Richtlijn “Leefregels bij kinderen met kanker”

Versie 2
Mei 2022

INITIATIEF
Nederlandse Vereniging voor Kindergeneeskunde

IN SAMENWERKING MET
Nederlands Instituut van Psychologen
Stichting Kinderoncologie Nederland
Vereniging Kinderkanker Nederland
Verpleegkundigen & Verzorgenden Nederland

MET ONDERSTEUNING VAN
Prinses Máxima Centrum voor Kinderoncologie, Utrecht

FINANCIERING
De richtlijnontwikkeling werd gefinancierd uit de Stichting Kwaliteitsgelden Medisch Specialisten (SKMS).

COLOFON
RICHTLIJN LEEFREGELS BIJ KINDEREN MET KANKER ©, 2022

Nederlandse Vereniging voor Kindergeneeskunde
Postbus 20059, 3502 LB Utrecht
Tel. 088 282 33 06
nvk@nvk.nl
www.nvk.nl

INHOUDSOPGAVE

LIJST MET AFKORTINGEN

AML	Acute myeloïde leukemie
ASCO	American Society of Clinical Oncology
BSI	Blood stream infection
CHG	Chloorhexidine
CLABSI	Central line associated blood stream infection
EtD	Evidence-to-decision
GIN	Guidelines International Network
GRADE	Grading Recommendations Assessment, Development and Evaluation
IDSA	Infectious Diseases Society of America
IGHG	International Guideline Harmonization Group
IPOG	International Pediatric Oncology Group
NICE	National Institute for Health and Care Excellence
NIP	Nederlands Instituut van Psychologen
NVK	Nederlandse Vereniging voor Kindergeneeskunde
PICC lijn	Perifeer ingebrachte centrale lijn
RCT	Randomized controlled trial
RR	Risk ratio
SKION	Stichting Kinderoncologie Nederland
VKN	Vereniging Kinderkanker Nederland
V&VN	Verpleegkundigen & Verzorgenden Nederland

SAMENSTELLING VAN DE WERKGROEP

Samenstelling kernwerkgroep:

- Drs. D.C. (Debbie) Stavleu, arts-onderzoeker kinderoncologie Prinses Máxima Centrum, Utrecht en Beatrix Kinderziekenhuis (Universitair Medisch Centrum Groningen), op persoonlijke titel
- Dr. E.A.H. (Erik) Loeffen, AIOS kindergeneeskunde, epidemioloog en postdoc onderzoeker kinderoncologie Prinses Máxima Centrum, Utrecht en Beatrix Kinderziekenhuis (Universitair Medisch Centrum Groningen), NVK
- Dr. R.L. (Renée) Mulder, postdoc onderzoeker, richtlijn ontwikkelaar, methodoloog, Prinses Máxima Centrum, Utrecht, op persoonlijke titel
- Drs. D.M. (Demi) Kruimer, ANIOS kindergeneeskunde, MSc Healthcare Management en arts-onderzoeker kinderoncologie Prinses Máxima Centrum, Utrecht, op persoonlijke titel
- Prof. Dr. L.C.M. (Leontien) Kremer, kinderarts, hoogleraar late effecten in kinderoncologie, Prinses Máxima Centrum, Utrecht en hoogleraar gepaste zorg, Amsterdam UMC, Amsterdam, NVK
- Prof. Dr. W.J.E. (Wim) Tissing, kinderoncoloog, hoogleraar Supportive Care, Prinses Máxima Centrum, Utrecht en Beatrix Kinderziekenhuis (Universitair Medisch Centrum Groningen), NVK

Samenstelling werkgroep “Leefregels bij kinderen met kanker”:

- Drs. L.R. (Laura) Beek, klinisch psycholoog, Prinses Máxima Centrum, Utrecht, NIP
- Mw. J.H.P. (Janneke) Evers, MANP, verpleegkundig specialist, Prinses Máxima Centrum, Utrecht, V&VN
- Dr. M.M. (Melanie) Hagleitner, kinderoncoloog, Prinses Máxima Centrum, Utrecht, NVK
- Dr. D.H.J. (Daniëlle) Martens, kinderarts, Isala, Zwolle, NVK
- Dr. J.G. (Jeroen) Noordzij, kinderarts, Reinier de Graaf Gasthuis, Delft, NVK
- Mw. I. (Ida) Ophorst, MSc, kinderoncologie verpleegkundige, expert verpleegkundig onderzoek, Prinses Máxima Centrum, Utrecht, V&VN
- Mw. J. (Janneke) Ottens, verpleegkundig specialist kinderoncologie, Beatrix Kinderziekenhuis (Universitair Medisch Centrum Groningen), V&VN
- Mw. W. (Willemijn) Plieger, beleidsmedewerker VKN (Vereniging Kinderkanker Nederland), VKN
- Drs. M. (Marjolijn) Quaak, kinderarts, fellow kinderinfectieziekten en –immunologie, Sophia Kinderziekenhuis (Erasmus MC), NVK
- Mw. T. (Tirza) Schuerhoff, pedagogisch medewerker, Prinses Máxima Centrum, Utrecht, op persoonlijke titel
- Dr. J. (Judith) Spijkerman, kinderarts, fellow kinderoncologie, Prinses Máxima Centrum, Utrecht, NVK
- Dr. M.D. (Marianne) van de Wetering, kinderoncoloog, Prinses Máxima Centrum, Utrecht, SKION
- Dr. T.F.W. (Tom) Wolfs, kinderarts-infectieziekten, Wilhelmina Kinderziekenhuis, Utrecht, NVK

Bijzondere dank aan:

- Mw. E. (Erika) Heerema, onafhankelijk voorzitter

SAMENVATTING (NEDERLANDS)

Onderstaande is een samenvatting van de belangrijkste aanbevelingen uit de richtlijn "Leefregels bij kinderen met kanker". In deze samenvatting ontbreken het wetenschappelijk bewijs en de overwegingen die tot de aanbevelingen geleid hebben. Lezers van deze samenvatting worden voor deze informatie verwezen naar de volledige richtlijn. Deze samenvatting van aanbevelingen staat niet op zichzelf.

Samenvatting van de aanbevelingen:

A. Badspeelgoed

STERKE aanbeveling, ZEER LAGE KWALITEIT evidence	Wij raden het gebruik af van badspeelgoed met een reservoir (waarin water kan achterblijven) of badspeelgoed dat niet goed afgedroogd kan worden.

B. Bubbelbad

ZWAKKE aanbeveling, ZEER LAGE KWALITEIT evidence	Wij adviseren tegen het gebruik van warme (publieke) bubbelbaden.

ZWAKKE aanbeveling, EXPERT evidence	De werkgroep is van mening dat het gebruik van een bubbelbad thuis toegestaan is, zolang het bad grondig schoongemaakt kan worden en dat het water compleet ververst kan worden na elk bad.

C. Chloorhexidine gebruik

ZWAKKE aanbeveling, ZEER LAGE KWALITEIT evidence	Wij adviseren tegen het gebruik van chloorhexidine in bad of andere hygiëne doekjes, omdat dit geen toegevoegde waarde lijkt te zijn op standaard hygiëne maatregelen.

D. Omgeving/milieu factoren (inclusief zandbak)

STERKE aanbeveling, ASCO richtlijn (1)*	Wij adviseren het vermijden van langdurig contact met een omgeving met een hoge concentratie van schimmelsporen (zoals een bouwplaats of plaats waar sloopwerkzaamheden plaatsvinden, blootstelling aan grond door tuinieren of graven, verbouwwerkzaamheden thuis) voor kinderen met kanker en neutropenie.

*Aanbeveling overgenomen van “ASCO and IDSA Clinical Practice Guideline” (1)

ZWAKKE aanbeveling, EXPERT evidence	De werkgroep is van mening dat kinderen met kanker in de zandbak kunnen spelen, zolang ze hun handhygiëne goed toepassen.

E. Bloemen

STERKE aanbeveling, EXPERT evidence	De werkgroep is sterk van mening dat bloemen en planten in huis zijn toegestaan.

F. Activiteiten met hoogte- of druk verschil

ZWAKKE aanbeveling, EXPERT evidence	De werkgroep is van mening dat klinisch stabiele kinderen met kanker zonder ernstige neutropenie (i.e. neutrofielen $<0.5x10^9$/L) of trombocytopenie (i.e. trombocyten $<50x10^9$/L), bepaalde activiteiten met hoogte- of druk verschil, zoals in het vliegtuig of duiken, kunnen uitvoeren zolang dit in overeenstemming is met hun behandelend arts.

G. Hygiëne (algemeen)

STERKE aanbeveling, GOOD PRACTICE STATEMENT	Zorgvuldige handhygiëne moet worden toegepast door patiënten, ouders/ verzorgers en zorgverleners.

H. Hygiëne (persoonlijk)

STERKE aanbeveling, EXPERT evidence	De werkgroep is sterk van mening dat reguliere persoonlijke hygiëne (betreft wassen, schoonmaken, schone kleren aantrekken) voldoende is voor kinderen met kanker en hun huishouden.

I. Huisdieren, dierentuin of kinderboerderij

ZWAKKE aanbeveling, ZEER LAGE KWALITEIT evidence	Wij adviseren het toestaan van huisdieren bij kinderen met kanker.

ZWAKKE aanbeveling, EXPERT evidence	Wij adviseren het toestaan van het bezoeken van een dierentuin of kinderboerderij door kinderen met kanker.

ZWAKKE aanbeveling, EXPERT evidence	Wij adviseren dat kinderen met kanker niet de kattenbak of hokken van de huisdieren schoonmaken.

J. Openbaar vervoer

ZWAKKE aanbeveling, EXPERT evidence	De werkgroep is van mening dat kinderen met kanker het openbaar vervoer kunnen gebruiken of drukke plaatsen (zoals een concert of een theater) kunnen bezoeken.

ZWAKKE aanbeveling, EXPERT evidence	De werkgroep is van mening dat het niet raadzaam is voor kinderen met kanker in neutropenie om het openbaar vervoer te gebruiken of drukke plaatsen (zoals een concert of een theater) te bezoeken tijdens een periode met een hoge incidentie van virale infecties en dus een hogere kans om een infectie op te lopen.

K. School en kinderopvang

STERKE aanbeveling, ZEER LAGE KWALITEIT evidence	Wij adviseren het toestaan van naar school of naar de kinderopvang te gaan door kinderen met kanker (tenzij iemand in de klas of groep een infectieuze ziekte heeft zoals waterpokken).

L. Sport en activiteiten met hoge snelheid

STERKTE aanbeveling, EXPERT evidence	De werkgroep is sterk van mening dat kinderen met kanker aangemoedigd moeten worden om te sporten en bewegen.

ZWAKKE aanbeveling, EXPERT evidence	De werkgroep is van mening dat kinderen met trombopenie (i.e. trombocyten <50x10^9/L) geen sporten zouden moeten beoefenen met een hoog risico op bloedingen (contact sport, sporten of activiteiten met een hoge impact of hoge snelheid, activiteiten met een hoog risico op vallen).

M. Zwemmen

ZWAKKE aanbeveling, ZEER LAGE KWALITEIT evidence	Wij adviseren het toestaan van zwemmen voor kinderen met kanker (ongeacht het hebben van neutropenie).

STERKE aanbeveling, EXPERT evidence	De werkgroep is sterk van mening dat kinderen met kanker en een niet-getunnelde lijn zoals een PICC lijn niet mogen zwemmen.

N. Reizen naar het buitenland

STERKE aanbeveling, EXPERT evidence	De werkgroep is van mening dat kinderen met kanker naar het buitenland kunnen reizen, onder de voorwaarden dat ze een land bezoeken met een vergelijkbaar zorgsysteem en dat het kind in klinisch goede gezondheid verkeert.

ALGEMENE INLEIDING (NEDERLANDS)

Aanleiding voor het maken van de richtlijn

Jaarlijks krijgen in Nederland ongeveer 600 kinderen kanker. Met het stijgen van de overleving van kinderen met kanker, is er meer plaats gekomen voor het verlagen van morbiditeit (door de behandeling) en het verhogen van kwaliteit van leven. Er is veel aandacht hiervoor en dit krijgt een steeds prominentere plek in de behandeling. Nog steeds is er veel variatie in de aanbevelingen die worden gebruikt in de klinische praktijk, wat een negatieve invloed heeft op de zorg. Hierom is het belangrijk om evidence-based richtlijnen te ontwikkelen. (2)

De behandeling van kanker is zwaar, intensief en langdurig, en gaat gepaard met veel bijwerkingen en toxiciteit. Zo is er bijvoorbeeld een kans op bloedingen of op infecties. Kinderen met kanker krijgen tijdens hun ziekte en behandeling daarvan te maken met bepaalde leefregels waaraan zij zich dienen te houden. Het doel van het instellen van deze leefregels is bijvoorbeeld het infectierisico of het risico op een bloeding zo veel mogelijk te verminderen. Het is echter een lastige balans tussen zoveel mogelijk bijwerkingen of complicaties voorkomen en de kwaliteit van leven zo optimaal mogelijk te houden.

Veel van de leefregels die in de huidige praktijk gebruikt worden, zijn niet gebaseerd op literatuur. De leefregels en sommige beperkingen die daarmee worden opgelegd, kunnen van invloed zijn op de kwaliteit van leven van kinderen met kanker. Daarom is het belangrijk dat er kritisch wordt gekeken naar al deze huidige aanbevelingen, aangevuld met nieuwe klinische vragen. In deze evidence-based richtlijn bespreken wij in een multidisciplinaire groep alle relevante aspecten per onderwerp en bespreken we uitgebreid alle voor- en nadelen. We maken een afgewogen beslissing met daarin de mogelijke complicaties, toxiciteit of negatieve effecten en de kwaliteit van leven in acht nemend.

Er is behoefte aan een praktische leidraad voor zorgverleners, kinderen met kanker en hun ouders of verzorgers. In deze richtlijn is er door de werkgroep getracht duidelijke evidence-based leefregels op te stellen. Voor de klinische vragen waar geen literatuur beschikbaar voor was, is een aanbeveling op basis van gedeelde *expert opinion* gemaakt. Dit om ervoor te zorgen dat er een praktische, bruikbare richtlijn beschikbaar voor zorgprofessionals met handvatten om patiënten en hun ouders te informeren.

Belangrijke onderwerpen in de ontwikkeling van deze richtlijn zijn dus de zaken uit het dagelijks leven van kinderen met kanker en hun ouders, o.a.: kunnen kinderen met kanker naar school of de kinderopvang, naar de dierentuin of kinderboerderij, in de achtbaan, kunnen ze sporten, zwemmen, activiteiten met hoge snelheid uitvoeren, en welke hygiëne maatregelen zijn nodig?

Doel van de richtlijn

Het doel van deze richtlijn is dat er eenduidige, heldere leefregels komen voor kinderen met kanker, met een goede balans tussen negatieve gevolgen (bijwerkingen, toxiciteit, etc.) en kwaliteit van leven.

Afbakening van de richtlijn

De richtlijn is gericht op kinderen met kanker (0 tot 18 jaar) en hun ouders of verzorgers.

Beoogde gebruikers van de richtlijn
Deze richtlijn is geschreven voor alle zorgverleners die betrokken zijn bij de zorg voor kinderen met kanker. Deze aanbevelingen zullen ook beschikbaar worden, met een meer toegankelijke uitleg, voor kinderen met kanker en hun ouders en verzorgers.

Definities en begrippen
De definities en begrippen die worden gebruikt, zijn zo veel mogelijk toegelicht in de afzonderlijke aanbevelingen.

VERANTWOORDING ALGEMEEN (NEDERLANDS)

Geldigheid
Voor het beoordelen van de actualiteit van deze richtlijn is de werkgroep niet in stand gehouden. Uiterlijk in 2027 bepaalt het bestuur van de Nederlandse Vereniging voor Kindergeneeskunde of de modules van deze richtlijn nog actueel zijn. De geldigheid van de richtlijn komt eerder te vervallen indien nieuwe ontwikkelingen aanleiding zijn een herzieningstraject te starten.
De Nederlandse Vereniging voor Kindergeneeskunde is regiehouder van deze richtlijn en eerstverantwoordelijke op het gebied van de actualiteitsbeoordeling van de richtlijn. De andere aan deze richtlijn deelnemende wetenschappelijke verenigingen of gebruikers van de richtlijn delen de verantwoordelijkheid en informeren de regiehouder over relevante ontwikkelingen binnen hun vakgebied.

Initiatief
Nederlandse Vereniging voor Kindergeneeskunde

Algemene gegevens
De richtlijnontwikkeling werd gefinancierd uit de Stichting Kwaliteitsgelden Medisch Specialisten (SKMS). De financier heeft geen enkele invloed gehad op de inhoud van de richtlijn.

Doelgroep
Deze richtlijn is geschreven voor alle leden van de beroepsgroepen die betrokken zijn bij de zorg voor kinderen met kanker.

Samenstelling werkgroep
Voor het ontwikkelen van de richtlijn is in 2019 een werkgroep ingesteld, bestaande uit vertegenwoordigers van alle relevante specialismen die betrokken zijn bij de zorg voor kinderen met kanker te maken hebben (zie hiervoor de samenstelling van de werkgroep op pagina 6).

Belangenverklaringen
Alle werkgroep leden hebben schriftelijk verklaard of zij directe financiële belangen (betrekking bij een commercieel bedrijf, persoonlijke financiële belangen, onderzoeksfinanciering) of indirecte belangen (persoonlijke relaties, reputatiemanagement, kennisvalorisatie) hebben gehad. Een overzicht van de belangen van werkgroep leden en het oordeel over het omgaan met eventuele belangen vindt u in onderstaande tabel. De ondertekende belangenverklaringen zijn op te vragen bij het secretariaat van de Nederlandse Vereniging voor Kindergeneeskunde.

Tabel 1: (Neven)functies en belangen werkgroep leden

Werkgroeplid	Functie	Nevenfuncties	Gemelde belangen	Ondernomen acties
D.C. Stavleu	Arts-onderzoeker kinderoncologie Prinses Máxima Centrum, Utrecht en Beatrix Kinderziekenhuis (Universitair Medisch Centrum Groningen)	-	Geen	Geen

E.A.H. Loeffen	AIOS kindergeneeskunde, epidemioloog en postdoc onderzoeker kinderoncologie Prinses Máxima Centrum, Utrecht en Beatrix Kinderziekenhuis (Universitair Medisch Centrum Groningen)	Voorzitter Stichting Kinderboek & Wetenschap (onbetaald).	Geen	Geen
R.L. Mulder	Postdoc onderzoeker, richtlijn ontwikkelaar, methodoloog, Prinses Máxima Centrum, Utrecht	-	Geen	Geen
D.M. Kruimer	Arts-onderzoeker kinderoncologie Prinses Máxima Centrum, Utrecht	ANIOS Kindergeneeskunde	Geen	Geen
L.C.M. Kremer	Kinderarts, hoogleraar late effecten in kinderoncologie, Prinses Máxima Centrum, Utrecht en hoogleraar gepaste zorg, Amsterdam UMC, Amsterdam	Adviseur kenniscentrum palliatieve zorg, beurzen via KiKa, KWF, ZonMW in het kader van werkzaamheden onderzoeksgroep Late Effecten.	Geen	Geen
W.J.E. Tissing	Kinderoncoloog, hoogleraar Supportive Care, Prinses Máxima Centrum, Utrecht en Beatrix Kinderziekenhuis (Universitair Medisch Centrum Groningen)	Geen relevante nevenfuncties.	Geen	Geen
L.R. Beek	Klinisch psycholoog, Prinses Máxima Centrum, Utrecht	Lid van congrescommissie “Samen nog beter” en lid van bestuur LVMP kinder- & jeugd.	Geen	Geen
J.H.P. Evers	Verpleegkundig specialist, Prinses Máxima Centrum, Utrecht	-	Geen	Geen
M.M. Hagleitner	Kinderoncoloog, Prinses Máxima Centrum, Utrecht	-	Geen	Geen
D.H.J. Martens	Kinderarts, Isala, Zwolle	-	Geen	Geen
J.G. Noordzij	Kinderarts, Reinier de Graaf Gasthuis, Delft	-	Geen	Geen
I. Ophorst	Kinderoncologie verpleegkundige, expert verpleegkundig onderzoek, Prinses Máxima Centrum, Utrecht	-	Geen	Geen

J. Ottens	Verpleegkundig specialist kinderoncologie, Beatrix Kinderziekenhuis (Universitair Medisch Centrum Groningen)	-	Geen	Geen
W. Plieger	Beleidsmedewerker VKN (Vereniging Kinderkanker Nederland)	-	Geen	Geen
M. Quaak	Kinderarts, fellow kinderinfectieziekten en – immunologie, Sophia Kinderziekenhuis (Erasmus MC)	Lid NVK commissie Pleitbezorging: voor verbetering leefomstandigheden voor kinderen en opkomen voor de rechten van het kind (onbetaald).	Geen	Geen
T. Schuerhoff	Pedagogisch medewerker, Prinses Máxima Centrum, Utrecht	-	Geen	Geen
J. Spijkerman	Kinderarts, fellow kinderoncologie, Prinses Máxima Centrum, Utrecht	-	Geen	Geen
M.D. van de Wetering	SKION taakgroep Supportive Care, Kinderoncoloog, Prinses Máxima Centrum, Utrecht	-	Geen	Geen
T.F.W. Wolfs	Kinderarts-infectieziekten, Wilhelmina Kinderziekenhuis, Utrecht	Redactielid tijdschrift Praktische Pediatrie (betaald), Beroepslid Centraal Tuchtcollege voor de Gezondheidszorg, (onkostenvergoeding)	Geen	Geen

Inbreng patiëntenperspectief
Er werd ruim aandacht besteed aan het patiëntenperspectief door de Nederlandse Vereniging Kinderkanker Nederland (VKN) af te vaardigen in de werkgroep en in nauw contact te blijven gedurende het hele proces.

