Cot death</td>
<td></td>
</tr>
<tr>
<td>OR</td>
<td>Diagnosis of Infanticide</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
relation to the relative position of the child at death concluding that sleeping position is a contributory factor but that the supine position may not protect those with small mandibles. Given that sudden infant death is now much rarer than in previous years but is still a potential avenue of investigation, establishment of airway occlusion as a contributory factor can assist in deeming a death as non-suspicious.20

Given the context of head injuries,9 establishment of the presence of intracranial lesion is particularly significant. Cohen et al.,’s 2010 study concerned itself primarily with intracranial pathology and they acknowledge the controversies that exist in establishing the causes of intradural, subdural haemorrhages and hypoxia. In concordance with findings elsewhere, the emphasis is on the interprofessional approach and a combination of imaging and other established techniques. They describe these pathologies as frequent occurrences that can be linked to more natural causes of death but that subdural haemorrhage in particular could be viewed as more suspicious. Of particular interest was their link between prolonged cardiopulmonary resuscitation and raised intracranial pressure which could be important in cases where cause of death is viewed as suspicious.21 Many collapsed victims will have cardiopulmonary resuscitation (CPR) performed upon them and establishing a link between CPR and the change in intracranial pressure, in conjunction with other clinical manifestations such as rib fractures could be significant in identifying a more natural cause of death.

A noticeable and inevitable factor that hampers the ability to research the impact of imaging in sudden deaths of children is the small numbers of cases which makes establishing an impact of cross sectional imaging difficult. Coupled to this, the ethical and medico-legal challenges faced by researchers in investigating deaths that are viewed as suspicious appear to have impacted on the ability to recruit such cases to prospective studies. Much of the published literature on the use of MRI in particular arises from a single centre. That centre deserves considerable credit for their work but the question of whether other centres could match the localised expertise would have to be questioned.

The published literature indicates that post mortem MRI in the investigation of child deaths can be a beneficial intervention but stop short of extolling it as a sole method of investigation, seeing it more in combination with other techniques. The notion of minimally invasive autopsy makes for particularly interesting reading and may negate some of the reasons that autopsy is refused.22 In cases where the death of a child is regarded as suspicious, the issue of consent for autopsy is negated. The key is the ability to differentiate between a natural, accidental or traumatic death as quickly as possible using the techniques that are best supported by the evidence base.

The advantage of imaging is that it can allow anatomy to be viewed without dissection that give the potential for the invasiveness of an autopsy to be reduced. The improvements that have occurred in cross-sectional imaging that allow multi-planar and three dimensional reconstruction are particularly significant. Levy and Harke (2011) suggest that in some cases, imaging could be regarded as a “triage technique” that could take place before more interventional autopsy.6 This notion has considerably merit as the emphasis can sometimes be on speed but also, a dissection could change the bodies post mortem physiology which could affect appearances on CT or MRI.

Reece et al., quoted in Brogdon (2011) as early as 1994 suggested that CT was preferable for demonstrating subarachnoid haemorrhage and fracture detection, MRI was preferable for sub-dural haematoma, concussive injury and shear injury whilst CT and MRI were of equal efficacy for demonstrating epidural haematoma.6 Given the high incidences of head injuries with shaking in non-accidental injury cases rather than blunt or penetrating trauma to the head, this 1994 conclusion could at least in part explain the greater emphasis on MRI in paediatric deaths despite the conventional wisdom that CT is more readily available. Brogdon acknowledges that much of the evidence for post mortem imaging is related to adults but that evidence is available that evaluates infants and children for abuse, sudden death, accidental trauma, skeletal age, air embolism and intracranial and soft tissue changes before and after death.6 Given that evidence exists that both CT and MRI can demonstrate significant pathology a combination approach may be regarded as the most appropriate course but there is no available evidence that such an approach would be dramatically beneficial and cost and practicalities are likely to preclude such a measure in most centres.

The importance of histology and toxicology in conjunction with other investigative techniques should not be underestimated. Imaging may display the results of toxic poisoning but would not demonstrate the chemical composition or amount of any such poison. Biochemical testing remains a significant contributor to identifying cause of death and can evaluate areas that imaging could not, these include anaphylaxis, dehydration, endocrine disorders, renal failure and errors of metabolism. Such testing can also be suggestive of hypoxia. Intra-ocular assessment remains a useful indicator of non-accidental injury in terms of identifying haemorrhage and detachment of the retina which are potential signs of abuse.7 In assessing whether a death is suspicious or otherwise, imaging should be seen only as part of a wider investigation and proponents of its use should acknowledge its limitations in evaluating all causes of paediatric death.

