WHO recommendations on Iodine Thyroid Blocking

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Radiation-induced Thyroid Cancer

In the **early phase** of such an accident, there is a significant risk for thyroid cancer resulting from external and internal radiation exposure (inhalation and ingestion of food and/or milk products). Internal exposures are dominant risk factors.

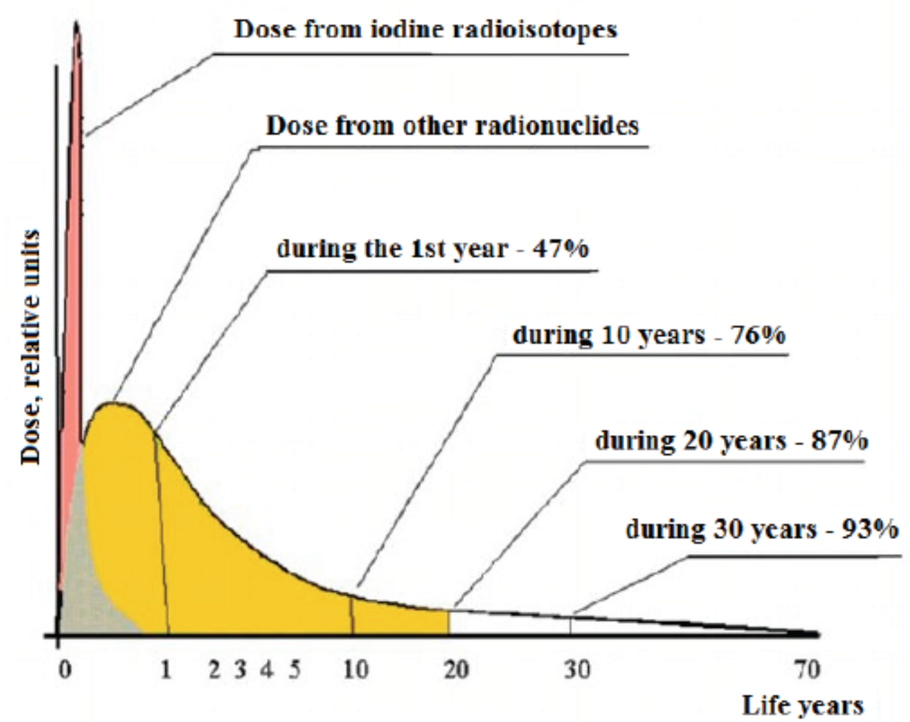
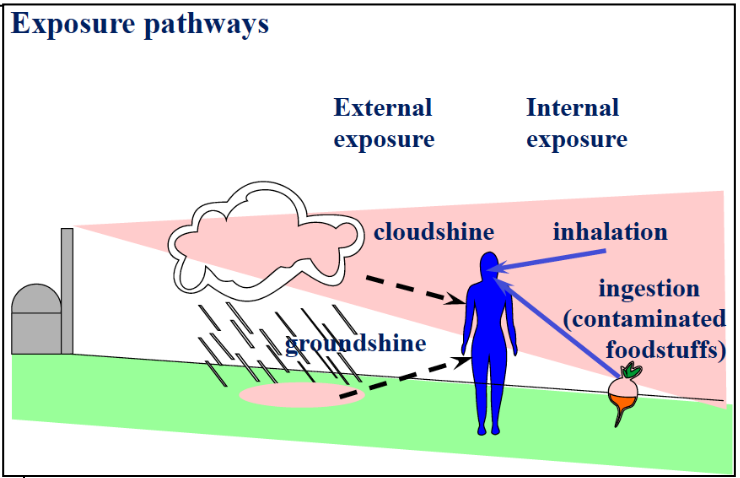


Figure 1.17. Dynamics of emergency radiation doses to critical group of Ukrainian population – children born in 1986 [2]

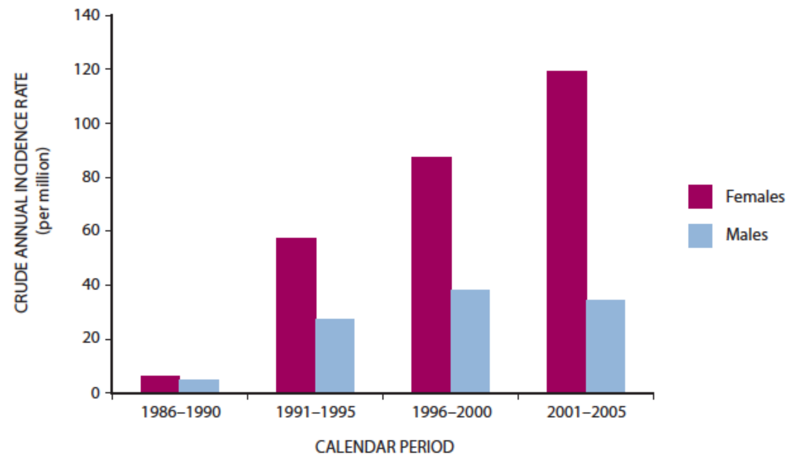


Thyroid Cancer Risk after Chernobyl

By 1995, the incidence of childhood thyroid cancer related to the Chernobyl accident increased to **4 cases per 100,000 per year** as compared to **0.03–0.05 cases per 100,000 per year** prior to the accident.

The increase in thyroid cancer incidence observed among those exposed as children or adolescents in Belarus, the Russian Federation and Ukraine showed **no signs of diminishing up to 20 years after exposure**.

