













Recommendations for the surveillance of education and employment outcomes in survivors of childhood, adolescent, and young adult cancer: A report from the International Late Effects of Childhood Cancer Guideline Harmonization Group

Katie A. Devine, PhD, MPH ¹; Salome Christen, BSc, MA ²; Renée L. Mulder, PhD ³,
 Morven C. Brown, BSc (Hons), MSc ^{4,5}; Lisa M. Ingerski, PhD ^{6,7}; Luzius Mader, MSc, PhD ^{8,9};
 Emma J. Potter, BSc (Hons), PGCert¹⁰; Charlotte Sleurs, PhD ¹¹; Adrienne S. Viola, MPH, PhD ¹;
 Susanna Waern, BSc, PsychD, PGDip¹⁰; Louis S. Constine, MD^{12,13}; Melissa M. Hudson, MD ^{14,15};
 Leontien C. M. Kremer, MD, PhD³; Roderick Skinner, PhD, MB ChB (Hons), DCH^{5,16}; Gisela Michel, PhD ²;
 Jordan Gilleland Marchak, PhD ^{6,7}; Fiona S. M. Schulte, PhD ¹⁷; and for the International Guidelines Harmonization Group Psychological Late Effects Group

Educational achievement and employment outcomes are critical indicators of quality of life in survivors of childhood, adolescent, and young adult (CAYA) cancer. This review is aimed at providing an evidence-based clinical practice guideline (CPG) with internationally harmonized recommendations for the surveillance of education and employment outcomes in survivors of CAYA cancer diagnosed before the age of 30 years. The CPG was developed by a multidisciplinary panel under the umbrella of the International Late Effects of Childhood Cancer Guideline Harmonization Group. After evaluating concordances and discordances of 4 existing CPGs, the authors performed a systematic literature search through February 2021. They screened articles for eligibility, assessed quality, and extracted and summarized the data from included articles. The authors formulated recommendations based on the evidence and clinical judgment. There were 3930 articles identified, and 83 of them, originating from 17 countries, were included. On a group level, survivors were more likely to have lower educational achievement and more likely to be unemployed than comparisons. Key risk factors for poor outcomes included receiving a primary diagnosis of a central nervous system tumor and experiencing late effects. The authors recommend that health care providers be aware of the risk of educational and employment problems, implement regular surveillance, and refer survivors to specialists if problems are identified. In conclusion, this review presents a harmonized CPG that aims to facilitate evidence-based care, positively influence education and employment outcomes, and ultimately minimize the burden of disease and treatment-related late adverse effects for survivors of CAYA cancers. **Cancer** 2022;0:1-15. © 2022 The Authors. *Cancer* published by Wiley Periodicals LLC on behalf of American Cancer Society This is an open access article under the terms of the Creative Commons Attribution-NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

LAY SUMMARY:

- A multidisciplinary panel has developed guidelines for the surveillance of education and employment outcomes among survivors of childhood, adolescent, and young adult cancer.
- On the basis of evidence showing that survivors are at risk for lower educational achievement and unemployment, it is recommended that all survivors receive regular screening for educational and employment outcomes.

KEYWORDS: childhood, adolescent, and young adult cancer, education, employment, evidence-based guidelines, late effects, survivorship.

Corresponding Authors: Katie A. Devine, MPH, PhD, Rutgers Cancer Institute of New Jersey, 195 Little Albany St, New Brunswick, NJ 08903 (Katie.Devine@rutgers.edu). Fiona S. M. Schulte, PhD, University of Calgary, Calgary, Alberta, Canada (fmschul@ucalgary.ca).

¹Department of Pediatrics, Rutgers Cancer Institute of New Jersey, Rutgers, The State University of New Jersey, New Brunswick, New Jersey; ²Health Science and Health Policy, Department of Health Sciences and Medicine, University of Lucerne, Lucerne, Switzerland; ³Princess Máxima Center for Pediatric Oncology, Utrecht, the Netherlands; ⁴Population Health Sciences Institute, Newcastle University, Newcastle Upon Tyne, United Kingdom; ⁵Newcastle University Centre for Cancer, Newcastle Upon Tyne, United Kingdom; ⁶Department of Pediatrics, Emory University School of Medicine, Atlanta, Georgia; ⁷Aflac Cancer and Blood Disorders Center, Children's Healthcare of Atlanta, Atlanta, Georgia; ⁸Danish Cancer Society Research Center, Copenhagen, Denmark; ⁹Institute of Social and Preventive Medicine, University of Bern, Bern, Switzerland; ¹⁰The Royal Marsden Hospital, London, United Kingdom; ¹¹Department of Oncology, KU Leuven, Leuven, Belgium; ¹²Department of Radiation Oncology, University of Rochester Medical Center, Rochester, New York; ¹³Department of Pediatrics, University of Rochester Medical Center, Rochester, New York; ¹⁴Department of Oncology, St. Jude Children's Research Hospital, Memphis, Tennessee; ¹⁵Department of Epidemiology and Cancer Control, St. Jude Children's Research Hospital, Memphis, Tennessee; ¹⁶Department of Paediatric and Adolescent Haematology/Oncology, Great North Children's Hospital, Newcastle Upon Tyne, United Kingdom; ¹⁷Division of Psychosocial Oncology, Department of Oncology, Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada

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The first 2 authors contributed equally to this article.

The last 3 authors contributed equally to this article.

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INTRODUCTION

The current success in the treatment of childhood, adolescent, and young adult (CAYA) cancers is evident with overall survival rates of ~85%,¹ and it has resulted in a steadily growing population of long-term survivors. There are currently more than 1,000,000 survivors of CAYA cancer across North America² and Europe.³ Survivors of CAYA cancers are at risk for significant medical late effects (eg, secondary malignancies) and psychological late effects (eg, anxiety).⁴ In addition, survivors may experience long-term functional limitations, including poor educational achievement and employment difficulties.⁵ However, the literature is conflicting about whether survivors of CAYA cancer fare worse with respect to their education and employment outcomes than individuals who have not had cancer. As a result, long-term follow-up guidelines developed independently for North America⁶ and Europe⁷⁻⁹ are inconsistent with respect to their recommendations for educational and vocational surveillance.

Educational achievement and employment outcomes are critical indicators of the long-term quality of life for survivors.^{10,11} Specifically, survivors who do not complete the same levels of education as their peers are at a significant disadvantage for future employment opportunities.¹² Ultimately, the ability of survivors of CAYA cancer to achieve their academic and vocational goals and thrive as productive members of society may be significantly compromised. Thus, the development of evidence-based consensus recommendations for the surveillance of education and employment is critical to facilitate opportunities for preventive and remedial interventions.

