

2017-03-21

Improving the identification of cancer in young people: A scoping review

Gibson, F

<http://hdl.handle.net/10026.1/9383>

10.1080/23809000.2017.1307089

Expert Review of Quality of Life in Cancer Care

Informa UK Limited

All content in PEARL is protected by copyright law. Author manuscripts are made available in accordance with publisher policies. Please cite only the published version using the details provided on the item record or document. In the absence of an open licence (e.g. Creative Commons), permissions for further reuse of content should be sought from the publisher or author.



**Improving identification of cancer in young people: a
scoping review**

Journal:	<i>Expert Review of Quality of Life in Cancer Care</i>
Manuscript ID	ERQ-2016-0059.R1
Manuscript Type:	Reviews
Keywords:	Teenagers, Adolescents, Young Adults, timely cancer diagnosis, pathways to treatment

SCHOLARONE™
Manuscripts

1
2
3 **Improving the identification of cancer in young people: A scoping review.**
4
5
6
7

8 **Abstract 180/200**
9
10

11 **Introduction:** The challenges of achieving timely cancer diagnosis in adolescents and young adults are
12 recognised. However, contributing factors and associated clinical and psychosocial outcomes are
13 poorly understood.
14
15

16 **Areas covered:** We present a scoping review of existing evidence into time intervals to diagnosis and
17 potential mechanisms influencing the identification of cancer symptoms and impact on a timely
18 diagnosis. Charting data using Walters 'pathways to treatment' we summarise the diagnostic
19 pathway into four interval categories: appraisal, help-seeking, diagnostic, and pre-treatment, and
20 illustrate where evidence exists and where unanswered questions remain.
21
22

23 **Expert commentary:** Whilst the research base has expanded over the last decade in cancer care
24 there continues to be limited research that reveals the complexity of the timeliness of diagnosis in
25 this population. There are unique issues facing this age group in terms of rarity of cancer, complexity
26 of symptoms and problems with healthcare system access that create a constellation of challenges.
27 We offer explanations for diagnostic difficulties in this age group, and explain how, with the limited
28 available evidence, we are still seeking solutions to what is a uniquely complex problem.
29
30
31
32
33
34

35 **Key Words:** Teenagers; adolescents; young adults; timeliness of a cancer diagnosis; pathways to
36 treatment; scoping review
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1. Introduction

A diagnosis of cancer is a significant life event for anyone, but perhaps more so for adolescents and young adults (AYA's), as they are at a particularly vulnerable developmental stage [1]. The adjunct of a potentially life threatening diagnosis with the normative developmental tasks of adolescence can have an adverse impact on AYA's physical and emotional wellbeing: this potential impact can be profound. The symptoms of cancer, superimposed on the anxiety of the period leading up to a diagnosis, can evoke psychological distress, uncertainty and fear in young people. Many describe their diagnostic experience with a sense of loss, anger, and frustration [2]. However, with a definitive diagnosis the process of renegotiating a new sense of identity and place in the world can begin. Young people, using social media, have also described trying to make the best of their situation, finding ways to overcome negative emotions and an urgency to return to normal as soon as they could, even if this was to a 'new normal' [3].

Improving both the experience and outcomes of a cancer diagnosis through earlier intervention has become the focus of national policy in the United Kingdom [UK] [4-6], in the United States [US] [7], as well for international AYA clinical partnerships [8]. Specific to the UK context there are two relevant health policy initiatives. First, the 'two-week wait', introduced in 2000, whereby anyone with a suspected cancer would be referred to a specialist within fourteen days [9]. Second, the National Awareness and Early Diagnosis Initiative [10], introduced in 2008, that continues to spearhead an increased focus on the importance of earlier diagnosis and its potential association with reduced morbidity and mortality in some cancers [10]. It is recognized, however, that precisely quantifying the relationship between the time taken to diagnosis and survival is challenging but it is known that, for some cancers at least, a shorter time to diagnosis is associated with a poorer outcome [11]. Despite this, there is a general consensus that optimizing the time from symptom onset to a definitive cancer diagnosis is a worthwhile pursuit [5, 12-17]. Not least this is because strength of the patient voice across the cancer population suggests that 'rapid and adequate referral' is an important measure of quality [18], and subjective experience of high quality care [19]. Delayed and/or multiple referrals are associated with a greater chance of decreased confidence in either the patient's General Practitioner (GP) or another referring clinician [20,21]. Patterns of referral, and the subsequent patient journey, have been studied in the UK with the most common route to diagnosis for older adults aged between

1
2
3 50 and 79 being the two week urgent GP referral for suspected cancer [22]. In contrast the most
4 common route for those aged 15-24 is via non-two week wait GP referrals (26%), followed by
5 emergency presentation at Accident and Emergency [A&E] Departments (24%). In this first report
6 only 13% of AYA were diagnosed via the two-week wait initiative suggesting minimal impact from this
7 earlier referral policy for this population [23]. However, the most recent National Cancer Intelligence
8 Network data would suggest that while the most common routes to diagnosis are still via non-urgent
9 GP referral (28%) and A&E admissions (26%), the proportion being diagnosed by urgent two-week
10 referral has increased considerably to 22% reflecting a change in practice, and perhaps greater
11 awareness of the unique needs, of this age group [24]. The association between A&E cancer
12 diagnosis-related admissions and poorer outcomes has not been confirmed in AYA and insufficient
13 data exists, however the nature of presenting symptoms for some young people's cancers may mean
14 that A&E will be their first point of entry into the healthcare system.
15
16
17
18
19
20
21
22
23
24
25
26

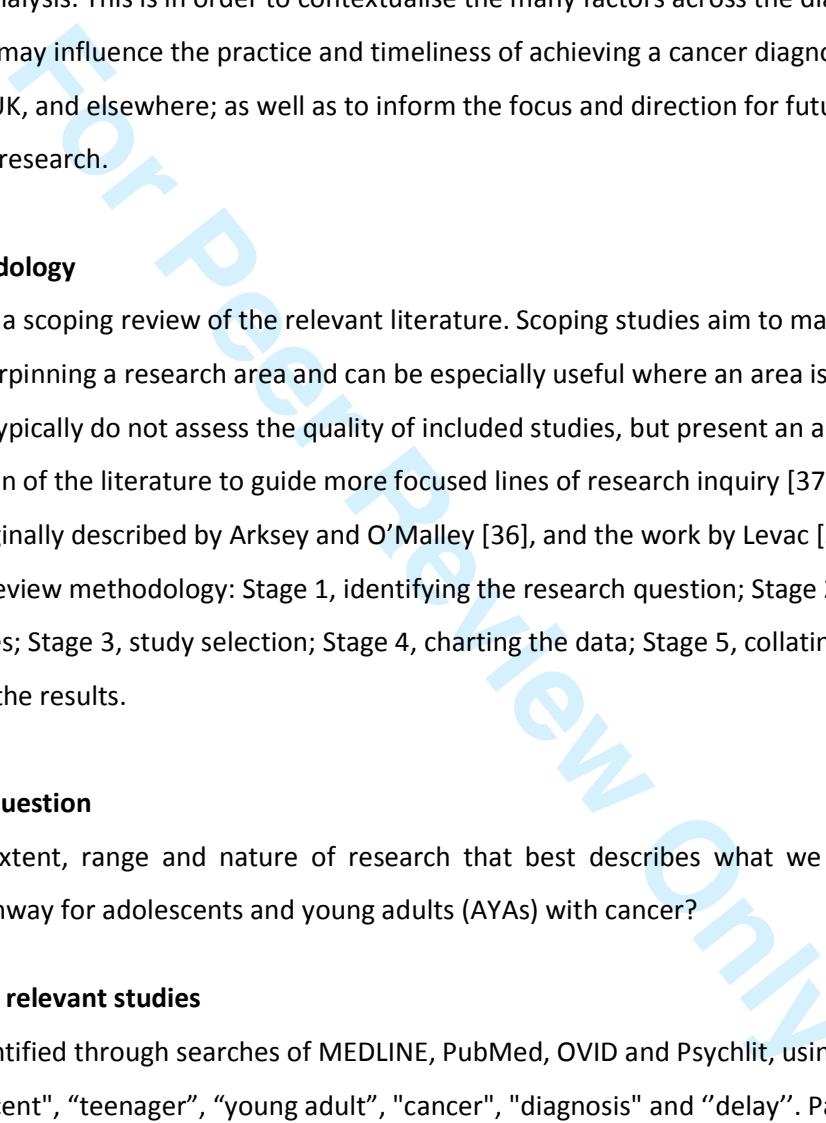
27 The NAEDI campaign in the UK also includes a focus on improving help-seeking behaviours through
28 screening, self-examination and the promotion of better cancer awareness [25-27]. The latest UK
29 campaign 'Be clear on cancer' [28], stresses the link between early diagnosis, higher success of
30 therapies and improved quality of life for patients. However, the relationship between greater
31 awareness, better cancer-related knowledge, improved interpretation of symptoms, and the
32 subsequent positive impact on timely access to health-care, and hence effective and timely therapies,
33 is a complex mix, and these various factors **are** only beginning to be examined in the AYA population
34 [29-30]. Hence there exists a continuing need to drive a national ambition to achieve earlier
35 diagnosis. Indeed, this is one of the six strategic priorities from the UK Cancer Taskforce [31], being
36 implemented through the ACE program: Accelerate, Coordinate, Evaluate [32], exploring innovative
37 concepts in early diagnosis pathways.
38
39
40
41
42
43
44
45
46
47

48 Much of the existing evidence regarding the time to diagnosis has been generated from research
49 with adult cancers; limiting its generalisability to the AYA population. The existing evidence,
50 therefore, provides little in the way of easily identifiable solutions to improve the timeliness of a
51 definitive diagnosis for this population. Part of the explanation for this situation is related to deficits
52 in the quality (as well as quantity) of published research which may be difficult to interpret through
53 lack of precise definitions, variations on health systems or lack of reproducible methodologies [33-
54
55
56
57
58
59
60]

1
2
3 34]. However, increasing evidence, from a number of sources, is now emerging that may have
4 greater specificity to younger people with cancer (Table 1). As a result, this ensures that the
5 timeliness of a cancer diagnosis remains close to the top of the UK cancer policy agenda [35].
6
7
8
9

10 Given this situation we sought to identify elements of the diagnostic pathway that have already been
11 subjected to analysis. This is in order to contextualise the many factors across the diagnostic
12 pathway, that may influence the practice and timeliness of achieving a cancer diagnosis in AYA
13 groups in the UK, and elsewhere; as well as to inform the focus and direction for future
14 interventional research.
15
16
17
18
19
20