Figure IX. Thyroid cancer incidence rate among those exposed as children and adolescents (age under 18 years in 1986) in Belarus



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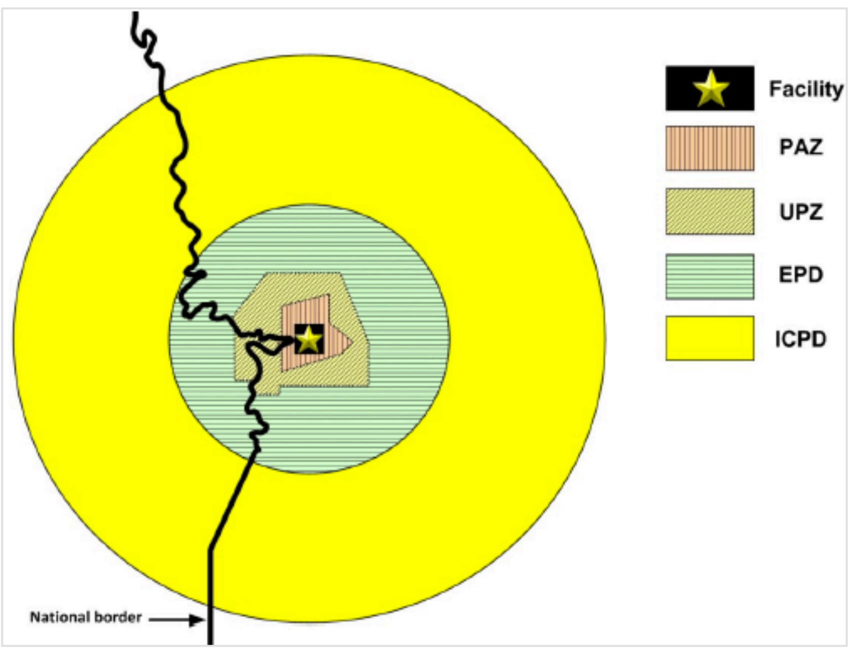
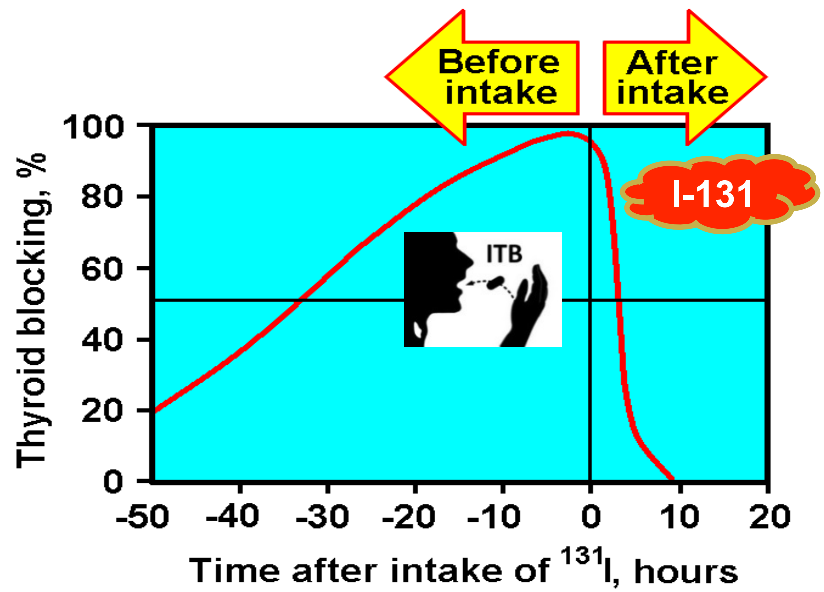
Iodine Thyroid Blocking (ITB)

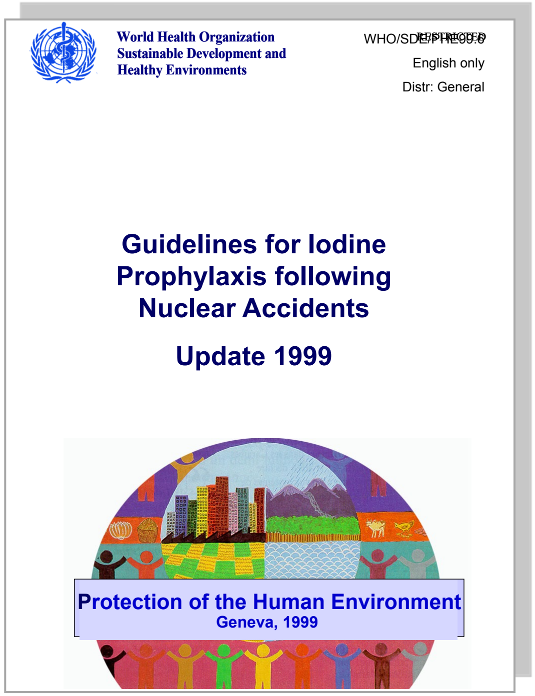
- ✓ An urgent protective action to reduce risk of thyroid cancer
- ✓ Should be administered within hours to be effective, based on the plant conditions, before or shortly after the release (precautionary)
- ✓ Implemented as early action, based on monitoring and assessment
- ✓ ITB effectiveness is significantly reduced by delay of administration





History of the WHO Guidelines on ITB

- Shortly after Chernobyl accident, WHO Regional Office for Europe published the "Guidelines for iodine prophylaxis following nuclear accidents" (1989).
- First epidemiological evidence of increase of childhood thyroid cancer became available few years later. In the light of this information the WHO 1989 guidelines were updated in 1999.
- Since then, numerous publications on preparedness and response to radiation emergencies were jointly developed by WHO and IAEA and addressed the ITB issue.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Sustainable Development and
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WHO/SDE/PHE/99.6
English only
Distr: General

