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Assessing and investigating children with suspected bone and abdominal tumours: an e-Delphi consensus process.

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Assessing and investigating children with suspected bone and abdominal

tumours: an e-Delphi consensus process.

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 Assessing and investigating children with suspected bone and abdominal tumours: an e-Delphi consensus process.

ABSTRACT

Background

The incidence of childhood cancer has risen by 15% since the 1990s. The overall five-year survival is 84% but bone and abdominal tumours have the lowest survival rates with many experiencing delays to diagnosis. This Delphiconsensus process was conducted to develop a new clinical guideline for children and young people (CYP) presenting with a suspected bone or abdominal tumour.

Methods

Invitation emails were sent to primary and secondary healthcare professionals (HCPs) to join the Delphi panel. 65 statements were derived from evidence review by a multidisciplinary team. Participants were asked to rank their level of agreement with each statement on a 5-point Likert scale (1 = strongly disagree, 9 = strongly agree), with responses >=7 taken to indicate agreement. Statements not reaching consensus were rewritten and re-issued in a subsequent round.

Results

All statements achieved consensus after two rounds. 96/133 (72%) participants responded to Round 1 (R1) and 69/96 completed Round 2 (R2). 62/65 (94%) statements achieved consensus in R1 with 29 (47%) gaining more than 90% consensus. Three statements did not reach consensus scoring between 60.9 and

69.1%. All reached numerical consensus at the end of Round 2. Strong consensus was reached on best practice of conducting the consultation, taking into account parental instinct and obtaining telephone advice from a paediatrician to decide the timing and place of review, rather than two week wait pathways. Dissensus in statements were due to unachievable targets within primary care and valid concerns over a potential over-investigation of abdominal pain.

Conclusions

This consensus process has consolidated statements that will be included in a new clinical guideline for suspected bone and abdominal tumours for use in both primary and secondary care. This evidence base will be translated into awareness tools for the public as part of the Child Cancer Smart national awareness campaign.

WHAT IS ALREADY KNOWN ON THIS TOPIC?

- Childhood cancer is the leading illness cause of death in children over 1 in the UK and globally.
- Bone and abdominal tumours have some of the lowest survival estimates of childhood cancers.
- They pose a diagnostic dilemma for clinicians, presenting with non-specific symptoms such as bone pain, limp and abdominal distension.

WHAT THIS STUDY ADDS?

- 64 new evidence-based statements on best practice, assessment, imaging and referral of CYP presenting with key bone and abdominal symptoms.
- Wide representation on the Delphi panel to include those from primary and secondary care resulting in pragmatic guidance to aid decision-making in both primary and secondary care.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

These data will form the basis of a new clinical guideline which will aid
 HCPs to instigate investigation of those with signs and symptoms that
 could be due to a bone or abdominal tumour.

- Empowering clinicians with this guidance will allow prompt recognition of those children with bone and abdominal tumours, improving their
- Jugh a new awareness cathe patient interval and promote. These data will be translated into public-facing materials for dissemination through a new awareness campaign called Child Cancer Smart to reduce

INTRODUCTION

Childhood cancer is not rare. An individual's cumulative risk of cancer from birth to age 15 years is 1 in 450, with 1840 new cases diagnosed in children and young people (CYP) aged 0-15 each year in the UK.(1) Incidence of childhood cancer has increased by 15% since the 1990s. Although survival estimates are also increasing (from 77% in 2001 to 84% in 2016 across all childhood cancers(1)) progress in the UK lags behind other Western European countries.(2, 3)

Many CYP experience delays in their cancer diagnosis.(4) Such delays are multifactorial. Unlike in adult cancers, prevention and screening strategies are not available, therefore early diagnosis is key to optimising outcomes, reducing morbidity, mortality and treatment burden.(5) A possible explanation behind delayed diagnosis lies with childhood cancer symptomatology posing a diagnostic dilemma. Symptoms are often non-specific, mimicking other more common ailments such as gastroenteritis, migraines or can masquerade as pain attributed to minor injury. The 2015 National Institute Health and Care Excellence (NICE) issued a guideline on "Suspected cancer: recognition and referral"(6) which covers all ages. There is a real need for paediatric-specific guidance, as adult cancers manifest and present differently. This current guidance is directed at primary care with the "end-point" being referral onto secondary care. Children with cancer experience diagnostic delay throughout the health service both at primary care and secondary care level and a referral from primary to secondary care can add significant length to the patient's diagnostic journey.

Furthermore, the recommendations lack a systematic evidence review and are based solely on expert consensus which notably did not include any paediatric oncologists or haematologists on the panel.

As a result, concern from the paediatric oncology community across the UK rose that the guidance was not fit for purpose.(7) A supplement to the NICE guideline was published in 2021 following a Delphi consensus process conducted amongst the Children's Cancer and Leukaemia Group membership.(8) A full systematic evidence review was not completed at this time, due to the urgent need for expert child-specific guidance to be published.

Currently, UK survival estimates for bone and abdominal tumours in CYP are the lowest of all childhood cancers.(1) Detailed tumour specific diagnostic guidance as that produced for childhood brain tumours(9) is needed, in order to empower clinicians to make decisions about those who need investigation and accelerate referrals for CYP with high-suspicion symptoms promoting earliest possible diagnosis.

As the questions of specificity, referral pathways, investigation indications and acceptable waiting times for CYP with suspected cancer cannot easily be addressed by quantitative research methods alone, a Delphi consensus process(10, 11) was employed to use professional expertise to incorporate the evidence from systematic reviews into a clinical guideline.

METHODS

The Delphi consensus process

The Delphi consensus process was conducted as the final step of the goldstandard AGREE-II approach to clinical guideline development (Figure 1).(12)

A Guideline Development Group (GDG) consisting of seven members with experience in developing clinical guidelines (two paediatric oncologists, a representative member of the Royal College of Paediatrics and Child Health (RCPCH), the Chief Executive of the Children's Cancer and Leukaemia Group (CCLG), a GP, a paediatric registrar, research assistant and parent representative) oversaw the guideline development. The initial stage comprised of a systematic review and meta-analysis of the literature. This provided contemporary evidence regarding the signs and symptoms of bone and abdominal tumours in CYP.(13, 14)

Multidisciplinary workshop

A multi-disciplinary workshop was held on 12th November 2019 with 15 participants (seven male, eight female). Participants consisted of doctors from primary, secondary and tertiary care (two general practitioners, three paediatric emergency department consultants, three paediatricians, three paediatric oncologists and two paediatric surgeons), and two parents of CYP who have been diagnosed with cancer.

The systematic review identified five bone tumour symptoms (pain, swelling, mass/lump and restricted movement or limp) and four abdominal tumour symptoms (mass, haematuria, pain and distension). For each sign/symptom, the group were asked to consider a set of questions on clinical presentation,

assessment and investigation strategies and suggest answers or possible approaches to care. The questions for discussion were:

- How would this sign/symptom present?
- How should an HCP assess a child/young person presenting with this sign/symptom?
- How should an HCP determine whether this presenting sign/symptom could be due to a bone or abdominal tumour (specificity)?
- What factors influence the specificity of this sign/symptom?
- What are appropriate thresholds for referral and/or investigation for a child/young person presenting with this sign/symptom?
- What would you regard as best practice for referral and/or investigation of a child/young person presenting with this sign/symptom?

The discussions were recorded, and contemporaneous notes taken. The discussion points and notes were collated and translated into a series of statements by the GDG at the end of the workshop. These were sent back to the workshop participants to check accuracy and content. The workshop participants did not participate in the Delphi consensus survey.

Delphi-consensus surveys

The statements derived from the workshop were sent to healthcare professionals using a modified e-Delphi consensus process(11). Invitation emails were sent out to HCPs to join the Delphi panel; it included doctors from primary, secondary and tertiary care across a wide range of specialties who may encounter CYP with these symptoms in their daily practice (general paediatricians, GPs, community paediatricians, paediatric surgeons, paediatric radiologists, paediatric orthopaedic surgeons, paediatric oncologists/haematologists and emergency paediatricians). HCPs were recruited from the Children's Cancer and Leukaemia

Group (CCLG) membership, Association of Paediatric Emergency Medicine (APEM) and through General Practice mailing lists.

The survey was built using Jisc Online Surveys and the Delphi panel members were asked to rank their agreement with the statements by means of a 9-point Likert scale (1 = strongly disagree; 5 = neither agree, nor disagree; 9 = strongly agree) with the ability to comment by free-text.

Definition of consensus

Based on existing guidelines, statements were defined as reaching consensus if 70% or more of the Delphi Panel respondents rated the statement as either 7, 8 or 9.(7) Statements were rejected if 25% or less of the Delphi Panel respondents rated the statement 7, 8 or 9.(10)

The rankings for each statement were collated. Any statement achieving the predetermined level of consensus was accepted. Statements not reaching consensus were rewritten and reviewed by the multi-disciplinary workshop participants. Free-text comments were used to help structure the re-written statement prior to being re-issued in Round 2.

Patient and Public involvement

Two parent representatives with experience of childhood cancer diagnosis volunteered to participate in the multi-disciplinary workshop and helped revise the statements following feedback from the Delphi panel.

Ethical approvals

This Delphi consensus process is part of clinical guideline development and healthcare professionals were recruited for their expertise by virtue of their professional role. Ethical approvals were not required however consent was obtained from all participants prior to the workshops and Delphi process, with explicit consent being asked for recording of sessions and use of quotes or feedback as part of the process.

RESULTS

150 HCPs practising in the UK were invited to take part. 133 agreed to take part consisting of 57 general practitioners, 28 general paediatricians, 18 paediatric emergency consultants, 13 paediatric surgeons, 6 paediatric radiologists and 11 paediatric oncologists. Sixty-five statements were derived from the workshop and reviewed by the RCPCH guideline development team as part of the endorsement process. The statements were split under categories: best practice in conducting the consultation (referral, imaging, predisposing factors), bone tumours (general, bone pain, swelling, mass/lump, restricted movement/limp) and abdominal tumours (general, abdominal pain, abdominal mass, haematuria, abdominal distension).