21 **2. Methodology**



22 We undertook a scoping review of the relevant literature. Scoping studies aim to map rapidly the key
23 concepts underpinning a research area and can be especially useful where an area is complex [36].
24 Such reviews typically do not assess the quality of included studies, but present an analytical
25 reinterpretation of the literature to guide more focused lines of research inquiry [37]. We used the
26 five stages originally described by Arksey and O'Malley [36], and the work by Levac [37] that aim to
27 enhance this review methodology: Stage 1, identifying the research question; Stage 2, identifying
28 relevant studies; Stage 3, study selection; Stage 4, charting the data; Stage 5, collating, summarizing
29 and reporting the results.
30
31
32
33
34
35
36
37

38 **2.1 Research question**

39 What is the extent, range and nature of research that best describes what we know about the
40 diagnostic pathway for adolescents and young adults (AYAs) with cancer?
41
42
43

44 **2.2 Identifying relevant studies**

45 Data were identified through searches of MEDLINE, PubMed, OVID and Psychlit, using the search
46 terms "adolescent", "teenager", "young adult", "cancer", "diagnosis" and "delay". Papers identified
47 from the search were cross-referenced with cited sources within the retrieved papers so that any
48 otherwise non-identified papers could be included. Relevant policy documents were also accessed by
49 online review and hand searching.
50
51
52
53
54

55 **2.3 Study selection**

Inclusion criteria:

1. Peer-reviewed research exploring the diagnostic process, including delay.
2. Published in English between 1990 and 2016.
3. Reporting on adolescents and young adults, defined as those between 16 to 24 years in the UK.
4. Reporting on child-AYA or adult-AYA in the same paper.

Exclusion criteria:

1. Reporting on adolescents or young adults, <16 years, >24 years.
2. Reporting a single population of 'adults' or 'child' in a paper.

Copies of the full articles were obtained for those studies that appeared to represent a 'best fit' with our research question.

2.4 Charting the data

One of the most influential models for describing pathways to a cancer diagnosis was proposed by Andersen et al in 1995 [38]. This original model describing 'total patient delay' has been summarised in three overall categories by Hansen et al 2008 [39]: patient delay, doctor delay, and system delay. Historically, patients and professionals have referred to 'delay in diagnosis' and 'diagnostic delay' however, there has been a move away from this terminology due to the negative connotations of 'delay' which may impose guilt and regret from a patient perspective if they have delayed seeking help for a symptom which turned out to be cancer related; it might also imply some degree of blame or neglect on the healthcare professional. The revised model by Walter et al 2012 [40] reflects more acceptable parlance and importantly illustrates that the pathways to diagnosis are often not linear as patients may transverse back and forward along the pathway as diagnostic tests are verified or dismissed [41]. Four categories of the diagnostic process are described [40]: appraisal, help-seeking, diagnostic, and pre-treatment intervals. These categories of interval provided an analytical framework to use when charting our data (Figure 1). Walters model also cites a number of contributing factors which influence these intervals: patient factors (demographics, psychological, social, cultural, previous experience); disease factors (size, growth rate); and healthcare provider and system factors (access, healthcare policy and delivery). Considering each of these factors allowed us to deliberate these in the context of young people and demonstrate how some of the contributing factors are unique to this group. This also assisted us in illustrating where evidence existed and

1
2 where unanswered questions remain. The framework was used to chart a narrative summary of
3 information gained from each publication. Charting against this framework helped further in
4 improving our understanding by building on existing knowledge that may be applicable in the real-
5 world context of policy and service development [42] Included therefore are additional publications
6 outside of our search parameters that are thought to be relevant to illuminate the 'whole story' on
7 timeless of achieving an accurate cancer diagnosis in this age group.
8
9
10
11
12
13
14

15 **2.5 Collating, summarizing and reporting results**

16

17 Electronic searches revealed a total of 340 articles, 297 were rejected and 43 full copies were
18 retrieved for eligibility assessment. We included all papers at this stage, irrespective of the research
19 methodology, and included editorials, letters, and research reports, if they dealt with cancer and
20 diagnostic intervals in the AYA population. After rejection of a further 18, three additional papers
21 identified through citations were also deemed eligible for inclusion giving a total of 28 papers for
22 review (Figure 2).
23
24
25

26 The majority of eligible publications included combined data on cancer diagnosis in children and
27 AYAs, and only eight focused specifically on the AYA group as a single population. Table 1 summarizes
28 the main characteristics of the final 28 publications: 19 retrospective and prospective studies on
29 diagnostic intervals, five papers on adolescents' knowledge, awareness and attitudes towards cancer,
30 three systematic reviews and one editorial (n=28).
31
32
33
34
35
36
37

38 **3. Results**

39

40 Here we present a narrative summary of the results discussed within discrete headings as per the
41 four intervals in the pathways to treatment (Figure 1).
42
43
44

45 **3.1 Appraisal interval**

46

47 This is defined as the time from awareness of a bodily change to perceiving the need to discuss
48 symptoms with a healthcare professional, such as a GP, or to make contact with the acute health care
49 system. Appraisal interval has been described in a number of helpful studies spanning child and early
50 adolescent cancers [43-44] This body of research, mostly utilizing retrospective analysis of medical
51 notes and cohort designs, suggests that age appears to be a significant factor [45-46] Those in their
52
53
54
55
56
57
58
59
60

1
2
3 teenage years are more likely to experience a longer interval from initial symptoms to reporting
4 symptoms to healthcare professionals than younger children [46, 47-52]. There is little research as
5 yet to underpin explanations of this longer interval in AYA, however in the context of Walters
6 contributing mediators there **are** some identifiable and unique factors.
7
8
9

10
11 **Disease factors: symptom pattern**
12

13 One possible explanation for the effect of age on a timely cancer diagnosis is symptom pattern.
14 Younger children may experience cancers with more identifiable signs at onset (such as an abdominal
15 mass in Wilms' tumour) than older children or AYAs. However, studies have reported a positive
16 association between age and diagnostic interval still being present even after the type of cancer was
17 controlled for [46, 53-54]. This would suggest that the effect of age on interval may, in part, be due to
18 more than simply differences in tumour-specific characteristics [45]. Appreciating the importance of
19 symptoms that lead to help-seeking behaviours, may lead to a better understanding of the time
20 between symptom onset and diagnostic trajectory. The following risk factors have been identified in
21 the literature to date: symptom recognition, psychological factors, socio-demographic influences and
22 ethnicity [40].
23
24

25
26 **Patient factors: cancer awareness**
27

28 The initial presentation of possible cancer symptoms, due to rarity and lack of specificity in this age
29 group, has been associated with prolonged time intervals [47, 50, 55-56]. Public awareness of early
30 warning signs of cancer has been identified as playing an important role in symptom recognition
31 (although it has also been identified as a prompt for seeking medical help by the 'worried well') [55,
32 57]. Two studies in the UK have shown that cancer awareness in adolescents is low [58-59]. In both
33 studies adolescents did not know the most common cancer in the AYA age group, and there was also
34 the belief that cancer was unrelated to age [28]. In a cross sectional study in the UK [29], teenagers
35 recall of cancer **signs** was good for lump/swelling, but their recall of other cancer warning **signs or**
36 **symptoms** was very poor (13.8% for both 'unexplained pain' and a 'change in the appearance of a
37 mole', 6.5% for 'weight loss' and 1.3% for 'a sore that does not heal') and one in four young people
38 could not name a sign or symptom of cancer. Moreover, studies from the UK, United States, Turkey
39 and The Netherlands have shown that self-examination for signs of cancers found in AYAs is also poor
40 [59-62]. For example, the number of young males knowing how to, or who have performed, testicular
41 self-examination was low [59-61] as was female adolescents' knowledge of breast self-examination
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2 [62].
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Health knowledge has been found to be a contributing factor in diagnostic processes and a lack of knowledge has been linked to AYA's intentions to delay health care seeking, even when signs and symptoms are present. It has been shown that adolescents who have never heard of testicular self-examination were more likely to report the intention of putting off health care seeking with symptoms of testicular cancer [63]. Conversely, three quarters of adolescents taking part in a Survey (Cancer Awareness Measure [CAM]) stated that they would seek help for a symptom they thought might be cancer within three days [29]. Hence, empowering AYAs for greater self-care and early detection of cancer are important and seem to be worthwhile pursuits [64]. It has been suggested that health education within schools should also reflect cancer topics including the importance of early recognition of possible signs and symptoms [58]. School environments provide fertile ground for public health campaigns, particularly when the materials used are age specific to aid relevance and retention [30].

Patient factors: demographics and psychosocial

Longer intervals from initial symptoms to the reporting of symptoms to healthcare professionals, when compared with younger children [44, 46, 47, 51], may be explained by a range of demographic and psychosocial factors. Young people's strong sense of independence and sense of invincibility may lead to a decrease in parental influence over this age group as well as to an undervaluation of symptoms; hence AYAs may be more likely to delay attracting attention to themselves [64]. In-depth interviews about young people's pre-diagnostic experiences has shown that they may normalize or wrongly attribute their symptoms to something other than cancer, and other people (such as parents, teachers, neighbours or co-workers) may play a significant role in prompting them to have troublesome symptoms investigated [65]. Gender-associated behavior expectations may also influence a longer appraisal interval, however findings have not been consistent, with one study reporting that males diagnosed with a medulloblastoma experienced a longer duration of symptoms than females [66]. Moreover, a powerful social desire to appear 'normal' and 'independent' often associated with adolescence may also contribute to a reluctance to trust adults – including the medical establishment [49]. Nevertheless, contrary to perceptions that AYAs may generally have less contact with health care services, Fern et al.'s study [67] found that this age group do indeed consult

1
2
3 with GPs with symptoms. Thus young people do consult their GP, however this is generally for
4 routine non-cancer reasons such as contraception and pregnancy and infection [67].
5
6
7
8

9 Overall, research evidence into the appraisal interval shows that from first symptom to consultation
10 with the healthcare system is not a straightforward process. Age may indeed have been associated
11 with an increased time interval, but age alone is insufficient to 'truly' understand prolonged symptom
12 appraisal. Attitudes, beliefs and social context clearly also influence the process of making a decision
13 to seek help. Increasing cancer awareness may deserve to be an important national health policy
14 imperative: as simply being able to talk about cancer is one determinant of medical help-seeking [68].
15
16
17
18
19
20
21