Knelpunteninventarisatie
Tijdens de voorbereidende fase inventariseerde de kernwerkgroep een aantal belangrijke en omvangrijke knelpunten. Deze werden vervolgens door de gehele werkgroep, inclusief alle afgevaardigden van de wetenschappelijke verenigingen, uitgebreid besproken en beoordeeld. Tevens zijn er nieuwe knelpunten aangedragen door de werkgroep leden. Hier is een volledige sessie aan gewijd met alle werkgroep leden in september 2019.
In deze knelpunteninventarisatie is expliciet rekening gehouden met zowel het klinische belang van deze uitkomsten en de organisatie van zorg zoals coördinatie, communicatie, (financiële) middelen, menskracht en infrastructuur.

Uitgangsvragen
Op basis van de uitkomsten van de knelpunteninventarisatie zijn door de kernwerkgroep concept-uitgangsvragen opgesteld. Deze zijn met de werkgroep gedeeld ter goedkeuring, waarna de werkgroep de definitieve uitgangsvragen heeft vastgesteld. Knelpunten gingen met name over naar school of naar de kinderopvang gaan, zwemmen, huisdieren, (contact) sporten, reizen en openbaar vervoer etc. Zie alle uitgangsvragen in de “Verantwoording Methodologie” vanaf pagina 18 voor een compleet overzicht. Alle besproken knelpunten zijn omgezet naar definitieve uitgangsvragen.

Kostenimplicaties
Door de toenemende aandacht voor de kosten in de gezondheidszorg neemt het belang van richtlijnen die doelmatig handelen bevorderen toe. Met de totstandkoming van deze richtlijn zijn kostenimplicaties meegenomen in de beoordeling van elke aanbeveling.

Kennislacunes
Tijdens de ontwikkeling van deze richtlijn is bij elke uitgangsvraag is door de werkgroep nagegaan of er (aanvullend) wetenschappelijk onderzoek gewenst is om de uitgangsvraag te kunnen beantwoorden. Een overzicht van de onderwerpen waarvoor (aanvullend) wetenschappelijk van belang wordt geacht, is beschreven in bijlage 1 “Kennislacunes”.

Implementatie
In de verschillende fasen van de richtlijnontwikkeling is rekening gehouden met de implementatie van de richtlijn en de praktische uitvoerbaarheid van de aanbevelingen. De implementatie zal plaatsvinden in het Prinses Máxima Centrum en de Shared Care centra en de werkgroep ziet geen grote belemmeringen. Een implementatieplan is bijgevoegd in bijlage 2.

Commentaar- en autorisatiefase
De conceptrichtlijn werd aan de betrokken (wetenschappelijke) verenigingen en (patiënt) organisaties voorgelegd ter commentaar. De commentaren werden verzameld en besproken met de werkgroep. Naar aanleiding van de commentaren werd de conceptrichtlijn aangepast en definitief vastgesteld door de werkgroep dd 19-05-2022. De definitieve richtlijn werd aan de deelnemende (wetenschappelijke) verenigingen en (patiënt) organisaties voorgelegd voor autorisatie en door hen geautoriseerd dan wel geaccordeerd dd XX-XX-XX.

VERANTWOORDING METHODOLOGIE (English)

This guideline was developed using the GRADE methodology (Grades of Recommendation, Assessment, Development and Evaluation Working Group). All necessary steps towards creating recommendations for clinical practice are described below.

First, already existing guidelines were extracted from guideline-databases (GIN, NICE, IPOG, ASCO) and those were evaluated for applicability and direct implementation.
In the absence of an applicable, usable guideline for children with cancer, then,, together with a multidisciplinary guideline panel, clinical questions were defined.

1. Clinical questions:
The purpose of this guideline is to provide recommendations for children with cancer, receiving anti-cancer treatment with **curative intent.** This accounts for all of the following patient groups. The guideline was not intended to provide recommendations for palliative care settings.

PICO (1)
What is the effect of social restrictions (regarding risk of infections) on infections (prevalence and infectious complications) and other outcomes in children with any type of cancer and/or after stem-cell transplantation?

P = Children (aged 0-18 years) with any type of cancer and/or after stem-cell transplantation receiving anti-cancer treatment with curative intent
I = Social restrictions regarding risk of infections (i.e. restriction in school attendance, kindergarten, visiting zoo or farm, pets, swimming (whirlpool, sauna visits), being in crowded places, public transport, intimacy, flowers, or other author defined social restrictions)
C = (No social restrictions)
O = Severe or mild infections (prevalence and infectious complications), quality of life, anti-cancer treatment-related complications (adjustments in therapy or delay), costs, mortality, event-free survival

PICO (2)
What is the effect of social restrictions (regarding bleeding risk) on hemorrhagic complications and other outcomes in children with any type of cancer and/or after stem-cell transplantation?

P = Children (aged 0-18 years) with any type of cancer and/or after stem-cell transplantation
I = Social restrictions regarding risk of bleeding (i.e. restriction in physical contact sports, high-velocity sports, high impact or high energetic sports, sports with high risk of falling such as skiing or skating, playing with high risk of falling such as slides, high or low altitude events such as scuba diving or flying, rollercoaster rides or other author-defined social restrictions)
C = (No social restrictions)
O = Hemorrhagic complications (mild and severe), quality of life, anti-cancer treatment related complications, (adjustments in therapy or delay), costs, mortality, event-free survival

PICO (3)
What is the effect of social restrictions, after a minor procedure or in patients with a venous access line with needle insertion, on infections and other outcomes in children with any type of cancer and/or after stem-cell transplantation?

P = Children (aged 0-18 years) with any type of cancer and/or after stem-cell transplantation after a minor procedure (i.e. lumbar puncture) or with venous access line (central venous access ports) with needle insertion
I = Social restrictions (e.g. being in crowded places, showering, taking a bath, swimming)
C = (No social restrictions)
O = Severe or mild infections (prevalence and infectious complications), quality of life, anti-cancer treatment-related complications (adjustments in therapy or delay), costs, mortality, event-free survival

PICO (4)
What is the effect of hygiene rules on infections and other outcomes in children with any type of cancer and/or after stem-cell transplantation?

P = Children (aged 0-18 years) with any type of cancer and/or after stem-cell transplantation
I = Hygiene rules (e.g. cleaning, laundry, renewing of clothes, personal hygiene)
C = (No hygiene rules)
O = Severe or mild infections (prevalence and infectious complications), quality of life, anti-cancer treatment-related complications (adjustments in therapy or delay), costs, mortality, event-free survival

The guideline panel formed these four general clinical questions. In case of specific clinical questions of individual interventions further on in the process, these PICO's will be divided into clinical sub-questions.

2. In- and exclusion criteria
Then, together with the guideline panel, in- and exclusion criteria were defined.

Population:
- Children with cancer;
- Aged 0-18 years.

- When not enough studies are found in this group: guidelines in other pediatric patient groups (infectious diseases, hematology) or adult guidelines will be searched (applicability depending per clinical question).

Outcomes:
- Severe infections (defined as: infections leading to hospital admission or any other author-defined severity);
- Mild infections (defined as: infections not leading to hospital admission or any other author-defined mild infections);
- Quality of life (self-reported or by-proxy reported);
- Anti-cancer treatment-related complications (adjustments in therapy or delay);
- Costs;
- Mortality;

- Event-free survival (author-defined);
- Mild hemorrhagic event (defined as: nose bleeds, small bleedings that can easily be controlled, petechiae of oral mucosa or skin, spontaneous hematoma);
- Severe hemorrhagic event (defined as hemorrhage leading to severe and permanent damage, severe morbidity, severe brain-bleeding, bleeding associated with severe hemodynamic instability, fatal bleeding).

Type of studies:

- Firstly, RCTs are preferred. Then, if these studies do not provide enough evidence, other controlled studies can be included;
- Case series and case reports will be excluded;
- No language resection;
- No year restriction;
- Databases: PubMed, Embase, Cochrane CENTRAL, CINAHL.

3. Search strategy

Together with a medical librarian, an extensive literature search was created and performed (see Appendix 3). We searched for all terms regarding social restrictions in pediatric oncology patients, as defined in the clinical questions. PubMed, Embase, Cochrane CENTRAL, CINAHL were searched, with a total of 6038 results (most recently: December 2020). The entire in- and exclusion process is shown in Appendix 4).

4. Quality of single studies

4.1 Evaluating methodological quality of included RCTs

Bias evaluation was performed according to the Cochrane handbook. (3)

- *Selection bias*: random sequence generation and the allocation concealment;
- *Performance bias*: blinding of participants and personnel;
- *Detection bias*: blinding of outcome assessors for all separate outcomes;
- *Attrition bias*: based on incomplete outcome data for all separate outcomes;
- *Reporting bias:* selective reporting;
- *Other potential sources of bias.*

4.2 Evaluating methodological quality of included non-RCTs

The methodology for Risk of Bias assessment had to be adjusted for the non-RCT studies. We combined the Risk of Bias tool for observational studies, as described in the IGHG Handbook (4), with a couple of aspects of the RCT tool as described earlier. By combining these tools, we aimed to have the best possible tool to assess the Risk of Bias in our types of studies. The tool that we used is shown in Table 2.

Table 2: Adjusted Risk of Bias criteria

Selection bias	Is the study group representative? Cases and controls were selected based on comparable patient characteristics (i.e. age, gender and tumor type) *Low risk if:* no significant differences between cases and controls with respect to age, gender and tumor type *High risk if:* cases and controls differ with respect to age, gender and tumor type (baseline imbalances caused by selection)
Attrition bias	Is complete outcome data for all the participants available in this study? Is the follow up adequate?

	Low risk if: no missing data, reasons for missing data not related to outcome, missing data balanced across groups, proportion missing or plausible effect size nog enough to have a clinically relevant effect *High risk if:* imbalance in numbers or reasons, proportion missing or plausible effect size enough to have a clinically relevant effect, inappropriate use of imputation, 'as treated' analysis with substantial departure from allocation
Detection bias	Are the outcome assessors blinded for important determinants related to the outcome?
	Low risk if: the outcome assessors were blinded for important determinants related to the outcome *High risk if:* no blinding or broken blinding ***and*** measurement likely to be influenced
Reporting bias	Is the report complete? Are the outcomes that were planned to be measured also reported?
	High risk if: Outcomes not reported as pre-specified or expected or outcomes reported incompletely so they cannot be entered in meta-analysis
Confounding bias	Are the analyses adjusted for important confounding factors?
	Low risk if: important prognostic factors (i.e. age, gender, diagnosis and risk stratification) were taken adequately into account *High risk if:* important prognostic factors (i.e. age, gender, diagnosis and risk stratification) were inadequately or not taken into account
Other bias	The following list of other potential sources of bias in a clinical study may aid detection of further problems. *High if:* • The conduct of the study is affected by interim results (e.g. recruiting additional participants from a subgroup showing more benefit). • There is deviation from the study protocol in a way that does not reflect clinical practice (e.g. *post hoc* stepping-up of doses to exaggerated levels). • There is pre-randomization administration of an intervention that could enhance or diminish the effect of a subsequent, randomized, intervention. • Inappropriate administration of an intervention (or co-intervention). • Contamination (e.g. participants pooling drugs). • Occurrence of 'null bias' due to interventions being insufficiently well delivered or overly wide inclusion criteria for participants (Woods 1995). • An insensitive instrument is used to measure outcomes (which can lead to under-estimation of both beneficial and harmful effects). • Selective reporting of subgroups. • Fraud. • Baseline imbalances for other reasons than through selection. • Other

4.3 Dual appraisal

All relevant steps (study identification, data extraction and management, assessment of risk of bias in included studies) were performed by two review authors (DS, DK), independently. Discrepancies will be resolved by consensus.

4.4 Summary of findings tables

For each clinical question a summary of findings table of the body of evidence will be completed. A summary of findings table provides key information of every single study about the main patient characteristics, the magnitude of effects for the defined outcomes and determinants, and the quality of that study.

5. Total body of evidence

5.1 Importance of outcomes

According to the GRADE methodology, the outcomes were defined as 'low important, important or critical'. The importance of outcomes and its hierarchy were discussed in the guideline panel meeting. Based on consensus, the following hierarchy of importance was determined by the guideline panel:

Table 3: Importance of outcomes social restrictions

Critical	9	Severe infections Severe hemorrhagic events Anti-cancer treatment-related complications Mortality
	8	Quality of life (self-reported)
	7	Quality of life (by-proxy reported) Event free survival
Important	6	Mild infections Mild hemorrhagic events
	5	
	4	
Low importance	3	
	2	
	1	Costs

5.2 Grading the quality of the body of evidence (GRADE)

Then, the quality of the body of evidence per outcome is assessed. According to the GRADE methodology, a randomized controlled trial starts at a high quality evidence level, whereas a cohort study or other type of study starts at a lower quality evidence level. Then, the following considerations can lower the quality of evidence: inconsistency (degree of consistency of effect between or within studies), imprecision (the precision of the results), indirectness (the generalizability of population and outcomes from each study to the population of interest), publication bias or other study limitations.

Some factors might increase the quality of the evidence: for example, a large magnitude of effect or a dose-response gradient.

A total GRADE score for the total body of evidence will be appointed per outcome:

⨁⨁⨁⨁ High quality evidence
⨁⨁⨁⊖ Moderate quality evidence
⨁⨁⊖⊖ Low quality evidence
⨁⊖⊖⊖ Very low quality evidence

6. Translate evidence into recommendations – Evidence-to-Decision Framework
Results of literature studies were used to formulate recommendations. If no studies were identified, we carefully considered expert consensus.

According to the GRADE methodology, an evidence-to-decision (EtD) framework was used to translate evidence into recommendations. Below examples of the questions in such a EtD framework are shown. These questions were answered by the guideline panel to help form a recommendation.

- PROBLEM:
  Is the problem a priority?
- BENEFITS AND HARMS:
  What is the overall certainty of this evidence?
  Is there important uncertainty about how much people value the main outcomes?
  Are the desirable anticipated effects large?
  Are the undesirable anticipated effects small?
  Are the desirable effects large relative to undesirable effects?
- RESOURCE USE:
  Are the resources required small?
  Is the incremental cost small relative to the net benefits?
  What would be the impact on health inequities?
- EQUITY:
  What would be the impact on health inequities?
- ACCEPTABILITY:
  Is the option acceptable to key stakeholders?
- FEASIBILITY:
  Is the option feasible to implement?

7. Terminology in recommendations
We used the GRADE terminology for evidence-based guidelines, such as ‘we suggest’ or ‘we recommend’. For our expert evidence recommendations, we used the terminology from the following article: “Lexicon for guidance terminology in pediatric hematology/oncology: A White Paper” (5). For example, we used ‘we believe’, to emphasize that these recommendations are based on expert opinion and group consensus, and not on a relevant body of identified studies. For further information about this terminology, we refer to this specific paper.

If necessary, in line with the GRADE methodology, we formulated good practice statements (6) for recommendations that we consider a part of good clinical practice, but are not researched specifically. These good practice statements definitely have a place in this guideline, but are not researched specifically (because this is not achievable or not deemed necessary).

General remarks applicable to all recommendations:
The purpose of this guideline is to provide recommendations for children with cancer, receiving anti-cancer treatment with curative intent. The guideline was not intended to provide recommendations for palliative care settings.

Module 1: Bath toy use (English)

A: Recommendations

Research question: What is the effect of bath toy use on infections in children with any type of cancer and/or after stem-cell transplantation?

A1.1: Recommendation (English)

STRONG recommendation, VERY LOW QUALITY of evidence	We recommend against the use of bath toys that have a reservoir (in which water can be retained) or bath toys that cannot be dried thoroughly.

B: Clinical question, search and selection

B1: Clinical question:
What is the effect of hygiene rules on infections and other outcomes in children with any type of cancer and/or after stem-cell transplantation?

P = Children (aged 0-18 years) with any type of cancer and/or after stem-cell transplantation
I = Hygiene rules (e.g. cleaning, laundry, renewing of clothes, personal hygiene)
C = (No hygiene rules)
O = Severe or mild infections (prevalence and infectious complications), quality of life, anti-cancer treatment-related complications (adjustments in therapy or delay), costs, mortality, event-free survival

B2: Literature search and study selection
For the complete methodology of this guideline development and the search strategy, we refer to pages 18-23.
Of 6038 unique citations identified in the literature search, one study with pediatric oncology patients (Buttery,1998 (7)) was included for this clinical question.

C: Results in pediatric and adult oncology patients

C1. Evidence in pediatric oncology patients
In our literature search, one study was included for this clinical question (Buttery, 1998) (7). In this study, the results of a case-control study in pediatric oncology patients are reported. Eight patients were infected with *Pseudomonas aeruginosa* and they subsequently matched these patients with controls (3:1 ratio) who were admitted on the pediatric ward at time of this *Pseudomonas* outbreak. Cases were defined as the eight patients with clinical infections with the outbreak *Pseudomonas* strain.

They identified several risk factors, such as the use of bath toys. 7 out of 8 cases reported bath toys use, whereas 7 out of 24 controls reported bath toys use (odds ratio 17 (95% CI 2.2, ∞), p=0.004). However: cases were significantly younger than controls. When bath toy use was

controlled for age (not reported how), the trend persisted, however it lost statistical significance (7). Importantly, they identified the same *Pseudomonas* strain on the bath toys as they identified in the patients.

Table 4: Study characteristics Buttery, 1998

Article Author, year Study type	**Population a. No. of patients b. Population**	**Case group* a. Group definition b. No. of patients, age, gender (% males)**	**Control Group a. Group definition b. No. of patients, age, gender (% males)**	**Included outcomes**	**Risk of bias assessment a. Selection bias b. Attrition bias c. Detection bias d. Reporting bias e. Confounding bias f. Other bias**
Buttery et al, 1998 Case-control study	a. 32 patients b. Cases and matched controls (with cancer diagnoses) during Pseudomonas outbreak, single-center, 1997.	a. Patients with clinical infections during Pseudomonas outbreak (with the same strain, on the pediatric ward) b. 8 patients, mean age 4.5 years, 62.5% males	a. Inpatients on the pediatric ward during the Pseudomonas outbreak but *without* infections (2) b. 24 patients, mean age 8.3 years, 62.5% males	- Number of infections	a. High b. Low c. Low d. Unclear e. High f. Low

*or possible risk factor group, or intervention group

Table 5: Outcomes Buttery, 1998 – Bath toy use

Author, study design	**No. of participants, total (cases vs controls) & Group definition**	**Results**	**Statistical methods**	**Effect size**	**Quality of evidence**
1) Buttery, 1998 Case-control study	1) 32 (8 vs 24) pediatric oncology patients. Cases with Pseudomonas infection, matched controls *without* Pseudomonas infection	1) 7/8 cases reported bath toys use (on which the Pseudomonas strain was identified); 7/24 controls reported bath toys use (on which the Pseudomonas strain was identified). *NB. When 'controlled for age' (not reported how', only a marginally significant association remained with p=0.06.*	1) Univariate and bivariate analyses, Cornfield method for Odds Ratio and confidence intervals	1) p=0.004 Odds Ratio 17 (2.2, ∞)	⨁◯◯◯[A] VERY LOW

A: GRADE: Grade quality assessment bath toy use: design is case-controlled study, inconsistency not serious, indirectness not serious, imprecision serious (downgraded one level because of small study population), publication bias unlikely, downgraded 1 level because of serious risk of bias (selection bias high, attrition bias low, detection bias low, reporting bias unclear, confounding bias high, other bias low).

C2. Additional recommendations guidelines (adults)

From our search for existing relevant guidelines, no additional guidelines were included for this clinical question.