The first round of the Delphi consensus process was open from 2 March to 23 March 2020. A Delphi survey containing 65 statements were sent out to all 133 participants. During this period, the COVID-19 pandemic was declared and the round was paused. The survey was re-issued on 9 September 2020, allowing those who still wished to complete it, to do so. In total, 96 (72%) participants

completed Round 1. The second round was open between 9 November and 30 November 2020 and was completed by 69 of 96 respondents who had taken part in Round 1. All 65 statements reached numerical consensus after two rounds (Figure 2).

Round One (R1)

96 of 133 (72%) participants responded to the first round.

62 of 65 (95%) statements achieved numerical consensus. Three of 65 (5%) statements did not achieve numerical consensus and no statements were rejected.

Of the 62 consensus-reaching statements, 29 (47%) gained more than 90% consensus, 25 (40%) statements gained between 80-90% consensus and 8 (13%) statements between 70-80% consensus.

Despite achieving numerical consensus, statement 3, which read "if a child or young person (CYP) warrants another appointment for the same problem, the timing of this review should comply with national diagnosis of all cancers (currently, diagnosis or all clear should be given to the patient within 4 weeks)", was revised and included in round two due to comments outlining ambiguity in the wording.

Statements 8, 19 and 53 did not reach consensus, with 69.1%, 66% and 60.9% rating the statement 7-9 respectively. These were revised by the multidisciplinary workshop participants based on the comments received and sent out in Round 2 (Table 1).

Round Two (R2)

69 of 96 participants responded to the second round.

All four statements reached numerical consensus at the end of R2. However, the statement regarding the investigation of abdominal pain which was revised and accepted was deemed similar to another statement and was omitted from the final list.

The final 64 statements are presented in Figures 3, 4 and 5.

DISCUSSION

Summary

These data provide the backbone of a new clinical guideline in the assessment and investigation of CYP with suspected bone or abdominal tumours. When developed, this will be the first clinical guideline to be published specifically for these tumour types, and the second stand-alone guidance for children and young people following the HeadSmart guidance for childhood brain tumours.(9)

The initial round achieved a consensus in 95% of the statements sent out for review and all statements reached consensus within two rounds. This was higher than expected, a testament to the work of the multi-disciplinary workshop participants in clarifying and negotiating statements that were applicable across specialties. Those statements that did not reach consensus achieved between 60.9% and 69.1% and required minor revisions before achieving consensus in R2.

Best practice in general approach

Overall, there was strong consensus regarding the best practice of conducting the consultation, taking into account parental concern or instinct which has been shown to be an important factor in diagnosis of childhood cancer. (15, 16) Referral pathways for childhood cancers currently use the Two Week Wait pathway but has been subject to criticism. Studies have shown that only 2% of childhood cancer is actually diagnosed via this route and the distress caused to parents being referred using this pathway far outweighs the rate of pick-up. (17, 18) Furthermore, for those for whom cancer is the diagnosis, this pathway adds a further two week delay before any investigation is requested. Reaching clear

consensus on obtaining telephone advice from a paediatrician to decide the timing and place of review will ensure that all CYP are appropriately triaged based on their history. This is in line with standards set by the RCPCH in the 2015 "Facing the Future" publication stating that GPs assessing or treating children should have access to immediate telephone advice from a consultant paediatrician.(19) Despite this guidance, there were some comments from primary care stating a lack of availability of advice in their region.

One recurring theme amongst the comments, was the regional differences within primary care. A number of GPs highlighted that there was no ability to request paediatric imaging directly from primary care and if there was, this could take weeks or even months to take place. A caveat was added to the investigation statements to state that requesting an investigation should not delay a referral.

Dissensus in R1

The dissensus in three statements were due to unachievable targets within primary care and valid concerns over a potential over-investigation of a common symptom respectively.

Measuring and plotting height and weight takes place routinely within secondary care paediatrics. However, GPs raised concerns around the ability to complete this within a 10-minute appointment and the lack of availability of appropriate growth charts. They also queried the importance of this over other information available in the history and examination that would warrant referral regardless of the child's height. Based on this feedback, the GDG felt that weight was important and whilst a single measurement would not be useful, weight loss is an

important feature to elicit, especially in the context of re-attendance for nonspecific symptoms. This highlighted the importance of ensuring guidance is feasible for both primary and secondary care.

Investigating abdominal pain also caused much debate due to the frequency of children seen with ongoing abdominal pain for whom constipation or functional abdominal pain is the most likely diagnosis. Primary care sees many more children with these symptoms that do not enter secondary care. It was agreed that abdominal pain should not be seen as a single symptom and investigation was warranted if there were other persistent symptoms present.

Strengths and Limitations

The methodology has followed the AGREE-II tool(12) which is the gold-standard process for guideline development. The multi-disciplinary team and Delphi panel comprised of a wide range of clinicians from both primary and secondary care. Representation of professional groups who see these symptoms in CYP on a daily basis has ensured that the final statements are pragmatic for all.

The workshop also included parent representatives ensuring that the guideline also meets the needs of the children, young people and their families.

The attrition of participants between rounds gave a smaller sample than expected. This was largely due to the pandemic as the first round was open during the time the UK went into lockdown and many panel members were front-line workers in emergency and primary care. However, the majority of consensus was gained in the first round prior to further attrition and as part of the RCPCH endorsement process, there will be further stakeholder review of the guideline prior to publication.

Implications for practice

Childhood cancer poses a diagnostic dilemma for clinicians due to non-specificity of symptoms. Early diagnosis is key to ensuring the best possible outcomes for CYP with cancer and this guideline will empower clinicians to investigate CYP for a prompt diagnosis but to also identify those CYP who do not need any further investigations.(5)

These data will also undergo further development methodologies to allow translation into decision support tools and awareness materials. These will be disseminated through public messaging, raising awareness of the signs and symptoms of abdominal and bone tumours through a new national awareness campaign called Child Cancer Smart.

Conclusion

This consensus process has provided expert guidance that will be included in a new clinical guideline for suspected bone and abdominal tumours for use in both primary and secondary care. This evidence base will be translated into awareness tools for the public as part of the Child Cancer Smart campaign.

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COMPETING INTERESTS

The authors have no conflicts of interest to declare.

CONTRIBUTORSHIP STATEMENT

DS, JFL, JN, SO and DW conceived the guideline development process. DS, JFL, DW, AP, SO and KV were involved with design of the process. DS drafted the manuscript which was reviewed and edited by all.

DATA SHARING STATEMENT

All data can be shared upon reasonable request.

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FIGURE LEGENDS

Figure 1: Steps in guideline development

Figure 2: The Delphi consensus process

Figure 3: Percentage consensus for final best practice statements

Figure 4: Percentage consensus for final bone tumour statements

Figure 5: Percentage consensus for final abdominal tumour statements

REFERENCES

- 1. England PH. UK CTYA Cancer Statistics report. 2021.
- 2. Pritchard-Jones K. Childhood cancer in Britain: incidence, survival and mortality. *Br J Cancer* 2007; 96 12:1927. doi: 10.038/sj.bjc.6603800. Epub 2007 Jun 12.
- 3. Pritchard-Jones K, Graf N, van Tinteren H, Craft A. Evidence for a delay in diagnosis of Wilms' tumour in the UK compared with Germany: implications for primary care for children. *Arch Dis Child* 2016; 101 5:417-20.
- 4. Lethaby CD, Picton S, Kinsey SE, Phillips R, van Laar M, Feltbower RG. A systematic review of time to diagnosis in children and young adults with cancer. *Arch Dis Child* 2013; 98 5:349-55.
- 5. Dang-Tan T, Franco EL. Diagnosis delays in childhood cancer: a review. *Cancer* 2007; 110 4:703-13.
- 6. Excellence NIoC. Suspected cancer recognition and referral. 2015.
- 7. Murray MJ, Ruffle A, Lowis S, Howell L, Shanmugavadivel D, Dommett R, et al. Delphi method to identify expert opinion to support children's cancer referral guidelines. *Arch Dis Child* 2020; 105 3:241-6.
- 8. Nicholson J, Murray M, Lowis S, Howell L, Dommett R, Shenton G, Shanmugavadivel S, Ruffle A, Gamble A on behalf of CCLG. CCLG referral guidance for suspected cancer in children and young people. 2021.
- 9. Aware HBBT, Aware HBBT, Walker D, Wilne S, Grundy R, Kennedy C, et al. A new clinical guideline from the Royal College of Paediatrics and Child Health with a national awareness campaign accelerates brain tumor diagnosis in UK children—"HeadSmart: Be Brain Tumour Aware". *Neuro-Oncology* 2015; 18 3:445-54.
- 10. Jones J, Hunter D. Consensus methods for medical and health services research. *Bmj* 1995; 311 7001:376-80.
- 11. Murphy MK, Black NA, Lamping DL, McKee CM, Sanderson CF, Askham J, et al. Consensus development methods, and their use in clinical guideline development. Health Technol Assess 1998; 2 3:i-iv, 1-88.
- 12. Brouwers MC, Kho ME, Browman GP, Burgers JS, Cluzeau F, Feder G, et al. AGREE II: advancing guideline development, reporting and evaluation in health care. *Canadian Medical Association Journal* 2010; 182 18:E839-E42.
- 13. Shanmugavadivel D, Liu JF, Walker D. A systematic review of the signs and symptoms of abdominal tumours in children and young people. SIOP ABSTRACTS. *Pediatric Blood & Cancer* 2019; 66 S4:e27989.
- 14. Shanmugavadivel D, Liu J, Stewart A, Gamble A, Walker D. P05 What are the signs and symptoms of bone tumours in childhood? are the great british public aware of them? *Archives of Disease in Childhood* 2020; 105 Suppl 1:A61-A2.
- 15. Dixon-Woods M, Findlay M, Young B, Cox H, Heney D. Parents' accounts of obtaining a diagnosis of childhood cancer. *Lancet* 2001; 357 9257:670-4.
- 16. Pedersen LH, Wahlberg A, Cordt M, Schmiegelow K, Dalton SO, Larsen HB. Parent's perspectives of the pathway to diagnosis of childhood cancer: a matter of diagnostic triage. *BMC Health Services Research* 2020; 20 1:969.
- 17. Mant JE, Nanduri V, Francis D. The 2 week urgent referral pathway for suspected cancer: the paediatric experience in a local oncology shared-care centre. *Archives of Disease in Childhood* 2011; 96 Suppl 1:A85-A.
- 18. Galloway P, Arumugam J, Hargreaves J, Tsouana E. G13 How effective is the 2 week urgent referral pathway in identifying paediatric cancer? experience from a general paediatric hospital and literature review. *Archives of Disease in Childhood* 2016; 101 Suppl 1:A8-A9.
- 19. (RCPCH) RCoPaCH. Facing the Future: Together for Child Health. 2015.

