Review Article

Cancer Pain in People With Intellectual Disabilities: Systematic Review and Survey of Health Care Professionals

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Abstract

Context. Owing to life expectancy improvements for people with intellectual disabilities, their risk of developing cancer is increasing. Pain is an inevitable aspect of cancerous diseases. However, as pain experience and expression can be atypical in people with intellectual disabilities, this population is vulnerable to late diagnosis of cancer and undertreatment of cancer pain.

Objectives. The objective of this study was to investigate what is currently known about cancer pain in people with intellectual disabilities and provide specific recommendations to improve this knowledge.

Methods. A systematic review using PubMed, PsycINFO, and CINAHL and an anonymous online survey of Dutch health care professionals were conducted.

Results. From 10,146 publications, with *intellectual disabilities* in the title, and *pain* or *cancer* in the title or abstract, 11 articles underwent qualitative synthesis. Discussions within these articles were predominantly unspecific and brief, frequently indicating challenges in symptom presentation, communication, as well as assessment and treatment of cancer pain. The survey received 102 responses. The 63 health care professionals experienced with cancer in people with intellectual disabilities indicated challenges recognizing, assessing, and treating their cancer pain.

Conclusion. Cancer pain in people with intellectual disabilities is a topic lacking specific and comprehensive research within scientific literature. We suggest this is due to inherent difficulties regarding the complex interplay of comorbidities and communication issues in people with intellectual disabilities. J Pain Symptom Manage 2019;58:1081–1099.

Key Words
pain, cancer, intellectual disabilities, treatment, assessment

Introduction

Increased life expectancy for people with intellectual disabilities (PWIDs) due to health care improvements[1–3] has led to new challenges for health services and carers, including increased deaths from age-related conditions, such as cancer.[3–5] Age has been described as one of the most important determinants of cancer in the general population[6] and in PWIDs.[7,8] However, particular levels of intellectual disabilities (IDs) and ID-associated syndromes have been linked with differing cancer profiles.[9] For example, there is an increased risk of gall bladder neoplasms in people with severe IDs, potentially due to sedentary lifestyles and/or high levels of medication due to comorbidities.[7] There are inequalities in health provision and care of PWIDs who have cancer,[9] as caregivers and health care professionals face challenges at all stages of cancer progression, including prevention, screening, detection, diagnosis, treatment, follow-up, and palliative care.[9–11] Most significantly, late diagnosis

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has been identified as a key issue precluding effective treatment of cancer in PWIDs as it results in poorer prognoses and avoidable deaths.[9,12] Reviews on cancer in PWIDs suggest that late diagnosis is, in part, due to difficulties regarding the presentation and assessment of pain symptoms.[9,13]

Despite the significance of pain in this population (e.g., comorbidities leading to multiple painful surgeries[14–18]), pain is underrecognized and undertreated due to communication difficulties, atypical pain expression, and suspected atypical pain experience.[19] First, self-report of pain, commonly used to identify and assess pain in the general population, can be difficult for PWIDs owing to communication issues.[20] As a consequence, symptoms are underreported and the presence of cancer can be hidden.[7,10] Second, assessment of pain relies on the interpretation of behaviors and facial expressions, but these behaviors and expressions may manifest atypically in this population. Behavioral pain indicators can be contradictory and situational, as well as highly individual: dependent on factors such as level of IDs, mental age, and learned behavior.[21,22] Third, atypical pain expression may reflect atypical pain experience (e.g., due to congenital or acquired brain damage, genetic syndromes, or psychopathology). Although atypical experience does not necessarily result in reduced sensitivity[23–26], caregivers may not take symptoms seriously because it can be difficult to discriminate pain indicators from anxiety, stress, attention seeking, or problem behaviors.[21] Cancer may only be suspected when symptoms become observable (e.g., visible tumors or weight loss), at which point it may be too late to use effective cancer treatment.[27] Therefore, greater understanding of pain as a symptom of cancer in PWIDs will become more critical as the population ages and could reduce the number of avoidable deaths due to late diagnosis.

As well as indicating presence of cancer, pain persists after diagnosis, either due to cancer treatments, or disease progression, or both in combination.[28,29] This cancer pain can be acute or chronic: the former is short term, usually less than three months, caused by surgery, dressing changes, or movement; the latter lasts longer than three months, caused by tumor pressure (i.e., on organs, bones, or nerves), chemical release, or nerve changes due to the disease or treatment.[30–32] Consequently, cancer pain is a highly important consideration at all stages of disease progression.[31] However, atypical pain expression and experience, resulting from the complex interplay of comorbidities and communication issues, could hinder effective cancer pain assessment and management in those with IDs.[20–22] The present article aimed to investigate what is currently known about cancer pain in PWIDs and provide recommendations to improve this knowledge. Greater understanding would aid earlier diagnoses as well as improve pain assessment and management during cancer treatment and progression, ultimately improving quality of life for PWIDs who have cancer. Owing to the clinical relevance of this investigation, two avenues of research were used: a systematic review of scientific literature and a survey of health care professionals.

Method

Systematic Review

Searching. A systematic search was first conducted in PubMed, PsychINFO, and CINAHL for articles from the last 20 years containing three terms in the title: intellectual disabilities, cancer, and pain. The search did not yield any articles with all three terms; for this reason, "IDs and pain" and "IDs and cancer" were independently searched using the inclusion criteria described in Table 1. All papers were required to have a title including "intellectual disabilities" and either "pain" or "cancer," and the third search term was required in the abstract or the main text when no abstract was available. The search strategy used for PubMed is illustrated in the following.

1. IDs and Pain

((intellectual disabilit*) OR (down* syndrome) OR (mental* retard*))
AND (pain* OR discomfort)

2. IDs and Cancer

((intellectual disabilit*) OR (down* syndrome) OR (mental* retard*))
AND (cancer*)

According to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), IDs are disorders involving both intellectual and adaptive functioning deficits in practical, social, or conceptual domains, with an onset during the developmental period.[33] Inclusion of *mental retardation* as a search term in the present systematic review improved the search for relevant articles, owing to the frequency of its use before the US federal statute.[34] *Down syndrome* was included as a search term as it is the most prevalent ID-associated syndrome.[35,36] Including other prevalent ID-associated syndromes (e.g., Fragile X syndrome) and conditions (e.g., learning disabilities, dyslexia, autism) as search terms did not improve outcomes, but these were still considered as inclusion criteria (Table 1). The term *cancer* was used in PubMed and CINAHL searches,[37] and the

Table 1
Inclusion and Exclusion Criteria for Systematic Literature Search

Inclusion Criteria	Exclusion Criteria
Articles (all study types [e.g., cross-sectional, case-control, case series])	Literature reviews, published commentaries and letters
Publication year 1998−2018	Publication year older than 1998
Written in English	Written in a language other than English
Human studies	Animal studies
Intellectual disabilities in title and abstract (synonyms include, developmental disabilities [if also having intellectual disabilities] and genetic syndromes [e.g., Fragile X syndrome, Rett syndrome, tuberous sclerosis complex])	Other developmental or neurological conditions (e.g., autism, cerebral palsy, or epilepsy), or learning disabilities (e.g., dyslexia or dyspraxia) without also having intellectual disabilities
Pain or discomfort in title, or in abstract if title contained cancer and intellectual disabilities (terms also accepted: painful, acute, and chronic)	Congenital insensitivity to pain, congenital sensory neuropathy, or hereditary sensory and autonomic neuropathy
This pain or discomfort could be identified as a symptom of cancer, resulting from cancer treatment [e.g., radiotherapy, chemotherapy, or surgery], or during palliative care of cancer patients	Description of distress in title or abstract, without also having pain or discomfort. (Distress may only relate to fear or anxiety, which was not the focus of the present article)
	Pain or discomfort during cancer screening procedures (e.g. mammography) without cancer being diagnosed
Cancer in title, or in abstract if title contained pain and intellectual disabilities (all forms of cancer were included [e.g., malignant tumors, leukemia, carcinoma])	Tumors found to be benign
	Other diseases or health issues (e.g., arthritis, gastro-oesophageal reflux disease) without also having cancer

terms *leukemia, leukaemia,* and *carcinoma* were additionally used in the PsychINFO search. Cancer *pain* is heterogeneous[30,32,38,39] and the search terms *pain* and *discomfort* were used to encompass all varieties.