D: Conclusion(s) of evidence (pediatric oncology patients)

⊕◯◯◯ (1 study)[A*] **VERY LOW** QUALITY of evidence	Significantly more bath toy use in group infected with *Pseudomonas* compared to the group without *Pseudomonas* infection.**

***** The letter refers to the specific GRADE assessment described in section C1.
** *Pseudomonas strain was identified in the culture of bath toys.*

E: Considerations

One study in pediatric oncology patients was found. In this study (7), significantly more bath toy use was reported in the group infected with *Pseudomonas* compared to the group without *Pseudomonas* infection (note, significance was lost when correcting for age, also, Pseudomonas strain was identified in the culture of bath toys). This study is small and retrospective, but it does show a (possible) effect of the use of bath toys, which is supported by our expert opinions.

The guideline panel agrees that bath toys with a reservoir in which water can be retained should not be used in children with cancer. The still standing water in the reservoir, for example in the inside of a bath toy as in the included study, is a reservoir for several bacteria like *Pseudomonas*, which can cause severe infections in these children. Also, toys that cannot be dried thoroughly are prone to formation of for bacteria and should therefore not be used.
It is not necessary to dispose all bath toys for (younger) children with cancer during their treatment. The panel agrees that if toys can be dried thoroughly and if there is no reservoir in which water can be retained, the toys are probably not an infectious risk and can be used safely.
Note that this also accounts for sponges, towels and other items that become wet during showering or bathing. As long as water is not retained in these items, we believe the infectious risk remains low.

Module 1: Badspeelgoed gebruik (NEDERLANDS)

F: Aanbeveling (Nederlands)

STERKE aanbeveling, ZEER LAGE KWALITEIT evidence	Wij raden het gebruik af van badspeelgoed met een reservoir (waarin water kan achterblijven) of badspeelgoed dat niet goed afgedroogd kan worden.

G: Overwegingen (Nederlands)

Er werd één studie gevonden over kinderen met kanker en het gebruik van badspeelgoed. In deze studie (7) werd er significant meer gebruik van badspeelgoed gerapporteerd in de groep met de *Pseudomonas* infectie, vergeleken met de groep zonder *Pseudomonas* infectie (significantie viel weg wanneer gecorrigeerd werd voor leeftijd, en ook, werd de *Pseudomonas* geïdentificeerd op het badspeelgoed). Deze studie is klein en retrospectief, maar het geeft een (mogelijk) effect aan van het gebruik van badspeelgoed, dat de werkgroep ook erkent.

De werkgroep is van mening dat badspeelgoed met een reservoir waarin water kan achterblijven afgeraden moeten worden voor kinderen met kanker. Het stilstaande water in het reservoir, zoals bijvoorbeeld in de badeenden in deze studie, is een goede bodem voor bacteriën zoals *Pseudomonas* om te groeien, wat kan zorgen voor ernstige infecties bij deze groep kinderen. Ook badspeelgoed dat niet goed afgedroogd kan worden zou niet gebruikt moeten worden door kinderen met kanker om dezelfde reden.
Het is niet nodig om al het (bad)speelgoed weg te gooien; als badspeelgoed wel goed afgedroogd kan worden en water hierin niet kan blijven staan (in een reservoir of iets soortgelijks) kan dit gewoon gebruikt worden omdat wij van mening zijn dat het risico op infectie hierdoor dan zeer minimaal is.
Let op, deze argumenten gelden ook voor het gebruik van sponzen, handdoeken en andere spullen die nat worden tijdens het douchen of in bad gaan.

Module 2: Bubble bath use (English)

A: Recommendations

Research question: What is the effect of bubble bath use on infections in children with any type of cancer and/or after stem-cell transplantation?

A1.1: Recommendation (English)

WEAK recommendation, VERY LOW QUALITY of evidence	We suggest not to use warm publically accessible bubble baths.

WEAK recommendation, EXPERT evidence	We believe the use of a bubble bath at home is allowed, as long as the bath can be cleaned thoroughly and water is refreshed completely after every bath.

B: Clinical question, search and selection

B1: Clinical question:

What is the effect of hygiene rules on infections and other outcomes in children with any type of cancer and/or after stem-cell transplantation?

P = Children (aged 0-18 years) with any type of cancer and/or after stem-cell transplantation
I = Hygiene rules (e.g. cleaning, laundry, renewing of clothes, personal hygiene)
C = (No hygiene rules)
O = Severe or mild infections (prevalence and infectious complications), quality of life, anti-cancer treatment-related complications (adjustments in therapy or delay), costs, mortality, event-free survival

B2: Literature search and study selection

For the complete methodology of this guideline development and the search strategy, we refer to pages 18-23.
Of 6038 unique citations identified in the literature search, one study with pediatric oncology patients (Buttery,1998) was included for this clinical question.

C: Results in pediatric and adult oncology patients

C1. Evidence in pediatric oncology patients

In our literature search, one study was included for this clinical question (Buttery, 1998) (7). In this study, the results of a case-control study in pediatric oncology patients are reported. Eight patients were infected with *Pseudomonas aeruginosa* and they subsequently matched these patients with controls (3:1 ratio) who were admitted on the pediatric ward at time of this *Pseudomonas* outbreak. Cases were defined as the eight patients with clinical infections with the outbreak *Pseudomonas* strain.

They identified several risk factors, and in addition to previously described bath toy used, they also identified another risk factor, i.e. the use of a bubble bath. Seven out of 8 cases reported bubble bath use, whereas 9 out of 24 controls reported bubble bath use. This corresponds to an odds ratio of 11.7 (95% CI 1.5, ∞) with a p-value of 0.014 (7). Note, they did not identify the *Pseudomonas* strain in the cultures of the bubble bath water. This outcome was not controlled for age.

Table 4: Study characteristics Buttery, 1998

Article **Author, year** **Study type**	**Population** **a. No. of patients** **b. Population**	**Case group*** **a. Group definition** **b. No. of patients, age, gender (% males)**	**Control Group** **a. Group definition** **b. No. of patients, age, gender (% males)**	**Included outcomes**	**Risk of bias assessment** **a. Selection bias** **b. Attrition bias** **c. Detection bias** **d. Reporting bias** **e. Confounding bias** **f. Other bias**
Buttery et al, 1998 Case-control study	a. 32 patients b. Cases and matched controls (with cancer diagnoses) during Pseudomonas outbreak, single-center, 1997.	a. Patients with clinical infections during Pseudomonas outbreak (with the same strain, on the pediatric ward) b. 8 patients, mean age 4.5 years, 62.5% males	a. Inpatients on the pediatric ward during the Pseudomonas outbreak but *without* infections (2) b. 24 patients, mean age 8.3 years, 62.5% males	- Number of infections	a. High b. Low c. Low d. Unclear e. High f. Low

*or possible risk factor group, or intervention group

Table 6: Outcomes Buttery, 1998 – Bubble bath use

Author, study design	**No. of participants, total (cases vs controls) & Group definition**	**Results**	**Statistical methods**	**Effect size**	**Quality of evidence**
1) Buttery, 1998 Case-control study	1) 32 (8 vs 24) pediatric oncology patients. Cases with Pseudomonas infection, matched controls *without* Pseudomonas infection	1) 7/8 cases reported bubble bath use; 9/24 controls reported bubble bath use (Pseudomonas strain not identified).	1) Univariate and bivariate analyses, Cornfield method for Odds Ratio and confidence intervals	1B) p=0.014 Odds Ratio 11.7 (1.5, ∞)	⨁◯◯◯[B] VERY LOW

B: GRADE: Grade quality assessment bubble bath use: design is case-controlled study, inconsistency not serious, indirectness not serious, imprecision serious (downgraded one level because of small study population), publication bias unlikely, downgraded 1 level because of serious risk of bias (selection bias high, attrition bias low, detection bias low, reporting bias unclear, confounding bias high, other bias low).

C2. Additional recommendations guidelines (adults)

From our search for existing relevant guidelines, no additional guidelines were included for this clinical question.

D: Conclusion(s) of evidence (pediatric oncology patients)

⊕◯◯◯ (1 study)[B*] **VERY LOW** QUALITY of evidence	Significantly more bubble bath use in group infected with *Pseudomonas* compared to the group without *Pseudomonas* infection.**

***** The letter refers to the specific GRADE assessment described in section C1.
**Pseudomonas strain was not identified in culture of bubble bath water.*

E: Considerations

One study in pediatric oncology patients was found. In this study (7), significantly more bubble bath use was reported in the group infected with *Pseudomonas* compared to the group without *Pseudomonas* infection (note, the *Pseudomonas* strain was not identified in culture of bubble bath water). This study is small and retrospective, but it does show a (possible) effect of the use of bubble baths on *Pseudomonas* infection.

Firstly, the guideline panel suggests not to use warm bubble baths in for example public swimming pools, saunas or other accommodations. We believe the infectious risk in these types of bubble baths is high because of the amount of people that enter the bubble baths, the constant high temperature of the bubble baths that form a good environment for bacteria and most importantly the fact that, for these publically accessible bubble baths, water is not frequently refreshed. Therefore we suggest not to use these types of -publically accessible- warm bubble baths.

The guideline panel agrees that there are harms for the use of bubble baths at home or at for example a vacation accommodation. These baths, unlike the publically accessible bubble baths, are not visited by other people and water can be refreshed easily. Therefore, the guideline panel believes that if the bath can be cleaned properly before the use of the bath, and water can be completely refreshed, the use of a bubble bath at home (or at a vacation accommodation) is allowed.

Module 2: Bubbelbad gebruik (NEDERLANDS)

F: Aanbeveling (Nederlands)

ZWAKKE aanbeveling, ZEER LAGE kwaliteit evidence	Wij adviseren tegen het gebruik van warme publiek toegankelijke bubbelbaden.

ZWAKKE aanbeveling, EXPERT evidence	De werkgroep is van mening dat het gebruik van een bubbelbad thuis toegestaan is, zolang het bad grondig schoongemaakt kan worden en dat het water compleet ververst kan worden na elk bad.

G: Overwegingen (Nederlands)

Er werd één studie gevonden over kinderen met kanker en het gebruik van een bubbelbad. In deze studie (7) werd er significant meer gebruik van het bubbelbad gerapporteerd in de groep met de *Pseudomonas* infectie, vergeleken met de groep zonder *Pseudomonas* infectie (de *Pseudomonas* werd **niet** geïdentificeerd in het water van het bubbelbad). Deze studie is klein en retrospectief, maar het geeft een (mogelijk) effect aan van het gebruik van een bubbelbad, dat de werkgroep grotendeels erkent.

Ten eerste adviseert de werkgroep tegen het gebruik van warme, publiek toegankelijke bubbelbaden in bijvoorbeeld zwembaden, sauna's of andere accommodaties. Wij zijn van mening dat er een groot infectierisico is in deze bubbelbaden vanwege de grote hoeveelheid mensen die hierin gaat, de constant hoge temperatuur van deze bubbelbaden wat een goede omgeving is voor bacteriën om te groeien, en het meest belangrijke argument, dat het water van deze publiek toegankelijke bubbelbaden niet frequent wordt ververst. Al deze argumenten vormen genoeg reden voor de werkgroep om adviseren tegen het gebruik publiek toegankelijke bubbelbaden in eerder genoemde accommodaties.

De werkgroep is van mening dat er géén argumenten zijn tegen het gebruik van bubbelbaden thuis of in een privé vakantie woning of accommodatie. Deze bubbelbaden, in tegenstelling tot eerder genoemde publiek toegankelijke bubbelbaden, worden niet door veel mensen bezocht (wellicht familieleden, maar dan wordt het water tussendoor ververst) en het water van het bad kan makkelijk ververst worden. Als het bubbelbad goed schoongemaakt kan worden voor gebruik en het water compleet ververst kan worden, is het gebruik van een bubbelbad thuis of in een privé accommodatie toegestaan.

Module 3: Chlorhexidine use (English)

A: Recommendations

Research question: What is the effect of chlorhexidine bathing or other bath wipe use on infections in children with any type of cancer and/or after stem-cell transplantation?

A1.1: Recommendation (English)

WEAK recommendation, VERY LOW QUALITY of evidence	We suggest not to use chlorhexidine bathing or other bath wipes as it does not seem to have an added value to basic hygiene measures.

B: Clinical question, search and selection

B1: Clinical question:

What is the effect of hygiene rules on infections and other outcomes in children with any type of cancer and/or after stem-cell transplantation?

P = Children (aged 0-18 years) with any type of cancer and/or after stem-cell transplantation
I = Hygiene rules (e.g. cleaning, laundry, renewing of clothes, personal hygiene)
C = (No hygiene rules)
O = Severe or mild infections (prevalence and infectious complications), quality of life, anti-cancer treatment-related complications (adjustments in therapy or delay), costs, mortality, event-free survival

B2: Literature search and study selection

For the complete methodology of this guideline development and the search strategy, we refer to pages 18-23.
Of 6038 unique citations identified in the literature search, three studies with pediatric oncology patients (Raulji 2015 (8), Zerr 2020 (9), Kjellin 2020(10)) were included.

C: Results in pediatric and adult oncology patients

C1. Evidence in pediatric oncology patients

C1.1. Bath wipes

One RCT by Kjellin et al (2020) (10), in which patients ≤21 years of age who were scheduled to undergo an autologous or allogeneic HCT received either experimental bath wipes or standard bath wipes. The experimental bath wipes contained allantoin, colloidal silver, preservatives, vitamin E, aloe, and lauryl glucoside. In total, 127 patients were included in the study.

Colonization of vancomycin-resistant enterococcus was found in in 1/61 patients (2%) in the group with experimental bath wipes versus 2/66 patients (3%) in the standard bath wipes group (p-value 1). The colonization with multidrug resistant organisms was 0 in both groups. In the group with experimental bath wipes, CLABSI was reported in 0/61 patients (0%) versus 2/66 patients* (3%) in the standard group (p-value 0.5) (10). (**Staphylococcus epidermidis & Pseudomonas)*

C1.2. Chlorhexidine bathing

Our literature search identified two studies answering this clinical question. Firstly, Raulji et al (2015) (8) performed a study that assessed daily bathing with chlorhexidine and its effect on nosocomial infection rates (i.e. infections that originate in the hospital) in pediatric oncology patients. In total, 330 patients were included in the study. 190 patients were included in the control group (i.e. no chlorhexidine bathing) and 140 patients were included in the study group and received daily chlorhexidine bathing. Raulji et al report that 170 out of 190 patients in the control group did not get an infection, versus 128 out of 140 in the intervention group who did not get an infection. This means, if calculated, 20 out of 190 patients in the control group got an infection versus 12 out of 140 patients in the intervention group (RR or p-value not reported). Seven incidences of blood stream infections were reported in the control group, and three incidences reported in the intervention group (p-value 0.70).
In this study, an incidence density per age group is reported, i.e. the rate of infection is quantified in number of occurrences per 100 days per age group. There was a significant difference in incidence density (ID) for infections in age group 12-21: in the control group, the ID is 3.91 versus 0.96 in the study group (p=value 0.03). Age groups 7-12 and 4-7 did not differ in incidence density (respectively, p-values 0.07 and 0.28). Remarkably, in the age group 0-4 years, the incidence density is higher in the study group, namely 2.28 versus 1.31 in the control group (p-value 0.29). They conclude that all the age groups in the study group, except 0-4 years old, had a lower occurrence of infection for 100 days compared to the control group (8). A significant difference was only reported in the age group 12-21 years.

Secondly, Zerr et al (2020) (9) performed a randomized controlled trial in pediatric oncology patients with externally tunneled central venous catheters who underwent once-daily bathing for 90 days with either cloths impregnated with mild cleansers or with 2% chlorhexidine-impregnated cloths. In total, 174 patients were included in the study. In the chlorhexidine group, they reported 5.44 CLABSI (central line associated blood stream infection) per 1000 line days compared to 3.1 CLABSI per 1000 line days in the control group, with adjusted incidence rate ratio 1.76 (95% CI 1.00-3.08), p= 0.049. In addition, in the chlorhexidine group, the estimated 90-day cumulative incidence of CLABSI was 34.6% (95% CI, 25.1-46.4%) versus 24.1% (95% CI 16.1-35.3%) in the control group (p=0.091) (9). This study also described cutaneous adverse events, when limited to events to be at least possibly related to the intervention, 10% in the chlorhexidine group versus 6% in the control group (p-value not reported).

Table 7: Study characteristics Raulji 2015

Article **Author, year** **Study type**	**Population** **a. No. of patients** **b. Population**	**Case group*** **a. Group definition** **b. No. of patients, age, gender (% males)**	**Control Group** **a. Group definition** **b. No. of patients, age, gender (% males)**	**Included outcomes**	**Risk of bias assessment** **a. Selection bias** **b. Attrition bias** **c. Detection bias** **d. Reporting bias** **e. Confounding bias** **f. Other bias**
Raulji et al, 2015 Pre- and post-intervention study	a. 330 patients b. All pediatric oncology inpatient admissions, single-center, 2008-2010.	a. Post-intervention group given daily sponge bathing with chlorhexidine b. 140 patients; 49 patients aged 0-4, 35 patients aged 4-7, 19 patients aged 7-12, 37 patients aged 12-21; 60.7% males	a. Pre-intervention group of children *not* receiving chlorhexidine baths b. 190 patients, 61 patients aged 0-4, 27 patients aged 4-7, 48	- Number of infections	a. High b. High c. Low d. Unclear e. High f. High

			patients aged 7-12, 54 patients aged 12-21; 50.5% males		

*or possible risk factor group, or intervention group

Table 8: Study characteristics Zerr 2020, Kjellin 2020 (RCTs)

Article Author, year Study type	**Population a. No. of patients b. Population**	**Case group* a. Group definition b. No. of patients, age, gender (% males)**	**Control Group a. Group definition b. No. of patients, age, gender (% males)**	**Included outcomes**	**RCT Risk of bias assessment a. Selection bias (random sequence generation) b. Selection bias (allocation concealment) c. Performance bias d. Detection bias e. Attrition bias f. Reporting bias g. Other bias**
Kjellin et al, 2020 RCT	a. 127 patients b. Patients ≤21 years of age who were scheduled to undergo an autologous or allogeneic HCT.	a. Bath wipes, used once daily for 60 days post-HCT, containing allantoin, colloidal silver, preservatives, vitamin E, aloe, and lauryl glucoside. b. 61 patients, median age 10 years (range 0.26-20.95 years), 27 males (44%).	a. Bath wipes, used once daily for 60 days post-HCT, contained rinse-free soap and lotion b. 66 patients, median age 6.1 years (range 0.43-21.12 years), 37 males (56%).	- Number of infections	a. Unclear b. Unclear c. High d. Low e. Low f. Unclear g. High
Zerr et al, 2020 RCT	a. 174 patients b. Pediatric oncology patients ≥2 months and <22 years who were receiving treatment or were undergoing allogeneic HCT, and had an eligible CVC (externally tunneled).	a. Patients underwent once-daily bathing for 90 days with either cloths impregnated with mild cleansers. b. 88 patients, median age 5.5 years (range 2-12 years), 53 males (60,2%).	a. Patients underwent once-daily bathing for 90 days with 2% CHG-impregnated cloths. b. 87 patients, median age 4 years (range 1-8 years), 51 males (58.6%).	- Number of infections - Adverse events	a. Low b. Low c. Low d. Unclear e. High f. Unclear g. Low

*or possible risk factor group, or intervention group

Table 9: Outcomes Kjellin 2020 – Bath wipes with chlorhexidine

Author, study design	No. of participants, total (cases vs controls) & Group definition	Results	Statistical methods	Effect size	Quality of evidence
1) Kjellin, 2020 RCT	1) Patients ≤21 years of age who were scheduled to undergo an autologous or allogeneic HCT received either experimental bath wipes (see table 1 for exact composition) or standard bath wipes.	1A) Experimental bath wipes; colonization of vancomycin-resistant enterococcus in 1/61 patients (2%). Standard bath wipes; colonization vancomycin-resistant enterococcus in 2/66 patients (3%). 1B) Colonization with multidrug resistant organisms 0 in both groups. 1C) Experimental bath wipes; CLABSI in 0/61 patients (0%). Standard bath wipes; CLABSI in 2/66 patients (3%). (*_Staphylococcus epidermidis & Pseudomonas)_	1) Fisher's exact test	1A) p=1 1B) Not applicable 1C) p=0.50	⊕⊕◯◯[C] LOW

C: GRADE: Grade quality assessment bath wipes: design is randomized controlled trial, inconsistency not serious, indirectness not serious, imprecision serious (because of few events and therefore halting the trial), publication bias unlikely, downgraded 1 level because of serious risk of bias (random sequence generation unclear, allocation concealment unclear, performance bias high, detection bias low, attrition bias low, reporting bias unclear, other bias high)

Table 10: Outcomes Raulji, 2015, Zerr, 2020 – Chlorhexidine bathing

Author, study design	No. of participants, total (cases vs controls) & Group definition	Results	Statistical methods	Effect size	Quality of evidence
1) Raulji, 2015 Pre- and post-intervention study	1) 330 (140 vs 190) pediatric oncology patients. Daily bathing with chlorhexidine versus no-chlorhexidine bathing	1A) Total amount of patients getting **any** infection 20/190 children (10,5%) with any infection in pre-intervention group (no chlorhexidine bathing); 12/140 (8.6%) in post-intervention group (chlorhexidine bathing). 1A1) Total amount of **blood stream infections** (BSI) infection per group: 7 incidences in control group, 3 incidences in chlorhexidine group. 1B1) Incidence density (number of occurrences of infection/100 days) in age group 12-21: 3.91 in control group; 0.96 in intervention (chlorhexidine) group. 1B2) Incidence density in age groups 4-7 and 7-12 lower in study group (respectively; 1.49 vs 0.00 and 2.62 vs 1.14). 1B3) In age group 0-4, incidence density of infection **higher** in study group, 2.28 versus 1.31 in control group.	1A) Not provided 1A1) Not provided 1B1) Not provided 1B2) Not provided 1B3) Not provided	1A) Not provided 1A1) p=0.70 1B1) p = 0.03 1B2) p-values respectively p=0.07 and p=0.28 1B3) p=0.29	⊕◯◯◯[D] VERY LOW

2) Zerr, 2020 RCT	2) Pediatric oncology patients with externally tunneled CVCs underwent once-daily bathing for 90 days with either cloths impregnated with mild cleansers or with 2% CHG-impregnated cloths.	2A) Chlorhexidine group: 5.44 CLABSI per 1000 line days Control group: 3.1 CLABSI per 1000 line days 2B) Chlorhexidine group: the estimated 90-day cumulative incidence of CLABSI was 34.6% [(95% CI, 25.1-46.4%]. Control group: the estimated 90-day cumulative incidence of CLABSI was 24.1% [95% CI 16.1-35.3%]. 2C) Cutaneous adverse events chlorhexidine group: 24% Cutaneous adverse events control group: 15% (When limited to events to be at least possibly related to the intervention, the frequency of events was lower (10% vs 6%).	2A) Adjusted incidence rate ratio 2B) Log rank test 2C) Not reported	2A) 1.76 [95% CI 1.00-3.08], p= 0.049 2B) p=0.091 2C) Not reported	⊕⊕◯◯[E] LOW

D: GRADE: Grade quality assessment chlorhexidine bathing: design is case-controlled study, inconsistency not serious, indirectness not serious, imprecision not serious, publication bias unlikely, downgraded 2 levels because of very serious risk of bias (selection bias high, attrition bias high, detection bias low, reporting bias unclear, confounding bias high, other bias high).