Table 1: Statements that did not reach consensus

Original statement for R1	Common themes in comments	Revised statement for R2
Statement 3		
R1 consensus 72%	Comments	R2 Consensus 89.8%
If a child or young person (CYP) warrants another appointment for the same problem, the timing of this review should comply with national diagnosis of all cancers (Currently, diagnosis or all clear should be given to the patient within 4 weeks)	□ Only relevant if there is a concern around cancer□ Depends on the clinical situation	Any healthcare professional deciding to review a patient to diagnose or exclude cancer should ensure that the timing of the review does not exceed the national 4-week limit to access a diagnostic test and obtain the result.
Statement 8 R1 consensus 69.1%	Comments	R2 consensus 89.6%
Discuss concerns with a secondary healthcare professional before referring a CYP from primary care in which the differential diagnosis includes a possible tumour (low index of suspicion) to ensure the CYP is seen within two weeks	□Would use two week wait □No available telephone service for paediatrics □Ambiguity over who to call.	Discuss concerns over the telephone with the consultant paediatrician hotline or local equivalent service before referring a CYP from primary care in which differential diagnosis includes a possible tumour to ensure the CYP is seen within the most suitable timeframe (ideally within 2 weeks).
Statement 19 R1 consensus 66%	Comments	R2 consensus 88.36%
Measure and plot height and weight measurements for CYP with signs or symptoms suggestive of a bone tumour on age-appropriate growth charts	 □ Not feasible in a 10 minute consultation within primary care □ Weight is more important than height. □ Growth charts not easily accessible in primary care 	Be aware that weight loss can be a sign of a bone or abdominal tumour. Measure weight and compare to any previous measurements in CYP with signs or symptoms suggestive of a bone or abdominal tumour. Plot these measurements on ageappropriate growth charts if available to you to monitor change when reviewing symptoms.
Statement 53 Round 1 consensus 60.9%	Comments	R2 consensus 77.9%
Request ultrasound imaging of the abdomen and kidneys for persistent (occurring on most days for a 2-week period) abdominal pain of unknown cause	☐ Abdominal pain very common symptom especially in primary care	Request ultrasound imaging of the abdomen and pelvis for new persistent abdominal pain (occurring on most days for a 2- week period) of unknown cause

		atements after two rounds of a Delphi consensus process. A Best Practice (Statements 1-13)	
	1	Explicitly ask young people, parents and carers about their concerns regarding what the cause of symptoms are in any consultation.	99.0%
	2	If a parent/carer expresses concerns about a bone/abdominal tumour this should be reviewed carefully. If a tumour is unlikely, explain why and give appropriate safety netting advice.	72.0%
	3	Any healthcare professional deciding to review a patient to diagnose or exclude cancer should ensure that the timing of the review does not exceed the national 4-week limit to access a diagnostic test and obtain the result.	89.8%
General	4	Offer a telephone or in person interpreter if the patient, parent / carer or healthcare professional are not fluent in English or Welsh.	95.9%
Б	5	Be aware that low parental educational level, social deprivation and lack of familiarity with the UK healthcare system may be associated with diagnostic delay. Consider a multi-disciplinary approach for these families (for example health visitor liaison) and provide clear written safety netting for when to seek further medical advice.	90.7%
	6	Be aware that the presence of complex neuro-disabilities or other communication difficulties (eg, Autistic Spectrum Disorder) may also be associated with diagnostic delay. Care should be taken to elicit concerns from parents or carers that know them best.	98.0%
Referral	7	In primary care, discuss concerns with your local consultant paediatrician hotline or the paediatric consultant on call the same day if there is a high index of suspicion regarding a possible bone or abdominal tumour in a CYP.	90.1%
	8	Discuss concerns over the telephone with the consultant paediatrician hotline or local equivalent service before referring a CYP from primary care in which differential diagnosis includes a possible tumour to ensure the CYP is seen within the most suitable timeframe (ideally within 2 weeks).	89.6%
	9	Abdominal tumours can progress rapidly over days, increasing in size and causing pressure effects (eg, breathing difficulties or bowel obstruction and ischaemia). If there is suspicion of an abdominal tumour this should be discussed in person with a paediatrician to decide the most appropriate time for review, which will often be the same day.	92.7%
ging	10	Request a plain x-ray in AP and lateral view as the initial investigation for a CYP who has a suspected bone tumour. This should not delay referral from primary care.	76.2%
Imaging	11	Request an ultrasound of the abdomen and pelvis as the initial investigation for a CYP who has a suspected abdominal tumour. This should not delay referral from primary care.	80.4%
Predisposing factors	12	Be aware that some predisposing factors are associated with an increased risk of childhood bone tumours. Verify the presence of predisposing factors with parents/patients as they may lower the threshold for referral and investigation.	79.4%
	13	Be aware that some predisposing factors are associated with an increased risk of childhood abdominal tumours. Verify the presence of predisposing factors with parents/patients as they may lower the threshold for referral and investigation.	83.5%

Figure 3: Percentage consensus for final best practice statements $200 \times 172 \text{mm} \ (300 \times 300 \text{ DPI})$

The fi	inal sta	atements after two rounds of a Delphi consensus process.	
Sect	ion E	Bone Tumours (Statements 14-38)	
	14	Take a detailed history, including the presence or absence of the other symptoms on the list above, history of injury, predisposing factors and a family history for CYP presenting with symptoms suggestive of a bone tumour.	99%
	15	Be aware that bone tumours can present with systemic symptoms such as fever, malaise and weight loss. Ask about these associated symptoms when seeing patients with other symptoms suggestive of a bone tumour.	96.8%
	16	Be aware that bone tumours causing spinal cord compression can affect bladder, bowel dysfunction. Ask for the presence of urinary or faecal incontinence (and erectile dysfunction in adolescent males) when taking a history, especially if the presenting complaint is back pain.	94.8%
<u>ra</u>	17	If there is an associated injury, take a detailed history of the injury including the mechanism of injury and timings of the onset of symptoms after the injury occurred.	95.9%
General	18	Examine the limb or joint in question, the joint above and below, and perform a neurological and musculoskeletal examination (eg. pGALS) in a CYP with signs/symptoms suggestive of a bone tumour.	90.7%
	19	Be aware that weight loss can be a sign of a bone tumour. Measure weight and compare to any previous measurements in CYP with signs or symptoms suggestive of a bone or abdominal tumour. Plot these measurements on age-appropriate growth charts if available to you to monitor change when reviewing symptoms.	88.3%
	20	Be aware that an initial normal x-ray does not exclude a bone tumour. If symptoms or clinical suspicion persists, a referral to secondary care is warranted. In secondary care, a discussion with a radiologist about the most appropriate repeat imaging is advised.	88.6%
	21	Be aware that pelvic bone tumours may not initially show on an x-ray. If the persistent symptom is pelvic pain and the x-ray has been reported as normal, referral to secondary care is warranted. In secondary care, discuss with a paediatric radiologist for further advice on imaging.	85.6%
	22	Ask about the presence of the other symptoms of a bone tumour (swelling, palpable lump, restricted movement/limp, fever, weight loss, back pain and bowel/bladder/erectile dysfunction) in a CYP presenting with persistent bone pain (occurring on most days for a 2-week period).	99%
	23	Be aware that children aged younger than 4 years, or those with communication difficulties, are frequently unable to describe pain; their behaviour eg, withdrawal, holding their leg, not weight bearing may indicate bone pain. Look for these signs on examination.	98%
Bone pain	24	Be aware that an initial normal x-ray does not exclude a bone tumour. If symptoms or clinical suspicion persists, consider discussion with a paediatric radiologist and repeat x-ray or further imaging.	85.6%
Sone	25	Request x-ray imaging for persistent bone pain (occurring on most days for a 2-week period). In primary care, request of imaging should not delay referral to secondary care.	83.5%
	26	Request x-ray imaging for localised bone pain that is waking a child or young person at night.	85.5%
	27	Request x-ray imaging for unexplained bone pain (ie, without any preceding injury).	81.5%
	28	Be aware that x-ray imaging is not always the most suitable imaging modality for persistent bony back pain. Discuss with a paediatric radiologist to decide upon the most suitable imaging of choice.	87.6%
	29	Ask about the presence of the other symptoms of a bone tumour (bone pain, palpable lump, restricted movement/limp, fewer, weight loss, back pain and bowel/bladder/erectile dystimution) in a CYP presenting with persistent swelling (occurring on most days for a 2-week period).	96.9%
Swelling	30	Be aware that delayed diagnosis has been associated with attributing a red warm swelling to infection despite no improvement with antibiotics. Arrange to see the CYP at the end of the course of antibiotics to assess response. If there has been no response, consider discussion with secondary care for advice or referral.	87.7%
0,	31	Request x-ray imaging for persistent swelling (present for 2 weeks or more) rapidly increasing in size.	75.2%
	32	Request x-ray imaging for persistent swelling (present for 2 weeks or more) not resolving despite treatment with regular anti-inflammatories OR antibiotics.	78.3%
/ss/	33	A bony mass or lump which is increasing in size can be a sign of an underlying bone tumour and requires referral to secondary care.	95.9%
Bone mass/ lump	34	Ask and examine for the other signs and symptoms suggestive of a bone tumour (bone pain, swelling, limp/restricted movement, fever, weight loss, back pain and bladder/bowel/erectile dysfunction) in CYP with a lump/mass.	93.8%
B	35	Request x-ray imaging for a rapidly increasing bony lump or mass. This should not delay referral from primary care.	86.6%
Restricted movement/limp	36	Ask about the presence of the other symptoms of a bone tumour (bone pain, palpable lump, restricted movement/limp, fever, velight loss, back pain and bowel/bladder/erectile dysfunction) in a CYP presenting with restricted movement or limp.	93.9%
Restricted vement/lin	37	Have a high level of concern for a CYP who is normally highly active or sporty but is no longer able to play sport due to the presenting symptom.	87.6%
nom Nom	38	Request x-ray imaging for a CYP who is non-weight bearing or has restricted movement despite adequate analgesia.	83.5%