Fig. 1 displays a flow diagram summarizing the systematic search results according to PRISMA guidelines.[40] In PubMed, PsychINFO, and CINAHL, the search for "IDs and pain," and for "IDs and cancer," found 2011 and 6819 titles, 556 and 92 titles, and 366 and 302 titles, respectively.

As all the included articles were case reports, quality assessment was conducted using two methods to specifically assess case report quality[41] and allow generalization and comparison using a tool for appraising heterogeneous literature.[42] Both authors of the present study rated the criteria independently, after which consensus was reached via discussion. Note that quality appraisal of the general article was conducted, rather than specifically appraising the quality of pain reporting. Furthermore, quality appraisal did not determine exclusion of relevant articles because ratings only indicate the quality of each case report.[43]

Narrative summary was the most appropriate way to synthesize the information from the case reports.[44] Sections of text were identified where pain was mentioned in relation to cancer in PWIDs. Using a "describe-compare-relate" approach, the first author (S. K. M.) then identified the predominant themes[45] within these extracts to integrate the information and assess how cancer pain in PWIDs is discussed within the literature. Specifically, the characteristics and boundaries of each possible theme were *described*, differences in these themes across varying demographic groups and contexts were *compared* (i.e., what levels and types of IDs, or types of cancer were common within the theme?), and themes were *related* to those already identified.[45] No disagreement was found with the second author (N. C. d. K.). If an article contained a literature review and case report, only the case report underwent appraisal and synthesis.

Survey of Health Care Professionals

Participants, Design, and Materials. Data were gathered anonymously via a Web-based survey (Qualtrics, Provo, UT) for Dutch health care professionals to explore cancer pain in PWIDs, written in Dutch by the second author (N. C. d. K.). Besides relevant characteristics to describe the respondents (i.e., profession and experience with cancer pain in PWIDs), survey questions were designed to investigate pain at different stages of cancer progression (e.g., diagnosis, treatment) as well as investigate challenges faced and solutions suggested by health care professionals.

The survey was sent to the formal contact person (i.e., secretary) of Dutch associations for the following occupations: physicians for PWIDs, behavioral specialists for PWIDs, dentists for PWIDs, nurses and nursing specialists, oncologists, disabled care, and palliative care. In addition, the survey link was sent to an online platform for Dutch health care practitioners working with PWIDs, to the second author's (N. C. d. K.) professional contacts working in care centers for IDs, a center for special dental care, general physicians, and was also displayed on the second author's (N. C. d. K.) LinkedIn profile. The survey was open between May and September 2018. Cross-sectional descriptive data were produced

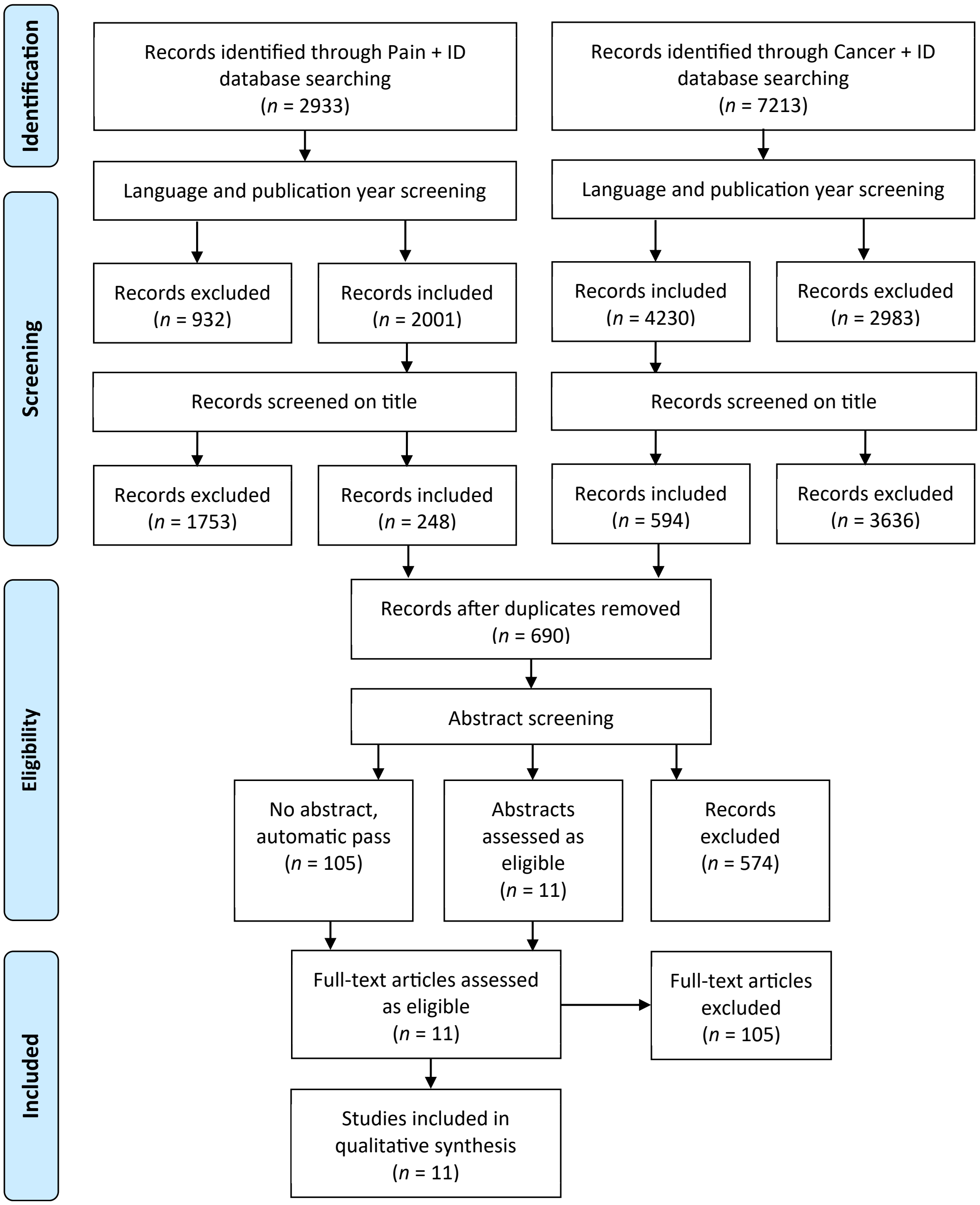

Fig. 1. Flow diagram (PRISMA) displaying the systematic selection process following database searches in PubMed, PsychINFO, and CINAHL for intellectual disabilities (IDs) and cancer or pain. Selection phases include identification, screening, eligibility, and final inclusion, using the inclusion and exclusion criteria in Table 1. From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. https://doi.org/10.1371/journal.pmed1000097. For more information, visit www.prisma-statement.org.

and analyzed qualitatively owing to the exploratory nature of this investigation.

Results

Systematic Review

The present systematic review revealed 11 articles that addressed cancer pain in PWIDs, either in the abstract or main text when no abstract was available. The included publications were all case reports of PWIDs who had cancer.[13,46–55]

Using the heterogeneous literature tool,[42] percentage quality ranged from 62.5% to 84.4%. Using the case report tool,[41] a "Yes" response to six or more of the eight quality questions was confirmed for nine of the articles, with one article only confirming four[48] and another five[13] of the questions (Table 2).