3.2 Help-seeking interval

Patient factors: psychological

22 This refers to the interval from perceiving a reason to share symptoms with a healthcare professional
23 to the first consultation. Within the adult literature recent findings have shown cross country
24 comparisons with adults putting off going to the doctor as they do not want to 'waste the doctors
25 time'. For young people emotional barriers to help-seeking were actually the most commonly
26 endorsed behaviours by more than half of participants in one study of cancer awareness ('worry
27 about what the doctor might find', 'too embarrassed', 'too scared', and 'not feeling confident to talk
28 about symptoms'), followed by service (e.g., 'difficulty talking to the doctor') and practical barriers
29 (e.g., being 'too busy') [30]. Similar findings have been described with an Italian population of
30 adolescents. They also described not wanting to alarm their parents, and avoided the need to have
31 their body examined or touched by adopting a 'wait and see approach' [69]. A similar approach was
32 also reported by Dixon-Woods et al [70]. In this study, parents did not want to appear 'anxious',
33 'overprotective' or 'neurotic' by consulting a GP too often or too early. Thus most parents adopted a
34 'wait and see' approach for mild symptoms e.g. viral symptoms, sore throat, or tiredness. General
35 Practitioners also discussed fear as the single most important factor, both consulting and delaying,
36 with a good professional/patient relationship being a prerequisite for patients' concerns being taken
37 seriously. Patients' accounts of their experiences prior to their diagnosis also show the importance of
38 this relationship. When young people were well known to the GP, action seemed to be taken more
39 quickly; conversely the lack of relationship had a negative influence on AYA's chances of been taken
40 seriously [65]. Hence, the lack of routine care prior to any cancer symptoms, as well as any co-
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

existing communication barriers, may have an impact on the relationship between patients and professionals and consequently on a timely diagnosis [49]. The differences described in barriers to help-seeking behaviour provides further evidence as to why studies carried out with adult populations cannot always be extrapolated across AYA's and why they should be studied as a unique group.

Patient factors: age and social

Exchanging opinions with peers, and seeking information online may also represent early steps in seeking help that avoids the need to consult with healthcare professionals directly [69]. Adolescents in the 21st century rely on technology much more than their adult counterparts for communication, accessing information, and generally, living life (e.g., using social Web sites, texting, and messaging) [71]. Thus these avenues may offer other routes for health information that avoid the need to ask questions of professionals, or communicate their fears by providing privacy, ease of access and even a sense of community [72-73]. The unreliability of some Internet content however is a concern for many AYAs [74]. At the current time, there is a substantial knowledge gap in the Internet on the matter of cancer in our population [69].

Healthcare provider and system factors: access

Access to medical care in some countries can also influence duration of the help seeking interval (e.g., in the US some young people are not covered by parents' health insurance) [49, 75]. For others social services barriers, such as being on income support, or unemployed, and having personal/family stability have also been described in terms of inequalities that impact on the diagnostic pathway [76]. In some countries the primary physician for children and AYA is a pediatrician, not a GP, where familiarity with cancers that occur in this age group may reduce the time to diagnosis: both health care systems and geographical differences are factors also known to affect the symptom interval and patient delay [77].

Overall, research into the help-seeking interval is limited. There is however much we can learn from adolescents as a population. We know that their health issues may be less closely monitored by their parents when compared to younger children, and we know they may be reluctant to talk openly about, and hence disclose, worrying symptoms that they may be experiencing. Lack of awareness

about health risks and their changing bodies, poor knowledge and limited experience of the healthcare system or how to access it, compounded by social and societal influences combine to impact negatively on help-seeking behaviours. Possible solutions, such as improving cancer awareness, are relatively inexpensive, as well as making more communication opportunities available so that AYA's can find accurate information about worrying symptoms.

3.3 Diagnostic interval

This refers to the interval between first consultation with a healthcare provider and a cancer diagnosis being made. This may involve referrals for diagnostic tests or to specialist services.

Healthcare provider and system factors: access, healthcare policy and delivery

The type of healthcare professional contacted initially has been reported as having a direct impact on the length of this interval [44, 45, 46, 47, 77-80]. For example, longer intervals have been reported for those presenting to their GP compared to Accident & Emergency (A&E) departments. In Dang-Tan et al's study [48] into children and adolescents with leukaemia and lymphomas in Canada, longer diagnostic intervals were found after referral to secondary care; patients first seen in a hospital emergency room also had a lower risk of delay than patients first seen by a GP. Presentation to A&E more commonly led to immediate X-rays than a GP consultation. It has been claimed that these increased intervals are not necessarily a reflection on GP's actions (or inaction) but may exemplify the weaknesses within the process of referral from professional to professional [81]. Parents may try to speed up this process with the use of private medical services, accessing alternative medicine or by resorting to A&E departments for immediate advice after failed referrals from primary care [68].

The prompt referral for a suspected cancer symptom from primary care is known to be challenging for this age group [80]. Reasons are not entirely clear, but may include atypical presentations, suboptimal clinical reasoning or other healthcare factors [82]. Young people have reported repeated interactions with a range of health care professionals when seeking a diagnosis, including optometrists, dentists, pediatricians' and other specialists [83]. A retrospective Italian study between September 2007 and March 2011, reported that the lag time between seeing a physician and being

referred to a specialist was longer for teenagers compared to children [84]. Young people have repeatedly reported multiple consultations prior to referral to a cancer specialist during an annual patient conference and this has recently gained further substantiation following analysis of the NHS Cancer Experience Survey [81,85]. Importantly young people aged 16-24 are twice as likely to have three or more consultations prior to referral compared to older adults. Approximately 40% of young people will consult three times or more prior to referral compared to 20% of older adults, thus 80% of older adults are referred on their first or second visit. Diagnosis via the A&E route has become associated with AYA experiencing repeated cycles of appraisal and help-seeking [86]. Referral guidelines for children and young people have been developed recently as a result, and are now in their second round of revisions (87-89). Evidence suggests from young people themselves however that there remain challenges when applying the guidance to AYA, or where there is a NICE qualifying symptom this may not always result in referral, and sometimes referrals were made but investigations did not occur [90]. Thus, the importance of the AYA cancer diagnostic interval continues to be recognised as inherently complex and an area worthy of further exploration [45, 46, 85,90].

Disease factors: symptoms and types of cancer

Quantitative studies using survey methods have shown that longer diagnostic intervals (rather than appraisal or help-seeking intervals) have been reported by AYAs [69]. This is also true in relation to cancers more often occurring in this age group, such as bone and soft tissue sarcoma and lymphomas [48]. Dang-Tan et al study [49] found that timeliness to diagnosis of bone cancers was influenced by longer diagnostic interval but shorter appraisal interval. Short appraisal interval and longer diagnostic interval and misdiagnoses have also been identified in a review of medical charts in South Africa [91].

Many physical signs and symptoms of young people's cancers such as fever, headache, fatigue, bone pain and weight loss may be attributed to more common problems such as, sporting injuries, stress and general fatigue [58, 79]. Pollock et al [46]. In a retrospective, multi-centred, study of children with a lymphoma or solid tumour, found longer lag time or symptom interval (time between presentation and diagnosis) in Hodgkin's disease and bone sarcomas (particularly Ewing's sarcoma) than in those with brain tumours or non-Hodgkin's lymphomas - the shortest lag time was for those children with neuroblastoma. Even after adjustment for age in a multivariate analysis of covariance, tumour type continued to have a statistically significant association with interval [46]. Factors may

1
2
3 include the slow-growing nature of Hodgkin's lymphoma and Ewing's sarcoma; their peak incidence
4 being in the second decade, together with an often longer diagnostic process compared to some
5 other cancers [12]. In Dang-Tan et al.'s study [48], cancer subtype was associated with diagnostic
6 interval - but not with patient appraisal - for lymphoma patients. Patients with non-Hodgkin's
7 lymphoma had longer delays as those with Hodgkin's disease. In this particular case, the differences
8 between disease symptoms and signs for these two different forms of lymphoma may have
9 contributed to this difference. Goyal et al [44]. study found that the site of the tumour (axial vs. limb)
10 affected diagnostic interval in that the same symptoms in the absence of an obvious 'visible mass' did
11 not seem to alert the suspicion of the healthcare professional in the same way that limb-associated
12 symptoms did. This is similar to other studies where more unusual symptoms (such as gait
13 abnormalities, ataxia or abdominal masses) also had a shorter time interval [51].
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Healthcare provider and system factors: healthcare policy and delivery

Although there has been less research about the in-depth experiences of healthcare professionals and why they may not suspect a cancer, it has been shown that several factors may impact on this situation. These include: perceptions of symptoms and the implications of the socio-economic status and age of the patient; past experiences with diagnosing cancer (it may be rare for GP to see AYA with cancer - a GP in the UK, for example, may be expected to see, on average, only one child under 15 with cancer every 15 years [81] or only 7 to 8 new cases of cancer, in all age groups, per year); and structural issues such as lack of time, lack of team working, lack of consistency in seeing patients, poor follow-up mechanisms and missed communications between different settings. These may all be considered important and relevant to the reasons for diagnostic delay in AYAs [89].

Moreover, although there is no evidence at present that lack of knowledge or awareness about AYA cancer is related to increased healthcare professional time intervals, it has been suggested that training in AYA cancer diagnosis could be beneficial in improving the recognition of classic cancer symptoms [83]. However, many will present with what are described as symptoms that have low or very low positive predictive values; and are often non-specific and vague in nature. Thus the 'alarm' symptoms - such as pain or physical changes – [92] that may generate a risk assessment in adult cancer care [93], are not always present or reliable in this population [94]. Presenting with non-alert symptoms, as categorized in the NICE guidance [88], is known to increase the diagnostic interval [95].

As part of a national audit of cancer diagnosis in primary care in the UK, 40% of young people who were identified attended the GP three times or more before being referred [96]. A significant event audit carried out under the aegis of NAEDI illustrated that GPs themselves spoke about the difficulties in engaging, and obtaining a diagnosis with this age group, and mentioned the perceived reluctance of some young people to seek advice. The importance of professional vigilance, effective communication and the appropriate management of unresolved symptoms have also been highlighted within the existing literature and remain relevant [96].

Young people themselves in in-depth interviews have also suggested that a wide variety of intervals to diagnosis are a recurring element of some young people's cancer trajectory [65]. For instance, some have reported not being taken seriously, not having their concerns addressed and often feeling that healthcare professionals might not attribute their ongoing symptomatology to cancer [65]. These findings suggest that young people were often not investigated for cancer until after they had visited their doctor several times, or until they, or their parents, also started to think something more serious was wrong. Young adults have expressed the opinion that GPs should consider serious illness earlier, even if it seems unlikely [65].