Figure 4: Percentage consensus for final bone tumour statements $209x297mm (300 \times 300 DPI)$

		C Abdominal Tumours (Statements 39-63)	
	39	Take a detailed history including the presence of any of the other symptoms on the list above, any predisposing factors and a family history.	94.89
	40	Examine the abdomen, including external genitalia and hernia orifices, visualise and palpate the spine and perform a neurological examination in a CYP with signs/symptoms that may be due to an abdominal turnour.	93.69
General	41	Perform a urine dipstick to exclude infection and identify any protein or blood that would warrant referral to secondary care.	89.79
Ğ	42	Consider recording blood pressure if the correct size cuff is available to identify hypertension.	74.29
	43	Be aware that weight loss can be a sign of an abdominal tumour. Measure weight and compare to any previous measurements in CYP with signs or symptoms suggestive of a bone or abdominal tumour. Plot these measurements on age-appropriate growth charts if available to you to monitor change when reviewing symptoms.	88.3%
	44	Ask about the presence of the other symptoms of an abdominal tumour (abdominal pain, haematuria, abdominal distension, weight loss, fever, malaise, jaundice, bone pain, neurological symptoms and bowel/bladder/erectile dysfunction) in a CYP presenting with an abdominal mass.	99%
al mass	45	Be aware that abdominal masses can cause neurological symptoms due to pressure on the spinal cord. The pressure can cause children to present as "off legs" or refusal to weight bear. Examine the abdomen when a CVP presents with refusal to weight bear.	94.99
Abdominal mass	46	Be aware that diagnostic delay is associated with failure to perform an abdominal examination in a child who is distressed/crying. Offer to examine the child once they have settled or ask a colleague to perform the examination.	94.89
A	47	Request ultrasound imaging of the abdomen and pelvis for a CYP with a palpable abdominal mass (unless this is felt to be faeces, in which case a review of the CYP after disimpaction is important).	83.69
	48	Request ultrasound imaging of the abdomen and pelvis for a CYP with suspected hepatomegaly or splenomegaly on examination.	83.59
	49	Ask about the presence of the other symptoms of an abdominal tumour (haematuria, abdominal distension, weight loss, fever, malaise, jaundice, bone pain, neurological symptoms and bowel/bladder/erectile dysfunction) in a CVP presenting with persistent abdominal pain.	92.89
pain	50	Examine the abdomen in a CYP with abdominal pain to elicit any masses or hepatomegaly and/or splenomegaly.	99%
lina	51	Be aware that if the tumour is retroperitoneal, the presenting complaint may be back pain. Examine the abdomen in a CYP presenting with back pain.	95.99
Abdominal pain	52	Be aware that delayed diagnosis has been associated with attributing abdominal pain to constipation despite no improvement with laxatives. Assess response to laxatives by reviewing the CYP at regular intervals and taking a full history and examining their abdomen.	87.79
	53	Request ultrasound imaging for persistent abdominal pain with one or more other symptoms that may be due to an abdominal tumour (abdominal distension, mass, haematuria, weight loss, fever, malaise, jaundice, bone pain, neurological symptoms and bowel/bladder/erectile dysfunction)	86.69
	54	Ask about the presence of the other symptoms of an abdominal tumour (abdominal pain, mass, weight loss, fever, malaise, jaundice, bone pain, neurological symptoms and bowel/bladder/erectile dysfunction) in a CYP presenting with haematuria in the absence of another known cause.	96.99
<u>ē</u>	55	Do a careful abdominal examination to elicit any potential retroperitoneal mass in all CYP with haematuria.	92.79
Haematuria	56	Be aware that delayed diagnosis has been associated with assuming persistent haematuria is due to a UTI despite no response to antibiotics. Arrange to see the CYP again at the end of the course of antibiotics to assess the response. If there is no response, consider discussion with paediatrician for advice.	82.49
Í	57	Request ultrasound imaging for unexplained persistent (occurring for 2 weeks or more) macroscopic haematuria.	87.79
	58	Request ultrasound imaging of the abdomen and pelvis for haematuria plus one or more other symptoms that may be due to an abdominal tumour (abdominal pain, abdominal distension, weight loss, fever, malaise, jaundice, bone pain, neurological symptoms and bowel/bladder/erectile dysfunction).	87.6%
sion	59	Ask about the presence of the other symptoms of an abdominal tumour (abdominal pain, haematuria, weight loss, fever, malaise, jaundice, bone pain, neurological symptoms and bowel/bladder/erectile dysfunction) in a CYP presenting with an abdominal distension.	97.99
Abdominal distension	60	Be aware that abdominal distension caused by a tumour will not fluctuate but will increase in size progressively over time. Arrange another appointment to review the symptoms and re-examine the CYP.	83.5%
	61	Be aware that delayed diagnosis has been associated with attributing abdominal distension to constipation despite no improvement with laxative treatment. Assess response to treatment in these CYP by seeing them at regular intervals.	84.5%
opq	62	Be aware that delayed diagnosis has been associated with failure to examine the abdomen at review of a CYP on treatment for constipation. Palpate the abdomen in CYP who are being reviewed for constipation.	94.99
4	63	Request ultrasound imaging of the abdomen and pelvis for a CYP with rapidly increasing abdominal distension. This should not delay referral from primary care.	83.59

Figure 5: Percentage consensus for final abdominal tumour statements $209x297mm (300 \times 300 DPI)$

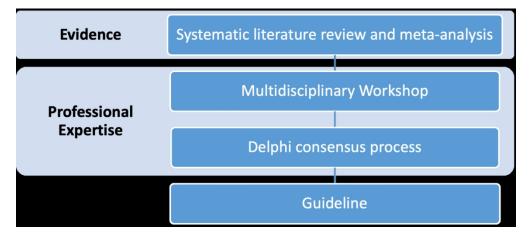


Figure 1: Steps in guideline development 125x55mm (300 x 300 DPI)

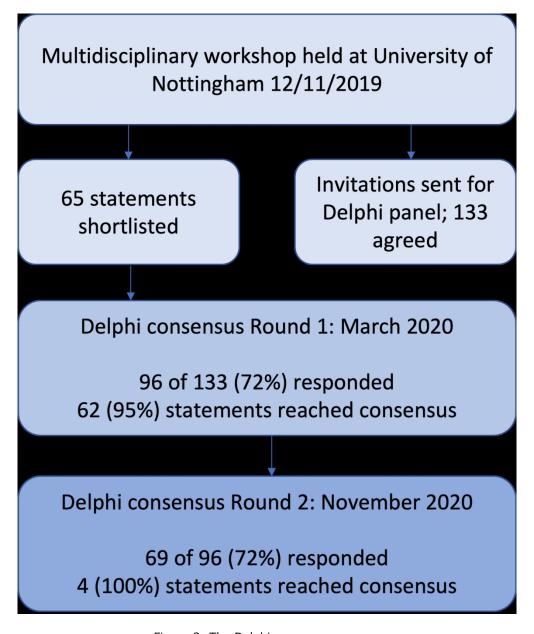


Figure 2: The Delphi consensus process $136x163mm (300 \times 300 DPI)$

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Assessing and investigating children with suspected bone and abdominal tumours: an e-Delphi consensus process.

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Assessing and investigating children with suspected bone and abdominal tumours: an e-Delphi consensus process.

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Assessing and investigating children with suspected bone and abdominal tumours: an e-Delphi consensus process.

ABSTRACT

Background

The incidence of childhood cancer has risen by 15% since the 1990s. Early diagnosis is key to optimising outcomes, however diagnostic delays are widely reported. Presenting symptoms are often non-specific causing a diagnostic dilemma for clincians. This Delphi-consensus process was conducted to develop a new clinical guideline for children and young people (CYP) presenting with signs/symptoms suggestive of a bone or abdominal tumour.

Methods

Invitation emails were sent to primary and secondary healthcare professionals (HCPs) to join the Delphi panel. 65 statements were derived from evidence review by a multidisciplinary team. Participants were asked to rank their level of agreement with each statement on a 9-point Likert scale (1 = strongly disagree, 9 = strongly agree), with responses >=7 taken to indicate agreement. Statements not reaching consensus were rewritten and re-issued in a subsequent round.

Results

All statements achieved consensus after two rounds. 96/133 (72%) participants responded to Round 1 (R1) and 69/96 (72%) completed Round 2 (R2). 62/65 (94%) statements achieved consensus in R1 with 29/65 (47%) gaining more than

90% consensus. Three statements did not reach consensus scoring between 61% and 69%. All reached numerical consensus at the end of Round 2. Strong consensus was reached on best practice of conducting the consultation, acknowledging parental instinct and obtaining telephone advice from a paediatrician to decide the timing and place of review, rather than generic adult cancer pathways. Dissensus in statements were due to unachievable targets within primary care and valid concerns over a potential over-investigation of abdominal pain.