Table 2

Subscores, Total Scores, and Percentage of Overall Quality for All Included Literature Review Articles Using the Heterogeneous Literature Tool[42] and Joanna Briggs Institute (JBI) Case Study Tool[41]

Criteria and References	Koorey et al., 2000[46]	Yang, Juang, Chuang, and Chou, 2000[47]	Sharaf El-Dean, Bakshi, and Giraldo, 2004[48]	Hellebostad, Carpenter, Hasle, Mitchell, and Vyas, 2005[49]	Tuffrey-Wijne, Curfs, and Hollins, 2008[13]	Hjorth, Vainer, Petersen, Larsen, and Hasle, 2010[50]	Kaako and Kolade, 2010[51]	Purvey, Hanna, Shaib, and Saif, 2010[52]	Gil, Brett, Cordinhã, and Gomes, 2013[53]	Satgé et al., 2013[54]	Roma et al., 2015[55]
Heterogeneous literature quality tool (4 = good, 3 = fair, 2 = poor, 1 = very poor)											
Abstract and title	1	4	1	1	4	1	4	1	4	4	4
Introduction and aims	2	3	3	3	3	3	2	3	3	3	3
Method and data	4	4	4	4	3	4	4	4	4	4	4
Sampling	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Data analysis	4	n/a	n/a	4	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Ethics and bias	2	2	2	3	3	2	2	3	2	4	4
Findings/results	4	4	4	4	4	4	4	4	4	4	4
Transferability/generalizability	4	4	4	4	3	4	4	4	4	4	4
Implications and usefulness	2	3	2	4	4	3	3	4	3	4	4
Quality rating	**23**	**24**	**20**	**27**	**24**	**21**	**23**	**23**	**24**	**27**	**27**
Total possible rating	36	32	32	36	32	32	32	32	32	32	32
Percentage quality	63.89	75	62.5	75	75	65.63	71.88	71.88	75	84.38	84.38
JBI case study quality											
Demographic characteristics	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Patient history	Yes	Yes	No	Yes	Unclear	No	Yes	No	Yes	Yes	Yes
Current clinical condition	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Diagnostic tests	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
Intervention procedures	Yes	Yes	Unclear	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Yes
Postintervention clinical condition	Unclear	Yes	n/a	Yes	Unclear	Yes	n/a	Yes	Yes	Yes	Yes
Adverse or unanticipated events	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Unclear	Yes	Yes
Takeaway lessons	No	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Table 3

Summary of Study Characteristics, Arranged by Date With Direct Quotes of Pain Descriptions

Authors	Type of Study	Patient	Form of Cancer	Form of Pain	Direct Quote Containing Discussion of Cancer Pain in People With IDs	Further Details (Diagnosis, treatment, and Outcomes)
Koorey, Basha, Tomaras, Freiman, Robson, and Smith, 2000[46]	Case report with genetic analysis	Adult female 26 years FAP and cytogenetically visible 5q deletions IQ level estimated at 70—80	Appendiceal carcinoma (i.e., a cancer that began in the tissue lining the appendix)	Right iliac fossa pain (i.e., pain in the hip bone)	"She presented acutely at 26 years of age with a 24 hour history of right iliac fossa **pain**. She was febrile and had **guarding** and rebound **tenderness** at the site of her pain" [46](p.73) "Eight months after hemicolectomy, she presented again with a **painful** right iliac fossa mass"[46](p.73)	• Cancer treatment at first occurrence consisted of a right hemicolectomy, performed to remove the carcinoma • Cancer treatment at second occurrence included 5-fluorouracil and folinic acid • The patient passed away 12 months after second occurrence • Genetic analysis showed links between FAP, cancer, and IDs
Yang, Juang, Chuang, and Chou, 2000[47]	Case report	Adult male 42 years DS	Low-grade MALT thyroid lymphoma	Anterior chest discomfort	The patient "presented with the chief complaints of anterior chest **discomfort** and bilateral leg weakness of four to five months' duration that was exacerbated in the previous week, and a right neck mass that he had had for several months."[47] (p.235)	• Treatment involved a total right thyroidectomy followed by conservative treatment with 20 mg of prednisolone each day due to the patient's poor condition • There was no tumor recurrence or distant metastasis nine months later
Sharaf El-Dean, Bakshi, and Giraldo, 2004[48]	Case report	Adult male 26 years DS	Primary pericardial malignant mesothelioma (i.e., a cancer that began in heart tissue)	Right-sided chest pain	"Presented with a 2-week history of exertional shortness of breath, orthopnea, paroxysmal nocturnal dyspnea, and dry cough. He also had an episode of right-sided chest **pain**, which was aggravated by breathing."[48] (p. e107)	• Cancer was not the initial diagnosis • Patient died a few days after hospitalization • Cancer discovered during autopsy • This form of cancer is not curable, 50% die within six months
Hellebostad, Carpenter, Hasle, Mitchell, and Vyas, 2005[49]	Case report with genetic analysis	Child female 3/6 years DS	AML age 3 ALL age 6	Bone pain	"She remained in complete continuous remission until aged 6 years, when she presented with bone **pain**"[49] (p. 408)	• Treated according to the NOPHO-AML93 protocol at the age of three yrs • Treated at second occurrence according to the NOPHO-ALL92 protocol in the standard-risk group • Two years after treatment, she was in continuous complete remission • Genetic analysis showed mutations in GATA1 exon 2 in the AML tissue sample but not in the ALL sample
Tuffrey-Wijne, Curfs, and Hollins, 2008[13]	Case report with literature review (literature review section excluded)	Adult male 66 years Severe IDs	Lung cancer		"It was difficult for her [a palliative care nurse] to assess Pete's needs and symptoms, because he often misunderstood her questions and did not clearly indicate his **pain**."[13] (p. 383)	• No cancer treatment was given as the cancer was at an advanced stage due to late diagnosis • Palliative care provided for several months, several issues concerning emotional aspects and practicalities of his care are described

					The patient "was given morphine to control his **pain**, but the carers were anxious about this. They weren't sure when they could give him extra analgesia, or what they should do when Pete was too weak to swallow the medication."[13] (p. 383)	
Hjorth, Vainer, Petersen, Larsen, and Hasle, 2010[50]	Case report	Adult female 39 years DS	ALL Infiltrations of the liver, spleen, and dura mater	Abdominal pain	The patient was "admitted to the hospital because of abdominal **pain** and neck stiffness."[50] (p. e297)	• Supported in an intensive care unit but died 22 hours after admission • Diagnosis of leukemia was not made until autopsy • This form of leukemia is common in young children with DS but not in adults, therefore it was not suspected
Kaako and Kolade, 2010[51]	Case report	Adult male 25 years Unspecified level and cause of IDs	Stage IV lung LCNEC (i.e., a cancer that began in the tissue lining the lung)	Back pain	The patient "was brought by his caregiver with a chief complaint of low back **pain** for four months. The **pain** was located in his lower back and radiated to the right hip. Initially intermittent, the **pain** became constant, with gradual increase in severity to the point that the patient had refused to walk for three days before presentation. **Pain** was exacerbated by movement; no significant relief was attained with rest and/or analgesics."[51] (p.37) "On physical exam the patient was uncooperative, couched in a fetal position, tachycardic, hyptertensive (154/94), and **tender** in the lumbar area"[51] (p.37) "Back **pain** is a common complaint in the outpatient setting. In the absence of 'red flags' this is often benign non-specific **pain**. Red flags include neurological symptoms, duration exceeding one month, **pain** at rest or night time, history of cancer, unexplained weight loss and refractoriness to conservative therapy."[51,67] (p.38)	• Caregiver had noticed that the patient was losing weight and had a poor appetite (i.e., mechanical symptoms) • No cancer treatment was given as the cancer was at an advanced stage due to late diagnosis • Palliative care provided for two weeks, at which point the patient developed pneumonia and died

(*Continued*)

Table 3
Continued

Authors	Type of Study	Patient	Form of Cancer	Form of Pain	Direct Quote Containing Discussion of Cancer Pain in People With IDs	Further Details (Diagnosis, treatment, and Outcomes)
Kaako and Kolade, 2010: continued[51]					"Our patient presented with chronic lower back **pain** for more than four weeks, associated with poor appetite, weight loss, no improvement with bed rest, and lumbar tenderness. These findings were suggestive of an infectious or malignant spinal lesion."[51] (p.38) "Diagnostic imaging studies are not recommended for nonspecific back **pain** in the first four to six weeks in the absence of 'red flag symptoms'.[67] In this particular case, in the context of [IDs], there was diagnostic delay and medical care was pursued four months after symptom onset. The diagnosis could have been made earlier if he had been evaluated for back **pain** soon after he reported it"[51] (p. 38) "This case of LCNEC is unique in its presentation as lower back **pain** in a non-smoking young male."[51] (p.38) "In a series of 21 LCNECs, five were asymptomatic, six had chest **pain**, four exhibited cough or hemoptysis, and six had nonspecific presentations including flu-like symptoms, dyspnea and night sweats"[51,68] (p.38)	
Purvey, Hanna, Shaib, and Saif, 2010[52]	Case report and literature review	Adult female 42 years DS	Metastatic pancreatic adenocarcinoma (i.e., a cancer that began in the tissue lining the pancreas)	Abdominal pain	The patient "presented with two to three months history of weight loss up to 9 kg and epigastric abdominal **pain**"[52] (p. 3) "A repeat CT scan after 5 months of therapy was performed due to worsening of abdominal **pain** and elevation of liver enzymes"[52] (p. 3) "Unfortunately the patient developed further elevation of liver function tests and showed worsening of her abdominal **pain**."[52] (p. 3)	• Treated at first occurrence with gemcitabine 1.00 mg/m^2 weekly for two weeks. • Treated at second occurrence with an endoscopic retrograde cholangiopancreatography • Owing to significant hypotension, the patient was not able to withstand the procedure and was therefore moved to an intensive care unit • Family decided to withdraw intubation "based on her comorbid factors and extensive metastasis of pancreatic cancer"[52] (p. 4)