The aims of this initiative under the umbrella of the International Guidelines Harmonization Group (IGHG), therefore, were to develop evidence-based guidelines to harmonize the recommendations for education and employment surveillance in survivors of CAYA cancer diagnosed before the age of 30 years.

MATERIALS AND METHODS

A detailed description of the IGHG methodology is provided elsewhere.¹³ The surveillance recommendations for education and employment were prepared by a multidisciplinary international group of 17 individuals representing expertise in pediatric oncology, survivorship, psychology, epidemiology, nursing, radiation oncology, and guideline methodology. Final consensus recommendations resulted from discussions with a wider group of 20 experts and 5 survivor representatives with lived experience (Supporting Table 1).

Scope

This clinical practice guideline (CPG) is intended to inform survivors, their families, and health care providers about education and employment outcomes for survivors of CAYA cancer; to identify risk factors for poorer outcomes; and to identify possible interventions to improve those outcomes.

Comparison of Existing Guidelines

In a first step, we evaluated concordances and discordances among existing guidelines from the Children's Oncology Group,⁶ the Dutch Childhood Oncology Group (DCOG),⁷ the Scottish Intercollegiate Guidelines Network,⁸ and the United Kingdom Children's Cancer Study Leukaemia Group Late Effects Group⁹ regarding the surveillance recommendations for psychosocial issues. In cases of discordance between the guidelines, we formulated clinical questions to achieve consensus about 5 key issues:

1. Who needs surveillance?
2. At what age or time from exposure should surveillance be performed?
3. At what frequency should surveillance be performed?
4. What surveillance modality should be used?
5. What should be done when abnormalities are found?

Search Strategy and Selection Criteria

We performed systematic literature searches in PubMed (MEDLINE) on October 27, 2016, and February 11, 2021, to identify available evidence. The search terms were devised by Cochrane Childhood Cancer and included *childhood cancer*, *survivors*, *late effects*, *education*, and *employment* along with synonyms and variations used to search the database (the detailed search strategy is provided in Supporting Tables 2a and 2b). The DCOG previously used the same search strategy for its guidelines for articles published from 2006 to 2009 to update the meta-analysis of de Boer (2006).^{7,14} Therefore, we updated their work and searched PubMed from January 2009 to February 11, 2021. The filters *humans* and *English language* were applied.

First, 2 authors independently screened each title and abstract and excluded irrelevant articles (K.A.D., S.C., F.S., E.J.P., M.C.B., C.S., and S.W. participated in the title/abstract screening). Next, the same pair of authors independently assessed the eligibility of the full-text articles (K.A.D., S.C., F.S., E.J.P., M.C.B., C.S., and S.W. participated in the full-text screening). A third reviewer (K.A.D. or F.S.) resolved discrepancies.

The inclusion criteria were as follows: 1) a diagnosis of childhood, adolescent, or young adult cancer; 2) $\geq 75\%$ of the study participants were younger than 30 years at their cancer diagnosis; 3) $\geq 50\%$ of the study participants were 2 or more years from their diagnosis; 4) the main outcome was education or employment; and 5) the sample size was 20 participants or greater (detailed inclusion and exclusion criteria can be found in Supporting Table 3). To answer clinical question 1, articles had to have included a control group to determine the risk in comparison with controls. To answer clinical question 2, articles had to use multivariable risk factor analyses to identify the risk associated with exposures among survivors. Relevant information from the articles was abstracted into evidence tables. The authors assessed the quality of the included articles using evidence-based methods provided by Cochrane Childhood Cancer (Supporting Table 4). The authors then formulated conclusions from the evidence to answer the clinical questions and graded the quality of the evidence according to evidence-based methods (Supporting Table 5).^{13,15} Finally, authors updated the conclusions of evidence from the DCOG guideline with the new conclusions from our search.

Translating Evidence Into Recommendations

We based the development of our recommendations on the evidence gathered, clinical judgments, costs, the benefits versus harms of the surveillance intervention, and the need to maintain flexibility of application across different health care systems. Decisions on recommendations were made through group discussions and unanimous consensus. The strength of the recommendations for the surveillance of education and employment were graded according to published evidence-based methods (Supporting Table 6).¹⁶ The harmonized recommendations for the surveillance of education and employment were critically appraised by 5 survivor representatives via telephone meetings and electronic communication and finalized after consideration of their comments (Supporting Table 1).

RESULTS

The 4 existing CPGs for psychosocial issues were concordant in designating all survivors at risk for poor psychosocial outcomes, with survivors of central nervous system (CNS) tumors or those exposed to CNS-directed therapy designated as high risk. The 4 guidelines were discordant in all other areas (Supporting Table 7).⁶⁻⁹ On the basis of the discordances, we formulated 3 clinical questions

to investigate the evidence in more detail (Supporting Table 8):

Clinical question 1: What is the risk of poor educational/employment outcomes?

Clinical question 2: What are the risk factors for poor educational/employment outcomes?

Clinical question 3: Which interventions can improve educational/employment outcomes among childhood cancer survivors?

We also present the evidence tables (Supporting Table 9) and detailed conclusions of the evidence (Supporting Table 10) as supporting information.

Eighty-three of the 3930 articles identified (3897 through database searching and 33 from the DCOG guideline) were included; 82 were original studies, and 1 study from the DCOG guideline was a meta-analysis. The 82 original studies came from 17 countries (Asia, $n = 6$; Europe, $n = 38$; and North America, $n = 38$). Fifty-two of the 83 articles were eligible from database searching, with a total sample of 41,074 survivors of CAYA cancer. The other 31 articles were eligible from the DCOG guideline. Thirty-four studies reported only educational outcomes, 34 studies reported both educational and employment outcomes, and 15 studies reported only employment outcomes (Fig. 1). The conclusions of evidence and the recommendations are presented in Tables 1 to 3.

Education

What is the risk of poor educational outcomes?