Conclusions

This consensus process has consolidated statements that will be included in a new clinical guideline for suspected bone and abdominal tumours for use in both primary and secondary care. This evidence base will be translated into awareness tools for the public as part of the Child Cancer Smart national awareness campaign.

WHAT IS ALREADY KNOWN ON THIS TOPIC?

- Childhood cancer is a global disease burden and is the leading illness
 cause of death in children between 1 and 14 in the UK.
- Bone and abdominal tumours have some of the lowest survival estimates of childhood cancers.
- They pose a diagnostic dilemma for clinicians, presenting with non-specific symptoms such as bone pain, limp and abdominal distension.

WHAT THIS STUDY ADDS?

- 64 new evidence-based statements on best practice, assessment, imaging and referral of CYP presenting with key bone and abdominal symptoms.
- Wide representation on the Delphi panel to include those from primary and secondary care resulting in pragmatic guidance to aid decision-making in both primary and secondary care.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

These data will form the basis of a new clinical guideline which will aid
 HCPs to instigate investigation of those with signs and symptoms that
 could be due to a bone or abdominal tumour.

- Empowering clinicians with this guidance will allow prompt recognition of those children with bone and abdominal tumours, improving their
- Jugh a new awareness cathe patient interval and promote. These data will be translated into public-facing materials for dissemination through a new awareness campaign called Child Cancer Smart to reduce

INTRODUCTION

Childhood cancer is often perceived to be rare, however, whilst individual childhood cancer types are rare, collectively they are more common than many believe. An individual's cumulative risk of cancer from birth to age 15 years is 1 in 450, with 1840 new cases diagnosed in children and young people (CYP) aged 0-15 each year in the UK.¹ Incidence of childhood cancer has increased by 15% since the 1990s. Although survival estimates are also increasing (from 77% in 2001 to 84% in 2016 across all childhood cancers¹) progress in the UK lags behind other Western European countries.¹-4

Many CYP experience delays in their cancer diagnosis⁵ ⁶. Such delays are multifactorial. Unlike in adult cancers, prevention and screening strategies are not available, therefore early diagnosis is key to optimising outcomes, reducing morbidity, mortality and treatment burden.¹ A possible explanation behind delayed diagnosis lies with childhood cancer symptomatology posing a diagnostic dilemma. Symptoms are often non-specific, mimicking other more common ailments such as gastroenteritis, migraines or can masquerade as pain attributed to minor injury. Furthermore, perceived rarity means childhood cancer is not often considered as a potential diagnosis by the parent or clinician. The 2015 National Institute Health and Care Excellence (NICE) issued a guideline on "Suspected cancer: recognition and referral" which covers all ages. There is a real need for paediatric-specific guidance, as adult cancers manifest and present differently. This current guidance is directed at primary care with the "end-point" being referral onto secondary care. Children with cancer experience diagnostic

delay throughout the health service both at primary care and secondary care level and a referral from primary to secondary care can add significant length to the patient's diagnostic journey.

Furthermore, the recommendations lack a systematic evidence review and are based solely on expert consensus which notably did not include any paediatric oncologists or haematologists on the panel.

As a result, concern from the paediatric oncology community across the UK rose that the guidance was not fit for purpose.⁸ A supplement to the NICE guideline was published in 2021 following a Delphi consensus process conducted amongst the Children's Cancer and Leukaemia Group membership.⁹ A full systematic evidence review was not completed at this time, due to the urgent need for expert child-specific guidance to be published.

Detailed tumour specific diagnostic guidance as that produced for childhood brain tumours is needed, in order to empower clinicians to make decisions about those who need investigation and accelerate referrals for CYP with high-suspicion symptoms promoting earliest possible diagnosis. Experience gained from developing and disseminating tumour specific evidence based guidance for diagnosis of childhood brain tumours through the HeadSmart campaign demonstrated that parents and clinicians were empowered by access to such guidance to identify the children who need investigation leading to a halving of the TDI across the UK for children with brain tumours¹⁰. Using this methodology for other tumour types, grouped by location, could accelerate diagnosis and improve outcomes.

Prolonged diagnostic intervals have been widely reported in bone tumours. Of the BRIGHTLIGHT cohort in the UK, adolescents and young adults with bone tumours had the longest median symptom-onset to diagnosis interval with multiple pre-referral consultations with general practice before diagnosis¹¹.

Abdominal tumours involving sympathetic nervous system (neuroblastoma), renal / urogenital tracts (Wilms tumour, bladder tumours), liver (hepatoblastoma), lymphatic tissues (lymphoma / leukaemia) and connective tissues (soft tissue sarcomas) account for approximately 15% of all childhood cancers, representing a substantial proportion. Furthermore, there is strong evidence that children in the UK with a Wilm's tumour have a significantly larger volume, a more advanced tumour stage at diagnosis and poorer survival compared with their European counterparts. ² ¹²

Based on this collective evidence, we prioritised focussing on these as the next step to improving childhood cancer awareness.

As the questions of specificity, referral pathways, investigation indications and acceptable waiting times for CYP with suspected cancer cannot easily be addressed by quantitative research methods alone, a Delphi consensus process¹³ ¹⁴ was employed to use professional expertise to incorporate the evidence from systematic reviews into a clinical guideline.

METHODS

The Delphi consensus process

The Delphi consensus process was conducted as the final step of the goldstandard AGREE-II approach to clinical guideline development (Figure 1).¹⁵

A Guideline Development Group (GDG) consisting of seven members with experience in developing clinical guidelines (two paediatric oncologists, a representative member of the Royal College of Paediatrics and Child Health (RCPCH), the Chief Executive of the Children's Cancer and Leukaemia Group (CCLG), a GP, a paediatric registrar, research assistant and parent representative) oversaw the guideline development. The initial stage comprised of a systematic review and meta-analysis of the literature. This provided contemporary evidence regarding the signs and symptoms of bone and abdominal tumours in CYP.^{16 17}

Multidisciplinary workshop

A multi-disciplinary workshop was held on 12th November 2019 with 15 participants (seven male, eight female). Participants consisted of doctors from primary, secondary and tertiary care (two general practitioners, three paediatric emergency department consultants, three paediatricians, three paediatric oncologists and two paediatric surgeons), and two parents of CYP who have been diagnosed with cancer.

The systematic review identified 29 bone tumour symptoms/signs and 97 abdominal tumour signs/symptoms but only those that occurred in 2% or more of the patients were reported as a list of pooled proportions. This list was reviewed and refined by the multi-disciplinary workshop participants to four bone tumour symptoms (pain, swelling, mass/lump and restricted movement or limp) and four

abdominal tumour symptoms (mass, haematuria, pain and distension). For each sign/symptom, the group were asked to consider a set of questions on clinical presentation, assessment and investigation strategies and suggest answers or possible approaches to care. The questions for discussion were:

- How would this sign/symptom present?
- How should an HCP assess a child/young person presenting with this sign/symptom?
- How should an HCP determine whether this presenting sign/symptom could be due to a bone or abdominal tumour (specificity)?
- What factors influence the specificity of this sign/symptom?
- What are appropriate thresholds for referral and/or investigation for a child/young person presenting with this sign/symptom?
- What would you regard as best practice for referral and/or investigation of a child/young person presenting with this sign/symptom?

The discussions were recorded, and contemporaneous notes taken. The discussion points and notes were collated and translated into a series of statements by the GDG at the end of the workshop. These were sent back to the workshop participants to check accuracy and content. The workshop participants did not participate in the Delphi consensus survey.

Delphi-consensus surveys

The statements derived from the workshop were sent to healthcare professionals using a modified e-Delphi consensus process¹⁴. Invitation emails were sent out to HCPs to join the Delphi panel; it included doctors from primary, secondary and tertiary care across a wide range of specialties who may encounter CYP with these symptoms in their daily practice (general paediatricians, GPs, community paediatricians, paediatric surgeons, paediatric radiologists, paediatric

orthopaedic surgeons, paediatric oncologists/haematologists and emergency paediatricians). HCPs were recruited from the Children's Cancer and Leukaemia Group (CCLG) membership, Association of Paediatric Emergency Medicine (APEM) and through General Practice mailing lists.

The survey was built using Jisc Online Surveys and the Delphi panel members were asked to rank their agreement with the statements by means of a 9-point Likert scale (1 = strongly disagree; 5 = neither agree, nor disagree; 9 = strongly agree) with the ability to comment by free-text.

Definition of consensus

Based on existing guidelines, statements were defined as reaching consensus if 70% or more of the Delphi Panel respondents rated the statement as either 7, 8 or 9.8 Statements were rejected if 25% or less of the Delphi Panel respondents rated the statement 7, 8 or 9.13

The rankings for each statement were collated. Any statement achieving the predetermined level of consensus was accepted. Statements not reaching consensus were rewritten and reviewed by the multi-disciplinary workshop participants. Free-text comments were used to help structure the re-written statement prior to being re-issued in Round 2.

Patient and Public involvement

Two parent representatives with experience of childhood cancer diagnosis volunteered to participate in the multi-disciplinary workshop and helped revise the statements following feedback from the Delphi panel.

Ethical approvals

This Delphi consensus process is part of clinical guideline development and healthcare professionals were recruited for their expertise by virtue of their professional role. Ethical approvals were not required however consent was obtained from all participants prior to the workshops and Delphi process, with explicit consent being asked for recording of sessions and use of quotes or feedback as part of the process.

RESULTS

150 HCPs practising in the UK were invited to take part. 133 agreed to take part consisting of 57 general practitioners, 28 general paediatricians, 18 paediatric emergency consultants, 13 paediatric surgeons, 6 paediatric radiologists and 11 paediatric oncologists. Sixty-five statements were derived from the workshop and reviewed by the RCPCH guideline development team as part of the endorsement process. The statements were split under categories: best practice in conducting the consultation (referral, imaging, predisposing factors), bone tumours (general, bone pain, swelling, mass/lump, restricted movement/limp) and abdominal tumours (general, abdominal pain, abdominal mass, haematuria, abdominal distension).