Gil, Brett, Cordinhã, and Gomes, 2013[53]	Case report	Child male 17 years TSC (i.e., a genetic neurocutaneous disorder, frequently coupled with IDs) Unspecified whether patient has IDs and of what level	Bilateral RCC (i.e., a cancer that began in the tissue lining the kidneys) Left kidney contained a clear cell RCC, Fuhrman Grade 3 Right kidney contained a chromophobe RCC, with positive EMA	Lumbar and abdominal pain	The patient "was admitted to his local hospital in March 2012 with right lumbar **pain**. The **pain** had started 24 hours prior to admission after a coughing bout and was described as a continuous **pain** that radiated to his right thigh."[53] (p.1) "On physical examination, he was found pale, had trouble walking and had symptoms of **pain** when pressure was applied to his right abdominal quadrant, which was **tender** on palpation but without rebound tenderness or rigidity."[53] (p. 1)	• Bilateral renal angiomyolipomas (i.e., common benign tumors found in TSC patients) were suspected at first • "Although malignancy could not be excluded as both lesions were highly vascularised"[53] (p. 2) • A biopsy confirmed malignancy in the form of RCC, clear cell type, Fuhrman Grade 1 (i.e., not advanced) • Treatment then involved a bilateral partial nephrectomy • Discovered of two different cancers, one in each kidney • Left kidney tumor found to be Fuhrman Grade 3 • Patient remained clinically stable after surgery
Satgé et al., 2013[54]	Case report and literature review	Adult male 36 years Severe IDs due to varicella encephalitis at 18 months old	A mucoepidermoid carcinoma of the mandible (i.e., an oral cancer)	Unspecified due to level of IDs, but oral pain was presumed based on cancer location	"Difficulties in communicating **pain** or **discomfort**, condition for access to medical centers, ability to cooperate during care procedures, and the ability of caregivers to perform routine hygiene are key factors for oral health in [people with IDs]."[54] (p. e22) After second surgery and insertion of a gastric tube, "There was no weight loss, and he seemed to accept the situation as long as the **pain** was controlled"[54] (p. e23) "The San Salvador **pain** assessment scale was used and adapted for him because he could not make the usual facial movements as a result of his tumor and the surgical treatment"[54] (p. e23)	• First treatment involved a molar extraction and tumor resection • One month after surgery, diagnosis of a carcinoma was confirmed • Further treatment involved a right mandibular resection with cervical lymph node dissection • No radiotherapy or chemotherapy were administered due to the patient's level of IDs • Local recurrence eight months after surgery, following this no further treatment administered • The patient died 20 months after initial discovery of the tumor
Roma et al., 2015[55]	Case report	Adult female 23 years KS with mild to moderate IDs	Spinal ependymoma (i.e., tumor of the spine)	Acute lumbar pain	The patient "presented with intermittent tactile hypoesthesia of the feet and worsening lumbar **pain**"[55] (p. 2)	• Treatment involved an L3 to L5 laminotomy, with gross total resection of the tumor • Biopsy confirmed Grade 2 cancer diagnosis • Patient remained in remission 14 months after diagnosis

ALL = acute lymphoid leukemia; AML = acute myeloid leukemia; DS = Down syndrome; EMA = endomysial antibodies; FAP = familial adenomatous polyposis; IDs = intellectual disabilities; KS = Kabuki syndrome; LCNEC = large-cell neuroendocrine carcinoma; MALT = mucosa-associated lymphoid type; NOPHO = Nordic society of Paediatric Haematology and Oncology; RCC = renal cell carcinoma; TSC = tuberous sclerosis complex.

Most case reports involved adults (9/11), with a mean age of 36 years (SD = 13.56; range = 23–66). The remaining two case reports involved children (i.e., younger than 18 years), with one diagnosed with cancer twice, at the ages of 3 and 6 years, and a 17-year-old. Most of the case reports did not specify the patients' level of IDs (7/11) but commonly involved individuals with Down syndrome (5/11). The remaining articles reported different ID-associated syndromes, stated that the IDs resulted from brain damage caused by a varicella encephalitis virus, or did not specify a cause. Most articles involved various forms of carcinoma (5/11) and leukemia (2/11); the remaining articles discussed a spinal tumor, thyroid lymphoma, lung cancer, and a case of pericardial mesothelioma (i.e., a rare heart tissue cancer). To summarize, most articles described cancer pain resulting from carcinomas in adults with IDs, especially Down syndrome, often with an unspecified level of IDs.

Cancer Pain Description Themes

From the articles reviewed, three main themes regarding cancer pain in PWIDs were identified. Table 3 shows the characteristics of the 11 accepted articles, with quotations of the exact pain descriptions (for a summary of patient characteristics within each theme, see Appendix Table 1).

Cancer Pain in Symptom Presentation. Articles were included in the *cancer pain in symptom presentation* category if a patient presented at, or was admitted to, hospital due to pain, or if pain was the revealing symptom of cancer. The majority of the reviewed articles described pain at symptom presentation (9/11). Of these, the pain was usually in adults (7/9) with an unspecified level of IDs (7/9) and Down syndrome (5/9), who were later diagnosed with a variety of cancers.

The majority of case reports were not specific about pain at presentation, with two reports merely describing pain location.[49,50,55] Other case reports additionally described pain duration: 24 hours,[46,53] two weeks,[48] two to three months,[52] or four to five months,[47,51] indicating that several individuals had been in pain for weeks or months before presenting at hospital with pain. Of the six articles that were either unspecific regarding pain duration or reported pain durations of two weeks or more, four passed away,[48,50–52] with cancer only diagnosed at autopsy in two cases.[48,50] Kaako and Kolade's article[51] was the only report that contained greater detail on cancer pain at presentation (Table 3). Details of lower back pain in a 25-year-old man with an unspecified level and cause of IDs were described in depth, including the consistency and intensity of pain over the four months before presentation. It was not stated exactly how this level of detail was attained. A large-cell neuroendocrine carcinoma of the lung in the advanced stage was discovered, with metastasis to the spine causing lower back pain. This late diagnosis resulted in immediate admittance to palliative care and was related to caregivers not acting on pain symptoms soon enough. The authors discuss the importance of recognizing and taking signals of pain seriously in PWIDs.[51]

Cancer Pain Communication. The *cancer pain communication category* included five articles (5/11) that describe how the patient expressed pain (i.e., with behavioral or verbal signals) or describing difficulties in pain communication. The pain was usually in adults (4/5) with an unspecified (3/5) or severe (2/5) level of IDs, with unspecified causes of IDs (2/5) or ID-associated syndromes (3/5), and who were diagnosed with carcinomas (4/5) or lung cancer.

Three articles, all of which did not state level of IDs, described the patients' pain behavior signals, such as body position, impaired movement, and responses to examination.[46,51,53] Gil and colleagues[53] stated that the patient showed "symptoms of pain" when pressure was applied during examination, without describing what these symptoms were (p. 1). Two other case reports described difficulties in the communication of pain signals in people with severe levels of IDs,[13,54] with one also stating that this contributed to late diagnosis and immediate admittance to palliative care.[13]

Cancer Pain Assessment and Treatment. Finally, articles in the *cancer pain assessment and treatment* category described how pain changed during cancer treatment (e.g., increased or decreased) or described how pain was assessed or treated (i.e., which measurement tools and medications were used). Two articles described pain assessment and treatment (2/11), both in adults with severe levels but unspecified causes of IDs, who were diagnosed with lung cancer and oral cancer.