Educational achievement

As a group, survivors of CAYA cancers are at risk for lower educational achievement with respect to comparison groups (Level C),¹⁷⁻⁶² and fewer survivors than comparisons have a university or college education (Level B).^{17,18,21,22,24-27,29,31,35-37,47,49,58,63-69} Specifically, we found 46 studies that compared educational achievement in survivors to that of siblings, peers, or the general population.¹⁷⁻⁶² In comparison with control groups, the educational attainment of survivors was lower in 19 studies (13 independent study samples),^{17,18,26,32,35-37,49-59} higher in 4 studies,^{21,22,30,33} and not significantly different in 23 studies (20 samples)^{19,20,23-25,27-29,31,34,38-48,61,62} (Supporting Table 11). Among 23 studies that evaluated the proportion of university/college graduates among survivors versus comparisons^{17,18,21,22-27,29,31,35-37,47,49,58,63-69} the proportion was lower in 12 studies (7

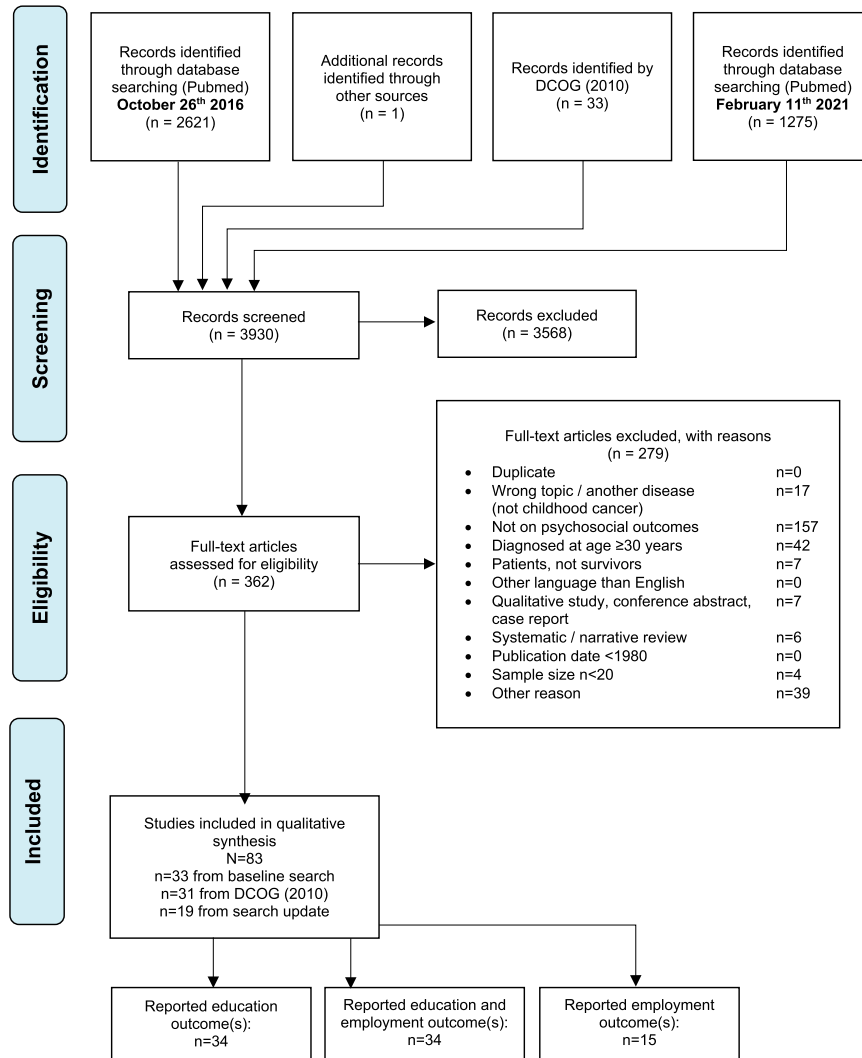


FIGURE 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flowchart. DCOG indicates Dutch Childhood Oncology Group.

samples),^{17,18,26,35-37,49,58,63,66,67,69} higher in 1 study,²¹ and not significantly different in 10 studies (6 samples) (Supporting Table 11).^{22,24,25,27,29,31,47,64,65,68} Survivors of CNS tumors were at increased risk for lower educational achievement^{26,57,60,61} and for not getting a college/university degree^{37,58,63,67} (both Level B; Table 1 and Supporting Table 10).

Educational delays

As a group, survivors are at risk for delays in completing their education (Level A)^{29,31,32,34,60,70-72} and for repeating a grade (Level B)^{20,38,70,73-78} in comparison with control groups. Specifically, in survivors versus siblings, peers, or the general population, an increased risk of academic delay was reported in 8 studies,^{29,31,32,34,60,70-72}

and an increased risk of grade repetition was reported in 6 studies.^{38,73,74,76-78} Three studies found no significant differences in grade repetition between survivors and comparison groups^{20,70,75} (Supporting Table 11). Survivors of CNS tumors were at increased risk for a delay in completing their education in comparison with controls (Level C)⁶⁰ (Table 1 and Supporting Table 10).

Participation in mainstream education

We found that survivors are less likely to attend mainstream education than controls (Level B; Table 1 and Supporting Table 10).^{31,36,50,51,75,77,79} Specifically, 5 studies reported that survivors were more likely to attend nonmainstream education than siblings or the general population,^{36,50,51,75,77} and 1 study reported no