Conclusions

The use of MRI in the investigation of child death whether viewed as suspicious or otherwise continues to grow but the notion that this technique will be the only method of investigation necessary appears fundamentally flawed and any results gleaned from MRI or other imaging needs to be seen in context of a wider approach and related to the circumstances of the patient in question. This is particularly true until there is greater appreciation of post mortem changes visualised by scanning, either CT or MRI. Undertaking an MRI scan of the head at minimum will only benefit an investigation. Much of the available research arises from a limited number of centres. Whilst expertise should not be spread too thinly, a greater number of research centres would give greater external validity to the use of cross sectional imaging.

Given the weight of evidence supporting the use of CT in major trauma,13,19 the limited research into its use in relation to child death investigation is surprising and further research could yet demonstrate CT as a potentially important intervention.21 This could be perceived as a knowledge gap, particularly given the evidence of CT usage in adult deaths.22

With the high percentage of traumatic child deaths being linked to intracranial pathology, concentration of evaluation of this area in a timely manner after death may be an area of future focus. The evidence appears to demonstrate
that such intracranial pathology can be present in traumatic and non-traumatic deaths which are further evidence that cross sectional imaging cannot be relied upon in isolation to differentiate between natural and non-natural deaths.

Limitations

This review ruled out publications before 2000 given the advances in technology and understanding that have taken place since then. Including publications before then could have added to the evidence base. Use of a greater number of databases could have ensured an even broader knowledge base could have been explored. Reports of small numbers of patients or case reports were discarded as of reduced academic significance.

Recommendations

There is evidence that where possible, MRI of any child who has died suddenly undertaken as rapidly as possible after death can contribute evidence as to the cause of death in conjunction with other techniques. However, the importance of trained paediatric radiologist interpreting the resultant images should not be underestimated, given the potential medico-legal context. The training of such radiologists would reduce the reliance on the small number of centres undertaking these procedures. More evidence is needed as to the potential benefit of CT, in particular should there be any suspicion of traumatic death. This should not be seen as a definitive answer to the cause of death but as part of a wider multi-disciplinary autopsy procedure. In the context of both CT and MRI, further research is needed in the specific area of paediatric death.

Greater appreciation should be given to the sub-speciality of forensic radiology to improve the understanding of post mortem changes on cross sectional imaging.

The challenging nature of getting ethical approval for research of this nature will remain but ethics committees need to consider carefully the potential long term benefits of improving investigations into sudden deaths of children.

Conflict of interest

None.

Uncited reference

16.

References


8

2. Royal College of Radiologists and Royal Society of Paediatrics and Child Health, Standards for radiological investigation of suspected non accidental injury, 2008, RCR/RSPCH; London.


**Queries and Answers**

**Query**: Please check the affiliation and the correspondence details, and correct if necessary.

**Answer**: Name is correct but note that the address should now be University of Bradford, Richmond Road, Bradford, West Yorkshire, BD7 1DP.

**Query**: As per the journal style sheet, the section heading “Introduction” is mandatory. Kindly provide the same.

**Answer**: Please change "Aim" to "Introduction".

**Query**: Please note that the Tables 2 to 4 were not cited in the text. Kindly check whether the citations suggested are in the appropriate place, and correct if necessary.

**Answer**: The citations now seem appropriate thank you.

**Query**: Please note that the text ‘The table below’ in the sentence ‘Carty and Pierce (2002)…’ has been changed to Table 4 citation. Kindly check and correct if necessary.

**Answer**: Fine

**Query**: Please check the section ‘Conflict of interest’ and correct if necessary.

**Answer**: Fine

**Query**: Please note that Ref. 16 was not cited in the text, hence provide citation for the reference or delete it from the reference list.

**Answer**: I have attempted to insert a 16 in the text

**Query**: Please update Ref. 16.

**Answer**: Should be ok as per query 6.

**Query**: Please confirm that given names and surnames have been identified correctly.

**Answer**: Name is correct but note that the address should now be University of Bradford, Richmond Road, Bradford, West Yorkshire, BD7 1DP.