The first round of the Delphi consensus process was open from 2 March to 23 March 2020. A Delphi survey containing 65 statements were sent out to all 133 participants. During this period, the COVID-19 pandemic was declared and the round was paused. The survey was re-issued on 9 September 2020, allowing those who still wished to complete it, to do so. In total, 96 (72%) participants completed Round 1. The second round was open between 9 November and 30 November 2020 and was completed by 69 of 96 (72%) respondents who had taken part in Round 1. All 65 statements reached numerical consensus after two rounds (Figure 2).

Round One (R1)

96 of 133 (72%) participants responded to the first round.

62 of 65 (95%) statements achieved numerical consensus. Three of 65 (5%) statements did not achieve numerical consensus and no statements were rejected.

Of the 62 consensus-reaching statements, 29 (47%) gained more than 90% consensus, 25 (40%) statements gained between 80-90% consensus and 8 (13%) statements between 70-80% consensus.

Despite achieving numerical consensus, statement 3, which read "if a child or young person (CYP) warrants another appointment for the same problem, the timing of this review should comply with national diagnosis of all cancers (currently, diagnosis or all clear should be given to the patient within 4 weeks)", was revised and included in round two due to comments outlining ambiguity in the wording.

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Table 1: Statements that did not reach consensus

Original statement for R1	Common themes in comments	Revised statement for R2
Statement 3 R1 consensus 72%	Comments	R2 Consensus 89.8%
If a child or young person (CYP) warrants another appointment for the same problem, the timing of this review should comply with national diagnosis of all cancers (Currently, diagnosis or all clear should be given to the patient within 4 weeks)	 Only relevant if there is a concern around cancer Depends on the clinical situation 	Any healthcare professional deciding to review a patient to diagnose or exclude cancer should ensure that the timing of the review does not exceed the national 4-week limit to access a diagnostic test and obtain the result.
Statement 8 R1 consensus 69.1%	Comments	R2 consensus 89.6%
Discuss concerns with a secondary healthcare professional before referring a CYP from primary care in which the differential diagnosis includes a possible tumour (low index of suspicion) to ensure the CYP is seen within two weeks	 Would use two week wait No available telephone service for paediatrics Ambiguity over who to call. 	Discuss concerns over the telephone with the consultant paediatrician hotline or local equivalent service before referring a CYP from primary care in which differential diagnosis includes a possible tumour to ensure the CYP is seen within the most suitable timeframe (ideally within 2 weeks).
Statement 19 R1 consensus 66%	Comments	R2 consensus 88.36%
Measure and plot height and weight measurements for CYP with signs or symptoms suggestive of a bone tumour on age-appropriate growth charts	 Not feasible in a 10 minute consultation within primary care Weight is more important than height. Growth charts not easily accessible in primary care 	Be aware that weight loss can be a sign of a bone or abdominal tumour. Measure weight and compare to any previous measurements in CYP with signs or symptoms suggestive of a bone or abdominal tumour. Plot these measurements on ageappropriate growth charts if available to you to monitor change when reviewing symptoms.
Round 1 consensus 60.9% Request ultrasound imaging of the abdomen and kidneys for persistent (occurring on most days for a 2-week period) abdominal pain of unknown cause	 Abdominal pain very common symptom especially in primary care Would not request ultrasound if not red flags 	R2 consensus 77.9% Request ultrasound imaging of the abdomen and pelvis for new persistent abdominal pain (occurring on most days for a 2-week period) of unknown cause where there is another symptom present from the checklist.

Round Two (R2)

69 of 96 (72%) participants responded to the second round.

All four statements reached numerical consensus at the end of R2. However, the similar to a.

.atements are presented in F statement regarding the investigation of abdominal pain which was revised and accepted was deemed similar to another statement and was omitted from the final list.

The final 64 statements are presented in Figures 3, 4 and 5.

DISCUSSION

Summary

These data provides professionally agreed backbone for best practice for use in a new clinical guideline in the assessment and investigation of CYP with suspected bone or abdominal tumours. When developed, this will be the first clinical guideline to be published specifically for these tumour types, and the second stand-alone guidance for children and young people following the HeadSmart guidance for childhood brain tumours.¹⁸

The initial round achieved a consensus in 95% of the statements sent out for review and all statements reached consensus within two rounds. This was higher than expected, a testament to the work of the multi-disciplinary workshop participants in clarifying and negotiating statements that were applicable across specialties. Those statements that did not reach consensus achieved between 60.9% and 69.1% and required minor revisions before achieving consensus in R2.

Best practice in general approach

Overall, there was strong consensus regarding the best practice of conducting the consultation, taking into account parental concern or instinct which has been shown to be an important factor in diagnosis of childhood cancer. ¹⁹ ²⁰ Referral pathways for childhood cancers include an urgent referral process for suspected cancer but has been subject to criticism. Studies have shown that only 2% of childhood cancer is actually diagnosed via this route and the distress caused to parents being referred using this pathway far outweighs the rate of pick-up.²¹ ²² Furthermore, for those for whom cancer is the diagnosis, this pathway could

potentially add a further two week delay, depending on waiting times for appointments, before any investigation is requested. Reaching clear consensus on obtaining telephone advice from a paediatrician to decide the timing and place of review will ensure that all CYP are appropriately triaged based on their history. This is in line with standards set by the RCPCH in the 2015 "Facing the Future" publication stating that GPs assessing or treating children should have access to immediate telephone advice from a consultant paediatrician.²³ Despite this guidance, there were some comments from primary care stating a lack of availability of advice in their region.

One recurring theme amongst the comments, was the regional differences within primary care. A number of GPs highlighted that there was no ability to request paediatric imaging directly from primary care and if there was, this could take weeks or even months to take place. A caveat was added to the investigation statements to state that requesting an investigation should not delay a referral.

Dissensus in R1

The dissensus in three statements were due to unachievable targets within primary care and valid concerns over a potential over-investigation of a common symptom respectively.

Measuring and plotting height and weight takes place routinely within secondary care paediatrics. However, GPs raised concerns around the ability to complete this within a 10-minute appointment and the lack of availability of appropriate growth charts, either electronically or in paper format. They also queried the importance of this over other information available in the history and examination

that would warrant referral regardless of the child's height. Based on this feedback, the GDG felt that weight was important and whilst a single measurement would not be useful, weight loss is an important feature to elicit, especially in the context of re-attendance for non-specific symptoms. This highlighted the importance of ensuring guidance is feasible for both primary and secondary care.

Investigating abdominal pain also caused much debate due to the frequency of children seen with ongoing abdominal pain for whom constipation or functional abdominal pain is the most likely diagnosis. Primary care sees many more children with these symptoms that do not enter secondary care. It was agreed that abdominal pain should not be seen as a single symptom and investigation was warranted if there were other persistent symptoms present.

Strengths and Limitations

The methodology has followed the AGREE-II tool¹⁵ which is the gold-standard process for guideline development. The multi-disciplinary team and Delphi panel comprised of a wide range of clinicians from both primary and secondary care. Representation of professional groups who see these symptoms in CYP on a daily basis has ensured that the final statements are pragmatic for all.

The workshop also included parent representatives ensuring that the guideline also meets the needs of the children, young people and their families.

The attrition of participants between rounds gave a smaller cohort than expected.

This was largely due to the pandemic as the first round was open during the time the UK went into lockdown and many panel members were front-line workers in emergency and primary care. However, the majority of consensus was gained in

the first round prior to further attrition and as part of the RCPCH endorsement process, there will be further stakeholder review of the guideline prior to publication.

Implications for practice

Childhood cancer poses a diagnostic dilemma for clinicians due to non-specificity of symptoms. Earlier diagnosis offers clinical presentations with smaller and less advanced tumours, requiring less therapy and therefore better outcomes. This guideline, which will be published by Summer 2023, will empower clinicians to investigate CYP for a prompt diagnosis but to also identify those CYP who do not need any further investigations.

These data will also undergo further development methodologies to allow translation into decision support tools and awareness materials. These will be disseminated through public messaging, raising awareness of the signs and symptoms of abdominal and bone tumours through a new national awareness campaign called Child Cancer Smart in September 2023.

Conclusion

This consensus process has provided expert guidance that will be included in a new clinical guideline for suspected bone and abdominal tumours for use in both primary and secondary care. This evidence base will be translated into awareness tools for the public as part of the Child Cancer Smart campaign.

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COMPETING INTERESTS

The authors have no conflicts of interest to declare.

CONTRIBUTORSHIP STATEMENT

DS, JFL, SO and DW conceived the guideline development process. DS, JFL, DW, AP, ABG, SO and KV were involved with design of the process. DS drafted the manuscript which was reviewed and edited by all.

DATA SHARING STATEMENT

All data can be shared upon reasonable request.