TABLE 1. Overall Conclusions of the Evidence

1. What Is the Risk of Poor Educational/Employment Outcomes?				
What is the risk of poor educational outcomes in childhood, adolescent and young adult (CAYA) cancer survivors?				
Survivors are at risk for lower educational achievement vs. controls	Level C ¹⁷⁻⁶²			
Fewer survivors than comparisons have university/college education vs. controls	Level B ^{17,18,21,22,24-27,29,31,35-37,47,49,58,63-69}			
Survivors are at risk for completing their education with a delay vs. controls	Level A ^{29,31,32,34,60,70-72}			
Survivors are at risk for repeating a grade vs. controls	Level B ^{20,38,70,73-78}			
Survivors are less likely to attend mainstream education vs. controls	Level B ^{31,36,50,51,62,69,75,77,79}			
CNS tumor survivors are at increased risk for lower educational achievement, not getting a college/university degree, or completing their education with a delay vs. controls	Level B-C ^{26,37,57,58,60,61,63,67}			
What is the risk of poor employment outcomes in CAYA cancer survivors?				
Increased risk of unemployment in CAYA cancer survivors vs. controls	Level B ^{14,17,19,21,22,23,24,25,28,31,32,33,34,35,36,37,38,52,53,59,61,62-69,71,84-96}			
CNS tumor survivors are at increased risk of unemployment vs. controls	Level A ^{14,37,61,63,67,87,88,95}			
2. What Are the Risk Factors for Poor Educational/Employment Outcomes?				
Treatment or Demographic Factor	Lower Educational Achievement ^s	Repeating a Grade ^s	Special Education ^s	Unemployment ^s
Treatment-related risk factors				
Surgery	Yes [†] C after an amputation ⁸⁰ No ^{B,d} 26,29	—	—	Yes [†] C after surgery ^d 22,91,97, after an amputation or limb-saving surgery vs. none ^C 80,84,85 and cerebral surgery ^C 84,85
Chemotherapy	Yes [†] C after treatment with alkylating agents ⁸⁰ Yes [‡] C after treatment with anthracyclines ⁸⁰ No ^{B,e} 17,26,29,83	—	No ^C after treatment with intrathecal methotrexate ⁷⁵	Yes [†] C after treatment with alkylating agents or vincristine ⁸⁰ No ^{B,e} 17,22,91,97
Radiotherapy (any field)	—	—	No ^C 75	No ^{B,f} 17,22,91,97
Cranial radiotherapy (CRT)	Yes [†] C 17,26,29,37,81,83	No ^{C,k} 73	—	Yes [†] A,j 14,37,81,84,85,88,91
Stay at an intensive care unit	Yes [†] C 22	—	—	—
Stem cell transplantation	No ^C 29	No ^B 73,74	—	No ^B 22,97
Treatment duration	No ^C 22	—	—	No ^C 22
Clinical risk factors				
Age at diagnosis	Yes [†] C,m 17,18,22,26,29,32,81,83	Conflicting ^{73,74}	—	Conflicting ^{17,22,61,81,84,91}
Time since diagnosis	No ^C 17	—	—	Yes [†] C 17,85
Diagnosis	Yes [†] B in CNS tumor survivors ^{17,22,24,26,29,61} Yes [†] C in leukemia survivors treated with CRT ^{24,26} Yes [‡] C in Ewing's sarcoma survivors ⁸⁰	No ^C 74	Yes [†] C for all diagnoses ⁷⁵	Yes [†] B in CNS tumor survivors ^{17,24,61,91} Yes [†] C in osteosarcoma survivors ⁹ 81 No ^B 17,22,97
Tumor location	Yes [†] C in upper vs. lower extremity sarcoma survivors ⁸⁰	—	—	No ^C 81
SMN or recurrence	Yes [†] C 17,22,26,29	No ^C 73	—	Yes [†] B 22,85,91
Late effects	Yes [†] C with late effects ^h 17,81, with psychological distress ^C 19, epilepsy/seizures ^C 26, or visual/hearing problems ^C 22,26,81 Yes [†] A with neuropsychological functioning deficits ^{19,22,82}	No ^{C,e} 74	—	Yes [†] A with late effects ^h 17,81,97, or with neuropsychological functioning deficits ^{19,22,39,82,98} Yes [†] B with psychological distress ^{19,39,98} , epilepsy/seizures ^{14,91} , or vision problems ^{81,91} Yes [†] C with hearing problems ⁹¹
Physical disability	—	—	—	Yes [†] B 14,39
Quality of life	—	—	—	Yes [†] C,i 98
Demographic risk factors				
Sex	Yes [†] C for females ^{17,19,22,26,29,61,80,81}	Yes [†] C for males ⁷³	No studies	Yes [†] B for females ^{14,17,19,22,61,80-82,84,85,88,91,97}
Age	Yes [‡] C with older age at follow-up ^{17,19,22,26,29,80,81}	—	—	Yes [†] C for survivors with younger age at follow-up ^{14,17,19,22,80-82,84,85,91,97}
Race/ ethnicity/ immigration status	Yes [†] A for non-white survivors, and survivors with a migration background ^{17,29,80}	—	—	Yes [†] C for non-white survivors, and survivors with a migration background ^{17,80,84,85}
Educational achievement	—	—	—	Yes [†] A with lower educational achievement ^{14,17,97}
Parents' education	Yes [‡] B with parents' higher level of education ^{29,61}	Yes [†] B with parents' lower level of education ^{73,74}	—	Yes [†] C with lower parents' education ⁶¹
Sibling status	No ^C 29	—	—	—
Financial difficulties ⁱ	—	Yes [†] C 73	—	—
History of repeating a grade	—	Yes [†] C 73	—	—
Help at school	—	Conflicting ^{73,74}	—	—
Marital status	—	—	—	Yes [‡] C in unmarried survivors ¹⁷
Having children	—	—	—	Yes [†] C for survivors with children ²²
IQ	—	—	—	Yes [†] C with lower IQ ¹⁴

TABLE 1. Continued

3. Which Interventions Can Improve Educational/Employment Outcomes Among Childhood Cancer Survivors?	
No studies evaluating interventions to improve education or employment outcomes in survivors of childhood, adolescent and young adult cancers identified.	No studies

Abbreviations: CAYA, childhood, adolescent, and young adult; CNS, central nervous system; CRT, cranial radiotherapy; IQ, intelligence quotient; SMN, second malignant neoplasm.

Dark grey indicates Level A evidence, medium grey indicates Level B evidence, light grey indicates Level C evidence; grey indicates conflicting evidence.

^ALevel A evidence.

^BLevel B evidence.

^CLevel C evidence.

^SConflicting indicates conflicting evidence; No indicates no statistically significant association; Yes indicates statistically significant association ↑, ↓, and — indicate an increased risk for, a decreased risk for, and not tested.

^dSurgery (not further specified).

^eChemotherapy (not further specified).

^fRadiotherapy (not further specified).

^gVersus soft-tissue sarcoma survivors.

^hLate effects (not further specified).

ⁱFinancial difficulties at diagnosis.

^jAfter higher doses of cranial radiation.

^kAmong ALL and AML survivors.

^lLower quality of life associated with increased risk for unemployment.

^mYounger age at diagnosis associated with increased risk for unemployment.

significant differences in comparison with siblings.³¹ One study found that a low number of survivors of medulloblastoma attended mainstream education, but it did not include a comparison group (Supporting Table 11).⁷⁹

What are the risk factors for poor educational outcomes?

The existing surveillance recommendations concordantly identified radiotherapy to the brain (total body, cranial, and craniospinal irradiation) and a history of a CNS tumor or CNS-directed therapy as risk factors for poor psychosocial outcomes. The recommendations were discordant regarding all other potential risk factors (Supporting Table 7).⁶⁻⁹

Risk factors for lower educational achievement

We identified 14 studies that investigated risk factors for lower educational achievement in survivors of CAYA cancer.^{17-19,22,24,26,29,32,37,61,80-83} Demographic risk factors included female sex (Level C),^{17,19,22,26,29,61,80,81} a lower parental level of education (Level B),^{29,61} and non-White race or a history of a migration background (for specific geographical regions, Level A).^{17,29,80} An older age at follow-up was associated with a decreased risk for lower educational achievement (Level C)^{17,19,22,26,29,80,81} (Table 1).