E: GRADE: Grade quality assessment chlorhexidine bathing: design is randomized controlled trial, inconsistency not serious, indirectness not serious, imprecision not serious, publication bias unlikely, downgraded 2 levels because of very serious risk of bias (random sequence generation low, allocation concealment low, performance bias low, detection bias unclear, attrition bias high, reporting bias unclear, other bias low)

C2. Additional recommendations guidelines (adults)
From our search for existing relevant guidelines, no additional guidelines were included for this clinical question.

D: Conclusion(s) of evidence (pediatric oncology patients)

D1.1 Bath wipes

⊕⊕◯◯ (1 study)[C*] **LOW** QUALITY of evidence	No significant differences in prevalence of infections were seen in the experimental bath wipes group versus the standard bath wipes group.

D1.2 Chlorhexidine bathing

⊕◯◯◯ (1 study)[D*] **VERY LOW** QUALITY of evidence	In one study, overall, no significant differences in prevalence of infections between patients with vs. without chlorhexidine bathing.

⊕◯◯◯ (1 study)[D*] **VERY LOW** QUALITY of evidence	In one study, significantly lower prevalence of infections in patients with vs. without chlorhexidine bathing in specific age group 12-21 years.

⊕⊕◯◯ (1 study)[E*] **LOW** QUALITY of evidence	In one study, no significant differences in prevalence of infections were seen in the chlorhexidine bathing group versus the control group.

***** The letter refers to the specific GRADE assessment described in section C1.

E: Considerations

E1.1 Bath wipes

One study (10) in pediatric oncology patients was found. In conclusion, no significant differences in prevalence of infections were seen in the experimental bath wipes group versus the standard bath wipes group. The guideline panel does not see any reason to suggest the use of these types of bath wipes, as the panel does not see any added value to basic hygiene measures.

This recommendation is based on evidence on bath wipes with ingredients such as allantoin, colloidal silver, preservatives, vitamin E, aloe, and lauryl glucoside (10). There was no evidence for any other types of bath wipes, and therefore we feel that bath wipes *in general* would not have any added value. Therefore, the panel suggests not to use bath wipes as it does not seem to have an added value to basic hygiene measures.

E1.2 Chlorhexidine bathing

Two studies in pediatric oncology patients were found. In one study (8), overall, no significant differences in prevalence of infections between patients with versus without chlorhexidine bathing were found. In this study, significantly lower prevalence of infections in patients with versus without chlorhexidine bathing in specific age group 12-21 years was reported. We believe that this specific reported lower prevalence of infections in the specific age group 12-21 years is mostly coincidental. The age groups were not predefined in the study and therefore it is difficult to assess the validity this outcome. Possibly, this is an age group in which basic hygiene measures might not be followed strictly, and that this result is possibly the result of a different intervention (namely 'regular basic hygiene measures' rather than 'chlorhexidine bathing'). Also in all the other age groups, no differences were seen between the two groups.

In one study (9), significant differences in prevalence of infections were seen in the chlorhexidine bathing group versus the control group were reported. This study, however, showed higher CLABSI rates in the chlorhexidine group. This study was of low quality and was stopped early because of poor accrual but does not support the use of routine chlorhexidine bathing in children with cancer.

Summarizing, two studies (8, 9) show inconsistent results as one of the studies even pointed towards more CLABSI in the chlorhexidine group, and the outcome from the other study that does show a significant difference in favor of the chlorhexidine group, is difficult to interpret. The guideline panel does not see any added value for chlorhexidine bathing, and we consider it more of a burden to these children. Therefore, the panel suggests not to use chlorhexidine bathing as it does not seem to have an added value to basic hygiene measures.

In summary, the guideline panel feels that both chlorhexidine bathing and bath wipes do not have an added value and that just following basic hygiene measures should be sufficient.

Module 3: Chloorhexidine gebruik (NEDERLANDS)

F: Aanbeveling (Nederlands)

ZWAKKE aanbeveling, ZEER LAGE KWALITEIT evidence	Wij adviseren tegen het gebruik van chloorhexidine in bad of andere hygiëne doekjes, omdat dit geen toegevoegde waarde lijkt te zijn op standaard hygiëne maatregelen.

G: Overwegingen (Nederlands)

G1.1. Hygiëne doekjes met chloorhexidine
Er werd één studie gevonden over het gebruik van hygiëne doekjes met chloorhexidine bij kinderen met kanker. In deze studie (10) werd er geen significant verschil gezien in de prevalentie van infecties tussen de groep met de experimentele hygiëne doekjes versus de standaard hygiëne doekjes. De werkgroep ziet geen enkele reden om dit type hygiëne doekjes te gebruiken, omdat de werkgroep geen enkele toegevoegde waarde ziet van deze middelen op gewone, basis persoonlijke hygiëne maatregelen.
Deze aanbeveling is gebaseerd op een studie met hygiëne doekjes met ingrediënten zoals allantoïne, colloidaal zilver, conservatieven, vitamine E, aloë en lauryl glucoside (10). Er is ook geen bewijs voor hygiëne doekjes met enige andere samenstelling, en daarom vindt de werkgroep dat deze hygiëne doekjes geen toegevoegde waarde zullen hebben. Concluderend is de werkgroep van mening dat basis hygiëne maatregelen voldoende zijn en dat (enig type) hygiëne doekjes geen effect zullen hebben.

G1.2. Chloorhexidine bad
Twee studies zijn gevonden over het gebruik van een bad met chloorhexidine bij kinderen met kanker. In één studie (8), over het geheel gezien, werd er geen verschil gezien in de prevalentie van infecties tussen de patiënten in de groep met als interventie een bad met chloorhexidine versus de patiënten in de groep met een bad zonder chloorhexidine. In deze studie werd wel een significant lagere prevalentie van infecties gerapporteerd in patiënten met de leeftijd 12-21 jaar. Wij zijn van mening dat deze specifieke uitkomst waarschijnlijk een toevalsbevinding is. De leeftijdsgroepen zijn niet van te voren gedefinieerd in deze studie, en daarom is het lastig om de waarde van deze uitkomst te bepalen. Mogelijk is het zo dat in deze leeftijdsgroep de basis hygiëne maatregelen niet optimaal uitgevoerd worden, waardoor een interventie met dagelijks hygiëne toepassen al een groot effect kan hebben (de interventie die dus effect heeft is dan ‘dagelijks hygiëne maatregelen toepassen’ in plaats van ‘in een bad met chloorhexidine’).

In één studie (9), werd er wel een significant verschil gezien in de prevalentie van infecties tussen de patiënten in de groep met als interventie een bad met chloorhexidine versus de patiënten in de groep met een bad zonder chloorhexidine. Echter, deze studie rapporteert een hoger aantal lijninfecties in de groep *met* chloorhexidine. Deze studie was van lage kwaliteit en is eerder gestopt vanwege trage inclusie en ondersteunt dus duidelijk *niet* het gebruik van chloorhexidine in bad bij kinderen met kanker.

Samengevat laten twee studies (8, 9) inconsistente resultaten zien, omdat één van deze studies zelfs *meer* lijninfecties laat zien in de groep met de interventie chloorhexidine en de andere

studie, met wel een beschreven significant effect, een moeilijk te valideren uitkomst rapporteert. Daarom is de werkgroep van mening dat er geen toegevoegde waarde is van het gebruik van chloorhexidine zowel in bad als met hygiëne doekjes de werkgroep ziet het zelf meer als een last voor de kinderen.

Daarom adviseren wij tegen het gebruik van chloorhexidine in bad of andere hygiëne doekjes, omdat dit geen toegevoegde waarde lijkt te zijn op standaard hygiëne maatregelen.

Module 4: Environmental factors (including sandbox) (English)

A: Recommendations

Research question: What is the effect of environmental factors on infections in children with any type of cancer and/or after stem-cell transplantation?

A1.1: Recommendation (English)

STRONG recommendation, ASCO guideline*	We suggest that children with cancer and neutropenia should avoid prolonged contact with environments that have high concentrations of fungal spores (i.e. construction or demolition sites, exposure to soil through gardening or digging, household renovation).

*Recommendation adapted from "ASCO and IDSA Clinical Practice Guideline"(1)

WEAK recommendation, EXPERT evidence	We believe that children with cancer can play in the sandbox as long as they carefully consider their hand hygiene.

B: Clinical question, search and selection

B1: Clinical question:

What is the effect of hygiene rules on infections and other outcomes in children with any type of cancer and/or after stem-cell transplantation?

P = Children (aged 0-18 years) with any type of cancer and/or after stem-cell transplantation
I = Hygiene rules (e.g. cleaning, laundry, renewing of clothes, personal hygiene)
C = (No hygiene rules)
O = Severe or mild infections (prevalence and infectious complications), quality of life, anti-cancer treatment-related complications (adjustments in therapy or delay), costs, mortality, event-free survival

B2: Literature search and study selection

For the complete methodology of this guideline development and the search strategy, we refer to pages 18-23.
Of 6038 unique citations identified in the literature search, zero studies with pediatric oncology patients were included for this clinical question.

C: Results in pediatric and adult oncology patients

C1. Evidence in pediatric oncology patients

In our literature search, 0 studies were included for this clinical question.

C2. Additional recommendations guidelines (adults)

One evidence-based guideline was found, namely: "Antimicrobial Prophylaxis for Adult Patients With Cancer-Related Immunosuppression: ASCO and IDSA Clinical Practice Guideline Update Summary" (1). They recommend: "Outpatients with neutropenia from cancer therapy should avoid prolonged contact with environments that have high concentrations of airborne fungal

spores (eg, construction and demolition sites, intensive exposure to soil through gardening or digging, household renovation) (Type of recommendation: consensus-based; benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: strong) (1).” No additional evidence was cited in this guideline.

D: Conclusion(s) of evidence (pediatric oncology patients)

0 studies in pediatric oncology patients were found.	-

E: Considerations

No evidence in pediatric oncology patients was found. However, a recommendation by the ASCO and IDSA (1) guideline was used for the decision by the guideline panel.

The guideline panel strongly agrees with the recommendation from the ASCO and IDSA guideline (1), as we agree that these environmental sites (construction or demolition sites, exposure to soil through gardening or digging, household renovation (1)), indeed could contain higher levels of fungal spores and could therefore be a potential danger.
Although this recommendation was not specifically made for children, we agree that it is also applicable to children with cancer. Therefore, we adapt the recommendation made by the ASCO and IDSA guideline panel (1). For more information we refer to the original guideline (1).

The guideline specifically made a recommendation about playing in the sandbox, as this is a clinically relevant subject for parents and children. No evidence in pediatric oncology patients or other guidelines were found.
The guideline panel believes that children with cancer should be allowed to play in the sandbox, either at home, at the playground or at school, as long as they carefully consider their hand hygiene. We believe that hand hygiene is most important after playing in the sandbox. We are aware that the sandbox, most of all the publically accessible ones, might not always be clean. However, we feel that it is a burden to the children if they have to be held out of the sandbox while all of their friends or classmates are playing in it. We feel that if children carefully wash their hands after playing in the sandbox, the infectious risk should be minimal. Therefore, we believe that children with cancer can play in the sandbox as long as they carefully consider their hand hygiene.

Module 4: Milieu en omgevingsfactoren (inclusief zandbak) (NEDERLANDS)

F: Aanbeveling (Nederlands)

STERKE aanbeveling, ASCO richtlijn *	Wij adviseren het vermijden van langdurig contact met een omgeving met een hoge concentratie van schimmelsporen (zoals een bouwplaats of plaats waar sloopwerkzaamheden plaatsvinden, blootstelling aan grond door tuinieren of graven, verbouwwerkzaamheden thuis) voor kinderen met kanker en neutropenie.

*Aanbeveling overgenomen van “ASCO and IDSA Clinical Practice Guideline” (1)

ZWAKKE aanbeveling, EXPERT evidence	De werkgroep is van mening dat kinderen met kanker in de zandbak kunnen spelen, zolang ze hun handhygiëne goed toepassen.

G: Overwegingen (Nederlands)

Er werd geen literatuur gevonden over dit onderwerp bij kinderen met kanker. Wel werd er een aanbeveling gevonden in een ASCO en IDSA richtlijn (1) die gebruikt werd door de werkgroep.

De werkgroep is het eens met de aanbeveling die beschreven wordt in de ASCO en IDSA richtlijn (1), omdat we het eens zijn met het feit dat in deze omgeving (zijnde een bouwplaats of plaats waar sloopwerkzaamheden plaatsvinden, blootstelling aan grond door tuinieren of graven, verbouwwerkzaamheden thuis(1)), inderdaad een hoge concentratie van schimmelsporen aanwezig kunnen zijn die een gevaar voor de gezondheid kunnen vormen. Hoewel de aanbeveling in de ASCO en IDSA richtlijn (1) niet specifiek gemaakt is voor kinderen met kanker, vindt de werkgroep dat deze wel toepasbaar is voor deze groep. Daarom nemen wij deze aanbeveling van de werkgroep van de ASCO en IDSA (1) over. We gaan verder niet in op de inhoud en de achtergrond van deze aanbeveling, hiervoor verwijzen wij naar het originele artikel. (1).

De werkgroep heeft een specifieke aanbeveling gemaakt over het spelen in de zandbak, aangezien dit een veelvoorkomende en belangrijke vraag is voor kinderen en hun ouders. Er werd geen literatuur gevonden over dit onderwerp.
De werkgroep is van mening dat kinderen met kanker in de zandbak kunnen spelen, zowel thuis als op school of in de speeltuin, zolang ze hun handhygiëne goed toepassen. Wij vinden dat handhygiëne het meest belangrijk is na het spelen in de zandbak. Wij zijn erkennen dat zandbakken, vooral in speeltuinen of op school, niet altijd even schoon zijn. Maar, wij vinden het een last voor kinderen als zij hier niet in mogen terwijl al hun klasgenoten of vrienden hier wel in mogen. Wij denken dat als kinderen goede handhygiëne toepassen na het spelen in de zandbak, het risico op infecties zeer minimaal is. Daarom is de werkgroep van mening dat kinderen met kanker in de zandbak kunnen spelen, zolang ze hun handhygiëne goed toepassen.

Module 5: Flowers (English)

A: Recommendations

Research question: What is the effect of having flowers or plants on infections in children with any type of cancer and/or after stem-cell transplantation?

A1.1: Recommendation (English)

STRONG recommendation, EXPERT evidence	We strongly believe that indoor flowers or plants at home should be allowed.

B: Clinical question, search and selection

B1: Clinical question:

What is the effect of hygiene rules on infections and other outcomes in children with any type of cancer and/or after stem-cell transplantation?

P = Children (aged 0-18 years) with any type of cancer and/or after stem-cell transplantation
I = Hygiene rules (e.g. cleaning, laundry, renewing of clothes, personal hygiene)
C = (No hygiene rules)
O = Severe or mild infections (prevalence and infectious complications), quality of life, anti-cancer treatment-related complications (adjustments in therapy or delay), costs, mortality, event-free survival

B2: Literature search and study selection

For the complete methodology of this guideline development and the search strategy, we refer to pages 18-23.
Of 6038 unique citations identified in the literature search, zero studies with pediatric oncology patients were included for this clinical question.

C: Results in pediatric and adult oncology patients

C1. Evidence in pediatric oncology patients

In our literature search, 0 studies were included for this clinical question.

C2. Additional recommendations guidelines (adults)

From our search for existing relevant guidelines, no additional guidelines were included for this clinical question.

D: Conclusion(s) of evidence (pediatric oncology patients)

0 studies in pediatric oncology patients were found.	-

E: Considerations

No evidence in pediatric oncology patients was found. Therefore, the recommendation is based on expert opinions. The guideline panel believes that indoor flowers and plants at home should be allowed. We believe the risk of infection of just having plants or flowers in the house, is very minimal. The panel does suggest additional hygiene measures, such as refreshing the water of the flowers often, and proposes that the children do not play with or help cleaning the soil of the plants. We believe that this also accounts for a Christmas tree and we see no reason why this should not be allowed in the house.

Again, basic hygiene measures should be appropriate to minimize the risk of infections through plants and flowers. Therefore, we believe that indoor flowers or plants at home should be allowed.

Module 5: Bloemen (NEDERLANDS)

F: Aanbevelingen (Nederlands)

STERKE aanbeveling, EXPERT evidence	De werkgroep is sterk van mening dat bloemen en planten in huis zijn toegestaan.

G: Overwegingen (Nederlands)

Er werd geen literatuur gevonden over dit onderwerp bij kinderen met kanker. Daarom is deze aanbeveling gebaseerd op de meningen van de experts in de werkgroep.

De werkgroep is van mening dat bloemen en planten in huis zijn toegestaan. Wij denken dat het risico op infectie door alleen het hebben van planten of bloemen in het huis, zeer minimaal is. De werkgroep is wel van mening dat er rekening moet worden gehouden met een aantal additionele hygiëne maatregelen, zoals bijvoorbeeld frequent het water van bloemen verversen, en het voorstel dat kinderen niet spelen met - of helpen met het schoonmaken van - de aarde van planten. Wij zijn ook van mening dat een kerstboom prima in huis kan worden gehouden. Nogmaals als basis hygiëne maatregelen worden toegepast en rekening wordt gehouden met bovenstaande aantal additionele hygiëne maatregelen rondom bloemen en planten, is de kans op infectie minimaal. Daarom is de werkgroep sterk van mening dat bloemen en planten (inclusief kerstboom) in huis zijn toegestaan.

Module 6: Events with altitude or pressure differences (English)

A: Recommendations

Research question: What is the effect of high or low altitude events on hemorrhagic complications in children with any type of cancer and/or after stem-cell transplantation?

A1.1: Recommendation (English)

WEAK recommendation, EXPERT evidence	We believe that clinically stable children with cancer without neutropenia (i.e. neutrophil count <0.5x10^9/L) or thrombocytopenia (i.e. platelet count <50x10^9/L) can perform events with altitude or pressure differences, such as going on a plane or scuba diving in agreement with their treating physician.

B: Clinical question, search and selection

B1: Clinical question:

What is the effect of social restrictions (regarding bleeding risk) on hemorrhagic complications and other outcomes in children with any type of cancer and/or after stem-cell transplantation?