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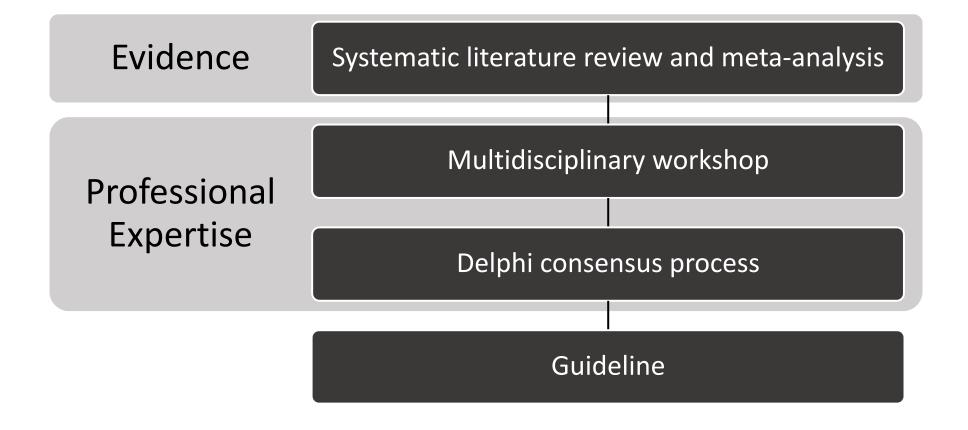
FIGURE LEGENDS

- Figure 1: Steps in guideline development
- Figure 2: The Delphi consensus process
- **Figure 3:** Percentage consensus for final best practice statements
- **Figure 4:** Percentage consensus for final bone tumour statements
- Figure 5: Percentage consensus for final abdominal tumour statements

REFERENCES

- 1. Public Health England. Children, teenagers and young adults UK cancer statistics report 2021 London2021 [Available from: https://www.qub.ac.uk/research-centres/nicr/FileStore/PDF/UKReports/Filetoupload,1024819,en.pdf accessed 19/01/2023.
- Aguirre-Neto JCd, Camargo Bd, Tinteren Hv, et al. International Comparisons of Clinical Demographics and Outcomes in the International Society of Pediatric Oncology Wilms Tumor 2001 Trial and Study. JCO Global Oncology 2022(8):e2100425. doi: 10.1200/go.21.00425
- 3. Pritchard-Jones K. Childhood cancer in Britain: incidence, survival and mortality. *British Journal of Cancer* 2007;96(12):1927-27. doi: 10.1038/sj.bjc.6603800
- 4. Pritchard-Jones K, Graf N, van Tinteren H, et al. Evidence for a delay in diagnosis of Wilms' tumour in the UK compared with Germany: implications for primary care for children. Archives of Disease in Childhood 2016;101(5):417-20. doi: 10.1136/archdischild-2015-309212
- 5. Lethaby CD, Picton S, Kinsey SE, et al. A systematic review of time to diagnosis in children and young adults with cancer. *Archives of Disease in Childhood* 2013;98(5):349-55. doi: 10.1136/archdischild-2012-303034
- 6. Dang-Tan T, Franco EL. Diagnosis delays in childhood cancer: a review. *Cancer* 2007;110(4):703-13. doi: 10.1002/cncr.22849 [published Online First: 2007/07/11]
- 7. National Institute for Health & Clinical Excellence (NICE). Suspected cancer: recognition and referral: NICE; 2015 [updated 15 December 2021. Available from: https://www.nice.org.uk/guidance/ng12 accessed 19/01/2023.
- 8. Murray MJ, Ruffle A, Lowis S, et al. Delphi method to identify expert opinion to support children's cancer referral guidelines. *Archives of Disease in Childhood* 2020;105(3):241-46. doi: 10.1136/archdischild-2019-317235
- Children's Cancer & Leukaemia Group (CCLG). Referral guidance for suspected cancer in children and young people UK2021 [Available from: https://www.cclg.org.uk/write/MediaUploads/Professionals/Guidelines/CCLG_referral_guidance_April_2021_(Web).pdf accessed 19/01/2023.
- Shanmugavadivel D, Liu JF, Murphy L, et al. Accelerating diagnosis for childhood brain tumours: an analysis of the HeadSmart UK population data. *Arch Dis Child* 2020;105(4):355-62. doi: 10.1136/archdischild-2018-315962 [published Online First: 2019/10/28]
- 11. Herbert A, Lyratzopoulos G, Whelan J, et al. Diagnostic timeliness in adolescents and young adults with cancer: a cross-sectional analysis of the BRIGHTLIGHT cohort. *The Lancet Child & Adolescent Health* 2018;2(3):180-90. doi: https://doi.org/10.1016/S2352-4642(18)30004-X
- 12. Pastore G, Znaor A, Spreafico F, et al. Malignant renal tumours incidence and survival in European children (1978-1997): report from the Automated Childhood Cancer Information System project. *Eur J Cancer* 2006;42(13):2103-14. doi: 10.1016/j.ejca.2006.05.010
- 13. Jones J, Hunter D. Consensus methods for medical and health services research. *Bmj* 1995;311(7001):376-80. doi: 10.1136/bmj.311.7001.376 [published Online First: 1995/08/05]
- 14. Murphy MK, Black NA, Lamping DL, et al. Consensus development methods, and their use in clinical guideline development. *Health Technol Assess* 1998;2(3):i-iv, 1-88. [published Online First: 1998/04/30]
- 15. Brouwers MC, Kho ME, Browman GP, et al. AGREE II: advancing guideline development, reporting and evaluation in health care. *Cmaj* 2010;182(18):E839-42. doi: 10.1503/cmaj.090449 [published Online First: 2010/07/07]

- 16. Shanmugavadivel D, Liu JF, Walker D. A systematic review of the signs and symptoms of abdominal tumours in children and young people. SIOP ABSTRACTS. *Pediatric Blood & Cancer* 2019;66(S4):e27989. doi: https://doi.org/10.1002/pbc.27989
- 17. Shanmugavadivel D, Liu J, Stewart A, et al. P05 What are the signs and symptoms of bone tumours in childhood? are the great british public aware of them? *Archives of Disease in Childhood* 2020;105(Suppl 1):A61-A62. doi: 10.1136/archdischild-2020-rcpch.146
- 18. Walker D, Wilne S, Grundy R, et al. A new clinical guideline from the Royal College of Paediatrics and Child Health with a national awareness campaign accelerates brain tumor diagnosis in UK children—"HeadSmart: Be Brain Tumour Aware". *Neuro-Oncology* 2015;18(3):445-54. doi: 10.1093/neuonc/nov187
- 19. Dixon-Woods M, Findlay M, Young B, et al. Parents' accounts of obtaining a diagnosis of childhood cancer. *Lancet* 2001;357(9257):670-4. doi: 10.1016/s0140-6736(00)04130-1 [published Online First: 2001/03/15]
- 20. Pedersen LH, Wahlberg A, Cordt M, et al. Parent's perspectives of the pathway to diagnosis of childhood cancer: a matter of diagnostic triage. *BMC Health Services Research* 2020;20(1):969. doi: 10.1186/s12913-020-05821-2
- 21. Galloway P, Arumugam J, Hargreaves J, et al. G13 How effective is the 2 week urgent referral pathway in identifying paediatric cancer? experience from a general paediatric hospital and literature review. *Archives of Disease in Childhood* 2016;101(Suppl 1):A8-A9. doi: 10.1136/archdischild-2016-310863.13
- 22. Mant JE, Nanduri V, Francis D. The 2 week urgent referral pathway for suspected cancer: the paediatric experience in a local oncology shared-care centre. *Archives of Disease in Childhood* 2011;96(Suppl 1):A85-A85. doi: 10.1136/adc.2011.212563.198
- 23. Royal College of Paediatrics & Child Health. Facing the Future together for child health 2015 [Available from: https://www.rcpch.ac.uk/resources/facing-future-together-child-health accessed 19/01/2023.



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Multidisciplinary workshop held at University of Nottingham 12/11/2019 Invitations sent for 65 statements Delphi panel; 133 shortlisted agreed Delphi consensus Round 1: March 2020 96 of 133 (72%) responded 62 (95%) statements reached consensus Delphi consensus Round 2: November 2020 69 of 96 (72%) responded 4 (100%) statements reached consensus

The f	inal sta	atements after two rounds of a Delphi consensus process.	
Sect	ion A	Best Practice (Statements 1-13)	
	1	Explicitly ask young people, parents and carers about their concerns regarding what the cause of symptoms are in any consultation.	99.0%
	2	If a parent/carer expresses concerns about a bone/abdominal tumour this should be reviewed carefully. If a tumour is unlikely, explain why and give appropriate safety netting advice.	72.0%
General	3	Any healthcare professional deciding to review a patient to diagnose or exclude cancer should ensure that the timing of the review does not exceed the national 4-week limit to access a diagnostic test and obtain the result.	89.8%
	4	Offer a telephone or in person interpreter if the patient, parent / carer or healthcare professional are not fluent in English or Welsh.	95.9%
	5	Be aware that low parental educational level, social deprivation and lack of familiarity with the UK healthcare system may be associated with diagnostic delay. Consider a multi-disciplinary approach for these families (for example health visitor liaison) and provide clear written safety netting for when to seek further medical advice.	90.7%
	6	Be aware that the presence of complex neuro-disabilities or other communication difficulties (eg, Autistic Spectrum Disorder) may also be associated with diagnostic delay. Care should be taken to elicit concerns from parents or carers that know them best.	98.0%
	7	In primary care, discuss concerns with your local consultant paediatrician hotline or the paediatric consultant on call the same day if there is a high index of suspicion regarding a possible bone or abdominal tumour in a CYP.	90.1%
Referral	8	Discuss concerns over the telephone with the consultant paediatrician hotline or local equivalent service before referring a CYP from primary care in which differential diagnosis includes a possible tumour to ensure the CYP is seen within the most suitable timeframe (ideally within 2 weeks).	89.6%
	9	Abdominal tumours can progress rapidly over days, increasing in size and causing pressure effects (eg, breathing difficulties or bowel obstruction and ischaemia). If there is suspicion of an abdominal tumour this should be discussed in person with a paediatrician to decide the most appropriate time for review, which will often be the same day.	92.7%
Imaging	10	Request a plain x-ray in AP and lateral view as the initial investigation for a CYP who has a suspected bone tumour. This should not delay referral from primary care.	76.2%
lma	11	Request an ultrasound of the abdomen and pelvis as the initial investigation for a CYP who has a suspected abdominal tumour. This should not delay referral from primary care.	80.4%
Predisposing factors	12	Be aware that some predisposing factors are associated with an increased risk of childhood bone tumours. Verify the presence of predisposing factors with parents/patients as they may lower the threshold for referral and investigation.	79.4%
Predis _e fact	13	Be aware that some predisposing factors are associated with an increased risk of childhood abdominal tumours. Verify the presence of predisposing factors with parents/patients as they may lower the threshold for referral and investigation.	83.5%

Figure 3: Percentage consensus for final best practice statements $200x172mm (300 \times 300 DPI)$