We identified several clinical risk factors associated with an increased risk for lower educational achievement in survivors of CAYA cancer, including a primary diagnosis of a CNS tumor (Level B),^{17,22,24,26,29,61} a younger age at diagnosis (Level C),^{17,18,22,26,29,32,81,83} an upper extremity

sarcoma tumor versus a lower extremity one (Level C),⁸⁰ a history of relapse (Level C),^{17,22,26,29} experiencing late effects such as impaired neurocognitive functioning (Level A),^{19,22,82} psychological distress (Level C),¹⁹ and visual or hearing problems (Level C; Table 1).^{22,26,81}

Among the treatment-related risk factors, some evidence suggested that cranial radiotherapy (Level C),^{17,26,29,37,81,83} amputation for sarcoma tumors versus no amputation (Level C),⁸⁰ treatment with alkylating agents (Level C),⁸⁰ and staying in an intensive care unit (Level C)²² were associated with an increased risk for lower educational achievement, whereas treatment with anthracyclines (Level C)⁸⁰ was associated with a decreased risk for lower educational achievement among survivors of sarcomas. There was low- to moderate-quality evidence suggesting that chemotherapy (not further specified; Level B),^{17,26,29,83} surgery (not further specified; Level B),^{26,29} stem cell transplantation (Level C),²⁹ and duration of treatment (Level C)²² did not affect educational achievement (Table 1).

Risk factors for educational delays

We identified 2 studies investigating risk factors for repeating a grade in survivors of CAYA cancer.^{73,74} Parents' lower level of education (Level B),^{73,74} male sex (Level C),⁷³ financial difficulties at diagnosis (Level C),⁷³ and a history of repeating a grade (Level C)⁷³ were associated with an increased risk for repeating a grade in survivors. Stem cell transplantation (Level B),^{73,74} cranial radiotherapy (Level C),⁷³ the primary cancer diagnosis (Level C),⁷⁴ a second malignant neoplasm or recurrence (Level C),⁷³ and late effects (Level C)⁷⁴

TABLE 2. Surveillance Recommendations for Education in Survivors of CAYA Cancers

Who Needs Surveillance?
Health care providers, teachers, caregivers, survivors of CAYA cancers, and survivors' schools should be aware that, on a group level, survivors of CAYA cancer are at risk for Lower educational achievement (Level C evidence). Experiencing a delay in completing their education (Level A evidence). Requiring educational accommodations (Level B evidence). Particular attention is needed for survivors of CAYA cancer with the following risk factors ^a for lower educational achievement: primary diagnosis of a CNS tumor (Level B evidence), CNS-directed therapies (concordant in existing guidelines, expert opinion), impaired neurocognitive functioning (Level A evidence), non-White race or immigration status (Level A evidence for specific geographical regions), and parents' lower level of education (Level B).
At What Age or Time From Exposure Should Surveillance Be Initiated?
Surveillance of educational outcomes is recommended for all ages to begin at diagnosis and continue through survivorship until young adulthood (expert opinion).
What Surveillance Modality Should Be Used and at What Frequency Should Surveillance Be Performed?
Regular assessment of educational outcomes ^b via parent report or self-report is recommended at every long-term follow-up visit or general medical checkup at least annually ^c until education is completed (expert opinion).
What Should Be Done If Abnormalities Are Identified?
Documentation of educational problems in the survivor's medical record is recommended to facilitate sharing with all members of the care team (expert opinion). Referral ^d to an educational specialist, psychologist, and/or social worker for assessment and implementation of relevant educational and/or disability services is recommended for survivors who report educational problems upon screening (expert opinion).

Abbreviations: CAYA, childhood, adolescent, and young adult; CNS, central nervous system.

Green indicates a strong recommendation to do.

^aThe main risk factors were all factors that were associated with an increased risk for lower educational achievement with at least Level B evidence (ie, demonstrated statistically significant increased risk in >50% of studies) or showed concordance in existing guidelines. A complete list of all risk factors is presented in Table 1.

^bQuestions to ask include the following: "How are you doing in school?," "Has your performance been affected in any way? In what way?," "Are there certain areas/subjects you struggle with?," "Are there areas of your education that cause you stress or anxiety?," and "Have you ever received or asked for any support?"

^cIf the survivor is not scheduled for annual visits, screening can be performed via the phone or telehealth or can be delegated to a suitable professional in the school of the survivor.

^dThe referring health care professional is responsible for the following:

- Following up with the referred survivor regarding receipt of support.
- Documenting the progress of educational outcomes in the survivor's medical records.

The referring health care professional can transfer this responsibility to another person (eg, the educational specialist or school), but it needs to be communicated clearly to the survivor, the referring health care professional, and the educational specialist who is responsible for this.

were not significantly associated with repeating a grade. Evidence was conflicting for age at diagnosis and help at school (Table 1).^{73,74}

Risk factors for special education

We identified 1 study investigating risk factors for special education in survivors of CAYA cancer.⁷⁵ Evidence

TABLE 3. Surveillance Recommendations for Employment in Survivors of CAYA Cancers

Who Needs Surveillance?
Health care providers, caregivers, and survivors of CAYA cancers should be aware that, on a group level, survivors of CAYA cancer are at risk for unemployment (Level B evidence). Particular attention is needed for survivors of CAYA cancer with the following risk factors ^a for unemployment: female sex (Level B evidence), lower educational achievement (Level A evidence), primary diagnosis of a CNS tumor (concordant in existing guidelines, Level A evidence), CNS-directed therapies (concordant in existing guidelines, Level A evidence), any adverse long-term side effects (Level A evidence), impaired neurocognitive functioning (Level A evidence), second malignancy or recurrence (Level B evidence), psychological distress (Level B evidence), and physical disability (Level B evidence).
At What Age or Time From Exposure Should Surveillance Be Initiated?
Vocational planning and employment surveillance are recommended to begin in adolescence to support survivors to transition from education to employment (expert opinion).
What Surveillance Modality Should Be Used and at What Frequency Should Surveillance Be Performed?
Regular assessment of vocational planning ^b and employment status via parent report or self-report is recommended at every long-term follow-up visit or general medical checkup (expert opinion).
What Should Be Done if Abnormalities Are Identified?
Documentation of vocational problems in the survivor's medical record is recommended to facilitate information sharing with all members of the care team (expert opinion). Referral ^c to a vocational counselor, psychologist, and/or social worker for assessment and implementation of relevant vocational and/or disability services is recommended for survivors who report vocational problems upon screening (expert opinion).

Abbreviations: CAYA, childhood, adolescent, and young adult; CNS, central nervous system.

Green indicates a strong recommendation to do.

^aThe main risk factors were all factors that were associated with an increased risk for unemployment with at least Level B evidence (ie, demonstrated statistically significant increased risk in >50% of studies) or showed concordance in existing guidelines. A complete list of all risk factors is presented in Table 1.