P = Children (aged 0-18 years) with any type of cancer and/or after stem-cell transplantation
I = Social restrictions regarding risk of bleeding (i.e. restriction in physical contact sports, high-velocity sports, high impact or high energetic sports, sports with high risk of falling such as skiing or skating, playing with high risk of falling such as slides, high or low altitude events such as scuba diving or flying, rollercoaster rides or other author-defined social restrictions) (D)
C = (No social restrictions)
O = Hemorrhagic complications (mild and severe), quality of life, anti-cancer treatment related complications, (adjustments in therapy or delay), costs, mortality, event-free survival (E)

B2: Literature search and study selection

For the complete methodology of this guideline development and the search strategy, we refer to pages 18-23.
Of 6038 unique citations identified in the literature search, zero studies with pediatric oncology patients were included for this clinical question.

C: Results in pediatric and adult oncology patients

C1. Evidence in pediatric oncology patients

In our literature search, 0 studies were included for this clinical question.

C2. Additional recommendations guidelines (adults)

From our search for existing relevant guidelines, no additional guidelines were included for this clinical question.

D: Conclusion(s) of evidence (pediatric oncology patients)

0 studies in pediatric oncology patients were found.	-

E: Considerations

No evidence in pediatric oncology patients was found. Therefore, the recommendation is based on expert opinions.

The guideline panel believes that children with cancer can perform high or low altitude events such as going on a plane or scuba diving. We believe that children in a stable phase of their treatment without severe neutropenia or thrombocytopenia, should be allowed to perform this events. We see no obvious reasons why these events with altitude or pressure differences should be contraindicated in stable children.
However, this should always be a careful consideration for the child as an individual, and therefore this always needs to be discussed and be allowed by the treating physician.

Module 6: Activiteiten met hoogte- of druk verschil (NEDERLANDS)

F: Aanbevelingen (Nederlands)

ZWAKKE aanbeveling, EXPERT evidence	De werkgroep is van mening dat klinisch stabiele kinderen met kanker zonder ernstige neutropenie (i.e. neutrofielen <0.5x10^9/L) of trombocytopenie (i.e. trombocyten <50x10^9/L), bepaalde activiteiten met hoogte- of druk verschil, zoals in het vliegtuig of duiken, kunnen uitvoeren zolang dit in overeenstemming is met hun behandelend arts.

G: Overwegingen (Nederlands)

Er werd geen literatuur gevonden over dit onderwerp bij kinderen met kanker. Daarom is deze aanbeveling gebaseerd op de meningen van de experts in de werkgroep.

De werkgroep is van mening dat kinderen met kanker activiteiten met hoogte- of druk verschil zoals vliegen of duiken kunnen uitvoeren. Wij vinden dat deze kinderen in een stabiele fase van hun behandeling moeten zijn, zonder neutropenie of trombocytopenie. Wij zien in dat geval geen duidelijke redenen waarom deze activiteiten met hoogte- of druk verschil dan niet uitgevoerd zouden kunnen worden.
Echter, dit moet wel altijd in overleg met de behandeld arts waarbij de individuele gezondheid van het kind moet worden beoordeeld en een eventueel risico worden afgewogen.

Module 7: Hygiene (general) (English)

A: Recommendations

Research question: What is the effect of hygiene rules on infections and other outcomes in children with any type of cancer and/or after stem-cell transplantation?

A1.1: Recommendation (English)

STRONG recommendation, GOOD PRACTICE STATEMENT	Proper hand hygiene should be performed by patients, caregivers and medical personnel.

B: Clinical question, search and selection

B1: Clinical question:

What is the effect of hygiene rules on infections and other outcomes in children with any type of cancer and/or after stem-cell transplantation?

P = Children (aged 0-18 years) with any type of cancer and/or after stem-cell transplantation
I = Hygiene rules (e.g. cleaning, laundry, renewing of clothes, personal hygiene)
C = (No hygiene rules)
O = Severe or mild infections (prevalence and infectious complications), quality of life, anti-cancer treatment-related complications (adjustments in therapy or delay), costs, mortality, event-free survival

B2: Literature search and study selection

For the complete methodology of this guideline development and the search strategy, we refer to pages 18-23.
Of 6038 unique citations identified in the literature search, zero studies with pediatric oncology patients were included for this clinical question.

C: Results in pediatric and adult oncology patients

C1. Evidence in pediatric oncology patients

In our literature search, 0 studies were included for this clinical question.

C2. Additional recommendations guidelines (adults).

One evidence-based guideline was found, namely: “Antimicrobial Prophylaxis for Adult Patients With Cancer-Related Immunosuppression: ASCO and IDSA Clinical Practice Guideline Update Summary” (1). They recommend: “All health care workers should comply with hand hygiene and respiratory hygiene/cough etiquette guidelines to reduce the risk for aerosol- and direct or indirect contact-based transmission of pathogenic microorganisms in the health care setting. (Type of recommendation: consensus-based; benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: strong). (1)“ No additional evidence was cited in this guideline.

D: Conclusion(s) of evidence (pediatric oncology patients)

0 studies in pediatric oncology patients were found.	-

E: Considerations

No evidence in pediatric oncology patients was found for this clinical question. The recommendation from the ASCO and IDSA (1) guideline was used, and expert opinions were discussed.

The guideline panel strongly agrees that proper hand hygiene is very important for patients, caregivers and medical personnel. We therefore agreed to a recommendation in line with the recommendation from the ASCO and IDSA guideline. There is no clear evidence that supports this recommendation, but it is supported by a combination of general logic, common sense and expert opinions. Therefore, this recommendation is a ‘best practice statement’.

Module 7: Hygiëne (algemeen) (NEDERLANDS)

F: Aanbevelingen (Nederlands)

STERKE aanbeveling, GOOD PRACTICE STATEMENT	Zorgvuldige handhygiëne moet worden toegepast door patiënten, ouders/ verzorgers en zorgverleners.

G: Overwegingen (Nederlands)

Er werd geen literatuur gevonden over dit onderwerp bij kinderen met kanker. Wel werd er een aanbeveling gevonden in een ASCO en IDSA richtlijn (1) die gebruikt werd door de werkgroep in combinatie met de meningen van de experts in de werkgroep.

De werkgroep is het volledig eens met de aanbeveling die beschreven wordt in de ASCO en IDSA richtlijn (1) over het toepassen van juiste handhygiëne door patiënten, verzorgers en zorgverleners. Wij hebben daarom besloten een aanbeveling te maken in lijn met de ASCO en IDSA richtlijn (1). Er is geen duidelijke literatuur die deze aanbeveling ondersteunt, maar wordt wel ondersteunt door een combinatie aan logisch redeneren, gezond verstand en de meningen van de experts. Daarom is deze aanbeveling een ‘best practice statement’.

Module 8: Hygiene (personal) (English)

A: Recommendations

Research question: What is the effect of personal hygiene on infections and other outcomes in children with any type of cancer and/or after stem-cell transplantation?

A1.1: Recommendation (English)

STRONG recommendation, EXPERT evidence	We strongly believe that regular personal hygiene (regarding doing laundry, cleaning, renewing clothes) is sufficient for children with cancer and their households.

B: Clinical question, search and selection

B1: Clinical question:

What is the effect of hygiene rules on infections and other outcomes in children with any type of cancer and/or after stem-cell transplantation?

P = Children (aged 0-18 years) with any type of cancer and/or after stem-cell transplantation
I = Hygiene rules (e.g. cleaning, laundry, renewing of clothes, personal hygiene)
C = (No hygiene rules)
O = Severe or mild infections (prevalence and infectious complications), quality of life, anti-cancer treatment-related complications (adjustments in therapy or delay), costs, mortality, event-free survival

B2: Literature search and study selection

For the complete methodology of this guideline development and the search strategy, we refer to pages 18-23.
Of 6038 unique citations identified in the literature search, zero studies with pediatric oncology patients were included for this clinical question.

C: Results in pediatric and adult oncology patients

C1. Evidence in pediatric oncology patients

In our literature search, 0 studies were included for this clinical question.

C2. Additional recommendations guidelines (adults)

From our search for existing relevant guidelines, no additional guidelines were included for this clinical question.

D: Conclusion(s) of evidence (pediatric oncology patients)

0 studies in pediatric oncology patients were found.	-

E: Considerations

No evidence in pediatric oncology patients was found for this clinical question. Therefore, the recommendation is based on expert opinions.

The guideline panel agrees that basic hygiene measures are sufficient for children with cancer. There is no need for washing clothes separately or extra, cleaning the house in extreme form, or renewing clothes multiple times a day. We believe that as long as the household is cleaned in a normal way, this would be a sufficient amount of hygiene measures. There is no need to intensify any of this personal hygiene measures such as cleaning the house or doing laundry. Therefore, we strongly believe that regular personal hygiene (regarding doing laundry, cleaning, renewing clothes) is sufficient for children with cancer and their households.

Module 8: Hygiëne (persoonlijk) (NEDERLANDS)

F: Aanbevelingen (Nederlands)

STERKE aanbeveling, EXPERT evidence	De werkgroep is sterk van mening dat reguliere persoonlijke hygiëne (betreft wassen, schoonmaken, schone kleren aantrekken) voldoende is voor kinderen met kanker en hun huishouden.

G: Overwegingen (Nederlands)

Er werd geen literatuur gevonden over dit onderwerp bij kinderen met kanker. Daarom is deze aanbeveling gebaseerd op de meningen van de experts in de werkgroep.

De werkgroep is van mening dat als basis hygiëne maatregelen worden toegepast de kans op infectie zeer minimaal. De werkgroep ziet geen reden om andere maatregelen te adviseren, zoals het extra of apart wassen van kleding, extra schoonmaken of meerdere keren op een dag schone kleren aantrekken. Als het huis op een normale manier wordt schoongemaakt, is dit voldoende. Er is geen reden om dit schoonmaken of wassen te intensiveren. De werkgroep is sterk van mening dat reguliere persoonlijke hygiëne (betreft wassen, schoonmaken, schone kleren aantrekken) voldoende is voor kinderen met kanker en hun huishouden.

Module 9: Pets, zoo and farm (English)

A: Recommendations

Research question: What is the effect of visiting the zoo or having pets on infections in children with any type of cancer and/or after stem-cell transplantation?

A1.1: Recommendation (English)

WEAK recommendation, VERY LOW quality of evidence	We suggest allowing to keep domestic pets in the households of children with cancer.

WEAK recommendation, EXPERT evidence	We suggest allowing children with cancer to go to the zoo or visit a farm.

WEAK recommendation, EXPERT evidence	We suggest that children with cancer do not clean the litterbox or cages of their domestic pets.

B: Clinical question, search and selection

B1: Clinical question:

What is the effect of social restrictions (regarding risk of infections) on infections (prevalence and infectious complications) and other outcomes in children with any type of cancer and/or after stem-cell transplantation?

P = Children (aged 0-18 years) with any type of cancer and/or after stem-cell transplantation receiving anti-cancer treatment with curative intent

I = Social restrictions regarding risk of infections (i.e. restriction in school attendance, kindergarten, visiting zoo or farm, pets, swimming (whirlpool, sauna visits), being in crowded places, public transport, intimacy, flowers, or other author defined social restrictions)

C = (No social restrictions)

O = Severe or mild infections (prevalence and infectious complications), quality of life, anti-cancer treatment-related complications (adjustments in therapy or delay), costs, mortality, event-free survival

B2: Literature search and study selection

For the complete methodology of this guideline development and the search strategy, we refer to pages 18-23.

Of 6038 unique citations identified in the literature search, one study with pediatric oncology patients (Tramsen, 2016 (11)) was included.

C: Results in pediatric and adult oncology patients

C1. Evidence in pediatric oncology patients

In our literature search, one study was included for this clinical question. Tramsen et al (2016) (11) performed a retrospective cohort study, including children with acute myeloid leukemia treated according to AML-BFM 2004, between 2004 and 2010 in Germany, Austria, Switzerland and the Czech Republic. They reported on a survey about anti-infective measures. In total, 37 hospitals completed the survey.The survey included questions about restriction in social contacts, pets at home, and food.
Pet restrictions evaluated were related to dogs, cats, turtles, hamsters or guinea pigs, and birds at home. Restrictions were categorized as always restricted (2 points), restricted under certain circumstances (1 point) or never restricted (0 points). Therefore, higher numbers represent more restrictions. They gathered data about infectious complications and calculated an incidence rate ratio of infection per score.

For the restriction in pets, Tramsen (2016) reported a pet restriction score with a median of 8 (range 2-10) for a question with five items (highest possible score 10). For the unadjusted analysis, a higher restriction in pet score was associated with a decreased incidence of pneumonia (IRR 0.86, 95% CI 0.76-0.97, p=0.015) (11).
However, when the results were adjusted for gender, age, weight groups, risk stratification and antibiotic prophylaxis, restriction of pets was **not** significantly associated with the risk of any infection. For fever of unknown origin, an IRR of 0.99 was reported (95% CI 0.95-1.03, p=0.59); for bacteremia an IRR of 0.99 was reported (95% CI 0.94-1.05, p=0.75); for pneumonia an IRR of 0.91 was reported (95% CI 0.82-1.02, p=0.11) and for gastroenteritis an IRR of 1.05 was reported (95% CI 0.95-1.17, p=0.316) (11).

Table 11: Study characteristics Tramsen 2016

Article **Author, year** **Study type**	**Population** **a. No. of patients** **b. Population**	**Group information and study protocol**	**Included outcomes**	**Risk of bias assessment** **a. Selection bias** **b. Attrition bias** **c. Detection bias** **d. Reporting bias** **e. Confounding bias** **f. Other bias**
Tramsen et al, 2016 Retrospective cohort study	a. 339 patients b. Children with acute myeloid leukemia treated accordingly AML-BFM 2004, between 2004 and 2010 in Germany, Austria, Switzerland and the Czech Republic.	37 hospitals completed a survey about anti-infective measures. The survey included questions about restriction in social contacts, pets at home, and food. (5) Restrictions were categorized as always restricted (2 points), restricted under certain circumstances (1 point) or never restricted (0 points). Therefore, higher numbers represent more restrictions. They gathered data about infectious complications and calculated an incidence rate ratio of infection per score.	- Number of infections	a. Low b. Low c. Low d. Unclear e. High f. Low

*or possible risk factor group, or intervention group

Table 12: Outcomes Tramsen 2016 – Restriction in pets

Author, study design	No. of participants, total (cases vs controls) & Group definition	Results	Statistical methods	Effect size	Quality of evidence
1) Tramsen 2016 Retrospective cohort study	1) 339 pediatric AML patients. Hospitals filled in restriction scores regarding pets and social contacts.	1A1) When the results were adjusted for gender, age, weight groups, risk stratification and antibiotic prophylaxis, restriction of pets was **not** significantly associated with decreased risk of fever of unknown origin. 1A2) For adjusted results (see above), restriction of pets was **not** significantly associated with decreased risk of bacteremia. 1A3) For adjusted results (see above), restriction of pets was **not** significantly associated with decreased risk of pneumonia. 1A4) For adjusted results (see above), restriction of pets was **not** significantly associated with decreased risk of gastroenteritis.	1) Poisson regression and associated 95% CI	1A1) IRR 0.99, 95% CI 0.95-1.03, p=0.59 1A2) IRR 0.99, 95% CI 0.94-1.05, p=0.75 1A3) IRR 0.91, 95% CI 0.82-1.02, p=0.11 1A4) IRR 1.05, 95% CI 0.95-1.17, p=0.316	⊕◯◯◯[F] VERY LOW

F: GRADE: Grade quality assessment *restriction in pets at home:* design is retrospective cohort study, inconsistency not serious, indirectness not serious, imprecision serious, publication bias unlikely, downgraded 1 level because of serious risk of bias (selection bias low, attrition bias low, detection bias low, reporting bias unclear, confounding bias high, other bias low).

C2. Additional recommendations guidelines (adults)

From our search for existing relevant guidelines, no additional guidelines were included for this clinical question.

D: Conclusion(s) of evidence (pediatric oncology patients)

⊕◯◯◯ (1 study)[F*] **VERY LOW** QUALITY of evidence	Restriction of pets at home was not significantly associated with a decreased risk of any type of infection.**

***** The letter refers to the specific GRADE assessment described in section C1.

***Pet restrictions evaluated were related to dogs, cats, turtles, hamsters or guinea pigs, and birds at home.*

E: Considerations

One study in pediatric oncology patients was included for this clinical question (11), in which, restriction of pets at home was not significantly associated with a decreased risk of any type of infection. However, this study described the restriction advice that was given by the doctors, and does not report on the actual adherence of the patients. This study is retrospective and may not show the exact restriction of pets of the patients. However, there was no effect found of the restriction, which is supported by our expert opinions.

The guideline panel agreed that any restriction in pets at home is not necessary. If children carefully consider their hand hygiene after playing with or touching their pet, we see no reason why any other form of restriction should be advised. We believe risk of infection from a pet is minimal, considering adequate hand hygiene, and that the quality of life would decrease if there would be any form of restriction regarding the pets. Under these conditions, the guideline panel feels that children with cancer can keep and play with their pets.
We also believe that children with cancer should be allowed to visit the zoo or farm. If the children remain at distance from the animals, we see no problems regarding infectious risks. If the children, for example on a farm, touch the pets or feed them, they should again consider their hand hygiene. Under these conditions, the guideline panel feels that children with cancer can safely visit the zoo or farm.

However, we do suggest that children with cancer do not clean the cages and/or litter boxes of the pets. We consider the infectious risk higher for these tasks, and it can easily – with no to minimal decrease in quality of life – be avoided by children with cancer.
Additionally, we also suggest that the pets of these children are seen by a veterinarian and that they are in good health.

In summary, taking adequate hand hygiene into consideration, we believe children with cancer can keep and play with their pets, and safely visit the zoo or farm, as the risk of infection would be very minimal and the quality of life would decrease with any form of restriction.

Module 9: Huisdieren, dierentuin en kinderboerderij (NEDERLANDS)

F: Aanbeveling (Nederlands)

ZWAKKE aanbeveling, ZEER LAGE kwaliteit van evidence	Wij adviseren het toestaan van huisdieren bij kinderen met kanker.

ZWAKKE aanbeveling, EXPERT evidence	Wij adviseren het toestaan van het bezoeken van een dierentuin of kinderboerderij door kinderen met kanker.

ZWAKKE aanbeveling, EXPERT evidence	Wij adviseren dat kinderen met kanker niet de kattenbak of hokken van de huisdieren schoonmaken.

G: Overwegingen (Nederlands)

Er werd één studie gevonden die dit onderwerp beschreef bij kinderen met kanker. In conclusie liet deze studie (11) zien dat restricties in het hebben van huisdieren thuis niet significant geassocieerd was met een verminderd risico op een infectie. Echter, de studie beschrijft dat deze restricties geadviseerd werden door zorgverleners, en er werd niet gerapporteerd in welke mate ouders en kinderen zich hieraan hebben gehouden. Deze studie is retrospectief en laat misschien de exacte aantal restricties rondom huisdieren niet zien, maar het laat wel een effect ziet, die wordt erkend door onze experts.

De werkgroep is van mening dat er geen restricties nodig zijn rondom het hebben van huisdieren thuis. Zolang kinderen hun handhygiëne zorgvuldig toepassen na het spelen of aaien van hun huisdieren, zien wij geen reden waarom enkele vorm van restricties moeten worden toegepast. Wij zijn van mening dat het risico op infectie door een huisdier minimaal is, handhygiëne in acht nemend, en dat de kwaliteit van leven flink verminderd zal worden als een huisdier bijvoorbeeld weg zou moeten. Onder deze voorwaarden adviseren wij het toestaan van huisdieren bij kinderen met kanker.

Met dezelfde argumentatie vinden wij ook dat kinderen met kanker naar een dierentuin of kinderboerderij kunnen gaan. Zolang kinderen afstand bewaren van de dieren is er een zeer minimaal risico op infectie. Als kinderen, bijvoorbeeld op de kinderboerderij, de dieren aaien of voer geven, moeten ze hierna handhygiëne toepassen. Onder deze voorwaarden adviseren wij het toestaan van het bezoeken van een dierentuin of kinderboerderij door kinderen met kanker

Echter, adviseert de werkgroep wel dat kinderen met kanker niet de kattenbak of hokken van de huisdieren schoonmaken. Wij denken dat het risico op infectie bij deze handelingen iets hoger

ligt en het is een handeling die makkelijk vermeden kan worden – zonder een vermindering in kwaliteit van leven. Ook stellen wij voor dat de huisdieren van kinderen met kanker door een dierenarts worden gezien en dat de huisdieren in goede gezondheid zijn.

Samenvattend, zolang juiste handhygiëne wordt toegepast, kunnen kinderen met kanker met hun huisdieren spelen en kunnen ze veilig naar de dierentuin of kinderboerderij, omdat het risico op infectie dan minimaal is en de kwaliteit van leven zo optimaal mogelijk blijft.

Module 10: Public transport (English)

A: Recommendations

Research question: What is the effect of using public transport on infections in children with any type of cancer and/or after stem-cell transplantation?