Both articles also featured in the cancer pain communication category, demonstrating overlap between these themes when an individual has severe levels of IDs and thus communication issues. In 2013, Satgé and colleagues[54] described the necessity of developing an individualized pain rating scale due to the patient's poor communication but did not state whether this was effective or what pain treatments were used. In 2008, Tuffrey-Wijne, Curfs, and Hollins[13] stated that morphine was used to control and treat pain in a palliative care patient, while also describing difficulties experienced by caregivers in administering this treatment due to the patient's poor communication (Table 3).

Table 4

Respondents' Methods for Measuring (in Gray) and Treating Cancer Pain in People With Intellectual Disabilities (IDs)

Methods for Measuring or Treating Cancer Pain	Used?[a] ($n = 63$)		In Which Phase of Cancer Development?				Effective?			
	Yes	No	Early	Advanced	Palliative	Does not apply	Yes	Somewhat	No	Does not apply
Individual pain behaviors/ knowing the patient	58 (92.06)	5 (7.94)	n/a	n/a	n/a	n/a	40 (68.97)	17 (29.31)	1 (1.72)	0 (0.00)
Using standard pain behavior observation lists	42 (66.67)	21 (33.33)	n/a	n/a	n/a	n/a	13 (30.95)	25 (59.52)	4 (9.52)	0 (0.00)
Self-reports by patient	32 (50.79)	31 (49.21)	n/a	n/a	n/a	n/a	11 (34.38)	19 (59.38)	4 (12.50)	0 (0.00)
Other[b]	16 (25.40)	47 (74.60)	n/a	n/a	n/a	n/a	10 (62.50)	6 (37.50)	0 (0.00)	0 (0.00)
Strong opiates (e.g., morphine, methadone)	54 (85.71)	9 (14.29)	1 (1.85)	14 (25.93)	38 (70.37)	1 (1.85)	47 (87.04)	6 (11.11)	0 (0.00)	0 (0.00)
Acetaminophen/paracetamol	51 (80.95)	12 (19.05)	41 (80.39)	7 (13.73)	3 (5.88)	0 (0.00)	26 (50.98)	22 (43.14)	3 (5.88)	0 (0.00)
NSAIDs (e.g., ibuprofen, diclofenac, naproxen)	44 (69.84)	19 (30.16)	18 (40.91)	24 (54.55)	2 (4.55)	0 (0.00)	16 (36.36)	26 (59.09)	2 (4.55)	0 (0.00)
Weak opiates (e.g., codeine, tramadol, fentanyl)	44 (69.84)	19 (30.16)	2 (4.55)	37 (84.09)	5 (11.36)	0 (0.00)	26 (59.09)	18 (40.91)	0 (0.00)	0 (0.00)
Without medication[c]	40 (63.49)	23 (36.51)	14 (35.00)	8 (20.00)	12 (30.00)	6 (15.00)	16 (40.00)	22 (55.00)	0 (0.00)	2 (5.00)
Without medication[d]	38 (60.32)	25 (39.68)	20 (52.635)	8 (21.05)	6 (15.79)	4 (10.53)	12 (31.58)	24 (63.16)	2 (5.26)	0 (0.00)
Without medication[e]	33 (52.38)	30 (47.62)	11 (33.33)	10 (30.30)	10 (30.30)	2 (6.06)	10 (30.30)	21 (63.64)	1 (3.03)	1 (3.03)
Medications for neuropathic pain	22 (34.92)	41 (65.08)	3 (13.64)	13 (59.09)	6 (27.27)	00.00)	8 (36.36)	13 (59.09)	1 (4.55)	0 (0.00)
Other[f]	13 (20.63)	50 (79.37)	3 (23.08)	2 (15.38)	3 (23.08)	5 (38.46)	5 (38.46)	2 (15.38)	0 (0.00)	6 (46.15)

Frequency and percentages (%) for effectiveness of each method and phase in which treatment was applied only for respondents who had used each method ($n = 63$).
Table ordered with most frequently used methods first.

[a] Multiple answers permitted.

[b] Caregivers' reports, trial basis analgesia, and self-report facial scales.

[c] Physiotherapy or aids (e.g., seat cushion, other mattress).

[d] Distraction and/or reassurance.

[e] Heat/cold, massage, and/or music.

[f] Combinations of multiple treatments or emotion-oriented care, as well as responses explaining that the respondent is not a physician so did not use any pain treatment.

Survey of Health Care Professionals

Sample Characteristics. In total, 63 of the 102 health care professionals that responded to the online survey had some experience with cancer in PWIDs (61.8%), of which the most common occupation was a physician for PWIDs (42.9%, see Appendix Table 2). These 63 respondents then answered a series of cancer pain–related questions. When questions permitted multiple answers, the percentage of the 63 professionals who responded affirmatively to each answer is given.

Cancer Pain Experience

According to respondents, pain is the symptom that ultimately leads to the diagnosis of cancer in 36.6% of cases (SD = 29.2%, range = 0%–100%). In addition, 34.2% of respondents believed that organ cancers (e.g., lung, intestine, liver) were the most painful forms of cancer for PWIDs. However, another frequent response (31.8%) was that they did not have enough experience to make a judgment. Several respondents indicated that cancer pain does not differ from other forms of pain in PWIDs (30.2%), whereas others suggested it was either more (19.1%) or less severe (20.6%) than other forms of pain.

Fifteen of 63 respondents stated that they could not compare cancer pain in people with and without IDs due to lacking experience with both groups (23.8%). Other respondents stated that cancer pain seems less severe in PWIDs (20.6%). However, notably, 10 respondents wrote that communication and signaling of cancer pain was more difficult or different in those with IDs compared to those without. A further eight wrote that assessment of cancer pain was more difficult, and six wrote that cancer pain was experienced differently in PWIDs compared to those without.

Cancer Pain Assessment and Treatment

Most professionals stated that observations made by themselves or other health care professionals usually identified cancer pain in PWIDs (90.5%). Observations of behavior changes by family (55.6%) and self-reports by the patient (31.8%) were the next most frequent recognition methods used. As displayed in Table 4, 54 professionals usually measured cancer pain by knowing the patient's individual pain behaviors (85.7%) and said it was effective (69%).

Most respondents reported use of strong opiates (85.7%) and paracetamol (81%; Table 4). Respondents usually employed strong opiates during palliative cancer care (70.4%) and stated that they were generally effective in relieving cancer pain in PWIDs (87%). By contrast, paracetamol was typically used in the early phases of cancer (80.4%), with 51% stating the treatment was effective. Several respondents commented that they use a variety of drugs or therapies to treat cancer pain in PWIDs, including alternative therapies such as massage, music, physiotherapy, and distraction.

Challenges in Clinical Practice

The most common challenge experienced by the respondents was patient communication and cooperation (92.1%), followed by pain signaling (87.3%). Other prominent challenges included the medical complexity of PWIDs (77.8%), assessment of pain (76.2%), and lack of research (65.1%). Appendix Tables 3 and 4 show full lists of experienced challenges and anonymous case examples given by respondents.

Finally, respondents were asked to suggest future research avenues that would be of value to them. Dominant themes included research into pain signaling, recognition, assessment, communication, and treatment. Validation of scales and tools for pain assessment and to inform patients about their illness and treatment options was suggested. One respondent clarified that these tools should be easy to use, short and concise, longitudinally applicable, and focused on different levels of IDs. Respondents desired step-by-step guidance through all phases of a cancer's development (i.e., from screening to palliative care). A final future research suggestion involved improving understanding of the distinction between pain, anxiety, and fear in PWIDs.

