



**International Guideline  
Harmonization Group**  
for Late Effects of Childhood Cancer

# International Guideline Harmonization Group Meeting

19 June 2025  
Seattle

# Agenda

<b>12.45 – 12.50</b>	Melissa Hudson	Welcome
<b>12.50 – 13.10</b>	Elvira van Dalen	Methodology & guidelines in progress
<b>13.10 – 13.35</b>	Kiri Ness	Health promotion
<b>13.35 – 13.55</b>	Monica Muraca	Update premature ovarian insufficiency surveillance
<b>13.55 – 14.10</b>	Matt Ehrhardt	ARIA survivorship care guidelines
<b>14.10 – 14.15</b>	Leontien Kremer	Closing remarks

# Published guidelines

- Secondary breast cancer (TLO 2013; JCO 2020)
- Cardiomyopathy (TLO 2015; TLO 2023)
- Premature ovarian insufficiency (JCO 2016)
- Male gonadotoxicity (TLO 2017)
- Secondary thyroid cancer (Cancer Treat Rev 2018)
- Ototoxicity (TLO 2019)
- Cancer-related fatigue (JCS 2020)
- Obstetric care (AJOG 2021)
- Subsequent CNS neoplasms (TLO 2021)
- Fertility preservation (TLO 2021)
- Coronary artery disease (EJC, 2021)
- Bone mineral density (TLDE 2022)
- Hepatic toxicity (Cancer Treat Rev 2022)
- Mental health problems (TLO 2022)
- Education and employment outcomes (Cancer 2022)
- Hypothalamic-pituitary dysfunction (Endocrine Reviews 2022)
- Dexrazoxane cardioprotection (TLO 2023)
- Pulmonary dysfunction (eClinicalMedicine 2024)
- **Metabolic syndrome (Eur J Endocrinol 2025)**
- **Nephrotoxicity (JCO 2025)**
- **Anthracycline equivalence dose for cardiotoxicity (JACC: CardioOncology 2025)**

# Guidelines in progress

## Guidelines in manuscript phase

- Breast cancer after anthracyclines
- Subsequent colorectal cancer
- Splenic dysfunction
- Health promotion

## Ongoing guidelines

- Premature ovarian insufficiency (update)
- Growth hormone replacement
- Neurocognitive problems
- Primary thyroid dysfunction
- Osteonecrosis
- Dyslipidemia
- Dexrazoxane cardioprotection mitoxantrone

# IGHG's methodology

# Guideline development process

- Step 1** Determine **concordances and discordances** among existing guidelines
- Step 2** Formulate **clinical questions** based on discordant guideline areas
- Step 3** **Identify** available **evidence** for formulated clinical questions
- Step 4** **Summarize evidence** in evidence tables and appraise quality of evidence using GRADE
- Step 5** **Formulate recommendations** according to the evidence, clinical considerations, and patient values

# GRADE levels of evidence

⊕⊕⊕⊕ **HIGH**

Further research is unlikely to change the confidence in the estimate of effect

⊕⊕⊕⊖ **MODERATE**

Further research is likely to have an important impact on the confidence in the estimate of effect and may change the estimate

⊕⊕⊖⊖ **LOW**

Further research is very likely to have an important impact on the confidence in the estimate of effect and is likely to change the estimate

⊕⊖⊖⊖ **VERY LOW**

Any estimate of effect is very uncertain.

# Recommendations

**STRONG recommendation “is recommended”**

**MODERATE recommendation “is reasonable”**

**NOT TO DO recommendation “is not recommended”**



# Update of ongoing guidelines

# Ongoing guidelines

- Growth hormone replacement
- Neurocognitive problems
- Primary thyroid dysfunction
- Osteonecrosis
- Dyslipidemia
- Dexrazoxane cardioprotection mitoxantrone
- Premature ovarian insufficiency (update)

# Growth hormone replacement

**Chairs:** Hanneke van Santen, Wassim Chemaitilly, Simon Bailey

**Coordinators:** Laura van Iersel, Jiska van Schaik

**Aim:**

To formulate recommendations for the use of growth hormone in CAYA cancer patients and survivors and CAYA with cancer predisposition syndromes