A1.1: Recommendation (English)

WEAK recommendation, EXPERT evidence	We believe that children with cancer are allowed to use public transport or visit crowded places (i.e. big events such as visiting a concert or theater).

WEAK recommendation, EXPERT evidence	We believe that it is not advisable for children with cancer with neutropenia to use public transport or visit crowded places when there is a higher incidence of viral infections and thereby a higher chance of getting infected.

B: Clinical question, search and selection

B1: Clinical question:

What is the effect of social restrictions (regarding risk of infections) on infections (prevalence and infectious complications) and other outcomes in children with any type of cancer and/or after stem-cell transplantation?

P = Children (aged 0-18 years) with any type of cancer and/or after stem-cell transplantation receiving anti-cancer treatment with curative intent
I = Social restrictions regarding risk of infections (i.e. restriction in school attendance, kindergarten, visiting zoo or farm, pets, swimming (whirlpool, sauna visits), being in crowded places, public transport, intimacy, flowers, or other author defined social restrictions)
C = (No social restrictions)
O = Severe or mild infections (prevalence and infectious complications), quality of life, anti-cancer treatment-related complications (adjustments in therapy or delay), costs, mortality, event-free survival

B2: Literature search and study selection

For the complete methodology of this guideline development and the search strategy, we refer to pages 18-23.
Of 6038 unique citations identified in the literature search, zero studies with pediatric oncology patients were included for this clinical question.

C: Results in pediatric and adult oncology patients

C1. Evidence in pediatric oncology patients

In our literature search, 0 studies were included for this clinical question.

C2. Additional recommendations guidelines (adults)

From our search for existing relevant guidelines, no additional guidelines were included for this clinical question.

D: Conclusion(s) of evidence (pediatric oncology patients)

0 studies in pediatric oncology patients were found.	-

E: Considerations

No evidence in pediatric oncology patients was found for this clinical question. Therefore, the recommendation is based on expert opinions.

The guideline panel agrees that basic hygiene measures are sufficient for children with cancer. We believe there is no need to avoid public transport as long as basic hygiene measures such as hand hygiene are performed. Then, we believe the risk of infection remains minimal.

The guideline panel does feel that there is an exception for children with cancer and neutropenia, who should avoid the public transport or crowded places when there is a higher incidence of viral infections. In these months, there is a higher incidence of viral infections and thereby they have a higher chance of getting infected. As the potential consequences of a viral infection can be big (for example, hospital admission because of fever, delay of chemotherapy or the need for antiviral medication), we believe the public transport should be avoided when there is a higher incidence of viral infections.

Module 10: Openbaar vervoer (NEDERLANDS)

F: Aanbeveling (Nederlands)

ZWAKKE aanbeveling, EXPERT evidence	De werkgroep is van mening dat kinderen met kanker het openbaar vervoer kunnen gebruiken of drukke plaatsen (zoals een concert of een theater) kunnen bezoeken.

ZWAKKE aanbeveling, EXPERT evidence	De werkgroep is van mening dat het niet raadzaam is voor kinderen met kanker in neutropenie om het openbaar vervoer te gebruiken of drukke plaatsen (zoals een concert of een theater) te bezoeken tijdens een periode met een hoge incidentie van virale infecties en dus een hogere kans om een infectie op te lopen.

G: Overwegingen (Nederlands)

Er werd geen literatuur gevonden over dit onderwerp bij kinderen met kanker. Daarom is deze aanbeveling gebaseerd op de meningen van de experts in de werkgroep.

De werkgroep is van mening dat als basis hygiëne maatregelen worden toegepast de kans op infectie zeer minimaal. Wij vinden dat er geen reden is om openbaar vervoer of andere drukke plaatsen te vermijden, zolang deze basis hygiëne maatregelen worden toegepast. Dan is het risico op infectie minimaal.

De werkgroep is wel van mening dat kinderen met kanker **in neutropenie** niet het openbaar vervoer kunnen gebruiken of drukke plaatsen (zoals een concert of een theater) kunnen bezoeken tijdens een periode met een hoge incidentie van virale infecties. Dit omdat er dan een dus een hogere kans om een infectie op te lopen. Omdat de potentiële gevolgen van een virale infectie groot kunnen zijn (bijvoorbeeld opname in het ziekenhuis vanwege koorts, uitstel van chemotherapie of het starten van anti-virale middelen), vinden wij dat kinderen met kanker **in neutropenie** het openbaar vervoer of andere drukke plekken moeten vermijden in deze ‘hoog risico’ periode.

Module 11: School and kindergarten (English)

A: Recommendations

Research question: What is the effect of going to school or kindergarten on infections in children with any type of cancer and/or after stem-cell transplantation?

A1.1: Recommendation (English)

STRONG recommendation, VERY LOW quality evidence	We recommend allowing children with cancer to attend school or kindergarten (unless someone in their class or group has an infectious disease such as chickenpox).

B: Clinical question, search and selection

B1: Clinical question:

What is the effect of social restrictions (regarding risk of infections) on infections (prevalence and infectious complications) and other outcomes in children with any type of cancer and/or after stem-cell transplantation?

P = Children (aged 0-18 years) with any type of cancer and/or after stem-cell transplantation receiving anti-cancer treatment with curative intent
I = Social restrictions regarding risk of infections (i.e. restriction in school attendance, kindergarten, visiting zoo or farm, pets, swimming (whirlpool, sauna visits), being in crowded places, public transport, intimacy, flowers, or other author defined social restrictions)
C = (No social restrictions)
O = Severe or mild infections (prevalence and infectious complications), quality of life, anti-cancer treatment-related complications (adjustments in therapy or delay), costs, mortality, event-free survival

B2: Literature search and study selection

For the complete methodology of this guideline development and the search strategy, we refer to pages 18-23.
Of 6038 unique citations identified in the literature search, one study with pediatric oncology patients (Tramsen, 2016 (11)) was included. Evidence was extracted and assessed using the GRADE methodology.

C: Results in pediatric and adult oncology patients

C1. Evidence in pediatric oncology patients

In our literature search, one study was included for this clinical question. Tramsen et al (2016) (11) performed a retrospective cohort study, including children with acute myeloid leukemia treated accordingly AML-BFM 2004, between 2004 and 2010 in Germany, Austria, Switzerland and the Czech Republic. They reported about a survey about anti-infective measures. In total, 37 hospitals completed a survey about anti-infective measures. The survey included questions about restriction in social contacts, pets at home, and food.
Social restrictions evaluated were related to indoor public places, outdoor public places, friends visiting at home, daycare centers, kindergarten, and school beyond kindergarten. Restrictions were categorized as always restricted (2 points), restricted under certain circumstances (1 point)

or never restricted (0 points).

For the social restrictions, Tramsen (2016) reported a median score of 9 (range 7-12) for a score with six items and consequently the highest possible score of 12. For the unadjusted analysis, a higher restriction in social contact score was associated with an increased incidence of bacteremia (IRR 1.21, 95% CI 1.07-1.37, p=0.003).
However, when the results were adjusted for gender, age, weight groups, risk stratification and antibiotic prophylaxis, restriction of social contacts was **not** significantly associated with the risk of infection. Namely, for fever of unknown origin, an IRR of 0.99 was reported (95% CI 0.92-1.08, p=0.9); for bacteremia an IRR of 1.15 was reported (95% CI 0.99-1.33, p=0.066); for pneumonia an IRR of 0.99 was reported (95% CI 0.77-1.28, p=0.96) and for gastroenteritis an IRR of 0.94 was reported (95% CI 0.73-1.21, p=0.63).

Table 11: Study characteristics Tramsen 2016

Article Author, year Study type	**Population a. No. of patients b. Population**	**Group information and study protocol**	**Included outcomes**	**Risk of bias assessment a. Selection bias b. Attrition bias c. Detection bias d. Reporting bias e. Confounding bias f. Other bias**
Tramsen et al, 2016 Retrospective cohort study	a. 339 patients b. Children with acute myeloid leukemia treated accordingly AML-BFM 2004, between 2004 and 2010 in Germany, Austria, Switzerland and the Czech Republic.	37 hospitals completed a survey about anti-infective measures. The survey included questions about restriction in social contacts, pets at home, and food. (5) Restrictions were categorized as always restricted (2 points), restricted under certain circumstances (1 point) or never restricted (0 points). Therefore, higher numbers represent more restrictions. They gathered data about infectious complications and calculated an incidence rate ratio of infection per score.	- Number of infections	a. Low b. Low c. Low d. Unclear e. High f. Low

*or possible risk factor group, or intervention group

Table 13: Outcomes Tramsen 2016 – Restriction in social contact (school and kindergarten)

Author, study design	**No. of participants, total (cases vs controls) & Group definition**	**Results**	**Statistical methods**	**Effect *size***	**Quality of evidence**
1) Tramsen 2016 Retrospective cohort study	1) 339 pediatric AML patients. Hospitals filled in restriction scores regarding pets and social contacts.	1A1) When the results were adjusted for gender, age, weight groups, risk stratification and antibiotic prophylaxis, restriction of social contact was **not** significantly associated with decreased risk of fever of unknown origin. 1A2) For adjusted results (see above), restriction of social contact	1) Poisson regression and associated 95% CI	1A1) IRR 0.99, 95% CI 0.92-1.08, p=0.9 1A2) IRR 1.15, 95%	⨁◯◯◯[G] VERY LOW

		was **not** significantly associated with decreased risk of bacteremia. 1A3) For adjusted results (see above), restriction of social contact was **not** significantly associated with decreased risk of pneumonia. 1A4) For adjusted results (see above), restriction of pets was **not** significantly associated with decreased risk of gastroenteritis.		CI 0.99-1.33, p=0.066 1A3) IRR 0.99, 95% CI 0.77-1.28, p=0.96 1A4) IRR 0.94, 95% CI 0.73-1.21, p=0.63	

G: GRADE: Grade quality assessment *restriction in social contacts:* design is retrospective cohort study, inconsistency not serious, indirectness not serious, imprecision serious, publication bias unlikely, downgraded 1 level because of serious risk of bias (selection bias low, attrition bias low, detection bias low, reporting bias unclear, confounding bias high, other bias low).

C2. Additional recommendations guidelines (adults)
From our search for existing relevant guidelines, no additional guidelines were included for this clinical question.

D: Conclusion(s) of evidence (pediatric oncology patients)

⊕◯◯◯ (1 study)[G*] **VERY LOW** QUALITY of evidence	Restriction of social contact was not significantly associated with a decreased risk of any type of infection.**

***** The letter refers to the specific GRADE assessment described in section C1.
**Social restrictions evaluated were related to indoor public places, outdoor public places, friends visiting at home, daycare centers, kindergarten, and school beyond kindergarten.

E: Considerations
One study in pediatric oncology patients was included for this clinical question. In conclusion, restriction of social contact was not significantly associated with a decreased risk of any type of infection. However, this study described the restriction advice that was given by the doctors, and does not report on the actual adherence of the patients. This study is retrospective and may not show the exact social restrictions of the patients, but it does show an effect of the social restriction, which is supported by our expert opinions.

In line with the above mentioned study, the guideline panel feels that any social restriction such as restriction in school or kindergarten is not necessary. If children carefully consider their hand hygiene during the day, we see no reason why any other form of social restriction should be advised.

The guideline panel recognizes that the risk of infection at schools or kindergarten may be a concern to parents. However, we agree that going to school or kindergarten increases the

quality of life of these children in such a way that it outweighs the harms. Going to school is very important for the development of any child, also for children with cancer. It also has an important social aspect of seeing their friends at school and continuing with their life in the best possible way.
However, we recognize that if a lot of children in the class or at kindergarten are sick, parents would choose to keep their children at home. We strongly suggest that children stay at home when someone in their class or group has an contagious disease such as chickenpox. This only accounts for children who did not had chickenpox before or have no antibody titer. If there is an infectious disease in the class or at kindergarten, the guideline panel suggests that this will then be discussed by the treating physician for the specific patient.

In summary, taking adequate hand hygiene into consideration, we believe children with cancer should attend school or kindergarten (unless someone in their class or group has an infectious disease such as chickenpox), as the risk of infection would be minimal and the quality of life would decrease with any form of restriction.

Module 11: School en kinderopvang (NEDERLANDS)

F: Aanbeveling (Nederlands)

STERKE aanbeveling, ZEER LAGE kwaliteit evidence	Wij adviseren het toestaan van naar school of naar de kinderopvang te gaan door kinderen met kanker (tenzij iemand in de klas of groep een infectieuze ziekte heeft zoals waterpokken).

G: Overwegingen (Nederlands)

Er werd één studie gevonden over dit onderwerp in kinderen met kanker. Concluderend, in deze studie (11) werd een restrictie in sociaal contact (zoals school en kinderopvang) niet significant geassocieerd met een verminderd risico op infecties. Echter, de studie beschrijft dat deze restricties geadviseerd werden door zorgverleners, en er werd niet gerapporteerd in welke mate ouders en kinderen zich hieraan hebben gehouden. Deze studie is retrospectief en laat misschien de exacte aantal restricties rondom sociaal contact niet zien, maar het laat wel een effect ziet, die wordt erkend door onze experts.

In lijn met de eerder genoemde studie is de werkgroep van mening dat er geen restricties nodig zijn rondom het naar school of naar de kinderopvang gaan. Zolang kinderen hun handhygiëne zorgvuldig toepassen gedurende de dag, zien wij geen reden waarom enkele vorm van restricties moeten worden toegepast.

De werkgroep erkent dat het risico op infectie via school of de kinderopvang een zorg is voor ouders. Echter, het belang van naar school of naar de kinderopvang gaan is zo groot voor de kinderen en zorgt voor een betere kwaliteit van leven, dat de risico's opwegen tegen de voordelen. Wij vinden namelijk ook dat als kinderen niet naar school of de kinderopvang zouden mogen, dit een verlaging van hun kwaliteit van leven zou zijn. Wij vinden dat naar school gaan ontzettend belangrijk is voor de ontwikkeling van ieder kind, en natuurlijk geldt dat ook voor kinderen met kanker. Er speelt ook een belangrijk sociaal aspect, namelijk het zien van hun vrienden en leeftijdsgenoten en zoveel mogelijk met hun dagelijkse routine en activiteiten als vóór hun diagnose.

Echter, wij vinden het een begrijpelijke keuze als ouders hun kinderen thuis houden wanneer veel kinderen in de klas of op de opvang ziek zijn. Wij raden sterk aan dat kinderen thuis blijven als er een besmettelijke ziekte is in de groep, zoals bijvoorbeeld waterpokken. Dit geldt voor kinderen die nog nooit in aanraking zijn geweest met de waterpokken en hiervoor nog geen immuniteit hebben opgebouwd. Als er een besmettelijke ziekte in de groep heerst, raden wij aan om dit individuele geval te overleggen met de behandeld arts.

Samenvattend, zolang kinderen hun handhygiëne zorgvuldig toepassen gedurende de dag, zien wij geen reden waarom enkele vorm van restricties rondom school of de opvang moeten worden toegepast. Wij raden aan om kinderen met kanker naar school of naar de kinderopvang te laten gaan (tenzij iemand in de klas of groep een infectieuze ziekte heeft zoals waterpokken).

Module 12: Sports and high-velocity events (English)

A: Recommendations

Research question: What is the effect of sports or high-velocity events on hemorrhagic complications in children with any type of cancer and/or after stem-cell transplantation?

A1.1: Recommendation (English)

STRONG recommendation, EXPERT evidence	We strongly believe that children with cancer should be encouraged to exercise and perform sports.

WEAK recommendation, EXPERT evidence	We believe that children with cancer with thrombocytopenia (i.e. platelet count <50x10^9/L) should not perform events with increased risk of bleeding (contact sports, high-impact or high-velocity events, events with risk of falling).

B: Clinical question, search and selection

B1: Clinical question:

What is the effect of social restrictions (regarding bleeding risk) on hemorrhagic complications and other outcomes in children with any type of cancer and/or after stem-cell transplantation?

P = Children (aged 0-18 years) with any type of cancer and/or after stem-cell transplantation
I = Social restrictions regarding risk of bleeding (i.e. restriction in physical contact sports, high-velocity sports, high impact or high energetic sports, sports with high risk of falling such as skiing or skating, playing with high risk of falling such as slides, high or low altitude events such as scuba diving or flying, rollercoaster rides or other author-defined social restrictions) (D)
C = (No social restrictions)
O = Hemorrhagic complications (mild and severe), quality of life, anti-cancer treatment related complications, (adjustments in therapy or delay), costs, mortality, event-free survival (E)

B2: Literature search and study selection

For the complete methodology of this guideline development and the search strategy, we refer to pages 18-23.
Of 6038 unique citations identified in the literature search, zero studies with pediatric oncology patients were included for this clinical question.

C: Results in pediatric and adult oncology patients

C1. Evidence in pediatric oncology patients

In our literature search, 0 studies were included for this clinical question.

C2. Additional recommendations guidelines (adults)

From our search for existing relevant guidelines, no additional guidelines were included for this clinical question.

D: Conclusion(s) of evidence (pediatric oncology patients)

0 studies in pediatric oncology patients were found.	-

E: Considerations

No evidence in pediatric oncology patients was found for this clinical question. Therefore, the recommendation is based on expert opinions.

Firstly, the guideline panel strongly believes that children with cancer are allowed (and should be encouraged) to exercise and perform sports. Besides the reason of thrombocytopenia or other individual reasons, it is always encouraged for children to perform sports and other activities. This greatly benefits their physical state, but also their quality of life.

However, the guideline panel feels that an exception needs to be made for children with thrombocytopenia (i.e. thrombocytes $<50x10^9$/L). In some types of activities, such as contact sports like boxing or rugby, high-impact or high-velocity events, events with risk of falling, the risk of bleeding is just too big when a child has thrombocytopenia. Therefore, these activities should be avoided in the event of thrombocytopenia. We suggest encouraging these children to perform activities that are safe, to ensure the positive effects of performing activities and sports.

Module 12: Sporten en activiteiten met hoge snelheid (NEDERLANDS)

F: Aanbeveling (Nederlands)

STERKTE aanbeveling, EXPERT evidence	De werkgroep is sterk van mening dat kinderen met kanker aangemoedigd moeten worden om te sporten en bewegen.

ZWAKKE aanbeveling, EXPERT evidence	De werkgroep is van mening dat kinderen met trombocytopenie (i.e. trombocyten <50x10^9/L) geen sporten zouden moeten beoefenen met een hoog risico op bloedingen (contact sport, sporten of activiteiten met een hoge impact of hoge snelheid, activiteiten met een hoog risico op vallen).

G: Overwegingen (Nederlands)

Er werd geen literatuur gevonden over dit onderwerp bij kinderen met kanker. Daarom is deze aanbeveling gebaseerd op de meningen van de experts in de werkgroep.

Ten eerste is de werkgroep sterk van mening dat kinderen met kanker moeten en aangemoedigd moeten worden om te sporten en te bewegen. Behalve met ernstige trombocytopenie of andere individuele redenen om niet te sporten, moet sporten of andere activiteiten met beweging voor kinderen met kanker altijd worden bemoedigd. Dit verbetert hun fysieke gesteldheid en ook hun kwaliteit van leven.

Echter, de werkgroep is van mening dat er een uitzondering gemaakt moet worden voor kinderen met trombocytopenie (i.e. trombocyten <50x10^9/L). Zij zouden geen sporten moeten beoefenen met een hoog risico op bloedingen (contact sporten zoals boksen of rugby, sporten of activiteiten met een hoge impact of hoge snelheid, activiteiten met een hoog risico op vallen). Voor deze specifieke groep kinderen is het risico op bloedingen bij deze activiteiten te groot. Tijdens een periode van trombocytopenie moeten deze activiteiten dus ook vermeden worden. Wij stellen voor dat deze kinderen wordt aangeraden om aan andere activiteiten mee te doen die wel veilig uitgevoerd kunnen worden, om de positieve effecten van het sporten of bewegen te bevorderen.

Module 13: Swimming (English)

A: Recommendations

Research question: What is the effect of swimming on infections and other outcomes in children with any type of cancer and/or after stem-cell transplantation?

A1.1: Recommendation (English)

WEAK recommendation, VERY LOW quality of evidence	We suggest allowing children with cancer to swim (irrespective of neutropenia).

STRONG recommendation, EXPERT evidence	We strongly believe children with cancer with a non-tunneled central venous catheter such as PICC line should not swim.

B: Clinical question, search and selection

B1: Clinical question:

What is the effect of social restrictions (regarding risk of infections) on infections (prevalence and infectious complications) and other outcomes in children with any type of cancer and/or after stem-cell transplantation?