Guidelines for Iodine
Prophylaxis following
Nuclear Accidents

Update 1999

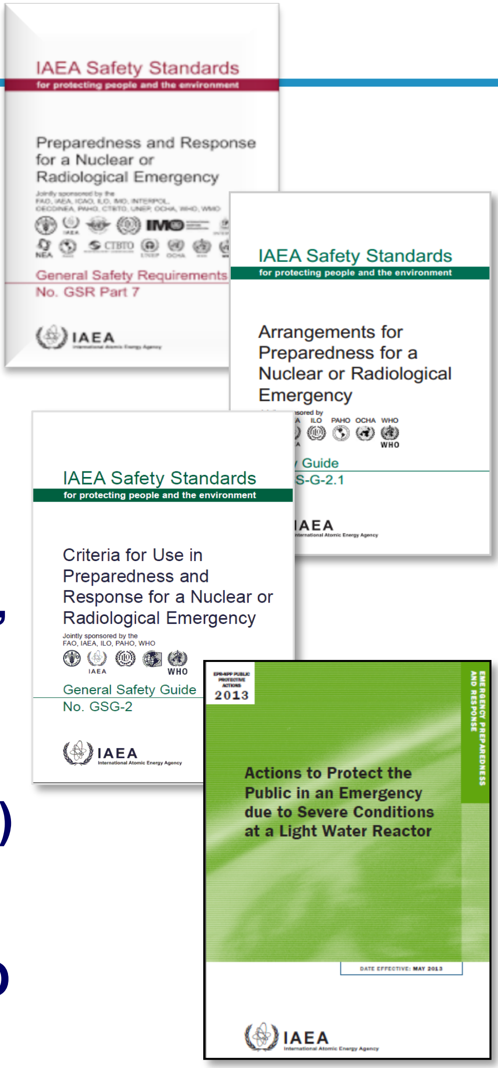
Protection of the Human Environment
Geneva, 1999

KI Thyroid Blocking guidelines revision

- WHO Guidelines on KI thyroid prophylaxis were published by the WHO European Regional Office in 1989 and updated in 1999
  - 10 mSv thyroid dose was used as a recommended intervention level for KI use at the time
- An updated intervention level for planning basis of KI use was revised in 2003 (IAEA's GSR-2, co-sponsored by WHO)
  - 50 mSv of effective thyroid dose remains unchanged in GSR Part 7
- WHO conducted literature review in 2009-2010 with the view of updating the 1999 WHO guidelines

Relevant international publications

- **Safety requirements: BSS – GSR Part 3 (2011) and GSR Part 7 (2015), cosponsored by WHO among other IOs**
- **Arrangements for preparedness for a nuclear or radiological emergency, GS-G-2.1, cosponsored by FAO, IAEA, ILO, PAHO, OCHA and WHO (2007)**
- **Criteria for use in preparedness and response for a nuclear or radiological emergency, cosponsored by FAO, IAEA, ILO, PAHO, OCHA and WHO, GSG-2 (2011)**
- **Actions to protect the public in an emergency due to severe conditions at a light water reactor (EPR-NPP 2013)**
- **Generic Procedures for medical response during a nuclear or radiological emergency, cosponsored by WHO (EPR Medical 2005)**



GSR Part 7 - page 64

TABLE II.2. GENERIC CRITERIA FOR PROTECTIVE ACTIONS AND OTHER RESPONSE ACTIONS IN AN EMERGENCY TO REDUCE THE RISK OF STOCHASTIC EFFECTS

Generic criteria		Examples of protective actions and other response actions[a]
Projected dose that exceeds the following generic criteria: Take urgent protective actions and other response actions		
$H_{thyroid}$	50 mSv[b] in the first 7 days	Iodine thyroid blocking[c]
E[d]	100 mSv in the first 7 days	Sheltering[e]; evacuation; prevention of inadvertent ingestion; restrictions on food, milk and drinking water[g] and restrictions on the food chain and water supply; restrictions on commodities other than food; contamination control; decontamination; registration; reassurance of the public
H_{fetus}[f]	100 mSv in the first 7 days	

[a] These examples are neither exhaustive nor grouped in a mutually exclusive way.

[b] The equivalent dose to the thyroid ($H_{thyroid}$) only due to exposure to radioiodine.

In actual emergencies…

- KI was not timely administered during response to Chernobyl accident in 1986 in the former Soviet Union
- KI was available but not administered by Fukushima population
- KI was over-used by TEPCO workers who are reported to have used up to 80 pills
- IAEA report on Fukushima (2015): " The arrangements prior to the accident included criteria for sheltering, evacuation and iodine thyroid blocking in terms of projected dose, but not in terms of measurable quantities…. Administration of stable iodine for iodine thyroid blocking was not implemented uniformly, primarily due to the lack of detailed arrangements"

Iodine Thyroid Blocking (ITB) considerations

- Existing guides offer a good planning basis based on radiation protection values and quantities, using projected dose concept
- Other technical publications offer OILs for monitoring the amount of radiation in the thyroid (AFTER the intake)
- Issues of timing of ITB administration are not fully addressed in existing guidance (e.g. when “late” becomes “too late”?)
- Question of repeated administration in case of continuing exposure also remains open (age effect, side effects, etc)
- Wide range of differences in national policies in terms of age groups, distances, and pre-distribution methods (RISKAUDIT report, 2010)
- Lessons learned from Fukushima (TEPCO workers)