The period prior to diagnosis is important in shaping the nature of adaptation and the subsequent reaction to the diagnosis itself [70]. Qualitative studies in childhood cancer focusing on parents' recall of the diagnosis of cancer in their child [70, 97, 98], suggest that difficulties in reaching a diagnosis has the potential to cause friction in the GP/parent relationship [99]. This is particularly so when parents did not think their concerns had been listened to [97]. Similar findings have been reported with the AYA age group [65]. Perceptions about diagnostic intervals are clearly significant, with a considerable overlap in the time reported by parents who felt that the diagnosis was not timely, as compared to those who did [97]. Patient confidence is known to be a core element of the doctor-patient relationship: and further research is needed to understand the impact the period prior to diagnosis has on this relationship in the long-term [99].

Overall, we would agree with Black et al (86 p13) that the pathway to receiving a cancer diagnosis in AYA's may be both 'prolonged and circuitous'. Where a GP route has not resulted in resolution, AYA may engage with other routes, such as A&E, where tests might be more rapidly forthcoming. NICE guidance [88], as it currently stands, might not assist with the nuances and differences in AYA's as

1
2
3 they do not take full account of the many contributing factors (identified by Walters) that present as
4 challenges to GPs and others.
5
6
7
8

3.4 Pre-treatment interval

9
10 This refers to the interval between a definite diagnosis being made and the initiation of cancer
11 control treatment. This is the part of the cancer trajectory where there has been the least research. It
12 has been recognized, and this paper has already demonstrated, that prompt diagnosis and referral
13 for treatment in AYA can be challenging from a clinical perspective, due to the wide range of
14 malignancies and the multiplicity of symptomatologies that may arise. Cancers in AYA can be
15 classified into three main categories: those that typically arise as 'late paediatric' cancers such as
16 Wilms' tumour; those that are described as 'early onset adult cancers' such as melanoma; and those
17 which have a peak incidence in this age group alone such as osteosarcoma [100]. The most common
18 cancers in adults comprise only a small proportion of cancer diagnosed in AYA; nevertheless, cancer
19 type has been associated with pre-treatment interval and lymphomas, bone tumours and soft tissue
20 sarcomas. which have a higher incidence in this age group, typically require molecular and other
21 diagnostic tests before administering first treatment [47]. Papers have identified delays in the
22 detailing of histological sub types [49, 91]; delays in both the referral to and correct reporting and
23 communication from imaging [79, 104]; and delay in referrals to the correct specialist [65, 81, 101].
24
25
26
27
28
29
30
31
32
33
34
35
36
37

38 Poor communication between services, poor reporting of results and the waiting for appointments
39 was found to be particularly stressful for young people, especially after a diagnosis of cancer had
40 been made [65]. In Klein-Gletink et al's study [101] (where outcomes were compared between
41 adolescents treated in adult-orientated and child cancer centres) the interval for referral of AYA to
42 adult-orientated centres was found to be twice as long as those for childhood cancer centres.
43
44
45

46 Whilst this may be the least researched phase of all across the cancer trajectory it remains important
47 as negative psychosocial reactions may be expected following cancer delay, or where disease is much
48 more advanced meaning that treatment is less likely to be curative [65]. It is also a phase where
49 positive relations can be established that can support the young person going forward into cancer
50 treatment.
51
52
53
54
55
56
57
58
59
60

1
2 These structural, organisational, resource and pathway related issues have generally been less
3 researched across all age groups but certainly warrant wider scale attention and programmes of work
4 in the future.
5
6
7
8
9

10 **4. Limitations of this review**

11 As this was a scoping review some papers may have been missed during the literature searching
12 process. If a full systematic review had been undertaken more databases would have been searched
13 and could have identified additional relevant studies. However, we suggest that the review captures
14 the state of the art in this field of research, with the remaining areas for future research clearly
15 identifiable.
16
17

18 We were also well aware of the methodological limitations of some of the research in this field that
19 have been well-documented [33,34]. Others have criticized research designs where information
20 collected through pre-existing records and/or patient/parent recall may not always be reliable [34].
21 Identifying possible sources of diagnostic delay from the perspective of patients and healthcare
22 providers is uniquely challenging due to symptom/disease complexities as well as the many steps
23 involved in the diagnostic trajectory superimposed on complex health systems. An earlier review
24 [102] emphasized the danger of attributing simplistic solutions to inherently complex phenomena.
25 The studies included here share and reflect these limitations. Furthermore, difficulties are
26 acknowledged in terms of the lack of research where the AYA age group have been studied as a
27 discreet group. Most papers do not focus specifically on this specific age group meaning that some
28 evidence has been drawn from studies of childhood cancer that included AYA in their populations in
29 recognition of their contribution to the conclusions.
30
31
32
33
34
35
36
37
38
39
40
41
42
43

44 **5. Expert commentary**

45 Whilst the research base has expanded over the last decade in AYA cancer care there continues to be
46 limited research that reveals the complexity of the timeliness of diagnosis in this population. There
47 are unique issues facing this age group in terms of rarity of cancer, complexity of symptoms and
48 problems with **accessing the healthcare system that creates** a constellation of challenges (Figure 3).
49 Given this complexity our use of a methodological framework to structure charting and analysis of
50 the literature has enabled a fuller description of the importance of the various interval factors to be
51 understood and examined further. In terms of the particular needs of the AYA age group, this review
52 has highlighted the importance of understanding the significance and range of factors such as
53
54
55
56
57
58
59
60

attitudes to health care, the nature of cancer symptoms, information needs and the social reality of young people's lives, that combine to impact negatively on timely help-seeking behaviour and eventual diagnosis.

Given the relatively rare incidence of cancer in the AYA population, superimposed on the complexity of primary and secondary health care systems, it is perhaps not surprising that a prolonged diagnostic pathway may occur in this age group. The existing evidence points to a combination of ways to firstly theorise and understand, and then improve, the diagnostic experience for younger people facing cancer. Here the evidence has been used to clarify what changes may be possible to modify in a positive way (such as greater AYA, parent, public and professional awareness; communication between services; and timely access to care) and to highlight others that remain problematic (such as vagueness of symptoms or health system failure). The threat of a cancer diagnosis or serious illness does not sit easily in the everyday world of AYAs. As a result, further research is needed to better understand how to improve outcomes by tackling the first two stages of symptom appraisal and help-seeking by concentrating on assessing the need to seek professional help and motivation to attend the first appointment.

The interval between the first consultation with a healthcare provider and a cancer diagnosis has often been seen as significant in the time to diagnosis. It may involve repeated visits before anything serious is suspected, and time being taken up for referral to diagnostic tests or to specialist services. Having key healthcare professionals respond, and allowing AYAs to have a voice and be heard, are key components to this stage of the AYA cancer trajectory. However, we currently have little empirical information about the impact of multiple consultations on young people. It must also be remembered that for many GPs it may be that clinical reasoning was appropriate as in many cases benign conditions were eliminated. Indeed, the healthcare professional, structural, disease and symptom related factors that contribute to this time interval exemplify why the time to diagnosis may be complex and prolonged and further support the need for evidence-based solutions. Although there is less research in this area, and the prognostic implications of lengthened diagnostic time intervals are not always clear, the link between time intervals and an increase in psychological stress in AYA's is apparent.

1
2
3 For instance, it is known that prolonged periods to diagnosis have been found to have a significant
4 clinical impact in terms of raising levels of anxiety, uncertainty and coping in children [51, 98]. Gibson
5 et al's [65] study pointed to the importance of young people feeling that they had a voice, and that
6 their symptoms and worries and concerns were heard, and when they were not, a significant lack of
7 trust and anger could develop. Tishelman and Sachs [103] found that after a process of constant
8 negotiation between popular and professional judgements, an eventual diagnostic outcome provided
9 the opportunity for a new framework of 'normality'. Similar findings emerged from an interview
10 study with AYA and nurses on the distressing and positive experiences of cancer. Over half responded
11 that a definitive diagnosis was better than pre-diagnostic uncertainty, with hope becoming more
12 realistic once the prognosis and treatments were explained [104].
13
14

15 Timeliness of a cancer diagnosis and the emotion it brings can thus have significant repercussions for
16 coping during the diagnostic period, treatment and adaptation to life after treatment. As mentioned
17 earlier there is very little research as yet for AYA in the pre-treatment phase, but after a diagnosis of
18 cancer, this is something which should addressed in future research. In the UK, healthcare providers
19 are assessed on the ability to provide cancer treatment within a certain time. The current target
20 waits between the date the hospital receives an urgent GP referral for suspected cancer and starting
21 treatment; starting treatment no more than 31 days after the meeting at which AYA and a medical
22 healthcare professional agree the treatment plan. If patients are delayed in the pre-treatment phase
23 it maybe to clarify precise details of tumour biology and pathology, making complex treatment plans
24 or identifying clear treatment pathways. <http://www.cancerresearchuk.org/about-cancer/cancers-in-general/cancer-questions/waiting-times-for-tests-and-treatment-after-cancer-diagnosis#treat>)
25
26 Generally hospitals are meeting this target for most of their patients. Although as Klein-Gletink [101]
27 state there are differences in this phase for AYA going to a children's cancer centre as opposed an
28 adult cancer centre. The reasons for this are unclear but may include lack of established care
29 pathways, less specialist nature of care in general adult compared to children's cancer together with
30 the possibility of different diagnostic groups and diagnostic pathways in adult and children's cancer
31 centres.
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

6. Five-year view

Understanding the reasons that impact on a timely and accurate cancer diagnosis is important for all

age groups and, in this population, would benefit from further research focused on the perspectives of young people themselves, the healthcare professionals who care for them, and research into structural and organisational barriers for timely access, referral and diagnosis. Such evidence ultimately needs to be strengthened by considering the range of data needed, such as diagnostic timelines; symptom profiles and disease outcomes; professional perceptions and roles; and service, referral and communication barriers - within the context of current service or policy developments: in the UK and elsewhere. Complex and multi-factorial phenomena, such as the diagnostic process, are likely to require complex, multi-method, multi-perspective research approaches. With the subsequent development of appropriative interventions (Table 3) and changes in practice and policy, it may be possible that under-researched patient groups such as AYAs may achieve more timely diagnoses of cancer.