		Bone Tumours (Statements 14-38)	
ral	14	Take a detailed history, including the presence or absence of the other symptoms on the list above, history of injury, predisposing factors and a family history for CYP presenting with symptoms suggestive of a bone tumour.	99%
	15	Be aware that bone tumours can present with systemic symptoms such as fever, malaise and weight loss. Ask about these associated symptoms when seeing patients with other symptoms suggestive of a bone tumour.	96.8%
	16	Be aware that bone tumours causing spinal cord compression can affect bladder, bowel dysfunction. Ask for the presence of urinary or faecal incontinence (and erectile dysfunction in adolescent males) when taking a history, especially if the presenting complaint is back pain.	94.8%
	17	If there is an associated injury, take a detailed history of the injury including the mechanism of injury and timings of the onset of symptoms after the injury occurred.	95.9%
General	18	Examine the limb or joint in question, the joint above and below, and perform a neurological and musculoskeletal examination (eg. pGALS) in a CYP with signs/symptoms suggestive of a bone tumour.	90.7%
Ü	19	Be aware that weight loss can be a sign of a bone tumour. Measure weight and compare to any previous measurements in CYP with signs or symptoms suggestive of a bone or abdominal tumour. Plot these measurements on age-appropriate growth charts if available to you to monitor change when reviewing symptoms.	88.3%
	20	Be aware that an initial normal x-ray does not exclude a bone tumour. If gymptoms or clinical suspicion persists, a referral to secondary care is warranted. In secondary care, a discussion with a radiologist about the most appropriate repeat imaging is advised.	88.6%
	21	Be aware that pelvic bone tumours may not initially show on an x-ray. If the persistent symptom is pelvic pain and the x-ray has been reported as normal, referral to secondary care is warranted. In secondary care, discuss with a paediatric radiologist for further advice on imaging.	85.6%
	22	Ask about the presence of the other symptoms of a bone tumour (swelling, palpable lump, restricted movement/limp, fever, weight loss, back pain and bowel/bladder/erectile dysfunction) in a CYP presenting with persistent bone pain (occurring on most days for a 2-week period).	99%
	23	Be aware that children aged younger than 4 years, or those with communication difficulties, are frequently unable to describe pain; their behaviour eg, withdrawal, holding their leg, not weight bearing may indicate bone pain. Look for these signs on examination.	98%
3one pain	24	Be aware that an initial normal x-ray does not exclude a bone tumour. If symptoms or clinical suspicion persists, consider discussion with a paediatric radiologist and repeat x-ray or further imaging.	85.69
3one	25	Request x-ray imaging for persistent bone pain (occurring on most days for a 2-week period). In primary care, request of imaging should not delay referral to secondary care.	83.59
ш	26	Request x-ray imaging for localised bone pain that is waking a child or young person at night.	85.59
	27	Request x-ray imaging for unexplained bone pain (ie, without any preceding injury).	81.59
	28	Be aware that x-ray imaging is not always the most suitable imaging modality for persistent bony back pain. Discuss with a paediatric radiologist to decide upon the most suitable imaging of choice.	87.69
Swelling	29	Ask about the presence of the other symptoms of a bone tumour (bone pain, palpable lump, restricted movement/limp, fever, weight loss, back pain and bowel/bladder/erectile dysfunction) in a CYP presenting with persistent swelling (occurring on most days for a 2-week period).	96.9%
	30	Be aware that delayed diagnosis has been associated with attributing a red warm swelling to infection despite no improvement with antibiotics. Arrange to see the CYP at the end of the course of antibiotics to assess response. If there has been no response, consider discussion with secondary care for advice or referral.	87.79
U)	31	Request x-ray imaging for persistent swelling (present for 2 weeks or more) rapidly increasing in size.	75.29
	32	Request x-ray imaging for persistent swelling (present for 2 weeks or more) not resolving despite treatment with regular anti-inflammatories OR antibiotics.	78.39
	33	A bony mass or lump which is increasing in size can be a sign of an underlying bone tumour and requires referral to secondary care.	95.99
dwnl	34	Ask and examine for the other signs and symptoms suggestive of a bone tumour (bone pain, swelling, limp/restricted movement, fever, weight loss, back pain and bladder/bowel/erectile dysfunction) in CYP with a lump/mass.	93.89
ğ	35	Request x-ray imaging for a rapidly increasing bony lump or mass. This should not delay referral from primary care.	86.69
dwil/tu	36	Ask about the presence of the other symptoms of a bone tumour (bone pain, palpable lump, restricted movement/limp, fever, weight loss, back pain and bowel/bladder/erectile dysfunction) in a CYP presenting with restricted movement or limp.	93.99
Restricted movement/limp	37	Have a high level of concern for a CYP who is normally highly active or sporty but is no longer able to play sport due to the presenting symptom.	87.69
	38	Request x-ray imaging for a CYP who is non-weight bearing or has restricted movement despite adequate analogsia.	83.59

Figure 4: Percentage consensus for final bone tumour statements $209x297mm (300 \times 300 DPI)$

		C Abdominal Tumours (Statements 39-63)	
General	39	Take a detailed history including the presence of any of the other symptoms on the list above, any predisposing factors and a family history.	94.89
	40	Examine the abdomen, including external genitalia and hernia orifices, visualise and palpate the spine and perform a neurological examination in a CYP with signs/symptoms that may be due to an abdominal tumour.	93.69
	41	Perform a urine dipstick to exclude infection and identify any protein or blood that would warrant referral to secondary care.	89.79
Ge	42	Consider recording blood pressure if the correct size cuff is available to identify hypertension.	74.29
	43	Be aware that weight loss can be a sign of an abdominal tumour. Measure weight and compare to any previous measurements in CYP with signs or symptoms suggestive of a bone or abdominal tumour. Plot these measurements on age-appropriate growth charts if available to you to monitor change when reviewing symptoms.	88.3%
	44	Ask about the presence of the other symptoms of an abdominal tumour (abdominal pain, haematuria, abdominal distension, weight loss, fever, malaise, jaundice, bone pain, neurological symptoms and bowel/bladder/rectlet dysfunction) in a CYP presenting with an abdominal mass.	99%
al mass	45	Be aware that abdominal masses can cause neurological symptoms due to pressure on the spinal cord. The pressure can cause children to present as "off legs" or refusal to weight bear. Examine the abdomen when a CYP presents with refusal to weight bear.	94.99
Abdominal mass	46	Be aware that diagnostic delay is associated with failure to perform an abdominal examination in a child who is distressed/crying. Offer to examine the child once they have settled or ask a colleague to perform the examination.	94.89
AF	47	Request ultrasound imaging of the abdomen and pelvis for a CYP with a palpable abdominal mass (unless this is felt to be faeces, in which case a review of the CYP after disimpaction is important).	83.69
	48	Request ultrasound imaging of the abdomen and pelvis for a CYP with suspected hepatomegaly or splenomegaly on examination.	83.59
	49	Ask about the presence of the other symptoms of an abdominal tumour (haematuria, abdominal distension, weight loss, fever, malaise, jaundice, bone pain, neurological symptoms and bowel/bladder/erectile dysfunction) in a CVP presenting with persistent abdominal pain.	92.89
pain	50	Examine the abdomen in a CYP with abdominal pain to elicit any masses or hepatomegaly and/or splenomegaly.	99%
ninal	51	Be aware that if the tumour is retroperitoneal, the presenting complaint may be back pain. Examine the abdomen in a CYP presenting with back pain.	95.99
Abdominal pain	52	Be aware that delayed diagnosis has been associated with attributing abdominal pain to constipation despite no improvement with laxatives. Assess response to laxatives by reviewing the CYP at regular intervals and taking a full history and examining their abdomen.	87.79
	53	Request ultrasound imaging for persistent abdominal pain with one or more other symptoms that may be due to an abdominal tumour (abdominal distension, mass, haematuria, weight loss, fever, malaise, jaundice, bone pain, neurological symptoms and bowel/bladder/erectile dysfunction)	86.69
	54	Ask about the presence of the other symptoms of an abdominal tumour (abdominal pain, mass, weight loss, fever, malaise, jaundice, bone pain, neurological symptoms and bowel/bladder/erectile dysfunction) in a CYP presenting with haematuria in the absence of another known cause.	96.99
ria	55	Do a careful abdominal examination to elicit any potential retroperitoneal mass in all CYP with haematuria.	92.79
Haematuria	56	Be aware that delayed diagnosis has been associated with assuming persistent haematuria is due to a UTI despite no response to antibiotics. Arrange to see the CYP again at the end of the course of antibiotics to assess the response. If there is no response, consider discussion with paediatrician for advice.	82.49
Í	57	Request ultrasound imaging for unexplained persistent (occurring for 2 weeks or more) macroscopic haematuria.	87.79
	58	Request ultrasound imaging of the abdomen and pelvis for haematuria plus one or more other symptoms that may be due to an abdominal tumour (abdominal pain, abdominal distension, weight loss, fever, malaise, jaundice, bone pain, neurological symptoms and bowel/bladder/erectile dysfunction).	87.69
Abdominal distension	59	Ask about the presence of the other symptoms of an abdominal tumour (abdominal pain, haematuria, weight loss, fever, malaise, jaundice, bone pain, neurological symptoms and bowel/bladder/erectile dysfunction) in a CYP presenting with an abdominal distension.	97.99
	60	Be aware that abdominal distension caused by a tumour will not fluctuate but will increase in size progressively over time. Arrange another appointment to review the symptoms and re-examine the CYP.	83.59
	61	Be aware that delayed diagnosis has been associated with attributing abdominal distension to constipation despite no improvement with laxative treatment. Assess response to treatment in these CYP by seeing them at regular intervals.	84.59
	62	Be aware that delayed diagnosis has been associated with failure to examine the abdomen at review of a CYP on treatment for constipation. Palpate the abdomen in CYP who are being reviewed for constipation.	94.99
	63	Request ultrasound imaging of the abdomen and pelvis for a CYP with rapidly increasing abdominal distension. This should not delay referral from primary care.	83.59

Figure 5: Percentage consensus for final abdominal tumour statements $209x297mm (300 \times 300 DPI)$