Revision of 1999 WHO Guidelines on ITB

- Project was launched at the 1st meeting of Guidelines Development Group (GDG) in Wuerzburg in May 2014
- In compliance with the new WHO requirements for development of guidelines/recommendations
- Follows the methodology of evidence-based medicine with a strong component of evaluation of quality of evidence by using GRADE approach
- Systematic reviews based on Cochrane Review methods were carried out in 2015, funded by the German Federal Radiation Protection Office (BfS)

Guidelines development process at WHO: transparency, quality assessment, bias reduction

Step	Process	Year
1	Scoping the document	2010
2	Setting up Guideline Development Group and External Review Group	2013
3	Management of Conflicts of Interest	2013-14
4	Formulation of the questions (PICOT), choice and rating of the relevant outcomes	2014
5	Evidence retrieval, assessment and synthesis (systematic review(s))	2015
	GRADE - evidence profile	
6	Formulation of the recommendations (GRADE)	2016
	Including explicit consideration of: ⦿ Benefits and harms, Values and preferences, and Resource use	Drafting and peer-review
7	Dissemination, implementation (adaptation)	
8	Evaluation of impact	
9	Plan for updating	

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Systematic reviews to inform the recommendations

- Systematic review protocol was published in 2015

Dreger *et al. Systematic Reviews* (2015) 4:126
DOI 10.1186/s13643-015-0106-3

SYSTEMATIC REVIEWS

PROTOCOL — Open Access

CrossMark

The effects of iodine blocking following nuclear accidents on thyroid cancer, hypothyroidism, and benign thyroid nodules: design of a systematic review

Steffen Dreger[1†], Manuela Pfinder[1,2,3*†], Lara Christianson[1], Stefan K Lhachimi[1,2,3] and Hajo Zeeb[1,4]

- Based on PICO approach: Population (P), Intervention (I), Comparator (C), Outcome (O)

Systematic reviews to inform the recommendations

- **PECO**: Which population sub-groups are at greatest risk of developing thyroid cancer, after exposure to radioiodine?
- **PICO 1**: In a population exposed to radioiodine release, should KI be administered to the potentially affected population within the emergency planning zone?
  - Two sub-questions will be: should KI be given to 0-18 age group as a priority? Should the >45 age group be receiving KI as well?
- **PICO 2**: In a population exposed to a single radioiodine release, should KI be administered prior to or within the first two hours after the release/exposure?
  - The underlying Question here is: When is administration of KI is protective and when it does it become harmful?
- **PICO 3**: In case of continuous/repeated release of radioiodine and if no evacuation is possible, should ITB be administered repeatedly to specific subgroups of population versus KI administration only once? (under the condition of the first KI being administered in a timely fashion)

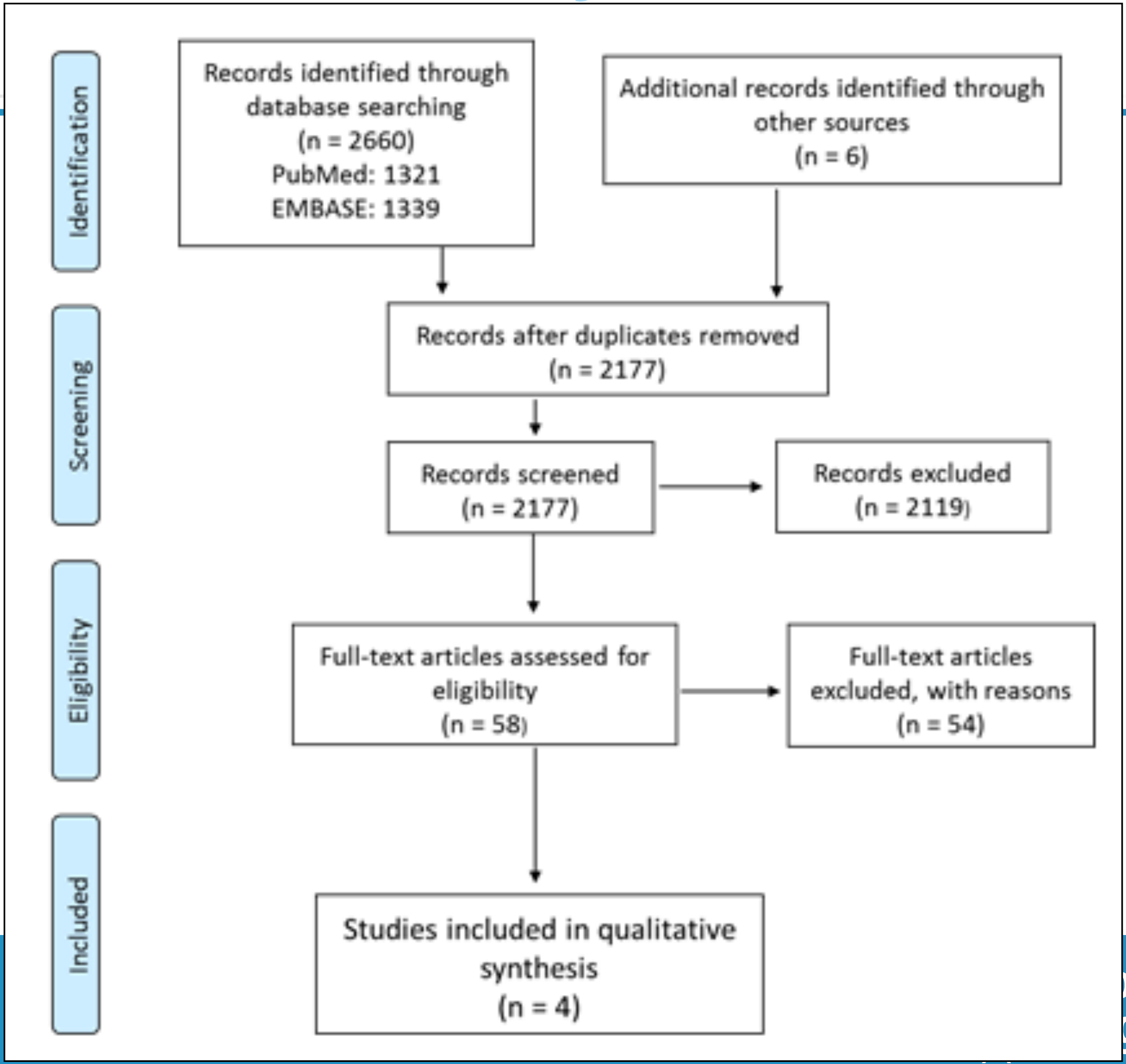
Revised PICOs:

From the main PICO, two sub-PICOs were derived:

- **Timing of KI administration**
  - **In a population exposed to a single radioiodine release (P), does the timing of the administration of KI (I) prior, shortly after, or later than two hours (C) affect the risk of developing thyroid cancer, hypothyroidism, or benign thyroid nodules (O)?**
- **Repeated ITB administration (in case of continuous or repeated exposure to radioactive iodine)**
  - **In specific subgroups of a population exposed to a continuous or repeated exposure to radioiodine (P), does a repeated administration of KI (I) against a single administration (C) affect the risk of developing thyroid cancer, hypothyroidism, or benign thyroid nodules (O)?**

NB: Extensive search of evidence did not bring results for these two sub-PICOs

Results of the systematic review



Eligible studies

- Bandurska-Stankiewicz E, Aksamit-Bialoszewska E, Stankiewicz A and Shafie D 2010 Did the Chernobyl atomic plant accident have an influence on the incidence of thyroid carcinoma in the province of Olsztyn? *Endokrynol Pol* **61** 437-442.

- Brenner AV, Tronko MD, Hatch M, Bogdanova TI et al. 2011 I-131 dose response for incident thyroid cancers in Ukraine related to the Chornobyl accident *Environ Health Perspect* **119** 933-939.
- Cardis E, Kesminiene A, Ivanov V, Malakhova I et al. 2005 Risk of thyroid cancer after exposure to 131I in childhood *Journal of the National Cancer Institute* **97** 724-732.

- Zarzycki W, Zonenberg A, Telejko B and Kinalska I 1994 Iodine prophylaxis in the aftermath of the Chernobyl accident in the area of Sejny in north-eastern Poland *Hormone and metabolic research = Hormon- und Stoffwechselforschung = Hormones et metabolisme* **26** 293-296.

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Grades of Recommendation Assessment, Development and Evaluation

GRADE

RATING QUALITY OF EVIDENCE AND STRENGTH OF RECOMMENDATIONS

GRADE: an emerging consensus on rating quality of evidence and strength of recommendations

Guidelines are inconsistent in how they rate the quality of evidence and the strength of recommendations. This article explores the advantages of the GRADE system, which is increasingly being adopted by organisations worldwide

www.gradeworkinggroup.org

2008 BMJ series

2011 JCE series

GRADE framework

- Emphasizes:
  - Systematic approach
  - Explicitness
  - Transparency
  - Quality of evidence
  - Patient important outcomes

- Uses standardized E-2-R matrix tables to present:
  - Summary of evidence (evidence profile)
  - The factors that affect the final recommendation (decision table)

Factors determining strength of recommendation

- Priority of the problem
- Quality of evidence
- Balance of benefits and harms
- Values and preferences
- Resource use
- Equity
- Feasibility
- Acceptability

All these factors must be included in the process of deriving recommendations

ITB Evidence-2-Recommendation matrix

Type of recommendation	We recommend against the option or for the alternative ☐	We suggest not to use the option or to use the alternative ☐	We suggest using either the option or the alternative ☐	We suggest using the option ☒	We recommend the option ☐

Recommendation

The panel suggests to administer KI over not administer KI to people exposed to radioiodine release in the environment in the setting of radiological or nuclear emergency (Conditional recommendation; Very low quality)

Key considerations:

- KITB should be implemented as a component of comprehensive public health approach in combination with other protection actions (evacuation and sheltering, restriction of contaminated food and drinking water consumption). KITB should not be considered as a single alternative.
- Provisions for KITB implementation need to be carefully considered at the planning stage (see implementation considerations below)
- Optimal timing of administration starts 24 hours prior to, and up to 2 hours after the expected onset of exposure. It would still be reasonable to administer KITB up to 8 hours after the estimated onset of exposure.
- Starting KITB later than 24 hours following the exposure may carry more harms then benefit (by prolonging the biological half-life of radioactive iodine in the thyroid).
- Single KI administration is typically sufficient. However, in the case of prolonged (beyond 24 hours) or repeated exposure, and unavoidable ingestion of contaminated food and water, and when evacuation is not feasible, consider repeated administration of KI. Neonates should not receive repeated KI.

Justification

There is well-documented evidence from various sources (epidemiological, experimental, pathophysiological, clinical, etc.) pointing to more benefits than harms of KITB

Subgroup considerations

- Individuals most likely to benefit include children, adolescents, pregnant and breast-feeding women, and those living in iodine deficiency areas.
- Individuals older than 40, are less likely to benefit from KITB.
- Neonates and elderly are at higher risk of adverse health effects of KI
- Individuals exposed to high dose (e.g., emergency workers) are likely to benefit from KITB irrespective of age.