In the meantime, we have to consider the pressures on health systems to process more demand, both in general practice and in hospital contexts, and AYA cancer care is only one of the multiple demands facing providers. Given this situation it is also important to contextualise what research will be needed to understand health systems as inherently complex and inter-connected, and where promoted values such as psychological adaptation to cancer, holism and patient safety must co-exist alongside concerns with service efficiency and cost-control.

We suggest that the existing research is already highlighting the existence of a problem with AYA cancer diagnosis that needs to be addressed in a number of ways. Firstly, policy is needed, based on evidence, that will help enhance access to age appropriate information and support. Secondly, research should build on existing gaps and address the most pertinent questions that should be asked to improve the diagnostic experience. Reviews such as this can help in this regard and more research is now being supported; such as the Lymphoma Research Foundation in the United States which has an AYA funding initiative.

Finally, the views of young people themselves should remain at the heart of accounts of where systems can be seen to encourage, or deter, them from seeking help. The third sector has a key role to play here and much opportunity exists for charities and lobby groups to influence awareness of the signs, symptoms and diagnostic trajectory for cancer across all age groups: for example, in the UK an online educational resource has recently been developed through the collaboration of two UK

charities <http://elearning.rcgp.org.uk/course/info.php?id=232> [105]. For the AYA population this review has highlighted the growing evidence that can be used to understand their needs in being diagnosed as quickly as possible in order to effect the best possible outcome.

Key issues

- Non-specific presenting symptoms, low awareness, system failures and rarity of cancer in this population impacts on the timeliness of achieving a cancer diagnosis.
- Effective communication, with an emphasis on diagnostic uncertainty in discussions between healthcare professionals and AYA, is essential so that AYA fully understand the decisions that are made.
- Adolescents and young adults must be encouraged to return to their GP if symptoms escalate: re-appraisal of symptoms and help-seeking is not linear.
- The prognostic implications of a possible time-lag remains unclear.
- Lack of AYA awareness about themselves and **their bodies**, their community and health care systems impacts on elements of the diagnostic pathway.
- **The support needs of parents and those closest to these young people is important as they also face the challenge of a cancer diagnosis.**
- Untimely diagnosis affects the overall patient experience negatively, and may not place the AYA in the best position in terms of future relationships with primary or specialist cancer services.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Funding

Lorna Fern is Funded by Teenage Cancer Trust.

For Peer Review Only

References

1. Docherty S, Kayle M, Maslow GR, Santacroce SJ. The adolescent and young adult with cancer: a
2 developmental life course perspective. *Seminars in Oncology Nursing* 2015;31:186-196
3. Gibson F, Hibbins S, Grew T, Morgan S, Pearce S, Stark D, Fern L. How young people describe
4 the impact of living with and beyond a cancer diagnosis: feasibility of using social media as a
5 research tool. *Psycho-Oncology* 2016;22:2585-2592
6. Department of Health. The Cancer Reform Strategy. London: Department of Health, 2007
7. Richards MA. The National Awareness and Early Diagnosis Initiative in England: assembling the
8 evidence. *British Journal of Cancer* 2009;(101):S1-S4
9. Department of Health. Improving outcomes: a strategy for cancer. London: Department of Health,
10 2011.
11. Cancer Diagnosis Program, National Cancer Institute. (<http://cancerdiagnosis.nci.nih.gov>).
12 Accessed 23/12/2016
13. Stark D, Bielack S, Brugieres L, et al. Teenagers and young adults with cancer in Europe: From
14 national programmes to a European integrated coordinated project. *European Journal of Cancer
15 Care* 2015;25:419-27
16. Department of Health. The NHS Cancer Plan. London: Department of Health, 2000
17. National Awareness and Early Diagnosis Initiative NAEDI Newsletter. 3:1.
18. http://info.cancerresearchuk.org/prod_consump/groups/cr_common/@nre/@hea/documents/gene
19. ralcontent/cr_053651.pdf.
20. Torring ML, Frydenberg M, Hamilton W, et al. Diagnostic interval and mortality in colorectal
21 cancer: u-shaped association demonstrated for three different datasets. *Journal of Clinical
22 Epidemiology*. 2013;65:669-678
23. Dang-Tan T, Trottier H, Merry LS, Morrison HI, Barr RD, Greenberg ML, Franco EL. Delays in
24 diagnosis and treatment among children and adolescents with cancer in Canada. *Pediatric Blood
25 and Cancer*. 2008;51:468-474
26. Fern LA, Birch R, Whelan J, Cooke M, Sutton S, Neal RD, Gerrard C, Hubbard G, Smith S,
27 Lethaby C, Dommett R, Gibson F. Why can't we improve the timeliness of cancer diagnosis in
28 children, teenagers, and young adults? *BMJ*. 2013; 347:f6493
29. Gatta C, Zigon G, Aareleid T, Ardanaz E, Bielska-Lasota M, Galceran J, Gó'zd'z S, Hakulinen T,
30 Martinez-Garcia C, Plesko I, Žakelj MP, Rachtan J, Tagliabue G, Vercelli M, Faivre J. Patterns of
31 care for European colorectal cancer patients diagnosed in 1996-98: a EUROCARE high-
32 resolution study'. *Acta Oncologica*. 2010; 4:776-83

- 1
2
3 15. Neal R. Do diagnostic delays in cancer matter? British Journal of Cancer. 2009;101:S9-S12
4
5 16. Thomson C S, Forman D. Cancer survival in England and the influence of early diagnosis: what
6 can we learn from recent EUROCARE results? British Journal of Cancer. 2009;101:S102–9.
7
8 17. Evans N T, Wakefield C E , McLoone J K, Cohn R J. Familial diagnostic experiences in paediatric
9 oncology. British Journal of Cancer. 2015;112:20–23
10
11 18. Booji JC, Zegers M, Evers PMPJ et al. Improving cancer patient care: development of a generic
12 cancer consumer quality index questionnaire for cancer patients. BMC Cancer. 2013; 203
13
14 19. Fern, L.A, Ashton, J., Broonan, K., Irving, C., Millington, H., Starkey, C., Wright, D., and Whelan,
15 J., Involving young people with cancer in research. The National Cancer Research Institute's
16 Teenage and Young Adult (TYA) Core Consumer Group (CCG) – a new and evolving model. In
17 National Cancer Research Institute International Conference, 2009, Birmingham.
18
19 20. Mendonca SC, Abel AG, Saunders CL et al Pre-referral general practitioner consultations and
21 subsequent experience of cancer care: evidence from the English Cancer Patient Experience
22 Survey. European Journal of Cancer Care 2015; 66:e171-81
23
24 21. Korsvold L, Lie HC, Mellblom AV et al Tailoring the delivery of cancer diagnosis to adolescent and
25 young adult patients displaying strong emotions: an observational study of two case. International
26 Journal of Qualitative Studies on Health and Well-Being. 2016;11:30763
27
28 22. Ellis-Brookes L, McPhail S, Ives A et al Routes to diagnosis for cancer-determining the patient
29 journey using multiple routine data sets. British Journal of Cancer. 2012;107:1220-1226
30
31 23. National Cancer Intelligence Network Routes to diagnosis: investigating the different pathways for
32 cancer referrals in England for Teenagers and Young Adults. NHS North West Cancer Intelligence
33 Service: 2013
34
35 24. http://www.ncin.org.uk/publications/routes_to_diagnosis Accessed 24/12/2016
36
37 25. Allgar V, Neil R. Delays in diagnosis of 6 cancers: analysis of data from the National Survey of
38 NHS Patients: Cancer. British Journal of Cancer. 2005;92:1959-1970
39
40 26. Waller J, Robb K, Stubbings S, Ramirez A, Macleod U, Austoker J, Hiom S, Wardle J. Awareness
41 of cancer symptoms and anticipated help-seeking among ethnic minority groups in England.
42 British Journal of Cancer. 2009;101:S24-30
43
44 27. Austoker J, Bankhead C, Forbes L, Atkin L, Martin F, Robb K, Wardle J, Ramirez A. Interventions
45 to promote cancer awareness and early presentation: a systematic review. British Journal of
46 Cancer. 2009;101(Suppl 2):S31-S39
47
48 28. <http://www.cancerresearchuk.org/health-professional/early-diagnosis-activities/be-clear-on-cancer>
49 Accessed 23/12/20016
50
51 29. Kyle R, Forbat L and Hubbard, G. Cancer awareness among adolescents in Britain: a cross-
52 sectional study. BMC Public Health. 2012;12:580.
53
54 30. Hubbard G, Stoddart I, Forbat L, Neal RD, O'Carroll R, Haw S & Kyle R. School-based brief
55 psycho-educational intervention to raise adolescent cancer awareness and address barriers to
56
57
58
59
60

- 1
2 medical help-seeking about cancer: a cluster randomised controlled trial, Psycho-Oncology. 2016;
3 25:760-771.
- 4
5 31. <http://www.cancerresearchuk.org/about-us/cancer-strategy-in-england> Accessed 23/12/2016
- 6
7 32. <http://www.cancerresearchuk.org/health-professional/early-diagnosis-activities/ace-programme>
8 Accessed 23/12/2016
- 9
10 33. Weller, D, Vedsted, P, Rubin, G, Walter, F, Emery, J, Scott, S, Campbell, C, Andersen, R,
11 Hamilton, W, Olesen, F, Rose, P, Nafees, S, van Rijswijk, E, Hiom, S, Muth, C, Beyer, M & Neal,
12 R. The Aarhus statement: improving design and reporting of studies on early cancer diagnosis.
13 British Journal of Cancer. 2012;106:1262-7
- 14
15 34. Lethaby CD, Picton S, Kinsey SE, Phillips R, van Laar M and Feltbower RG. A systematic review
16 of time to diagnosis in children and young adults with cancer. Archives of Disease in Childhood.
17 2013; 98:349-355.
- 18
19 35. <https://www.england.nhs.uk/wp-content/uploads/2016/05/cancer-strategy.pdf> Accessed
20 21/12/2016
- 21
22 36. Arksey H, O'Malley L Scoping studies: towards a methodological framework. International Journal
23 of Social Research Methodology 2005;8:19-32.
- 24
25 37. Levac D, Colquhoun H, O'Brien KK. Scoping studies: advancing the methodology. Implementation
26 Science 2010;5:69
- 27
28 38. Andersen B, Cacioppo J, Roberts D. Delay in seeking a cancer diagnosis. Delay stages and
29 psychophysiological comparison processes. British Journal of Social Psychology. 1995;343-352
- 30
31 39. Hansen RP et al. Socioeconomic patient characteristics predict delay in cancer diagnosis: A
32 Danish cohort study. BMC Health Services Research. 2008;8:49.
- 33
34 40. Walter F, Webster A, Scott S and Emery J. The Andersen Model of Total Patient Delay: a
35 systematic review of its application in cancer diagnosis. Journal of Health Services Research &
36 Policy 2012;17:110–118
- 37
38 41. Dobson CM, Russell AJ, Rubin GP. Patient delay in cancer diagnosis: what do we really mean
39 and can we be more specific. BMC Health Services Research 2014;14:387
- 40
41 42. NHS National Patient Safety Agency (2010) Delayed diagnosis of cancer: Thematic review. NPSA
42 March 2010.
- 43
44 43. Eden T, Saha V. Lag time for children with brain tumours (letter). Archives of Disease in
45 Childhood. 1996;75:766-767
- 46
47 44. Goyal S, Roscoe J, Ryder W, Gattamaneni H, Eden T. Symptom interval in young people with
48 bone cancer. European Journal of Cancer. 2004;40:2280-2286
- 49
50 45. Dang-Tan T, Franco EL. Diagnosis delays in childhood cancer: a review. Cancer. 2007;110:703-
51 713
- 52
53 46. Pollock B, Krischer J, Viettmi T. Interval between symptom onset and diagnosis of pediatric solid
54 tumors. Journal of Pediatrics. 1991;725-32