P = Children (aged 0-18 years) with any type of cancer and/or after stem-cell transplantation receiving anti-cancer treatment with curative intent

I = Social restrictions regarding risk of infections (i.e. restriction in school attendance, kindergarten, visiting zoo or farm, pets, swimming (whirlpool, sauna visits), being in crowded places, public transport, intimacy, flowers, or other author defined social restrictions)

C = (No social restrictions)

O = Severe or mild infections (prevalence and infectious complications), quality of life, anti-cancer treatment-related complications (adjustments in therapy or delay), costs, mortality, event-free survival

B2: Literature search and study selection

For the complete methodology of this guideline development and the search strategy, we refer to pages 18-23.

Of 6038 unique citations identified in the literature search, one study with pediatric oncology patients (Robbins, 1999 (12)) was included. Evidence was extracted and assessed using the GRADE methodology.

C: Results in pediatric and adult oncology patients

C1. Evidence in pediatric oncology patients

In our literature search, one study was included for this clinical question. Robbins et al (1999) (12) showed that pediatric oncology patients who swim with central venous catheters (CVC) are at increased risk of catheter-related infections. Their population was described as pediatric oncology patients with tunneled central venous catheters. “Swimming” was defined as swimming *at least once* while the catheter was in place. 46 patients did not swim at all, 49 patients did go swimming. They all swam in a public or private pool, nine of them additionally went swimming in a lake.

There were 34 catheter-related infections in the swimmers group compared to 13 infections among the non-swimmers. However, when rates of infection were calculated as number of infections per catheter per month, there were no significant differences between the groups. The swimmers group had their CVC in place significantly longer than the non-swimmers group. They report 34 infections in a total of 843 months (34/843) in the swimmers group versus 13 infections in 506 months (13/506). This means rates of an infection of 0.04% in the swimmers group, and 0.025% in the non-swimmers group, with a risk ratio of 1.6 (95% CI not reported) which they did not consider statistically significant (significance calculated based on 95% CI, but confidence intervals are not reported) (12).

They reported separate results for *tunnel or exit infections*, defined as pus or erythema and tenderness on the exit site (exit infection) or throughout the whole tunneled portion of the catheter (tunnel infection). A *bloodstream infection* was defined as sudden onset of fever in association with a positive blood culture.
In the swimmers group, 20 tunnel or exit infections were reported in 843 months (rate of 0.02%), versus 8 infections in 506 months in the non-swimmers group (0.016%). Regarding blood stream infections (BSI), in the swimmers group 14 BSI’s were reported in 843 months (rate 0.016%) versus 5 BSI’s in 506 months in the non-swimmers group (rate 0.0095). These results both did not differ significantly (12).

Robbins et al (1999) also evaluated if patients who swam **frequently** were at higher risk of infection than patients who swam only once or twice all summer. “Frequent swimming” was defined as swimming at least once a month, which was compared to patients who swam infrequently or not at all. They reported 35 frequent swimmers, versus 60 infrequent and non-swimmers. Of these, 19 catheter-related infections were reported in the frequent swimmers group versus 27 among the infrequent and non-swimmers. Also for these groups, a significant imbalance was seen in months of catheter in place. Therefore, the rates were calculated per months of catheter in place. The total number of infections in the frequent swimmers group, was 19 per 579 months (0.03%), versus 27 infections per 770 months in the infrequent/non-swimmers group (0.03%). Tunnel or exit infections were seen in 6/579 in the swimmers group (0.01%) versus 16/770 in the infrequent/non-swimmers group (0.02%). Bloodstream infections were reported in 13/579 (0.02%) in the swimmers group versus 11/770 in the infrequent/non-swimmers group (0.14%). None of the results differed significantly (12).

Table 14: Study characteristics Robbins 1999

Article **Author, year** **Study type**	**Population** **a. No. of patients** **b. Population**	**Case group*** **a. Group definition** **b. No. of patients, age, gender (% males)**	**Control Group** **a. Group definition** **b. No. of patients, age, gender (% males)**	**Included outcomes**	**Risk of bias assessment** **a. Selection bias** **b. Attrition bias** **c. Detection bias** **d. Reporting bias** **e. Confounding bias** **f. Other bias**
Robbins et al, 1999 Retrospective cohort study	a. 95 patients b. Pediatric oncology patients with a tunneled central venous catheter (CVC) in place (single- or double lumen), single-center, 1994-1996.	a. “Swimmers” (patients who swam at least once with catheter in place) b. 49 patients, median age 9 years, % males not provided.	a. “Non-swimmers”, (patients who did not swim at all) b. 46 patients, median age 8 years, % males not provided.	- Number of infections	a. Unclear b. High c. Low d. Unclear e. High f. High

Table 15: Outcomes Robbins 1999 – Swimming

Author, study design	**No. of participants, total (cases vs controls) & Group definition**	**Results**	**Statistical methods**	**Effect *size***	**Quality of evidence**
1) Robbins, 1999 Retrospective cohort study	1) 95 (49 swimmers vs 46 non-swimmers) pediatric oncology patients with tunneled central venous catheter. Swimmers (i.e. swimming at least once when catheter was in place) versus non-swimmers	1A) Total of infections: 34 in swimmers group, 13 in non-swimmer group (Note: baseline imbalances in months of catheter in place). 1B) **Total** infections per month in swimmers group: 34 infections per 843 months of catheter in place (0.04%). In non-swimmers group, 13 infections were reported in 506 months of catheter in place (0.025%). 1B1) **Tunnel or exit** infections per month in the swimmers group: 20 infections per 843 months of catheter in place (0.02%). In non-swimmers group, 8 infections were reported in 506 months of catheter in place (0.016%). 1B2) **Bloodstream infections** per month in the swimmers group: 14 infections per 843 months of catheter in place (0.016%). In non-swimmers group, 5 infections were reported in 506 months of catheter in place (0.009%).	1A) Not reported 1B) Relative Risk and Chi-squared test 1B1) Relative Risk and Chi-squared test 1B2) Relative Risk and Chi-squared test	1A) Not reported 1B) RR 1.6, not significant (p-value not reported) 1B1) RR 1.5, not significant (p-value not reported) 1B2) RR 1.7, not significant (p-value not reported)	⨁◯◯◯[H] VERY LOW

H: GRADE: Grade quality assessment swimming: design is case-controlled study, inconsistency not serious, indirectness not serious, imprecision serious (downgraded one level because of small study population), publication bias unlikely, downgraded 1 level because of serious risk of bias (selection bias unclear, attrition bias high, detection bias low, reporting bias unclear, confounding bias high, other bias high).

Table 16: Outcomes Robbins 1999 – Frequent swimming

Author, study design	**No. of participants, total (cases vs controls) & Group definition**	**Results**	**Statistical methods**	**Effect *size***	**Quality of evidence**
1) Robbins, 1999 Retrospective cohort study	1) 95 (35 frequent swimmers vs 60 infrequent swimmers) pediatric oncology patients with tunneled central venous catheter. Frequent swimmers (i.e. at least once a month) versus infrequent or non-swimmers	1A) 19 catheter-related infections in frequent swimmers; 27 among infrequent/non-swimmers (Note: baseline imbalances in months of catheter in place). 1B) **Total** infections per month in swimmers group: 19 infections per 579 months of catheter in place (0.03%). In infrequent/non-swimmers, 27 infections were reported in 770 months of catheter in place (0.03%). 1B1) **Tunnel or exit** infections per month in the swimmers group: 6 infections per 579 months of catheter in place (0.01%). In infrequent/non-swimmers 16 infections were reported in 770 months of catheter in place (0.02%). 1B2) **Bloodstream infections** per month in the swimmers group: 13 infections per 579 months of catheter in place (0.02%). In infrequent/non-swimmers, 11 infections were reported in 770 months of catheter in place (0.014%).	1A) Not reported 1) Relative Risk and Chi-squared test 1B1) Relative Risk and Chi-squared test 1B2) Relative Risk and Chi-squared test	1A) Not reported 1B) RR 0.9, not significant (p-value not reported) 1B1) RR 0.5, not significant (p-value not reported) 1B2) RR 1.6, not significant (p-value not reported)	⨁◯◯◯[I] VERY LOW

I: GRADE: Grade quality assessment frequent swimming: design is case-controlled study, inconsistency not serious, indirectness not serious, imprecision serious (downgraded one level because of small study population), publication bias unlikely, downgraded 1 level because of serious risk of bias (selection bias unclear, attrition bias high, detection bias low, reporting bias unclear, confounding bias high, other bias high).

C2. Additional recommendations guidelines (adults)

From our search for existing relevant guidelines, no additional guidelines were included for this clinical question.

D: Conclusion(s) of evidence (pediatric oncology patients)

⊕◯◯◯ (1 study)[H*] **VERY LOW** QUALITY of evidence	No significant difference in prevalence of infections in swimmers group versus non-swimmers group.

⊕◯◯◯ (1 study)[I*] **VERY LOW** QUALITY of evidence	No significant difference in prevalence of infections in frequent swimmers group versus infrequent/non-swimmers group.**

***** The letter refers to the specific GRADE assessment described in section C1.
** Frequent swimming defined as swimming more than once a month.

E: Considerations

One study in pediatric oncology patients was included for this clinical question. In conclusion, in one study (12), no significant difference in prevalence of infections in the swimmers group versus the non-swimmers group and in the frequent swimmers group versus infrequent/non-swimmers group were reported. This study is small and retrospective, but it does show a trend regarding the effects of swimming, which is supported by our expert opinions.

The guideline panel feels that an absolute restriction regarding swimming is not necessary. If basic hygiene measures are taken into consideration, we feel that children should be allowed to swim in chlorinated water, open water or the sea. We believe not allowing the children to swim, would decrease their quality of life, for example in summer holidays. The panel outweighed the benefits against the harms.

D1. Internal and external tunneled central venous catheters

We believe that children with an internal central venous catheter or an external tunneled central venous catheter, provided that the insertion site and dressings can be cleaned thoroughly should be allowed to swim.

The guideline panel feels that swimming with an internal venous catheter is allowed and would have minimal risks, both infectious and dislocation wise. A specific condition is that the child has an unwounded skin, so no needle should be inserted in the central venous access port or any other type of wound. This would create a potential entry port for bacteria or other and would increase the risk of infection.

The guideline panel agreed that swimming with an external tunneled central venous catheter is allowed and would have minimal risks, both infectious and dislocation wise. A specific condition is that the insertion site of the external venous catheter needs to be thoroughly dried and clean and dry bandages have to be applied after swimming. The guideline panel recognizes the fear for dislocation or problems with the external line from parents and children. Although not necessary, a suggestion is that the child can wear a wetsuit shirt (or a different type of tight shirt) so that the line is pushed against the body.

D2. Non-tunneled lines

There is no evidence for swimming with non-tunneled line. The guideline panel believes that swimming with a non-tunneled line such as a peripheral inserted central catheter (PICC) line,

should not be allowed. The guideline panel feels that there is an increased infection risk for non-tunneled lines.

D3. Swimming location
The guideline panel believes that swimming should be possible in all locations which are destined as swimming areas. For example, chlorinated water (and also swimming lessons), the sea, or in open water, given that there is no general advice against this from the local authorities. We feel that there is minimal difference in infectious risk between chlorinated water, open water and the sea.

In summary, the guideline panel recognizes that the risk of infection or dislocation of the line may be a concern to parents. However, we agree that swimming or swimming lessons increases the quality of life of these children in such a way, that it outweighs the harms. Therefore, we believe children with cancer should be able to swim under certain conditions as the risk of infection would be minimal and the quality of life would decrease with any form of restriction.

Module 13: Zwemmen (NEDERLANDS)

F: Aanbeveling (Nederlands)

ZWAKKE aanbeveling, ZEER LAGE kwaliteit evidence	Wij adviseren het toestaan van zwemmen voor kinderen met kanker (ongeacht het hebben van neutropenie).

STERKE aanbeveling, EXPERT evidence	De werkgroep is sterk van mening dat kinderen met kanker en een niet-getunnelde lijn zoals een PICC lijn niet mogen zwemmen.

G: Overwegingen (Nederlands)

Er werd één studie gevonden over zwemmen door kinderen met kanker. In conclusie, in deze studie, (12) werden er geen significante verschillen gerapporteerd in de prevalentie van infectie in de groep zwemmers en de groep niet-zwemmers; idem voor de groep frequente zwemmers versus infrequente/niet-zwemmers. De studie is klein en retrospectief, maar het geeft een idee over het effect van zwemmen, die erkend wordt door de werkgroep.

De werkgroep is van mening dat absolute restricties wat betreft zwemmen niet nodig zijn. Zolang basis hygiëne maatregelen genomen worden, vinden wij dat het toegestaan is voor kinderen met kanker om te zwemmen in gechloreerd water, open water of de zee. Wij zijn sterk van mening dat het niet toestaan van zwemmen de kwaliteit van leven verminderd, bijvoorbeeld in de zomervakantie of met zwemles. De voordelen wegen op tegen de risico's.

G1. Interne en externe getunnelde centraal veneuze lijnen

Wij vinden dat kinderen met interne en externe getunnelde centraal veneuze lijnen kunnen zwemmen, met de voorwaarde dat het verband rondom de eventuele insteekopening goed afgedroogd kunnen worden en vervangen kan worden na het zwemmen.
De werkgroep is van mening dat zwemmen met een interne centraal veneuze lijn toegestaan is en minimale risico's heeft, zowel qua infectie risico als qua dislocatie. Een voorwaarde hiervoor is dat de huid intact moet zijn, omdat een huid die niet intact is een porte d'entrée kan zijn voor bacteriën en hiermee er dus een hogere kans is op infecties.
De werkgroep is van mening dat zwemmen met een externe getunnelde centraal veneuze lijn ook is toegestaan is en minimale risico's heeft, zowel qua infectie risico als qua dislocatie. Zoals eerder genoemd is de voorwaarde dat het verband rondom de eventuele insteekopening goed afgedroogd kunnen worden en vervangen kan worden na het zwemmen. Wij erkennen mogelijke angst van ouders en kinderen op dislocatie of andere problemen met de externe lijn. Hoewel dit niet nodig is, kan een wetsuit of ander strak shirt worden gedragen zodat de lijn goed tegen het lichaam aangedrukt is en dit wellicht een veiliger gevoel geeft.

G2. Niet getunnelde lijnen

De werkgroep is sterk van mening dat zwemmen niet is toegestaan voor kinderen met kanker en een niet-getunnelde lijn zoals een PICC lijn. De werkgroep is van mening dat met dit soort

niet-getunnelde lijn is, er een groter risico is op infectie.

G3. Locatie van het zwemmen
De werkgroep is van mening dat zwemmen op alle locaties, die daarvoor bestemd zijn, toegestaan is zoals bijvoorbeeld gechloreerd water (en dus zwemles), de zee of open water. Bij het zwemmen in open water dient altijd het algemene zwemadvies van gemeenten gevolgd te worden. Wij denken dat er weinig verschil is in infectie risico tussen gechloreerd water, open water of de zee.

Concluderend, erkennen wij de angst voor infecties of dislocaties van de lijn door ouders of kinderen. We vinden echter dat het zwemmen en bijvoorbeeld ook zwemles de kwaliteit van leven verbeterd, en dat hierdoor de voordelen opwegen tegen de risico's. Wij denken dat de kwaliteit van leven afneemt als er restricties zijn in het zwemmen. Daarom adviseren wij het toestaan van zwemmen voor kinderen met kanker (ongeacht het hebben van neutropenie), behalve voor kinderen met een niet-getunnelde lijn zoals een PICC lijn.

Module 14: Travelling abroad (English)

A: Recommendations

Research question: What is the effect travelling abroad on infections in children with any type of cancer and/or after stem-cell transplantation?

A1.1: Recommendation (English)

STRONG recommendation, EXPERT evidence	We believe that children with cancer can travel abroad, provided that they visit a country with a comparable health system and provided that the child is in good clinical health.

B: Clinical question, search and selection

B1: Clinical question:

What is the effect of social restrictions (regarding risk of infections) on infections (prevalence and infectious complications) and other outcomes in children with any type of cancer and/or after stem-cell transplantation?

P = Children (aged 0-18 years) with any type of cancer and/or after stem-cell transplantation receiving anti-cancer treatment with curative intent

I = Social restrictions regarding risk of infections (i.e. restriction in school attendance, kindergarten, visiting zoo or farm, pets, swimming (whirlpool, sauna visits), being in crowded places, public transport, intimacy, flowers, or other author defined social restrictions)

C = (No social restrictions)

O = Severe or mild infections (prevalence and infectious complications), quality of life, anti-cancer treatment-related complications (adjustments in therapy or delay), costs, mortality, event-free survival

B2: Literature search and study selection

For the complete methodology of this guideline development and the search strategy, we refer to pages 18-23.

Of 6038 unique citations identified in the literature search, zero studies with pediatric oncology patients were included for this clinical question.

C: Results in pediatric and adult oncology patients

C1. Evidence in pediatric oncology patients

In our literature search, 0 studies were included for this clinical question.

C2. Additional recommendations guidelines (adults)

From our search for existing relevant guidelines, no additional guidelines were included for this clinical question.

D: Conclusion(s) of evidence (pediatric oncology patients)

0 studies in pediatric	-

oncology patients were found.	

E: Considerations

No evidence in pediatric oncology patients was found for this clinical question. Therefore, the recommendation is based on expert opinions.

The guideline panel believes that children with cancer can travel abroad, provided that they visit a country with a comparable health system and provided that the child is in good clinical health. We see no obvious reasons why this should be contraindicated in stable children.
However, this should always be a careful consideration for the child as an individual, and therefore this always needs to be discussed and be allowed by the treating physician. It should not interfere with treatment and parents should carry a letter of the treating physician, in the event something happens when abroad.

Module 14: Reizen naar het buitenland (NEDERLANDS)

F: Aanbeveling (Nederlands)

STERKE aanbeveling, EXPERT evidence	De werkgroep is van mening dat kinderen met kanker naar het buitenland kunnen reizen, onder de voorwaarden dat ze een land bezoeken met een vergelijkbaar zorgsysteem en dat het kind in klinisch goede gezondheid verkeert.

G: Overwegingen (Nederlands)

Er werd geen literatuur gevonden over dit onderwerp bij kinderen met kanker. Daarom is deze aanbeveling gebaseerd op de meningen van de experts in de werkgroep.

De werkgroep is van mening dat kinderen met kanker naar het buitenland kunnen reizen, onder de voorwaarden dat ze een land bezoeken met een vergelijkbaar zorgsysteem en dat het kind in klinisch goede gezondheid verkeert. Wij zien geen duidelijke reden waarom dit niet mogelijk zou zijn. Dit is natuurlijk altijd een zorgvuldige overweging voor het specifieke individu, en daarom is dit altijd in overeenstemming met de behandelend arts. Het reizen naar het buitenland zou niet de behandeling in de weg moeten staan en ouders zouden een brief mee moeten nemen van de behandelend arts met daarin belangrijke medische informatie, mocht er in het buitenland iets gebeuren.

Bijlage 1: Kennislacunes

Tijdens de ontwikkeling van de richtlijn Leefregels bij kinderen met kanker is systematisch gezocht naar onderzoeksbevindingen die nuttig konden zijn voor het beantwoorden van de uitgangsvragen. Een deel (of een onderdeel) van de uitgangsvragen is met het resultaat van deze zoekacties te beantwoorden, een zeer groot deel echter niet. Het is duidelijk geworden dat op het terrein van leefregels bij kinderen met kanker nog veel lacunes in de beschikbare kennis bestaan. De werkgroep is van mening dat (vervolg)onderzoek niet alleen wenselijk, maar ook noodzakelijk is, om in de toekomst een duidelijker antwoord te kunnen geven op vragen uit de praktijk.

Een aantal voorbeelden van deze kennislacunes werden benoemd:

- Wat is het effect van bepaalde leefregels op het voorkomen van infecties, maar ook op de kwaliteit van leven van kinderen met kanker?

  Deze vraag kan worden toegepast op alle onderwerpen die beschreven zijn in deze richtlijn, zoals bijvoorbeeld naar school gaan, zwemmen, activiteiten met hoge impact, openbaar vervoer etc.

Bijlage 2: Implementatieplan

Inleiding

Deze bijlage is opgesteld ter bevordering van de implementatie van de richtlijn Leefregels bij kinderen met kanker.

Werkwijze
De werkgroep heeft per aanbeveling geïnventariseerd:
- de verwachtte impact van implementatie van de aanbeveling op de zorgkosten;
- mogelijk barrières om de aanbeveling te kunnen implementeren;
- mogelijke acties om de implementatie van de aanbeveling te bevorderen;

Voor iedere aanbeveling is nagedacht over onder andere de hierboven genoemde punten. Deze richtlijn zal voornamelijk worden gebruikt in het Prinses Máxima Centrum en de Shared Care ziekenhuizen. Hierdoor is het verspreiden en het onder de aandacht van brengen van de richtlijn makkelijk. Hier zal met name de kernwerkgroep zich voor inzetten. Het streven is ook om samen met de VKN een implementatie plan te maken hoe we deze informatie op de juiste manier bij ouders en kinderen kunnen krijgen. Dit zal de kernwerkgroep in een later stadium met de VKN oppakken.