Discussion

Within 11 articles describing cancer pain in PWIDs, carcinomas were most frequently diagnosed. This may be due to the frequency of late cancer diagnosis in this population and the pains associated with carcinoma metastasis.[56–58] Most reviewed articles discussed cancer pain at symptom presentation but lacked depth beyond basic descriptions of pain location and duration. Only Kaako and Kolade[51] gave more detailed descriptions and discussed late diagnosis due to caregivers' slow reaction to pain symptoms. Cancer pain was related to communication in five of the articles, with some identifying it as an issue resulting in difficulties recognizing pain and others providing short descriptions of patients' pain behaviors. Two articles discussed assessment and treatment of cancer pain, both doing so only briefly, without reporting pain treatment effectiveness. To summarize, literature discussing cancer pain in PWIDs does exist but is limited. We found only a small number of case reports in which, despite good overall quality, the descriptions of cancer pain were largely unspecific and brief. Possible explanations for our

Table 5

Recommendations From Surveyed Health Care Professionals With Support From Surrounding Literature and Future Research Suggestions to Improve Recognition, Assessment, and Treatment of Cancer Pain for People With Intellectual Disabilities (PWIDs)

Areas of Improvement Related to Cancer Pain in PWIDs	Recommendations From Survey of Health Care Professionals		Support for Recommendations		
	Broad	Specific	Present systematic review	Guidelines and research in surrounding fields	Future Research Suggestions
Recognition	Caregivers are vital for noticing behavioral changes	• Facilitate communication between all involved • Possible pain signaling should be taken seriously • Be aware of functional deterioration (e.g., people with IDs may continue work and hobbies despite pain)	• Importance of behavioral signals due to communication issues in people with IDs[13,54] • Only a few articles described the behavioral signs[46,51] • Late cancer diagnosis can result from not acting on a patient's pain signaling[51]	• Observation of pain and discomfort related behaviors is recommended to recognize pain in the cognitively impaired, due to issues of communication[31,61] • Determination of pain behaviors universal for people with IDs is still not clear, so involvement of those who know the patient well is important to individualize pain observations[21,60] • Try to find a way to optimally communicate with the patient and those involved[62,69] • Atypical pain responses may be misinterpreted as challenging behavior or attributed to the person's IDs, such as self-injurious behavior[59,60,70,71] • "Ensuring that the person's baseline presentation is understood and recorded helps staff to identify if the person is experiencing pain."[72] (p. 37)	• Qualitative survey of people with IDs and cancer, as well as their family and carers. With the specific aim to understand how cancer pain is recognized and experienced. • Development of educational tools for families and caregivers of people with IDs about pain as a symptom of cancer.
Assessment/ measurement	Make extensive individualized pain signaling lists	Know about the patient's common pain behaviors and signals	Satgé and colleagues[54] individualized a pain assessment observation list to their patient	• Individualized approach advocated for pain management in people with IDs[30,60,72,73] • Create pain profiles in cooperation with patients, family, and caregivers. Save in electronic files and update[60,61] • Learn about the patient's past pain experiences (e.g., responses to pain, interventions, and their effectiveness) as well as their comprehension of pain. Consider the patient's level of functioning, communication abilities, physical and psychological health comorbidities[60,62]	Validation of practical tools for the individualized assessment of pain in people with IDs (e.g., 75). Tools should be applicable to the combination of acute and chronic pain states found in cancer and should be adaptable to individuals[30,60,74]

(*Continued*)

Table 5
Continued

Areas of Improvement Related to Cancer Pain in PWIDs	Recommendations From Survey of Health Care Professionals		Support for Recommendations		
	Broad	Specific	Present systematic review	Guidelines and research in surrounding fields	Future Research Suggestions
Assessment/ measurement	Conduct a thorough examination if pain is signaled or suspected	Examine for causes of pain Consider cancer on the list of possible diagnoses Examine under anesthesia if the patient is continuously uncooperative	Cancer was not considered during the initial diagnosis stage in several articles[48,50]	• Assume that what would bring you pain would also bring a patient with IDs pain[62] • People with IDs can suffer the same "neurological, physiological, psychological, and emotional consequences of pain"[61] (p. e44). • Overall deaths from cancer in the IDs population were not significantly different from the general population, despite the distribution of cancer sites being different. Therefore, cancer should be considered during diagnosis[75]	Awareness campaigns in hospitals and at General Practitioners that cancer should be considered in this population.
Treatment/ management	Use appropriate pain relief and evaluate treatment outcome	Be aware that you may underestimate the level of pain, so consider both your pain level estimation from observation, the type of cancer, and the stage of cancer See general population guidelines Use trial analgesics Communicate with the patient and family in assessment of pain to evaluate treatment outcome	Difficulties with delivering morphine to a patient: when to give extra doses and how to give it when the patient is unable to swallow[13]	• Involve patient, family, and caregivers in the creation of an individualized pain management plan[60,62] • Do not wait until the patient is in pain (act preventively), give medication according to a fixed schedule, adjusting dose to pain assessment[54] • Consider polypharmacy, physical and psychological comorbidities, level of IDs, and possible differences in metabolism of analgesics[76], as well as the patient's desired outcomes and quality of life[60] • Use the WHO analgesic pain ladder for chronic pain[60] • It is useful to consult pharmacists, the Dutch palliative care guidelines for people with IDs[62], and online databases (e.g., https://about.medicinescomplete.com/) for known drug-to-drug interactions.	Investigations into drug-to-drug interactions of medications for cancer, pain, and preexisting medications for comorbidities.

limited findings are as follows: strict inclusion criteria, insufficient focus, or insufficient knowledge on cancer pain in PWIDs.

The strict criterion used in the present systematic review (i.e., all three terms in the abstract) was beneficial because it revealed that cancer pain in PWIDs is a topic lacking specific and comprehensive research. Nevertheless, future research may benefit from a more lenient inclusion criterion (i.e., all three terms found in the main text). We suggest that this is first attempted by focusing on a specific type of cancer related to pain, such as bone cancer,[58] to provide in-depth analysis and reduce the workload that this more lenient criterion may produce. More valuable research would include wider empirical studies, as outlined in the recommendations below.

A second explanation could be that authors did not intend to describe patients' pain symptoms when writing case reports. Despite some authors demonstrating awareness of the importance of cancer pain in PWIDs,[51] generally most articles appeared to have insufficient focus on this topic. Third, brief cancer pain descriptions could be due to authors having insufficient knowledge of cancer pain in PWIDs. Communication issues[13,54] relate to *diagnostic overshadowing*, in which problem behaviors are mistaken as being due to the patients' IDs rather than signals of pain.[59] These difficulties may result from insufficient knowledge on the experience and expression of pain in PWIDs. Clear assessment and thus clear descriptions of pain are then hindered.

Whether the limited amount of research and brief descriptions of cancer pain in the systematic review are due to insufficient levels of knowledge or merely insufficient levels of focus on this topic is unclear, as both remain plausible. In either case, understanding gained from the literature is limited and issues relating to this topic will continue.

Assessment of Cancer Pain

Eight of the professionals in the survey suspected that apparent reduced pain severity in PWIDs might be due to difficulties in communication and assessment of pain. Some respondents commented on their own low knowledge of behavioral pain signals in PWIDs (see Appendix Table 4: clinical situation 7). However, knowing the patient and their individual behaviors was reported to be most helpful for recognizing and assessing cancer pain in PWIDs, which corresponds to previous literature.[8,60] Still, the present investigation indicates gaps in literature and clinical practice regarding effective recognition and assessment of cancer pain in PWIDs. Difficulties assessing cancer pain is a prominent issue, leading to serious consequences including the late diagnosis of cancer and difficulties with cancer pain treatment.

Treatment/ management	Treatment of pain should also include non-pharmacological methods	Consider what the individual enjoys or what comforts them as these activities or interventions could also relieve pain (Appendix Table 4: clinical situations 2 and 13) Consider what is best to improve the patient's quality of life. Increasing opiate doses may produce more side effects (Appendix Table 4: clinical situation 12)	A patient in palliative care was supported to do whatever he enjoyed in his last months, such as visiting a day center he had always enjoyed[13]	• Involve the patient and those around them to individualize nonpharmacological pain treatments[60] • An integrated approach to cancer pain management would include noninvasive techniques (e.g., rehabilitative and psychological interventions), as well as antitumor (i.e., surgery) and pharmacological treatments[31] • Consider changing seating position, cushions, massage, physiotherapy, and heat/cold[60]

ESMO = European Society for Medical Oncology; IDs = intellectual disabilities.

Late Diagnosis of Cancer

Cancer is less treatable if diagnosed at a late stage, leading to poorer prognosis.[9,12] The present literature review[13,48,50,51,54] and survey support suggestions from previous literature[7,9,10,20–22,61] that late diagnosis of cancer in PWIDs is a significant issue, due in part to difficulties regarding the assessment of pain symptoms, meaning that symptoms are underreported and the presence of cancer can be hidden. Multiple case report patients had pain for several weeks or months before they presented at hospital.[47,48,51,52] Three individuals had extensive metastasis[13,51,52] and cancer was only discovered during autopsy in two other individuals,[48,50] exhibiting the severity of late diagnosis. A possible cause could be communication issues[13] and caregivers not recognizing or acting on the pain soon enough.[51] This indicates overlap between *cancer pain communication* and *cancer pain at presentation* categories. Survey respondents stated that diagnosis using pain signaling is not straight forward, as communication, recognition, and assessment of pain were challenges they faced.