- 1
2
3 47. Dang-Tan T, Trottier H, Merry LS, Morrison HI, Barr RD, Greenberg ML, Franco EL. Delays in
4 diagnosis and treatment among children and adolescents with cancer in Canada. *Pediatric Blood*
5 and *Cancer*. 2008;51:468-474
6
7 48. Dang-Tan T, Trottier H, Mery LS, et al. Determinants of delays in treatment initiation in children
8 and adolescents diagnosed with leukemia or lymphoma in Canada. *Int J Cancer* 2010;126:1936–
9 1943
10
11 49. Ferrari A, Miceli R, Casanova M, et al. The symptom interval in children and adolescents with soft
12 tissue sarcomas. *Cancer* 2010;116:177–183
13
14 50. Haimi M, Peretz Nahum M, Ben Arush MW. Delay in diagnosis of children with cancer: a
15 retrospective study of 315 children. *Pediatr Hematol Oncol*. 2004;21:37–48
16
17 51. Fajardo-Gutierrez A, Sandoval-Mex AM, Mejia-Arangure JM, Rendon-Macias ME, Martinez-
18 Garcia Mdel C. Clinical and social factors that affect the time to diagnosis of Mexican children with
19 cancer. *Med Pediatr Oncol*. 2002;39: 25–31
20
21 52. Edgeworth J, Bullock P, Bailey A, Gallagher A, Crouchman M. Why are brain tumours still being
22 missed? *Archives of Disease in Childhood*. 1996;74:148-51
23
24 53. Saha V, Love S, Eden T, Micallef-Eynaud P, MacKinlay G. Determinants of symptom interval in
25 childhood cancer. *Archives Disease in Childhood*. 1993;68:771–774
26
27 54. Dobrovoljac M, Hengartner H, Boltshauser E, Grotzer MA. Delay in the diagnosis of paediatric
28 brain tumors. *European Journal Pediatrics*. 2002;161:663–667
29
30 55. De Nooijer J, Lechner L, de Vries H. Help-seeking behaviour for cancer symptoms: Perceptions of
31 patients and general practitioners. *Psycho-Oncology*. 2001;10:145-157
32
33 56. Mitchell E, Rubin G, Macleod U. Improving diagnosis of cancer.: a toolkit for general practice.
34
35 www.rcgp.org.uk/-/.../Cancer/Improving-Cancer-Diagnosis---A-Toolkit-for-General-...accessed
36
37 24/12/2016
38
39 57. Leydon G, Bynoe-Sutherland J, Coleman M. The journey towards a cancer diagnosis: the
40 experiences of people with cancer, their family and carers. *European Journal of Cancer Care*.
41 2003;12:317-326
42
43 58. Smith S, Case L, Fern L, Waterhouse K, Vaughan K, McCabe M. Poor cancer awareness in
44 young people in Greater Manchester advocates the need for age-specific interventions to raise
45 awareness. In NCRI Cancer Conference, 6-9 November, Liverpool, UK; 2011.
46
47 59. Rudberg L, Nilsson S, Wikblad K, Carlsson M. Testicular cancer and testicular self-examination:
50 knowledge and attitudes of adolescent Swedish men. *Cancer Nursing*. 2005;28:256-262
51
52 60. Lechner EHS, Oenema A, & Nooijer JM de. Testicular selfexamination (TSE) among Dutch young
53 men aged 1519: determinants of the intention to practice TSE. *Health Education Research* 2002;
54 17:73-84
55
56 61. Moore, R. and Topping, A. 'Young men's knowledge of testicular cancer and testicular self-
57 examination: a lost opportunity?' *European Journal of Cancer Care* 1999;8:137-142
58
59
60

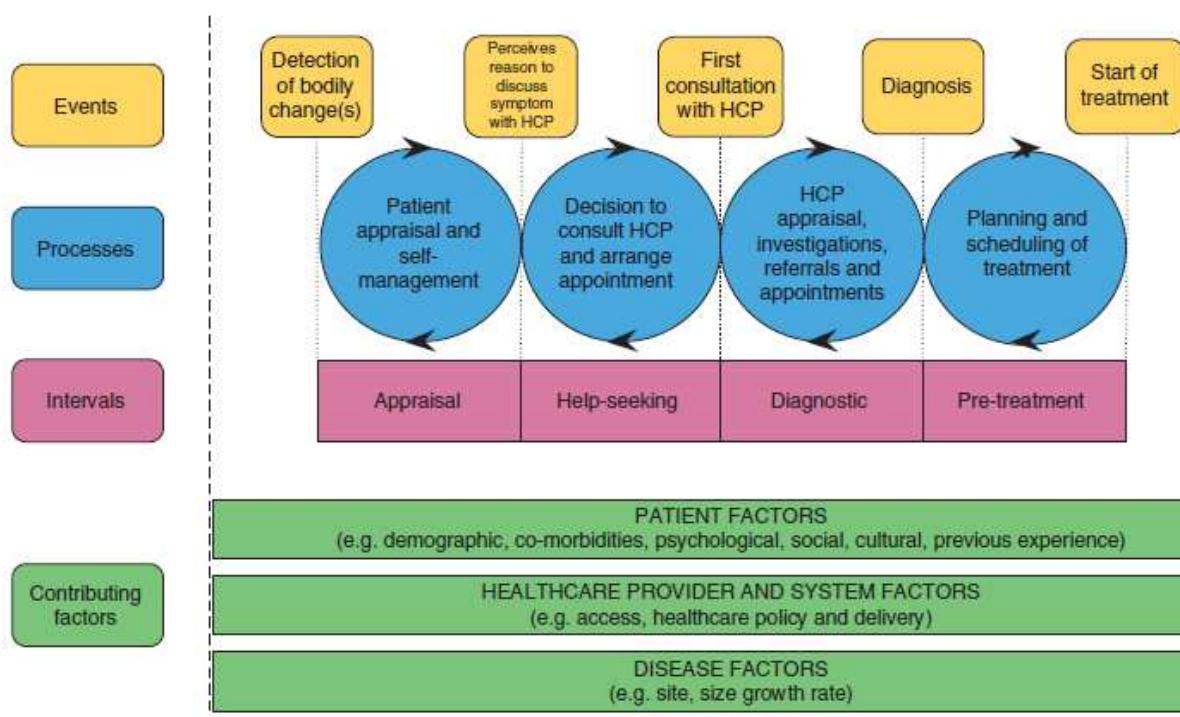
- 1
2
3 62. Karayurt O, Ozmen D, Cetinkaya AÇ. Awareness of breast cancer risk factors and practice of
4 breast self-examination among high school students in Turkey. BMC Public Health 2008;8:359-
5 366
6
7 63. Cronholm PF, Mao JJ, Nguyen GT, Paris RT. A dilemma in male engagement in preventive
8 services: Adolescent Males' Knowledge and Attitudes towards Testicular Cancer and Testicular
9 Self-Exam. Am J Men's Health. 2009;3:134-40
10
11 64. Albritton K and Bleyer WA. The management of cancer in the older adolescent. European Journal
12 of Cancer 2003;39:2584-2599
13
14 65. Gibson F, Pearce S, Eden T, Glaser A, Hooker L., Whelan J and Kelly D. Young people describe
15 their pre-diagnosis cancer experience. Psycho-Oncology. 2013;22:2585-92
16
17 • This was the first study to examine in detail young people's accounts of the pre-diagnostic
18 experience. The importance of narratives in research and clinical practice to understand the
19 impact of this period of time before people are in the 'safety' of specialist cancer care is
20 evidenced in this paper.
21
22 66. Halperin EC, Watson DM, George SL. Duration of symptoms prior to diagnosis is related inversely
23 to presenting disease stage in children with medulloblastoma. Cancer. 2001;91:1444-50
24
25 67. Fern LA, Campbell C, Eden TO, Grant R, Lewis I, Macleod U, Weller D, Whelan J. How frequently
26 do young people with potential cancer symptoms present in primary care? Br J Gen Pract. 2011
27 May;61(586):e223-30. doi: 10.3399/bjgp11X572418. Erratum in: Gen Pract. 2011;61(587):382
28
29 68. Ahrensberg JM, Fenger-Gren M, Vedsted P. Primary care use before cancer diagnosis in
30 adolescents and young adults- a nationwide register study. PLOS ONE. 2016;
31 DOI:10.1371/journal.pone.01559933
32
33 69. Magni C, Segre C, Finzi C et al. Adolescents health awareness and understanding of cancer and
34 tumor prevention: when and why an adolescent decides to consult a physician. Pediatric Blood
35 and Cancer 2016;63:1357-1361
36
37 • Reinforces the need for information campaigns dedicated to teenagers to focus not so much
38 on ensuring adolescents' awareness that cancer can develop at their age too, but rather on
39 how to interpret any symptom they experience, with a view to reducing the time elapsing
40 before they seek help, and thereby shortening the road to diagnosis.
41
42
43 70. Dixon-Woods M, Findlay M, Young B, Cox H, Heney D. Parents' accounts of obtaining a
44 diagnosis of childhood cancer. Lancet. 2001;357:670-674
45
46 71. Ghaddar SF, Valerio MA, Garcia, CM, Hansen L. Adolescent health literacy: the importance of
47 credible sources for online health information. Journal of School Health. 2012; 82:28-36
48
49 72. Schiffman JD, Csongradi E, Suzuki LK. Internet use among adolescent and young adults with
50 cancer. Pediatric Blood and Cancer. 2008;51:410-415
51
52
53
54
55
56
57
58
59
60