Er is door een multidisciplinaire werkgroep samen te stellen, geprobeerd zo veel mogelijk draagvlak te creëren voor de aanbevelingen. Hiermee hopen wij, samen met het geven van juiste informatie en voorlichten, barrières herkennen en te voorkomen.

Bijlage 3: Zoekstrategie

Search uitgevoerd door Mw. H.W.J. Deurenberg

Zoekstrategie Leefregels

ID Search

#1 (Cancer OR cancers OR cancer* OR oncology OR oncolog* OR neoplasm OR neoplasms OR neoplasm* OR carcinoma OR carcinom* OR tumor OR tumour OR tumor* OR tumour* OR tumors OR tumours OR malignan* OR malignant OR hematooncological OR hemato oncological OR hemato-oncological OR hematologic neoplasms OR hematolo*):ti,ab,kw (Word variations have been searched)

#2 "P variant breed":ti

#3 MeSH descriptor: [Stem Cell Transplantation] explode all trees

#4 stem NEAR/2 cell NEAR/3 transplan*:ti,ab

#5 stem NEAR/2 cell NEAR/3 transplan*:kw

#6 [mh "bone marrow transplantation"]

#7 "bone marrow" NEAR/5 transplant*:ti,ab,kw

#8 "stem cell" NEAR/5 transplant*:ti,ab,kw

#9 #3 OR #4 OR #5 OR #6 OR #7 OR #8

#10 "P variant stam cel transplantatie".ti.

#11 MeSH descriptor: [Leukemia] explode all trees

#12 (leukemia or leukemi* or leukaemi*):ti,ab,kw

#13 (aml or anll or lymphoma or lymphom* or hodgkin* or T-cell or B-cell or non-hodgkin or sarcoma or sarcom* or Ewing* or osteosarcom* or wilms* or nephroblastom* or neuroblastom* or rhabdomyosarcom* or teratom* or hepatom* or hepatoblastom* or PNET or medulloblastom* or PNET* or (neuroectodermal adj2 tumors NEAR/2 primitive) or retinoblastoma or retinoblastom* or meningiom* or gliom*):ti,ab,kw

#14 [mh "lymphatic vessel tumors"]

#15 MeSH descriptor: [Lymphatic Vessel Tumors] explode all trees

#16 [mh lymphoma] OR [mh "neoplasms, complex and mixed"] OR [mh "neoplasms, connective and soft tissue"] OR [mh "neoplasms, germ cell and embryonal"] OR [mh "neoplasms, glandular and epithelial"] OR [mh “neoplasms, gonadal tissue”] OR [mh “neoplasms, nerve tissue”] OR [mh “neoplasms, plasma cell”] OR [mh “neoplasms, vascular tissue"] OR [mh “neoplasms by site"] OR [mh “neoplasms, hormone-dependent"] OR [mh “neoplasms, radiation-induced"] OR [mh “neoplastic syndromes, hereditary”]

#17 ((brain NEAR/1 tumor*) OR (brain NEAR/1 tumour) OR (brain NEAR/1 neoplasm*) or (central NEAR/1 nervous NEAR/1 system NEAR/1 neoplasm*) OR (central NEAR/1 nervous NEAR/1 system NEAR/1 tumo*) or (central NEAR/1 nervous NEAR/1 system NEAR/1 cancer*) or (brain NEAR/1 cancer*) or (brain NEAR/1 neoplasm*) or (intracranial NEAR/1 neoplasm*) or (leukemia NEAR/1 lymphocytic NEAR/1 acute*)):ti,ab,kw

#18 #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17=P leukemia

#19 #1 OR #9 OR #18

#20 ((pediatric NEAR/3 oncolog*) OR (paediatric NEAR/3 oncol*) OR (child* NEAR/3 (cancer* OR tumor* OR tumour* OR neoplasm*))):ti,ab,kw

#21 [mh "young adult"] OR [mh child] OR [mh infant]

#22 ((young NEAR/1 adult*) OR child* OR infant* OR pediatr* OR paediatr* OR perinat* OR neonat* OR newborn* OR infan* OR boy OR boys OR girl OR girls OR kid OR kids or schoolage* or juvenil* or teenage* or adolescen* or toddler*):ti,ab,kw

#23 #20 OR #21 OR #22

#24 #18 AND #23

#25 [mh "Platelet Transfusion"]

#26 [mh Plateletpheresis]

#27 [mh "Blood Platelets"]

#28 ((platelet* OR thrombocyte*) NEAR/5 (prophyla* OR transfus* OR infus* OR administ* OR requir* OR need* OR product* OR component* OR concentrate* OR apheres* OR pooled OR single NEAR/1 donor OR random NEAR/1donor)):ti,ab,kw
#29 (thrombocytopheres* or plateletpheres*):ti,ab,kw
#30 #25 OR #26 OR #27 OR #28 OR #29
#31 [mh "blood component transfusion"] OR [mh "erythrocyte transfusion"]
#32 ((blood NEAR/3 transfus*) or (erythrocyt* NEAR/2 transfus*)):ti,ab,kw
#33 ((erythrocy* OR hemoglobin* OR haemoglobin*) NEAR/5 (prophyla* OR transfus* OR infus* OR administ* OR requir* OR need* OR product* OR component* OR concentrate* OR apheres* OR pooled OR single NEAR/1 donor OR random NEAR/1donor)):ti,ab,kw
#34 #31 OR #32 OR #33
#35 [mh "blood component transfusion"] OR [mh "erythrocyte transfusion"] OR [mh "platelet transfusion"]
#36 [mh "Platelet Count"]
#37 #35 OR #36
#38 #30 OR #34 OR #37
#39 #24 AND #38
#40 (#19 or #20) AND (#21 or #22)
#41 [mh "Social Participation"]
#42 (social NEAR/3 (participat* OR contact OR contacts OR reintegrat*)):ti,ab,kw
#43 (activity NEAR/2 limitat*):ti,ab,kw
#44 [mh "Social Isolation"]
#45 [mh "Interpersonal Relations"]
#46 social NEAR/2 (restriction* OR interaction* OR competenc* OR participat* OR contact* OR reintegrat*):ti,ab,kw
#47 (restrict* NEAR/2 participati* NEAR/5 (activities or relations*)):ti,ab,kw
#48 [mh hygiene] OR [mh "hand hygiene"] OR [mh "skin care"]
#49 showering OR bath* OR hygiene OR cleani* OR laundry OR (renew* NEAR/2 cloth*):ti,ab,kw
#50 [mh Pets]
#51 ((school NEAR/3 attendan*) OR (public NEAR/2 transpor*) or bus or train):ti,ab,kw
#52 [mh "Animals, Zoo"]
#53 [mh "schools, nursery"]
#54 [mh Nurseries] OR [mh "Child Day Care Centers"]
#55 (child* NEAR/2 day NEAR/2 care NEAR/3 center):ti,ab,kw
#56 [mh "Swimming Pools"]
#57 [mh Swimming] OR [mh boxing] OR [mh skating] OR [mh soccer] OR [mh hockey] OR [mh diving] OR [mh "weight lifting"] or [mh wrestling] OR [mh "youth sports"]
#58 (boxing OR skat* OR soccer OR diving OR (weight NEAR/1 lift*) OR wrestling OR swimming OR (scuba NEAR/2 diving) OR flying OR rollercoast* OR football* or hockey):ti,ab,kw
#59 #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55 OR #56 OR #57 OR #58
#60 #40 AND #59

Cochrane search

P= kinderen met kanker = set 18 AND set 23
1. kanker = set 18
2. leeftijd = set 23
3. leefregels ivm risico's door activiteiten =set 59
4. resultaat = set 60 = P kinderen met kanker + leefregels ivm risico's door activiteiten

Database: Ovid MEDLINE(R) ALL <1946 to December 11, 2020>
Search Strategy:
---
1 "coc social restrictions".ti. (0)
2 exp stem cell transplantation/ or exp hematopoietic stem cell transplantation/ (83929)
3 (stem adj2 cell adj3 transplan*).tw. (50727)
4 (stem adj2 cell adj3 transplan*).kf. (7551)
5 bone marrow transplantation/ (44746)
6 ("bone marrow" adj5 transplant$).tw. (38419)
7 ("bone marrow" adj5 transplant$).kf. (1865)
8 ("stem cell" adj5 transplant$).tw. (51747)
9 ("stem cell" adj5 transplant$).kf. (7713)
10 or/2-9 (151154)
11 exp Leukemia/ (234051)
12 (leukemia or leukemi* or leukaemi*).tw. (269738)
13 (leukemia or leukemi* or leukaemi*).kf. (32354)
14 (aml or anll or lymphoma or lymphom* or hodgkin* or T-cell or B-cell or non-hodgkin or sarcoma or sarcom* or Ewing* or osteosarcom* or wilms* or nephroblastom* or neuroblastom* or rhabdomyosarcom* or teratom* or hepatom* or hepatoblastom* or PNET or medulloblastom* or PNET* or (neuroectodermal adj2 tumors adj2 primitive) or retinoblastoma or retinoblastom* or meningiom* or gliom*).tw. (834591)
15 (aml or anll or lymphoma or lymphom* or hodgkin* or T-cell or B-cell or non-hodgkin or sarcoma or sarcom* or Ewing* or osteosarcom* or wilms* or nephroblastom* or neuroblastom* or rhabdomyosarcom* or teratom* or hepatom* or hepatoblastom* or PNET or medulloblastom* or PNET* or (neuroectodermal adj2 tumors adj2 primitive) or retinoblastoma or retinoblastom* or meningiom* or gliom*).kf. (90826)
16 exp lymphatic vessel tumors/ or exp lymphoma/ or exp "neoplasms, complex and mixed"/ or exp "neoplasms, connective and soft tissue"/ or exp "neoplasms, germ cell and embryonal"/ or exp "neoplasms, glandular and epithelial"/ or exp neoplasms, gonadal tissue/ or exp neoplasms, nerve tissue/ or exp neoplasms, plasma cell/ or exp neoplasms, vascular tissue/ or exp neoplasms by site/ or exp neoplasms, hormone-dependent/ or exp neoplasms, radiation-induced/ or exp neoplastic syndromes, hereditary/ (2727316)
17 ((brain adj tumo?r*) or (brain adj neoplasm?) or (central adj nervous adj system adj neoplasm?) or (central adj nervous adj system adj tumo?r?) or (central adj nervous adj system adj cancer?) or (brain adj cancer*) or (brain adj neoplasm*) or (intracranial adj neoplasm*) or (leukemia adj lymphocytic adj acute*)).tw. (49779)
18 ((brain adj tumo?r*) or (brain adj neoplasm?) or (central adj nervous adj system adj neoplasm?) or (central adj nervous adj system adj tumo?r?) or (central adj nervous adj system adj cancer?) or (brain adj cancer*) or (brain adj neoplasm*) or (intracranial adj neoplasm*) or (leukemia adj lymphocytic adj acute*)).kf. (10686)
19 or/11-18 (3380178)
20 "variant neurocognitive P".ti. (0)
21 "P variant breed".ti. (0)
22 ((p?ediatric adj3 oncolog*) or (child* adj3 (cancer? or tumo?r? or neoplasm?))).tw. (39721)
23 ((p?ediatric adj3 oncolog*) or (child* adj3 (cancer? or tumo?r? or neoplasm?))).kf. (2540)

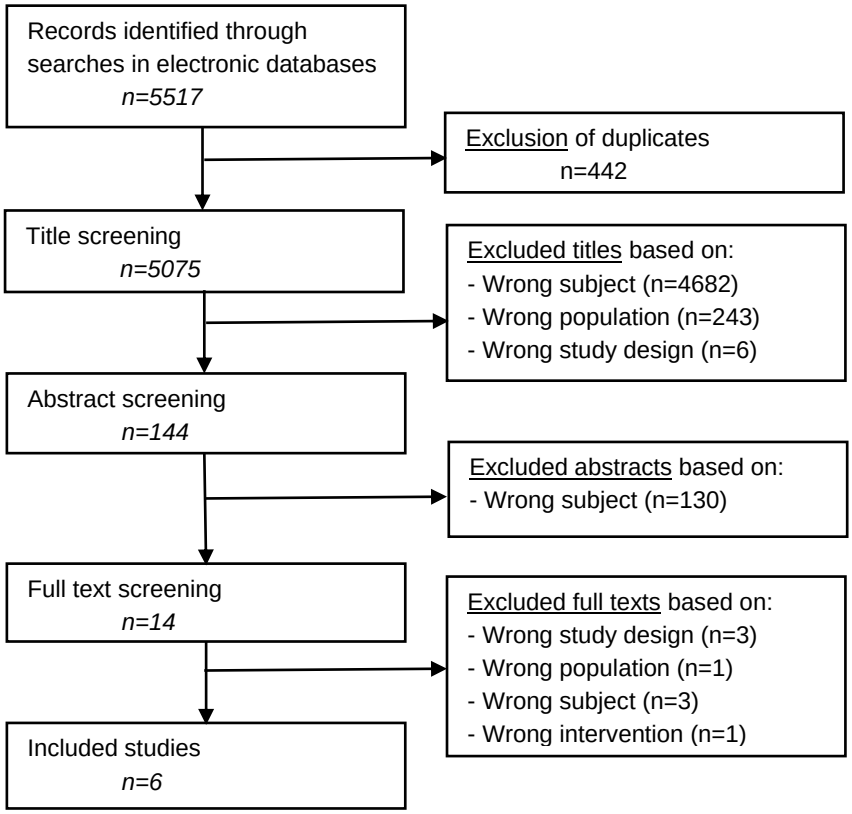
24 young adult/ or exp child/ or exp infant/ (3206941)
25 ((young adj adult?) or child??? or childhood or infant* or p?ediatr* or perinat* or neonat* or newborn* or infan* or boy? or girl? or kid? or schoolage* or juvenil* or teenage* or adolescen* or toddler?).tw. (2465097)
26 ((young adj adult?) or child??? or childhood or infant* or p?ediatr* or perinat* or neonat* or newborn* or infan* or boy? or girl? or kid? or schoolage* or juvenil* or teenage* or adolescen* or toddler?).kf. (336883)
27 (cancer* or oncolog* or neoplasm* or carcinom* or tumor* or tumour* or malignan* or hematooncological or hemato?oncological or hemato-oncological or (hematologic adj neoplasm*)).tw. (3361279)
28 (cancer* or oncolog* or neoplasm* or carcinom* or tumor* or tumour* or malignan* or hematooncological or hemato?oncological or hemato-oncological or (hematologic adj neoplasm*)).kf. (611739)
29 22 or 23 (40391)
30 10 or 19 or 29 (3481138)=stamcel transplantatie
31 24 or 25 or 26 (4126038)=kinderen
32 "zoekacties social restrictions en hygiene".ti. (0)
33 Social Participation/ (2558)
34 (social adj3 (participat* or contact? or reintegrat*)).tw. (10500)
35 (activity adj2 limitat*).tw. (3795)
36 Social Isolation/ (13929)
37 Interpersonal Relations/ (73010)
38 (social adj2 restriction?).tw. (649)
39 (restrict* adj2 participati* adj5 (activities or relations*)).tw. (141)
40 (interacti* adj3 social*).tw. (24227)
41 (social adj2 compet*).tw. (4008)
42 hygiene/ or hand hygiene/ or skin care/ (22978)
43 (showering or bath* or hygiene or cleani* or laundry or (renew* adj2 cloth*)).tw. (135913)
44 (showering or bath* or hygiene or cleani* or laundry or (renew* adj2 cloth*)).kf. (15536)
45 (social adj3 (participat* or contact? or reintegrat*)).kf. (756)
46 (activity adj2 limitat*).kf. (151)
47 (social adj2 restriction?).kf. (11)
48 (restrict* adj2 participati* adj5 (activities or relations*)).kf. (0)
49 (interacti* adj3 social*).kf. (1472)
50 (social adj2 compet*).kf. (276)
51 Pets/ (2641)
52 ((school adj3 attendan*) or (public adj2 transpor*) or bus* or train?).tw. (116944)
53 Animals, Zoo/ (5400)
54 schools, nursery/ (1474)
55 Nurseries/ (1087)
56 Child Day Care Centers/ (5063)
57 (child? adj2 day adj2 care adj3 center?).tw. (143)
58 (child? adj2 day adj2 care adj3 center?).kf. (21)
59 ((school adj3 attendan*) or (public adj2 transpor*) or buss* or train?).kf. (778)
60 exp Swimming Pools/ or exp Swimming/ (26392)
61 boxing/ or skating/ or soccer/ or hockey/ or diving/ or weight lifting/ or wrestling/ or youth sports/ (24034)
62 (boxing or skat* or soccer or diving or (weight adj lift*) or wrestling or swimming or (scuba adj2 diving) or flying or rollercoast* or football* or hockey*).tw. (69080)
63 (boxing or skat* or soccer or diving or (weight adj lift*) or wrestling or swimming or (scuba adj2 diving) or flying or rollercoast* or football* or hockey*).kf. (7172)

64 or/33-60 (432018)= standaard activiteiten met risico's
65 61 or 62 or 63 (79457)= risicovolle activiteiten
66 hemorrhage/ or blood loss, surgical/ or exp oral hemorrhage/ or exp postoperative hemorrhage/ (105696)
67 (bleeding or (blood adj3 loss) or rebleeding or hemorrhage* or h?emostasis or complicat*).tw,kf. (1490880)
68 66 or 67 (1519709)=bloedverlies
69 30 and 31 and 64 (3539)
70 30 and 31 and 65 (150)
71 30 and 31 and 68 (39860)
72 exp Case Reports/ (2140140)
73 (case adj2 serie?).ti,ab,kf. (81166)
74 72 or 73 (2206004)
75 69 not 74 (3127)
76 70 not 74 (95)
77 (30 and 31 and (64 or 65)) not 74 (3200)=stamceltransplantatie + kinderen + activiteiten geen case reports
78 77 (3200)
79 limit 78 to yr="2019 -Current" (320)

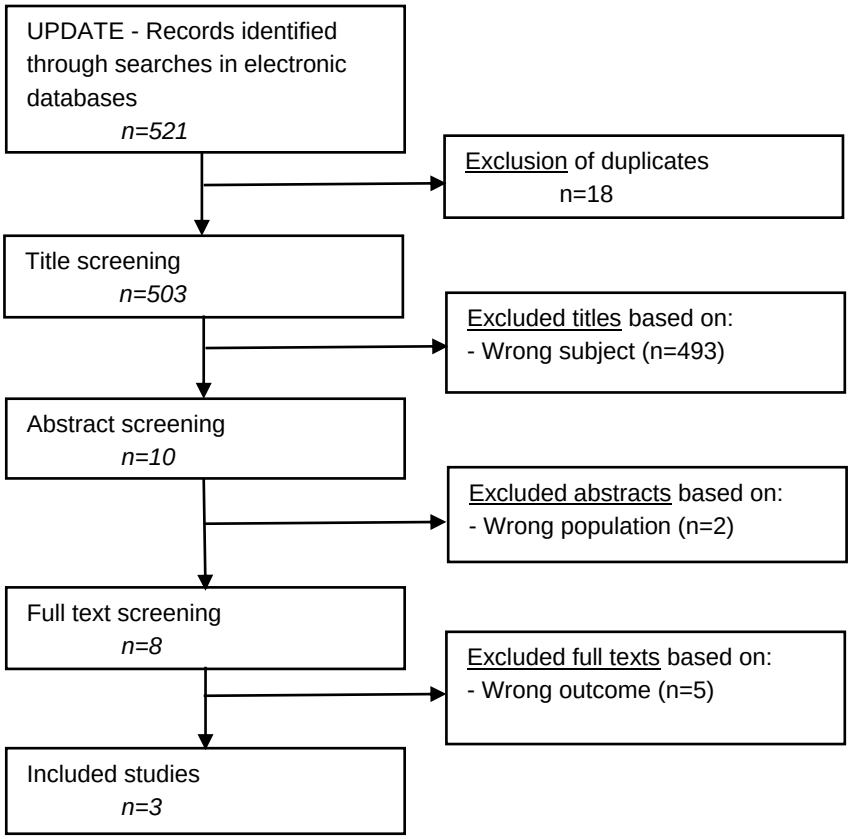
Medline search voor leefregels
P= kinderen met kanker = set 18 AND set 23
1. kanker = set 18
2. leeftijd inperking tot kinderen = set 23
3. leefregels ivm risico's door activiteiten =set 64 or set 65
4. resultaat = set 79 = set 77 na inperking tot na 2019 en P kinderen met kanker + stamceltransplantatie + leefregels ivm activiteiten vanaf 2019 zonder case reports

Bijlage 4: Inclusie en exclusie flowchart (2019 & 2020)

A) Search 2019



B) Search 2020 – Update



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