Undertreatment of Cancer Pain

We observed a general lack of focus on reporting the treatment of cancer pain within case reports. Excluding the surgical removal of tumors, only one article stated how cancer pain was treated (i.e., with morphine[13]). However, within this, caregivers did not know when to give the patient extra analgesia because the patient was unable to clearly indicate their pain. Difficulties treating cancer pain in PWIDs can also be seen in the survey results (Appendix Table 4).

In line with general population guidelines, the use of cancer pain treatments by survey respondents varied across the different phases of cancer, for example, strong opioids at late stages of cancer.[31] A few respondents use a variety of drugs or therapies to treat cancer pain in PWIDs, including alternative therapies. Recognizing the importance of combined therapies is critical due to potentially altered analgesic effectiveness and drug-to-drug interactions resulting from comorbidities in PWIDs.[62] Authors of the reviewed case reports may have known more about cancer pain treatment in PWIDs but did not report it as this was not the focus of their article.

Treatment of cancer pain in PWIDs was identified as a challenge experienced by over 60% of survey respondents. Issues of patient comorbidities, cooperation and understanding of treatments, as well as evaluation of treatment effectiveness were stated (Appendix Table 4, clinical situation 12 is a poignant example). Respondents' judgment of the effectiveness of cancer pain treatments in PWIDs in the present survey results should be viewed with caution due to inherent difficulties in pain assessment highlighted by the respondents themselves. Taken together, health care professionals appeared to know about appropriate cancer pain treatments and management but are also aware of knowledge gaps specific to PWIDs challenging their practice (i.e., mainly pain assessment). A major knowledge gap highlighted by both the literature review and survey was that no specific cancer pain management guidelines for PWIDs exist.

Limitations

A crucial limitation of the present investigation is that the survey results are opinions from only 63 Dutch professionals and therefore cannot be generalized to how cancer pain is recognized, measured, and treated worldwide. Yet, although low causality and generalizability are limitations, they clearly highlight necessity for further investigation into this topic. There are serious consequences to having low focus and knowledge on this topic, that is, late diagnosis of cancer and undertreatment of cancer pain. Thus, it is important to increase focus and knowledge on this topic to improve quality of life for PWIDs who have cancer. Several recommendations are provided below to combat the aforementioned issues.

Recommendations

Comprehensive cancer pain guidelines specifically for PWIDs are beyond the scope of the present article. However, Table 5 contains recommendations from surveyed health care professionals, supported by systematic review results and surrounding research, along with suggestions for future research avenues. Future development of guidelines for PWIDs would be valuable and might also be translatable to dementia due to comparable communication issues and alterations in pain-related neurophysiology.[12,31,63]

As pain discussions within case reports were largely unspecific and brief, we primarily recommend conducting a single-arm uncontrolled cohort study on cancer pain, after PWIDs and cancer. To differentiate it from a case series, such a study would require a set protocol, inclusion and exclusion criteria, standardized follow-up, and reported dropout numbers.[64] Building qualitative elements such as interviews into a cohort study would improve understanding of the experience of cancer pain for someone with IDs and cancer, also involving family and caregivers. The viewpoints of PWIDs will aid the development of cancer pain support that is suitable to and considerate of their needs.[65,66]

Conclusions

The present article intended to investigate what is known about cancer pain in PWIDs within scientific literature and clinical practice. A systematic review found only a limited number of case reports containing unspecific and brief descriptions of cancer pain in PWIDs. A survey of health care professionals indicated challenges in recognition, assessment, and treatment of cancer pain in PWIDs. In combination, the two investigations suggest that there is an insufficient level of knowledge and focus on cancer pain in PWIDs leading to continued difficulties with communication and cooperation, as well as recognition, assessment, and treatment of cancer pain. Expanding knowledge on cancer pain will become increasingly important as more PWIDs live to an age where the risk of cancer increases. Recommendations outlined here would aid earlier diagnosis of cancers in PWIDs as well as improve cancer pain assessment and treatment. This would ultimately increase quality of life for PWIDs who have cancer by reducing unnecessary suffering from pain.

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Appendix Table 1

Categories of Pain Descriptions in the Literature in People With Intellectual Disabilities (IDs) Who Have Cancer, From 11 Eligible Articles Found in the Systematic Literature Review

Categories of Pain Description	Number of Studies[a]	Case Report	Adult	Child	Down Syndrome	Other Causes of IDs	Borderline IDs Level	Mild IDs Level	Moderate IDs Level	Severe IDs Level	IDs Level Unspecified	Carcinoma	Leukemia	Other Form of Cancer
Cancer pain in symptom presentation	9	1,2,3,4, 6,7,8, 9,11	1,2,3, 6,7,8,11	4, 9	2,3,4,6,8	1 (i.e., FAP) 7 (cause unspecified) 9 (i.e., TSC) 11 (i.e., KS)	1	11	11	0	2,3,4,6,7,8,9	1,7,8,9	4,6	2 (i.e., thyroid lymphoma) 3 (i.e., pericardial mesothelioma) 11 (i.e., spinal ependymoma)
Cancer pain communication	5	1, 5,7, 9, 10	1,5,7, 10	9	0	1 (i.e., FAP) 5 (cause unspecified) 7 (cause unspecified) 9 (i.e., TSC) 10 (i.e., varicella encephalitis)	1	0	0	5,10	7,9	1,7,9,10	0	5 (i.e., lung cancer)
Cancer pain assessment and treatment	2	5,10	5,10	0	0	5 (cause unspecified) 10 (i.e., varicella encephalitis)	0	0	0	5,10	0	10	0	5 (i.e., lung cancer)

FAP = familial adenomatous polyposis; KS = Kabuki syndrome; TSC = tuberous sclerosis complex.

Article number: 1) Koorey et al., 2000[46]; 2) Yang et al., 2000[47]; 3) Sharaf El-Dean et al., 2004[48]; 4) Hellebostad et al., 2005[49]; 5) Tuffrey-Wijne et al., 2008[13]; 6) Hjorth et al., 2010[50]; 7) Kaako & Kolade, 2010[51]; 8) Purvey et al., 2010[52]; 9) Gil et al., 2013[53]; 10) Satgé et al., 2013[54]; 11) Roma et al., 2015.[55]

[a] Articles may contain multiple categories of pain descriptions. Most commonly addressed category is presented first.

Appendix Table 2

Respondents' Occupation and Level of Experience With Cancer in People With Intellectual Disabilities (IDs) ($N = 102$)

	How Often Have You Been Involved With Cancer in People With IDs?						
Respondent Occupation	Never, %	A Few Times, %	Several Times, %	Often, %	Total, %	Percentage of Total Respondents	Total With Experience, %
Physician for people with IDs	1 (3.6)	15 (53.6)	12 (42.9)	0 (0)	28 (100)	27.5	27 (42.9)
Behavioral expert	8 (42.1)	8 (42.1)	3 (15.8)	0 (0)	19 (100)	18.6	11 (17.5)
Dentist	18 (94.7)	1 (5.3)	0 (0)	0 (0)	19 (100)	18.6	1 (1.6)
Nurse or nurse specialist	2 (22.2)	3 (33.3)	3 (33.3)	1 (11.7)	9 (100)	8.8	7 (11.1)
Other occupation	4 (44.4)	2 (22.2)	3 (33.3)	0 (0)	9 (100)	8.8	5 (7.9)
Mentor	0 (0)	5 (71.4)	2 (28.6)	0 (0)	7 (100)	6.9	7 (11.1)
General practitioner	4 (57.1)	2 (28.6)	1 (14.3)	0 (0)	7 (100)	6.9	3 (4.8)
Palliative care consultant	0 (0)	0 (0)	2 (100)	0 (0)	2 (100)	2	2 (3.2)
Physiotherapist	2 (100)	0 (0)	0 (0)	0 (0)	2 (100)	2	0 (0)
Oncologist	N/A	N/A	N/A	N/A	N/A	0	0 (0)
Total	39 (38.2)	36 (35.3)	26 (25.5)	1 (1)	102 (100)	100	63 (61.8)

Table ordered on percentage of total respondents, followed by percentage of total respondents involved with cancer in people with IDs. No oncologists completed the survey. The "other" response included speech therapist, basic physician, physician's assistant, physician (previously general practitioner), services coordinator, dental hygienist, cluster manager, and a policy maker who is an acquaintance of a person with cancer and IDs.