1

Key considerations for the recommendation on ITB

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2

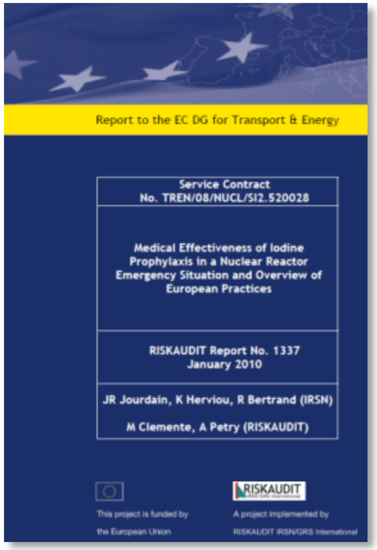
Key considerations for the recommendation on ITB

Sensitive subgroups:

- Individuals most likely to benefit include children, adolescents, pregnant and breast-feeding women, and those living in iodine deficiency areas.
- Individuals older than 40, are less likely to benefit from KITB.
- Neonates and elderly are at higher risk of adverse health effects of KI
- Individuals exposed to high dose (e.g., emergency workers) are likely to benefit from KITB irrespective of age.

New ITB Guide implementation monitoring

- To enable the monitoring of implementation, a national KI baseline survey was conducted in Aug-Oct 2016.
- Survey used EC's RISKAUDIT questionnaire template as a basis and includes seven groups of questions on:
- The survey question groups include:
  1. Galenic formulation and posology
  2. Emergency planning
  3. Intervention levels
  4. Decision-making process during an emergency
  5. Time of administration and effectiveness
  6. Public awareness and communication issues
  7. Roles of the various stakeholders
  8. Available guidelines and protocols for ITB program implementation