- 1
2
3 73. Gray NJ, Klein JD, Noyce PR et al. Health information-seeking behaviour in adolescence: the
4 place of the internet. *Social Science and Medicine*. 2004; 60:1467-1478
5
6 74. Dominguez M, Sapina L. 'Others like me' an approach to the use of the internet and social
7 networks in adolescents and young adults diagnosed with cancer. *Journal of Cancer Education*.
8 2016; DOI:10.1007/S13187-016-1055-9
9
10 75. Martin S, Ulrich C, Munsell M, Taylor S, Lange G, Bleyer A. Delays in cancer diagnosis in
11 underinsured young adults and older adolescents. *The Oncologist*. 2007;12:816–824
12
13 76. Primeau SW, Freund KM, Ramachandran A et al. Social Service barriers delay care among
14 women with abnormal cancer screening. *Journal of General Intern Medicine*. 2013;29:169-75
15
16 77. Jin SL, Hahn SM, Kim HS et al. Symptom interval and patient delay after survival outcomes in
17 adolescent cancer patients. *Yonsei Medical Journal*. 2016;57:572-579.
18
19 78. Yang J YK, Cheng F WT, Wong KC, Lee V, et al. Initial presentation and management of
20 osteosarcoma, and its impact on disease outcome. *Hong Kong Med J*. 2009;15:434-9
21
22 79. Shay V, Fattal-Valevski A, Beni-Adani L, Constantini S. Diagnostic delay of pediatric brain tumors
23 in Israel: a retrospective risk factor analysis. *Childs Nerv Syst*. 2012;28:93–100
24
25 80. Loh AHP, Ha C, Tan AM, Quah, TC, Chui CH. Diagnostic delay in pediatric solid tumors: A
26 population based study on determinants and impact on outcomes. *Pediatric Blood Cancer*.
27 2012;58:561–565
28
29 81. Lyratzopoulos G, Neal RD, Barbiere JM, Rubin GP, Abel GA. Variation in number of general
30 practitioner consultations before hospital referral for cancer: findings from the 2010 National
31 Cancer Patient Experience Survey in England. *Lancet Oncology*. 2012;13:353–365
32
33 82. Lyratzopolous G, Wardle J, Rubin G. Rethinking diagnostic delay in cancer: how difficult is the
34 diagnosis? *theBMJ*. 2014; 349:7400
35
36 83. <http://www.youngpeopleshealth.org.uk/wp-content/uploads/2016/06/The-best-chance-from-the-start-report.pdf> Accessed on 23/12/2016
37
38 84. Veroni L, Mariani L, Lo Vullo S, Favini F, Catania S, Pava MV, Massimino M and Ferrari A.
39 Symptom interval in pediatric patients with solid tumors: adolescents are at greater risk of late
40 diagnosis. *Pediatric Blood Cancer*. 2013;60:605-10
41
42 85. Smith S, Davies S, Wright D, Chapman C, Whiteson M. The experiences of teenagers and young
43 adults with cancer--results of 2004 conference survey. *European Journal of Oncology Nursing*.
44 2007;11:362-8
45
46 86. Black G, Sherringham J, Spencer-Hughes V et al. Patients' experiences of cancer **diagnosis** as a
47 result of an emergency presentation: a qualitative study. *PLOS One*
48 2015;DOI:10.1371/journal.pone.0135027
49
50 • An important study capturing the experience of young people across primary and secondary
51 care, presenting a three-part typology capturing novel insights into how presentations arise
52 and how patient pathways develop.
53
54
55
56
57
58
59
60

- 1
2
3 87. National Institute for Health and Clinical Excellence. Guidance on cancer services: Improving
4 outcomes in children and young people. London: National Institute for Health and Clinical
5 Excellence. 2005.
6
7 88. <https://www.nice.org.uk/guidance/NG12> Accessed 24/12/2016
8
9 89. National Institute for Health and Clinical Excellence. Referral Guidelines for Suspected Cancers.
10 London: National Institute for Health and Clinical Excellence. 2005.
11
12 90. Fern LA., Campbell C., Eden T., Grant R., Lewis I., Macleod., Weller D., Whelan J. Addressing
13 delayed cancer diagnosis in primary care: Patterns of attendance and symptoms of teenagers and
14 young adults seen in 3 general practices during one year. Abstract A108 *National Cancer*
15 *Research Institute Conference*, Birmingham 2008;
16 <http://www.ncri.org.uk/ncriconference/2008abstracts/abstracts/A108.htm>
17
18 91. Stefan DC and Siemonsma F. Delay and causes of the diagnosis of childhood cancer in Africa.
19 Pediatric Blood Cancer. 2011;56:80-85
20
21 92. Dommett RM, Redaniel T, Stevens MC, Martin RM, Hamilton W. Risk of childhood cancer with
22 symptoms in primary care: a population-based case-control study. British Journal of Cancer.
23 2013;108:2329-33
24
25 93. Whitaker KA, Macleod U, Winstanley K, Scott SE, Wardle J. Help seeking for cancer 'alarm'
26 symptoms. British Journal of General Practice. 2015; E96
27
28 94. Ahernesberg JM, Olesen F., Hansen RP, Schreder H, Vedsted P. Childhood cancer and factors
29 related to prolonged diagnostic intervals: a Danish population-based study. British Journal of
30 Cancer. 2013; DOI:10.1038/bjc.2013.88
31
32 • Focussing on primary care usage before a cancer diagnosis this study indicates that symptom
33 interpretation starts long before the diagnosis, specifically for some types of cancers in AYA.
34
35 Recognising even vague symptoms or minor changes in the help-seeking patterns seen in
36 primary care is highlighted as important.
37
38 95. Redaniel MT, Martin RM, Ridd MJ, Wade J, Jeffreys M. Diagnostic intervals and its association
39 with breast, prostate, lung, and colorectal cancer survival in England: historical cohort study using
40 the clinical practice research datalink. PLOS One. 2015;DOI:10.1371/journal.pone.0126608
41
42 96. Mitchell E, Macleod U, Rubin G. Report for the National Awareness and Early Diagnosis Initiative;
43 Cancer in Primary Care; An analysis of significant event audits (SEA) for diagnosis of lung cancer
44 and cancer in teenagers and young adults 2008-2009. Durham University: School of Medicine and
45 Health. 2009.
46
47 97. Sloper P. Needs and responses of parents following the diagnosis of childhood cancer. Child:
48 Care, Health and Development. 1996;22:187-202
49
50 98. Eiser C, Parkyn T, Havermans T, McNinch A. Parents recall on the diagnosis of cancer in their
51 child. Psycho-oncology. 1994;3:197-203
52
53
54
55
56
57
58
59
60

- 1
2
3 99. Larsen MB, Hansen RP, MOlesen F, Vedsted Patients' confidence in their GP before and after
4 being diagnosed with cancer. British Journal of General Practice. 2011;
5 DO110.3399/bjgp11x572409
6
7 100. Birch J. Why do teenagers get cancer? Fourth international conference on teenage and young
8 adult cancer medicine, Teenage Cancer Trust. London:Royal College of Physicians. 2006.
9
10 101. Klein-Gletink JE, Pogany LM, Barr RD, et al. Waiting times for cancer care in Canadian
11 children: Impact of distance, clinical, and demographic factors. Pediatric Blood Cancer.
12 2005;44:318–327
13
14 102. Facione N. Delay versus help seeking for breast cancer symptoms: A critical review of the
15 literature on patient and provider delay. Social Science and Medicine. 1993;36:1521-1534
16
17 103. Tischelman, C., Sachs, L. The diagnostic process and the boundaries of normality. Qualitative
18 Health Research. 1998;8:478-600
19
20 104. Macleod U, Mitchell E, Burgess C, et al. Risk factors for delayed presentation and referral of
21 symptomatic cancer: evidence of common cancers. British Journal of Cancer. 2009;101:S92-S101
22
23 105. <http://elearning.rcgp.org.uk/course/info.php?id=232> Accessed 04/03/17
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Figure 1. Model of pathways to treatment



From Walter et al 2012

Figure 2. Scoping studies

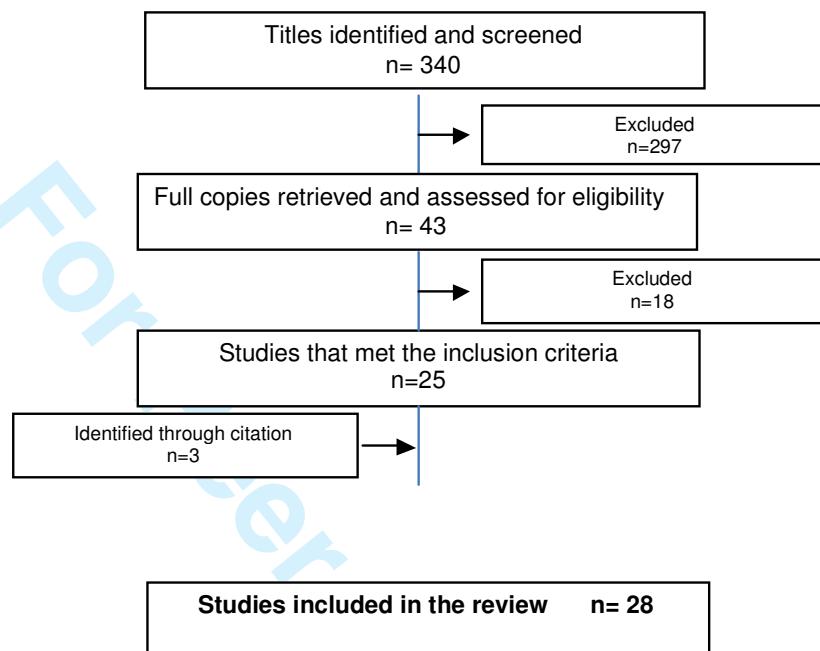


Figure 3: Factors affecting pathways to cancer diagnosis for adolescents and young adults