**Outcomes:**

Effects of growth hormone replacement on:

- Tumor progression or recurrence
- Mortality
- Subsequent neoplasms
- Other side effects

**Current situation:** formulation of recommendations nearly final (step 5)

# Neurocognitive problems

**Chair:** Kevin Krull

**Coordinator:** Chiara Papini

**Aim:**

To formulate recommendations for surveillance of neurocognitive problems in CAYA cancer survivors

**Outcomes:**

IQ, attention, memory, processing speed, visual-motor integration, fine motor skills, executive functions, language, academic abilities

**Current situation:**

Preparing the Summary of Findings tables/GRADE assessment (step 4)

# Primary thyroid dysfunction

**Chairs:** Hanneke van Santen, Paul Nathan, Sarah Clement

**Coordinators:** Marta Panciroli and Stephanie van der Leij

**Aim:**

To formulate recommendations for primary thyroid dysfunction surveillance in CAYA cancer survivors

**Outcomes:**

Primary thyroid dysfunction, defined as the presence of:

- primary hyperthyroidism
- primary hypothyroidism

**Current situation:**

Identifying the available evidence (step 3)

# Osteonecrosis

**Chairs:** Marry van den Heuvel and Lynda Vrooman

**Coordinators:** Demi de Winter and Emma Verwaaijen

**Aim:**

To formulate recommendations for surveillance and management of osteonecrosis during and after treatment for CAYA cancer

**Outcomes:**

- Symptomatic osteonecrosis
- Asymptomatic osteonecrosis

**Current situation:**

Identifying the available evidence (step 3)

# Dyslipidemia

**Chairs:** Maria Otth and Emily Tonorezos

**Coordinator:** Krystyna Lange

**Aim:**

To formulate recommendations for dyslipidemia surveillance in CAYA cancer survivors

**Outcomes:**

Dyslipidemia

**Current situation:**

- Formulation of the clinical questions and selection criteria (step 2)
- Preparing the search strategy for PubMed/MEDLINE (step 3)

# Dexrazoxane cardioprotection mitoxantrone

**Chairs:** Annelies Mavinkurve-Groothuis, Saro Armenian, Elvira van Dalen

**Coordinator:** -

**Aim:**

To formulate recommendations for primary cardioprotection with dexrazoxane in CAYA with cancer who are expected to receive mitoxantrone.

**Outcomes:**

- Cardiotoxicity (clinical heart failure and subclinical myocardial dysfunction)
- Tumor response, progression free survival and overall survival/mortality
- Adverse effects other than cardiac damage, including secondary neoplasms
- Quality of life

**Current situation:**

Finalization of the Summary of Findings tables/GRADE assessment and the conclusions of evidence (step 4)





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## Closing remarks

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# Future topics

- Metabolic syndrome components:
  - hypertension
  - obesity
  - diabetes
- Stroke
- Update male gonadotoxicity surveillance
- Update secondary thyroid cancer
- Fertility preservation for survivors
- Risk stratification follow-up care
- Neurovascular problems
- Melanoma and non-melanoma skin cancer
- Other subsequent neoplasms
- Dental abnormalities / oral health care management
- Eye abnormalities
- Arrhythmias, cardiac valvular abnormalities, pericardial disease
- Sexual health
- Risk of congenital abnormalities in offspring

# Resources

## Resources

- [www.ighg.org](http://www.ighg.org)
- Handbook for guideline development
- IGHG publications
- Interested? Email Renée Mulder ([r.l.mulder@prinsesmaximacentrum.nl](mailto:r.l.mulder@prinsesmaximacentrum.nl))

# Thanks to

## **Core group**

Melissa Hudson  
Leontien Kremer  
Renée Mulder  
Elvira van Dalen  
Rod Skinner  
Saro Armenian  
Smita Bhatia  
Louis Constine  
Lars Hjorth  
Wendy Landier  
Gill Levitt  
Kevin Oeffinger  
Hamish Wallace

**>500 guideline panel members**