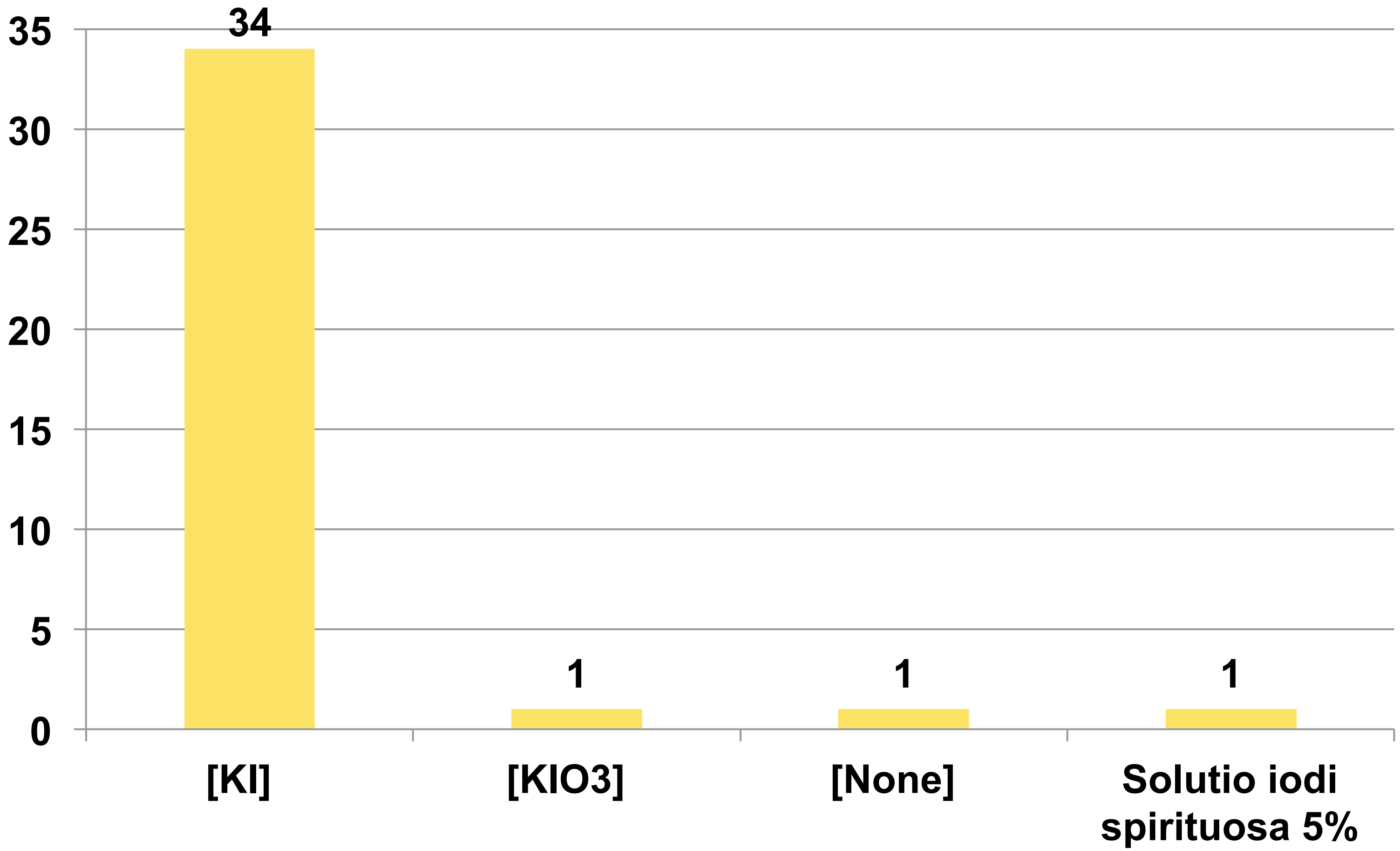


Preliminary Results

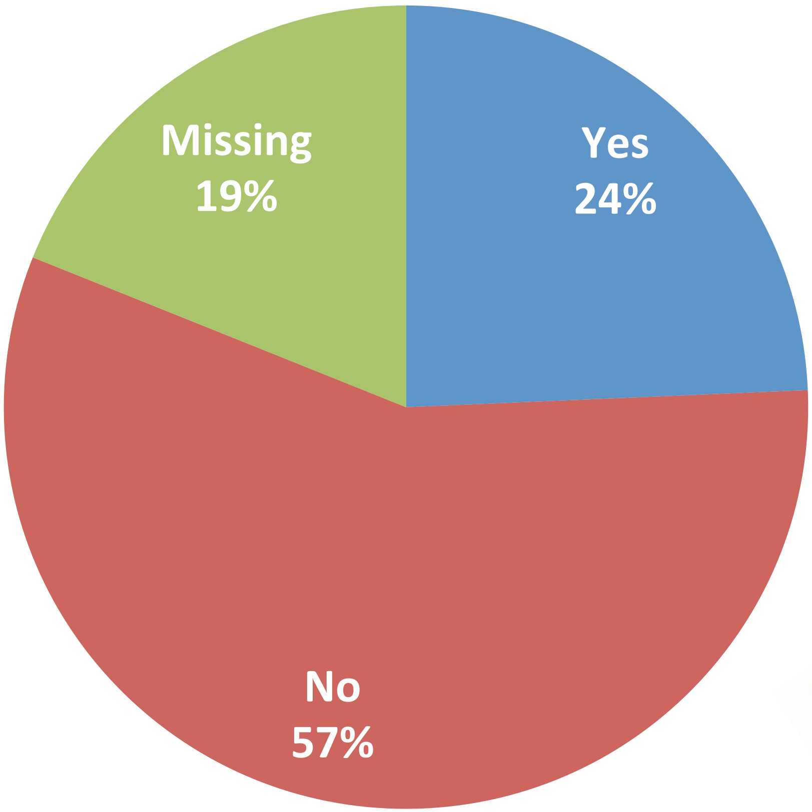
- **Total answers –37 member states**

Americas	2	5,4
South-East Asia	1	2,7
European Region	27	73,0
Eastern Mediterranean	1	2,7
Western Pacific	6	16,2
Total	37	100,0

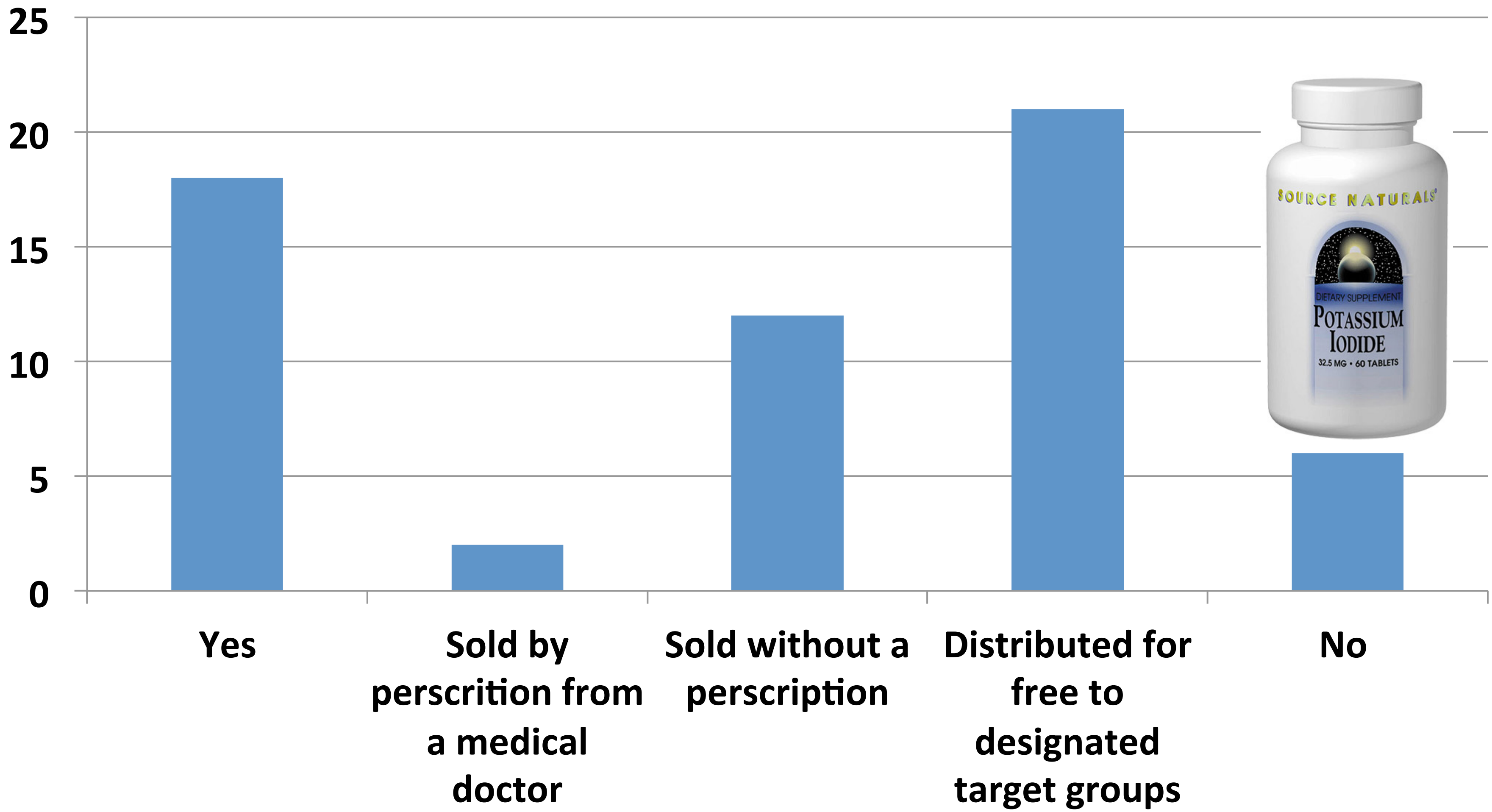
What is the active compound of the iodine formulation used in your country (n=37)