^bQuestions to ask include the following: "What profession would you like to pursue?," "Have you had difficulties when applying for a job?," "Do you have any problems keeping up with your work?," "Do you have any problems keeping a full-time job?," and "Have you ever received or asked for any support?"

^cThe referring health care professional is responsible for the following:

- Following up with the referred survivor regarding receipt of support.
- Documenting the progress of vocational outcomes in the survivor's medical records.

The referring health care professional can transfer this responsibility to another person (eg, the vocational counselor or rehabilitation specialist), but it needs to be communicated clearly to the survivor, the referring health care professional, and the vocational specialist who is responsible for this.

suggested that survivors of all primary cancer diagnoses were at risk for needing special education services (Level C).⁷⁵ Treatment with intrathecal methotrexate (Level C) and radiotherapy (any field) versus no radiotherapy (Level C) were not associated with special education (Table 1).⁷⁵

Which interventions can improve educational outcomes among childhood cancer survivors?

The existing surveillance recommendations were discordant regarding their recommendations,⁶⁻⁹ although

2 recommended referral to a (neuro)psychologist or to a social work team^{6,9} (Supporting Table 7).

We identified no studies investigating interventions to improve educational achievement in survivors of CAYA cancer (Table 1).

Employment

What is the risk of poor employment outcomes?

As a group, survivors of CAYA cancers are at increased risk for unemployment in comparison with control groups (Level B).^{14,17,19,21-25,28,31-38,52,53,59,61-69,71,84-96} Specifically, we found 43 studies from 29 different study samples that compared employment in survivors and siblings, peers, or the general population.^{14,17,19,21-25,28,31-38,52,53,59,61-69,71,84-96} Twenty-three of those studies (14 study samples and 1 meta-analysis) found that survivors were at increased risk for unemployment,^{14,21,52,84-87,95} not being currently employed,^{25,32,37,63,66,91-93} never being employed,^{35,61,88,89} health-related unemployment,^{85,91,93} being unable to work,¹⁹ or not working full time^{31,67} in comparison with control groups. Nineteen studies (16 study samples) found no statistically significant differences in employment status,^{17,22,33,38,53,59,64,69,90} employment rates,^{24,28,36,62,65,68,94} working ability,²³ problems keeping a job,⁷¹ or job distribution³⁴ in comparison with control groups. One study found that more leukemia survivors than expected in comparison with the general population were currently employed⁹⁶ (Table 1 and Supporting Table 12). Survivors of CNS tumors were at increased risk for unemployment in comparison with control groups (Level A)^{14,37,61,63,67,87,88,95} (Table 1 and Supporting Table 10).

What are the risk factors for poor employment outcomes?

We identified 16 studies (9 samples and 1 meta-analysis) that investigated risk factors for unemployment in survivors of CAYA cancers.^{14,17,19,22,24,37,39,61,80-85,88,91,97,98} Demographic risk factors for unemployment included lower educational achievement (Level A)^{14,17,97} and female sex (Level B)^{14,17,19,22,61,80-82,84,85,88,91,97} (Table 1).

Clinical risk factors for unemployment included a primary diagnosis of a CNS tumor (Level B)^{17,24,61,91}; a second malignancy or recurrence (Level B)^{22,85,91}; a longer time since diagnosis (Level C)^{17,85}; and suffering from late effects (not further specified; Level A),^{17,81,97} including impaired neurocognitive functioning (Level A),^{19,22,39,82,98} psychological distress (Level B),^{19,39,98} physical disability (Level B),^{14,39} vision problems (Level B),^{81,91} and hearing problems (Level C)⁹¹ (Table 1).

Among the treatment-related risk factors, evidence suggested that higher doses of cranial radiation (Level A),^{14,37,81,84,85,88,91} surgery (not further specified; Level C),^{22,91,97} amputation versus no amputation (Level C),^{80,84,85} limb-saving surgery versus no surgery (Level C),^{80,84,85} cerebral surgery (Level C),^{84,85} and treatment with alkylating agents or vincristine for sarcomas (Level C)⁸⁰ were associated with an increased risk for unemployment. However, there was moderate-quality evidence suggesting that chemotherapy (not further specified; Level B),^{17,22,91,97} radiotherapy (not further specified; Level B),^{17,22,91,97} stem cell transplantation (Level B),^{22,97} and treatment duration (Level C)²² were not significantly associated with the risk of unemployment. Evidence was conflicting for the association of age at diagnosis with unemployment^{17,22,61,81,84,91} (Table 1).

Which interventions can improve employment outcomes among childhood cancer survivors?

The existing surveillance recommendations did not specify interventions to improve employment outcomes among survivors of CAYA cancer (Supporting Table 7).⁶⁻⁹

We identified no studies investigating interventions to improve employment outcomes in survivors of CAYA cancer (Table 1).

Translating Evidence Into Recommendations

In translating the evidence into recommendations, the panel considered several key factors. Although an assessment of educational progress and employment status may already be included as part of routine clinical care, the evaluation of these factors may not be prioritized as highly as other clinical questions. Therefore, the panel unanimously endorsed the importance of raising awareness about the risk for poor educational outcomes and unemployment not only among health care professionals but also among survivors and families. Panel members were in agreement that schools and teachers represent important partners in the surveillance and support of survivors' educational progress.

We acknowledge that priorities for education and employment vary at different ages and developmental stages. Specifically, preparedness for school begins in most cases for toddlers and preschoolers. Formal education typically starts in early childhood and is completed by young adulthood. Vocational planning and employment status become important as adolescents approach the transition from education to employment, with

vocational planning usually starting in secondary school and occurring simultaneously with education and educational planning. Therefore, the panel recommends that the assessment of education begin at diagnosis when disruptions to education are common, whereas the assessment of employment should begin during adolescence when individuals typically start planning for future employment. The panel recognizes that often there is no prediagnosis assessment of educational or vocational difficulties, so early evaluation helps to establish a relative baseline from which to identify future problems. Educational surveillance is recommended through young adulthood or until the achievement of the individual's preferred highest educational degree. However, continuing surveillance of employment status through long-term survivorship is recommended because the risk of experiencing late effects or other health issues increases over time,⁹⁹ and this could negatively affect a person's ability to work.

Regular assessment of educational and vocational progress is recommended for all survivors at routine follow-up visits or general medical checkups, even in the absence of key risk factors. Annual surveillance can be brief with the goal of facilitating identification and referral, with it being recognized that discussion of problems in these areas may be sensitive or distressing. This recommendation aligns well with the recent publication regarding psychosocial follow-up as a standard of care in long-term survivorship.¹⁰⁰ If there is no indication for yearly long-term follow-up appointments, surveillance of educational progress can be delegated to the family physician or a suitable school professional. Underreporting of educational or employment problems by parents or survivors may occur because of feelings of shame or guilt. Schools and teachers may serve as valuable contacts for an outside assessment of educational problems, and vocational specialists may be useful for the evaluation of employment problems.