Disease factors

Cancer related

- Rare cancers
- Non-specificity of symptoms
- Symptom pattern
- Site of cancer

Physical factors

- Puberty
- Normal growth
- Sporting injuries

Patient factors

Demographic

- Age
- Gender

Knowledge

- Low cancer awareness
- Limited knowledge of complex healthcare systems

Psychological

- Fear
- Growing autonomy
- Confidence in communicating symptoms

Social

- Appearing normal
- Exchanging information with peers
- Accessing information from internet: provides privacy; accessible; creates community
- Influence of parents as reassurance of mediators or referral
- Competing life events

Healthcare factors

System

- Point of first contact GP vs A&E
- Primary physician
- Complex healthcare systems
- Insurance

Healthcare provider and interactions with AYA

- Age of patient
- Socioeconomic status of patient
- Perception of symptoms
- Previous experience of cancer in AYA
- Consultation time
- Continuity in care
- Communication with AYA
- Relationship between AYA-GP
- Previous consultations: not been taking seriously; issues not being addressed; reassurance from GP

Table 1 Why timeliness to diagnosis remains a top priority

Statement	Source	Level of evidence
13 Timelessness, 'delay' in diagnosis is frequently a theme in the lay press.	http://www.itv.com/news/2015-06-16/young-patients-facing-significant-delay-in-bowel-cancer-diagnosis/	+
17 Relationship of lack timeliness/ delay to poorer outcomes in lay press and research	http://www.clicsargent.org.uk/content/jess-story	+
21 A timely diagnosis is a key research priority for young people.	Fern et al 2009 (19), 2013 (13)	+++
23 Young people are often unaware of the more common cancers that affect their age group.	Hubbard et al 2016 (30)	++
26 Many young people consult their General Practitioner about their symptoms a number of times.	Gibson et al 2013 (65)	
29 Low awareness of cancer among primary-care personnel has been described.	http://www.mirror.co.uk/news/uk-news/gps-missing-cancer-children-because-6358489	+
33	http://www.clicsargent.org.uk/news/12-04-2016-day-action-tackle-delayed-diagnosis-young-cancer-patients	++
35 Level of evidence		
36 + lay press		
37 ++ charity report		
38 +++ peer reviewed		

Table 2. Publications outputs from the scoping review

	Year	Country	Patients (N, age range)	Cancer Type	Method	Delay Diagnosis: Influencing Factors
8	Authors					
9	Albrton & Bleyer	2003	UK	N/A		
10	Cronholm et al.	2009	USA	N=205 9 th and 10 th grade males	Testicular cancer	Review
11						Knowledge and attitudes towards testicular cancer and testicular self-exam
12	Dang-Tan & Franco	2007	-	Review of 23 studies (Patients' age range=0-29 years)	N/A	
13						
14						
15						
16	Dang-Tan et al.	2008	Canada	N=2,896 Age: 0-19 years	Leukemia; CNS; Lymphoma; Neuroblastoma; Retinoblastoma; Ranal Tumour; Hepatic Tumour; Bone Tumour; Sarcoma; Germ Cell neoplasm;	Retrospective review (1995-2000)
17						
18						
19						
20	Dang-Tan et al.	2010	Canada	N= 963 leukaemia and 397 lymphoma Age: <19-years	Leukaemia and Lymphoma	A prospective cohort study
21						
22	Fern et al.	2013	UK	N/A		Age professional delay (GP vs. A&E) cancer type
23	Ferrari et al.	2010	Italy	N=575 Age: ≤21 years of age	Soft Tissue Sarcomas (STS)	Editorial
24						
25						
26	Gibson et al.	2013	UK	N=24 Age: 16-25	Metastatic adenocarcinoma of the bowel, Osteosarcoma, 2B Hodgkin's lymphoma, 4B Hodgkin's lymphoma, Ovarian dysgerminoma, Ewing's kidney, Synovial sarcoma, ovarian cancer (granulosa cell tumour), B cell lymphoma, Medullablastoma, Osteosarcoma, Neuroblastoma, Ewing's sarcoma, Malignant peripheral nerve sheet tumour	Retrospective (Interviews)
27						
28						
29						
30						
31						
32	Goyal et al.	2004	UK	N=115 Age: 4-22 years	Osteosarcoma and Ewing's sarcoma	Retrospective review (January 1990- April 2002)
33						
34						
35	Haim	2004	Israel	N=315 Age: 0-20 years	Solid Tumour (excluding leukaemia)	Retrospective review
36						
37						
38	Halperin et al.	2001	-	N=122 Age:0 - ≥17	Medulloblastoma	Retrospective review (January 1974- October 1999)
39						
40						
41						
42						
43						
44						
45						
46						
47						
48						

Authors	Year	Country	Patients (N, age range)	Cancer Type	Method	Delay Diagnosis: Influencing Factors
Hubbard et al.	2016	UK	N=20173 Mean Age=12.4 (SD=.55)	N/A	Cluster randomised controlled trial	Cancer awareness, help-seeking barriers endorsed and cancer communication
Jin et al.	2016	Korea	N= 592 Age:0-18	Acute Lymphoid Leukemia; Acute Myeloid Leukemia; Non-Hodgkin Lymphoma; Central Nervous System tumors; Sarcomas; Neuroblastomas; and Wilms tumor	Retrospective review (2000-2007)	Patient delay (first symptoms/signs of disease and date medical help was first sought); symptom interval (first symptoms/signs of disease and date of diagnosis); patient delay proportion (Patient Delay divided by Symptom Interval); age
Klein-Geltink et al.	2005	Canada	N= 204 Age= 15-19 years	Leukaemia; Lymphomas; CNS; Bone; Soft tissue; Germ cell; Carcinoma; Other (hepatic tumours, renal tumours, sympathetic nervous system tumours, and other and unspecified malignant neoplasms)	Retrospective review (1995-2000)	Age Paediatric versus adult oncology treatment centres Referral delay (time between first health-care contact and assessment by a treating oncologist or surgeon)
Kyle et al.	2012	UK	N=478 Age=11-17	N/A	Survey	Cancer awareness
Lethaby et al.	2013	UK	N/A	N/A	Rapid Review	Type of cancer, age
Loh et al.	2012	Singapore	N=350 Age: 0-18	Solid Tumours	Retrospective review (1997-2007)	Age; site of presentation; points of first symptom detection; first healthcare contact; first suspicion of malignancy
Lytatzopoulos et al.	2012	UK	N=41299 Age: 16-85+	Multiple Myeloma, Pacreatic, Stomach, Lung, Hodgkin's Lymphoma, Colon, Ovary, Brain, Non-Hodgkin's Lymphoma, Mesothelioma, Rectal, Renal, Laryngeal, Oesophageal, Leukaemia, Prostate, Vulvar, Cervical, Bladder, Thyroid, Endometrical, Testicular, Melanoma, Breast	Survey	Type of cancer, age, gender
Magni et al	2016	Italy	N=500 Age:15-19	N/A	Survey	Health perception, understanding of oncological disease, reaction to early signs and symptoms potentially attributable to cancer
Martin et al.	2007	USA	N=235 Age: 15-29 years	Leukaemia, Hodgkin's and non-Hodgkin's lymphoma, sarcoma, brain tumours, thyroid cancer	Retrospective review (June 2001-June 2003)	Type of cancer; health insurance
Primeau et al.	2013	USA	N= 1,481 Age. ≥ 18	Breast and cervical cancer	Secondary analysis of the intervention arm of the Boston Patient Navigation Research Program (PNRP)	Social service barriers, site of care, age, race/ethnicity, primary language, and insurance

Authors	Year	Country	Patients (N, age range)	Cancer Type	Method	Delay Diagnosis: Influencing Factors
Redaniel et al.	2015	UK	N=22,051 Age >15	Breast, colorectal, lung and prostate cancers	Retrospective review (1998-2009)	Presenting symptoms (NICE-qualifying alert symptoms v non-alert symptoms); cancer site, tumour biology and clinical practice
Saha et al.	1993	UK	N=184 Age: 0-15 years	Acute leukaemia; brain tumour; bone tumour; lymphoma; neuroblastoma; rhabdomyosarcoma; nephroblastoma	Retrospective review (January 1982-December 1990)	Age; diagnostic group; geographical factors
Shay et al.	2012	Israel	N=330 Age: 0-18 years	Brain Tumours	Retrospective review Family interview	Delay in indicated imaging; Classic symptoms with a wrong diagnosis; Wrong imaging referral; Administrative delay; family; Wrong interpretation of imaging; Professional delay (GP vs. A&E)
Smith et al.	2007	UK	N=350	N/A	Conference survey	N/A
Stefan & Siemonsma	2011	South Africa	N= 194 children Age: 0-15 years	Lymphoma, Leukaemia, Blastoma, Sarcoma, Brain tumour, Teratoma, Histiocytosis, other tumours (i.e., less common)	Combined prospective and retrospective study (January 2000- July 2009)	Initial misdiagnoses delay in performing tests and waiting for a histopathology results
Veneroni et al.	2012	Italy	N=425 Age: 28% of them adolescents	Solid Tumours	A prospective series	Age Patient delay (time to first doctor appointment) Referral delay (time taken by the physician to the patient to a specialist - oncologist or surgeon)
Yang et al.	2009	China	N= 51 Age: <18 years	Osteosarcoma	Retrospective study (March 1994-October 2005)	First medical speciality consulted Preceding trauma or sports injury Misdiagnosis

Table 3 Examples of possible future interventional research

Time interval	Recommendation
Appraisal	<p>Target public awareness campaigns.</p> <p>Increase health knowledge and health education in schools.</p> <p>Raise awareness of the more common cancers that occur in this age group.</p> <p>Inform healthcare professionals and health systems of common delays.</p>
Help-seeking	<p>Increase the public's confidence that cancer is a survivable disease.</p> <p>Increase the quality of information available on the Internet.</p> <p>Develop and test strategies that help young people make the most of encounters with primary care.</p> <p>Improve access to primary care - getting appointments, length of appointments and consistency in healthcare professional on each occasion.</p>
Diagnostic	<p>Increase education and training in primary care.</p> <p>Involve young people in the design and review of existing services.</p> <p>Develop strategies to investigate earlier persistent symptoms of common illnesses.</p> <p>Patient as expert needs to be emphasised.</p> <p>Ensure rare cancers are managed in centres of excellence.</p>
Pre-treatment	<p>Explore pre-diagnostic experiences to establish trusting relationships with professionals and services.</p> <p>Offer choice of treatment location where possible.</p> <p>Encourage awareness and services that allow young people to remain in control once a diagnosis is made.</p> <p>Explore communication pathways and blocks between settings and departments of care.</p>