Appendix Table 3

Challenges Regarding Cancer Pain in People with Intellectual Disabilities (IDs), with Notable Examples Specified by Respondents

Challenges Experienced	Yes	No	Suggested Solutions
Communication/cooperation with the patient	58 (92.06%)	5 (7.94%)	If a patient shows anxiety and incomprehension: coordinate communication with specialized caregiver
Pain signaling (e.g., inability to communicate, anxiety, subjective or ambiguous behavior)	55 (87.30%)	8 (12.70%)	Example given of a patient who walks with broken leg due to autism: check abnormal posture or behavior
Medical complexity of the target group	49 (77.78%)	14 (22.22%)	Education, multidisciplinary cooperation, use multiple protocols, check drug-to-drug interactions, consult specialists
Pain assessment (e.g., lack of validated tools, lack of objective measurement, distinction from anxiety/fear)	48 (76.19%)	15 (23.81%)	Create individual pain profiles, check comprehension of rating scales
Lack of research	41 (65.08%)	22 (34.92%)	Case studies, practice-based, long-term medication, specific syndromes
Pain treatment (e.g., unable to evaluate effectiveness, family involvement, uncooperative behavior, comorbidities)	40 (63.49%)	23 (36.51%)	Distraction, evaluate treatment effectiveness, check drug-to-drug interactions
Communication/collaboration with other health care workers	35 (55.56%)	28 (44.44%)	Frequent team evaluation about shared patient file, check cushions/shoes before increasing pain medication
Knowledge about differences between tumor profiles and prevalence of cancers in different genetic syndromes	35 (55.56%)	28 (44.44%)	Search for information on tumor profiles, treat pain is a separate symptom, provide further scientific research, education, and clinical lessons
Communication/collaboration with the patient's family	30 (47.62%)	33 (52.38%)	Involve family early and frequently: design pain signaling plan
Lack of clear national guidelines for cancer pain in people with IDs	24 (38.10%)	39 (61.90%)	This does not hinder treatment, would be beneficial to specify guidelines for people with IDs
Other knowledge about cancer in people IDs (e.g., fear, reactions to medications, laws)	24 (38.10%)	39 (61.90%)	Use palliative care specialists and a biopsychological model, increase awareness in health care specialists
Lack of (inter)national conferences/symposiums	22 (34.92%)	41 (65.08%)	Ask what the needs are, organize symposium
Knowledge of existing national guidelines	20 (31.75%)	43 (68.25%)	Update and distribute guidelines, clinical lessons, use experts
Lack of (inter)national taskforces	20 (31.75%)	43 (68.25%)	Increase interest, Dutch palliative taskforce is almost set up
Other (e.g., giving the patient more knowledge on cancer pain, anxiety reduction, increase awareness of pain)	5 (7.94)	58 (92.06%)	Adapt information for people with IDs, mentors/caregivers should accompany patient to physician

Frequency and percentage (%) of responses displayed in order of commonality, with most frequent or notable solutions posed by health care professionals displayed ($n = 63$).

Appendix Table 4

Additional Challenges and Anonymous Clinical Examples Experienced by Health Care Professionals

Challenge or Clinical Situation	Outcome and Suggested Solution
1) Patient with mild [IDs] and autism with gastric carcinoma, in addition to pain also had vomiting symptoms. She was always afraid that she would have to go to the hospital if she indicated complaints (such as pain). This made it difficult to assess whether she had (pain) complaints.	Solution was to have very frequent contact during visits of nurse and doctor, for just a chat/weighing, etc. and clinical assessment. Giving explanation on her level, why she has pain. Patient involved in this by, for example, making VAS with faces for her. In terms of pain treatment, I was fine with existing guidelines
2) Male, 50 years old, severe IDs and colon carcinoma with metastasis. Discovered by severe anemia. Pain relief with fentanyl seemed inadequate.	Attention was spent on the things that this man always did and liked. Pain relief was adapted to his daily rhythm: pain relief before an activity or care moment restored the daily rhythm, with a beneficial effect on the overall well-being. The last weeks were spent on things that improved quality of life for this man (e.g., car trips with his brother and sister).
3) Patient with Down syndrome is deteriorating, health care professional suspect dementia, but mentor indicates that it is something else. She sees this in small signs of pain.	Patient appears to have a brain tumor. He gets medication against the pain and finally comes to rest to pass away.
4) Mature man who cannot speak and is always in good health, eats worse, stands bent over, and has blood in feces. He doesn't tolerate physical examination. This is only possible under anesthesia, but parents refuse.	After a few months of muddling, an MRI is done under anesthesia, in which esophageal cancer is diagnosed. The man lives a few weeks with efficient pain medication in a pleasant atmosphere of warm care and dies peacefully.
5) Patient was in an advanced stage of esophageal cancer but indicated that he had no pain. Pain meant for him that he would receive medication and according to him, his mother had died from medication use.	Family saw that he had a lot of pain but the doctor only wanted to take action if the patient reported pain. Pain relief was delayed for months, which was a heavy last period for the patient. The family and supervisors should have taken symptoms more seriously.
6) Cancer is usually only discovered at a late stage, such as a testicular carcinoma in a man with Down syndrome and dementia who didn't want to be examined or touched. Severe behavioral problems that increased in the last months and were recognised as pain, for which he received paracetamol. Dental examination under anesthesia revealed testicular carcinoma with peritonitis carcinomas.	Detection could have been earlier if there had been a general physical examination under anesthesia. This could have been combined with a dental examination.
7) As a team we had a patient with mild IDs who communicated pain signals. Owing to too little knowledge about her pain behaviors and pain behaviors in mild IDs in general, we could not reveal the cause. GP sent her back several times with simple pain relief. After a few months and at the urging of us as a team due to our "gut feeling," she was eventually examined and diagnosed with cancer. Patient dies after a very short and intense sickbed.	What we needed and certainly would have helped, was more knowledge about her pain behaviors, pain history, better communication with family/legal representatives and general practitioner, and taking our "gut feeling" seriously.
8) Caregiver of patient feels alarmed due to weight loss, less eating, less activity, changes in the face and posture. Tumors are detected during medical examination.	Extensive individual pain signaling list is made and acted on it. Patient eats better and is more active.
9) The routine of daily life can be so important for patients that pain is ignored. A man with metastatic bone cancer went to work every day and just danced the night before his death: it didn't go that well anymore, but he found peace in the daily routine.	Be aware of functional deterioration such as changes during work activities and hobbies.
10) Patient with brain tumor who displays self-injury but has always done this. Pain is not clear, caregivers are divided in what to do.	Pain relief is given on trial and is effective.
11) An older man who spoke a few words had a suddenly deteriorating mood. He looked gloomy and angry, but did everything else and had in the first instance no physical complaints. No abnormalities were shown in blood tests, so he was treated for depression. The adjustments only slightly improved his mood. Further physical examination showed metastatic cancer, which must have been painful.	It would be useful if a more thorough physical screening could be done (especially also for cancer).
12) Patient has metastatic gastric carcinoma. Wears a fentanyl patch. Has a vasovagal reaction when he gets out of bed, so remains in bed. Gets pressure sores. He clearly states by means of the VAS score that he has pain (in his heels). Fentanyl patch dose was increased. Resulted in allodynia: he screamed from the pain while we only looked at his legs. Further increase in fentanyl patch dose caused severe breathing depressions and delirium.	You would normally not give extra morphine for pressure sores (unless they are real decubitus ulcers). Patient already reacted strongly to the fentanyl. Such things happen due to a lack of background knowledge about pain relief and how you assess a patient.
13) Female, multiple disabilities (low intellectual level), autistic behavior, could not talk in complete sentences, sleeps at home under a heavy blanket for a feeling of safety. Has leukemia: showed visible pain, shivered constantly, and said "ouch". She could not cope with the pain due to tiredness because she slept badly.	I put four blankets from the hospital on her. She became visibly calm, her face showed a more satisfying expression. When we brought her own blanket, she slept better and the pain medication was more effective. She stopped shivering with pain.

IDs = intellectual disabilities; VAS = Visual Analogue Scale.

Responses translated from Dutch by first and second authors: S.K. Millard and N.C. de Knegt.