Evidence was insufficient to support recommending a particular method of assessment for either education or employment. Routine assessments can be performed through simple survivor or parent reporting regarding progress and should prompt further discussion and evaluation if problems are reported. Examples of questions to ask include "Do you have any problems keeping up with schoolwork?" and "Do you have any problems keeping a full-time job?" (Tables 2 and 3). Although self-report has limitations, securing reports from teachers and schools may not be feasible. However, establishing collaborations with local schools may facilitate surveillance of

educational outcomes. For assessing employment, there is a promising new measure of barriers to employment developed for childhood cancer survivors¹⁰¹ as well as a number of measures used in the broader vocational rehabilitation services literature.¹⁰²

DISCUSSION

We harmonized long-term follow-up recommendations for education and employment surveillance in survivors of CAYA cancer diagnosed before the age of 30 years to address gaps and inconsistencies in prior recommendations from different international groups. The current recommendations aim to raise awareness of CAYA survivors' risk of poor educational and employment outcomes and to encourage implementation of surveillance in long-term follow-up care. The goal is to disseminate these recommendations to all key stakeholders, including survivors of CAYA cancer and their families, health care providers, and schools.

On a group level, we found that survivors of CAYA cancers were at increased risk for poor educational and employment outcomes in comparison with controls (ie, siblings, peers, or the general population), with strong evidence found for the subgroup of CNS tumor survivors. This is in line with a recent meta-analysis that included several articles also considered in this review and found that although the odds of unemployment among survivors has declined over time, survivors still remain 1.5 times more likely to be unemployed than controls.¹⁰³ However, there was some heterogeneity across studies, with several studies finding no statistically significant differences between survivors and controls and a few identifying better outcomes. We attribute the variability of results to several possible explanations. First, the studies included represented 17 different countries. Educational systems vary greatly from country to country, as does the re-integration of severely ill children within these systems. In addition, levels of educational achievement and physical or cognitive disabilities may have different implications for job opportunities depending on the country. Second, there was significant heterogeneity in the populations studied (eg, primary cancer diagnoses, treatment durations, sample sizes, comparison groups, and ages at diagnosis or study) that could affect educational and employment outcomes. Third, the terminology used to describe employment status varied from study to study, with primary outcomes using terms such as *unemployment*, *health-related unemployment*, *being unable to work*, and *not working full-time*. Fourth, these outcomes focused on overall educational

achievement and employment status rather than more nuanced outcomes such as academic or job performance. Fifth, educational and employment outcomes are dependent on a variety of social and environmental factors, only some of which were assessed in the included studies and summarized in our review. Therefore, on the basis of the variability of the underlying evidence and to ensure that the recommendations would be applicable across various countries and health care systems, we formulated broad recommendations for the surveillance of education and employment. In the future, we encourage national adaptations of these recommendations to country-specific educational and vocational systems.

This review identified several risk factors for poor educational and employment outcomes among CAYA survivors, and this indicates that certain subgroups are at higher risk of poor outcomes. For example, factors that were consistently associated with increased risk included diagnosis of a CNS tumor, CNS-directed therapies, second malignant neoplasms or recurrence, late effects such as impaired neurocognitive functioning or vision or hearing problems, and amputation or limb-sparing surgery. Evidence from prior reviews¹⁰⁴⁻¹⁰⁶ and expert testimony from clinicians and survivors support the idea that CNS-directed therapies negatively affect educational outcomes. Importantly, however, it should be acknowledged that even in the presence of these risk factors, many survivors will still obtain outcomes comparable to those of their noncancer peers. Furthermore, many of the risk factors for unemployment identified in the current review, such as female sex, disability status, and lower educational achievement, are also present in the general US population¹⁰⁷ and might need to be addressed on a national level. In our review, there was conflicting evidence regarding the effect of age at diagnosis on educational and employment outcomes. Current studies did not cover a broad enough range of ages at diagnosis to investigate whether there is a vulnerable time period associated with poor future outcomes. Similarly, although unemployment decreased with the age of survivors, it is unclear whether health-related unemployment or receiving insurance benefits is associated with age; this would be expected if aging survivors developed more health problems. These gaps and areas for future research are presented in Table 4.

Importantly, there is a lack of focus on resiliency and specifically on the identification of factors that may protect against negative outcomes; this is perhaps a limitation of our work. Protective factors might include socioeconomic status and family functioning.¹⁰⁸ Moreover, despite the statistically significant differences in outcomes

TABLE 4. Gaps in Knowledge and Future Directions for Research

- Few studies have been performed in countries outside North America or Europe: Studies of the education and employment situation of CAYA cancer survivors in South and Central America, Africa, Middle East, Asia, and Australia/New Zealand are needed.
- Evidence is conflicting regarding the association of the age at primary cancer diagnosis and the risk for repeating a grade as well as the risk for unemployment. Future studies are needed to clarify the most vulnerable time.
- Although studies have found that the overall risk of unemployment decreases with the age of survivors, it is unclear whether this is also true for health-related unemployment, which may be expected to increase if aging survivors develop health complications that influence their ability to work.
- Rigorous trials (eg, randomized controlled trials and n-of-1 trials) investigating the effectiveness of interventions to improve educational or employment outcomes in CAYA cancer survivors are needed.

Abbreviations: CAYA, childhood, adolescent, and young adult; CNS, central nervous system.

between survivors and comparisons, a large proportion of survivors of CAYA cancers will experience a successful schooling career and professional life. Therefore, although there is strong consensus that all survivors of CAYA cancer can profit from ongoing surveillance of educational and employment outcomes to identify those most vulnerable, certainly these are not expected outcomes for every survivor of CAYA cancer. Future work in this domain must start to consider those resilience factors that seek to protect survivors of CAYA cancer from poorer educational and employment outcomes (Table 4).

Educational achievement and employment are widely recognized to have important influences on long-term quality-of-life outcomes.¹⁰⁹ The evidence is mixed if educational delays have negative consequences on educational achievement.¹¹⁰ However, grade repetition can in the short term further disrupt the life of severely ill children by separating them from their well-known social environment, namely from friends and teachers. The effect of repeating a grade or delayed school entry on longer term consequences may warrant further investigation.