Do you use a pediatric formulation for children (n=37)?



Are KI pills considered a pharmaceutical product in your country (n=37)?



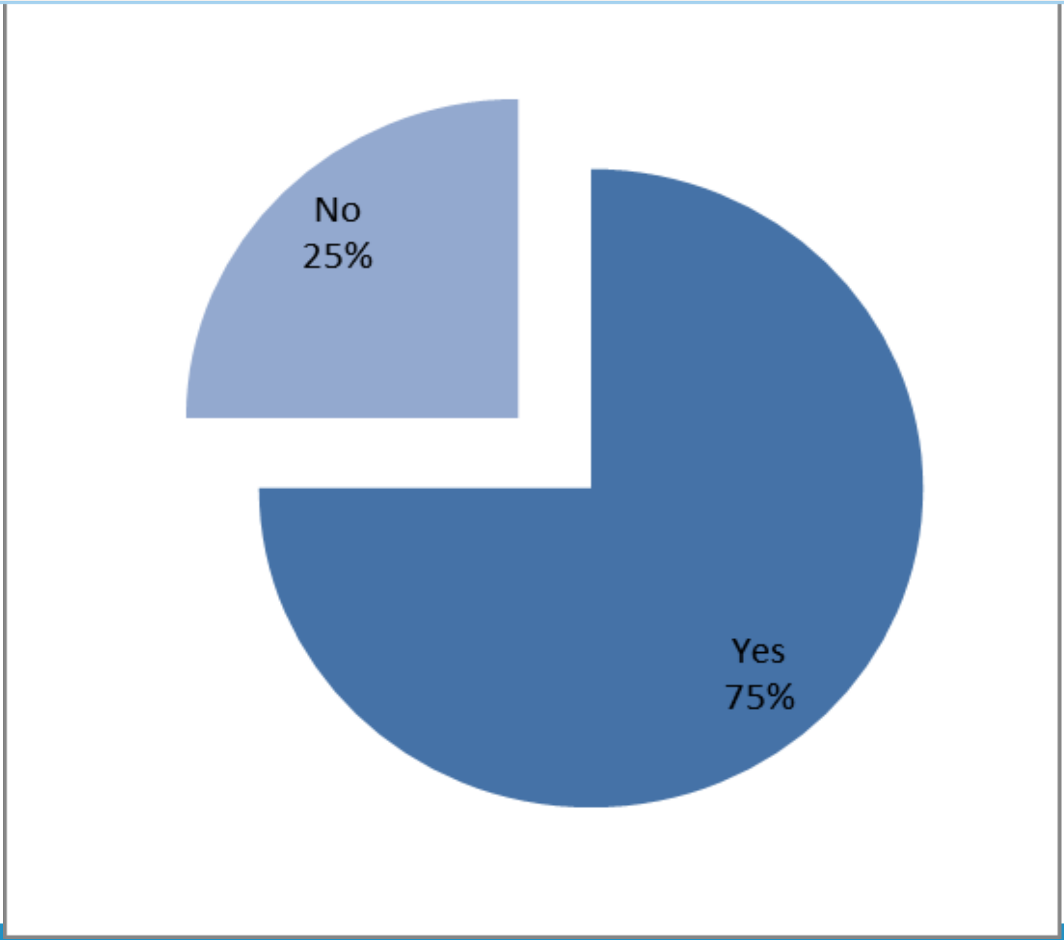
Age limit for iodine thyroid blocking?

- 26 replies 'no age limit',
- 11 replies 'yes, there is age limit' including:
  - 40 years – 7 replies
  - 45 years – 2 replies
  - >45 years – 1 reply
  - 50 years – 1 reply

Are KI pills pre-distributed to everyone or only to a targeted population?

[Everyone] = 11/37, [Target population only] = 11/37, no answer = 15/37

Is ITB recommended in combination with other countermeasures (e.g. sheltering, evacuation, ban of food/milk/drinking water)?



How long it will take to implement ITB to the affected population in your country?

Answers	# of answers	%
- no answer	18	48.6
More than 6 hrs	3	8.1
Less than 6 hrs:	13	35.1
- up to 1 hr	6	16.2
- 1 to 2 hrs	4	10.8
- 2 to 3 hrs	1	2.7
- 3 to 6 hrs	2	5.4
I do not know	3	8.1
Total	37	100.0

Are there communication plans regarding ITB before or during an emergency?

- **‘Yes’ – 19 replies**
- **‘No’ – 4 replies**
- **Missing answer – 14 replies**

- **To allow for a more complete picture on national KI policies, the survey was reopened in April for 8 weeks, will be closed on 31 May 2017.**

- **Full report expected by mid-2017**

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Thank you!

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