Communication among health care providers, survivors of CAYA cancer, families, schools, and vocational rehabilitations services is strongly encouraged to implement these recommendations. Documentation of educational or employment problems in the survivor's medical record is recommended to facilitate information sharing with all members of the care team. Because survivors of CAYA cancer often see multiple providers and psychosocial outcomes are often not recognized in follow-up care,¹⁰⁰ identifying 1 provider to take the primary role in assessing, documenting, and following up on psychosocial issues may be helpful. This role may be assumed by the referring health care professional or any other involved professional;

the responsible team member should be communicated to the survivor and her or his family to ensure consistency in care (see Grandinette¹¹¹ and Gilleland Marchak et al¹¹² for examples of communication tools).

Unfortunately, no studies evaluating specific interventions to improve educational and employment outcomes met our search criteria. This is not too surprising because of the focus on overall educational achievement and unemployment rather than more nuanced academic or vocational performance measures. To be effective, interventions need to be tailored to each survivor with her or his specific set of challenges and to the local educational and vocational system. In the United States, the use of certain vocational rehabilitation services, such as vocational training and job placement assistance, has been associated with increased odds of employment among young adult cancer survivors aged 18 to 25 years¹¹³ and adult cancer survivors.¹¹⁴ Despite limited published evidence, expert opinion has determined that survivors reporting any difficulties should be referred to an educational specialist, vocational counselor, psychologist, and/or social worker for further evaluation and relevant services aimed at supporting educational and vocational progress. These services should ideally be provided by a professional with experience in supporting survivors of CAYA cancer to ensure consideration of the complex challenges that many survivors face, including the management of regular health care appointments/medications, mental health concerns, dependency on caregivers, and adverse medical complications from their cancer treatment. Furthermore, ongoing vocational services or legal aid may be needed because survivors of CAYA cancer may experience workplace discrimination or other legal difficulties.¹¹⁵ Nevertheless, we encourage the development and scientific evaluation of interventions to improve educational and employment outcomes among CAYA survivors at risk. Effective interventions will need to be tailored to the unique needs of each patient and to the local resources available. Furthermore, investigators may consider rigorous designs for small-sample research such as n-of-1 trials¹¹⁶ (Table 4).

The strengths of this CPG include the evidence-based approach using a rigorous systematic literature review to summarize the relevant literature from a large number of studies, the transparency of each step of the process, and the multidisciplinary and international panel of experts involved in the process. The collaboration of these experts reduced duplication of efforts to develop CPGs. The multidisciplinary panel provided its expertise throughout the process, which was especially important when evidence was lacking. Another strength is that we involved survivors with lived experience to appraise the recommendations, and we

used their feedback to improve the recommendations. Limitations of this CPG are that nearly all the included studies were performed in North America or Europe. Educational systems around the world vary considerably, as do work environments. For an international CPG, it would be desirable to also include evidence from other geographical regions, especially those with middle to lower income countries (Table 4), although we are confident that the recommendations are broad enough to be applicable worldwide. Educational outcomes were restricted to educational achievement and did not include educational testing, performance, or neuropsychological testing, which may be used in determining specific strengths/weaknesses and making decisions regarding progressing grade levels or attending college or university. Neurocognitive outcomes were excluded because there is a separate working group of the IGHG developing guidelines for the surveillance of neurocognitive functioning (<https://www.ighg.org/guidelines/topics/neurocognitive-problems/>). Finally, we acknowledge that the recommendations as proposed apply to a large, heterogeneous population of survivors of childhood cancer and are not tailored to specific subpopulations with unique needs. Nevertheless, to ensure inclusivity across all potentially at-risk survivors, we recommend ongoing surveillance of educational and employment outcomes even though these outcomes may not be experienced by every survivor of CAYA cancer. Future guidelines may seek to consider greater specificity with respect to diagnosis and treatment protocols.

In conclusion, we describe the state of the evidence and provide internationally harmonized surveillance guidelines for education and employment in survivors of CAYA cancer. This guideline aims to raise awareness about educational and employment problems in survivors of CAYA cancer, encourage the implementation of routine surveillance of educational and vocational progress during survivorship care, and ultimately minimize the burden of disease for survivors and improve their overall quality of life.

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AUTHOR CONTRIBUTIONS

Katie A. Devine: Conception and design of the study, search strategy, data extraction, interpretation of the data, formulation of the recommendations, drafting of the manuscript, and approval of the final version of the manuscript. **Salome Christen:** Conception and design of the study, search strategy, data extraction, interpretation of the data, formulation of the recommendations, drafting of the manuscript, and approval of the final version of the manuscript. **Renée L. Mulder:** Conception and design of the study, search strategy, data extraction, interpretation of the data, formulation of the recommendations, critical revision of the manuscript, and approval of the final version of the manuscript. **Morven C. Brown:** Search strategy, data extraction, interpretation of the data, formulation of the recommendations, and approval of the final version of the manuscript. **Lisa M. Ingerski:** Search strategy, data extraction, interpretation of the data, formulation of the recommendations, and approval of the final version of the manuscript. **Luzius Mader:** Search strategy, data extraction, interpretation of the data, formulation of the recommendations, and approval of the final version of the manuscript. **Emma J. Potter:** Search strategy, data extraction, interpretation of the data, formulation of the recommendations, and approval of the final version of the manuscript. **Charlotte Sleurs:** Search strategy, data extraction, interpretation of the data, formulation of the recommendations, and approval of the final version of the manuscript. **Adrienne S. Viola:** Search strategy, data extraction, interpretation of the data, formulation of the recommendations, and approval of the final version of the manuscript. **Susanna Waern:** Search strategy, data extraction, interpretation of the data, formulation of the recommendations, and approval of the final version of the manuscript. **Louis S. Constine:** Conception and design of the study, critical revision of the manuscript, and approval of the final version of the manuscript. **Melissa M. Hudson:** Conception and design of the study, critical revision of the manuscript, and approval of the final version of the manuscript. **Leontien C. M. Kremer:** Conception and design of the study, search strategy, data extraction, interpretation of the data, formulation of the recommendations, critical revision of the manuscript, and approval of the final version of the manuscript. **Roderick Skinner:** Conception and design of the study, critical revision of the manuscript, and approval of the final version of the manuscript. **Gisela Michel:** Conception and design of the study, search strategy, data extraction, interpretation of the data, formulation of the recommendations, critical revision of the manuscript, and approval of the final version of the manuscript. **Jordan Gilleland Marchak:** Conception and design of the study, search strategy, data extraction, interpretation of the data, formulation of the recommendations, critical revision of the manuscript, and approval of the final version of the manuscript. **Fiona Schulte:** Conception and design of the study, search strategy, data extraction, interpretation of the data, formulation of the recommendations, drafting of the manuscript, and approval of the final version of the manuscript.

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