Alternative Methodology for Determining the Efficacy of Iodine Thyroid Blocking (ITB)

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NUS National University of Singapore | Singapore Nuclear Research & Safety Initiative

KAERI Korea Atomic Energy Research Institute

Background

- Why iodine is important in a nuclear event?
  - Large amount of radioiodine released in a nuclear event
  - Elevated thyroid dose as radioiodine accumulates in thyroid
- What is iodine thyroid blocking (ITB)?
  - Serves to saturate thyroid with stable iodine by taking stable iodine pills
  - Reduces the amount of (unstable) radioiodine absorbed by thyroid in the event of radioiodine exposure
  - Reduces the thyroid dose exposed by radioiodine

Iodine Pills (Photo Credits: HBO| Chernobyl)

Iodine Pills

Background

- Modeling of iodine thyroid blocking (ITB)
  - **Important to model** ITB as it is frequently part of the activation criterion for public protective actions

Organization	Activation criterion
IAEA (GSR Part 7)	50 mSv equivalent thyroid dose
Republic of Korea (원자력시설 등의 방호 및 방사능 방재 대책법 시행규칙 [별표 4])	100 mGy
US FDA (Guidance Potassium Iodide as a Thyroid Blocking Agent in Radiation Emergencies)	100 mGy (Adults)
WHO (Guidelines for Iodine Prophylaxis following Nuclear Accidents Update 1999)	100 mGy

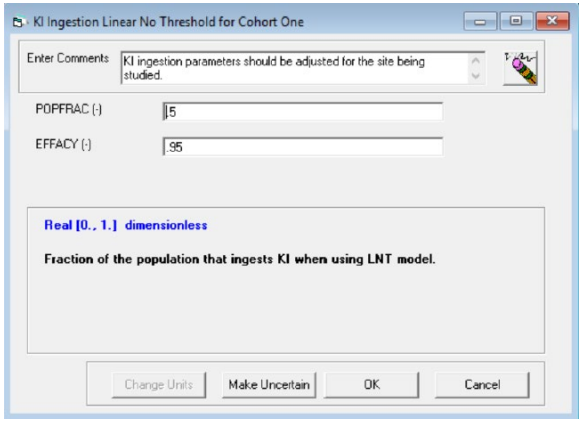
  - **Difficult to model** in a radiological consequence analysis
    - Depends on many factors that are bound to human behaviour and radioactive plume
    - Likely require expert opinion which may be hard to obtain in a timely manner

Background

- ITB Model in MACCS EARLY Module

$$DP_{I,thyroid} = (1 - \varepsilon_{KI}) * DB_{I,thyroid}$$

- $DP_{I,thyroid}$: **Thyroid dose (Sv)** an individual would receive from inhaling radioiodine **when applying KI ingestion**
- $DB_{I,thyroid}$: **Original thyroid dose** through inhalation pathway from radioiodine exposure **without considering KI ingestion**
- ε_{KI}: Efficacy of potassium iodine tablet in reducing thyroid doses radioiodine
  - **0**: No protection
  - **0.7**: Recommended value in MACCS
  - **1**: Total protection
- No time dependency in MACCS ITB model
  - Efficacy relying on expert judgement



KI Ingestion Linear No Threshold Form of MACCS

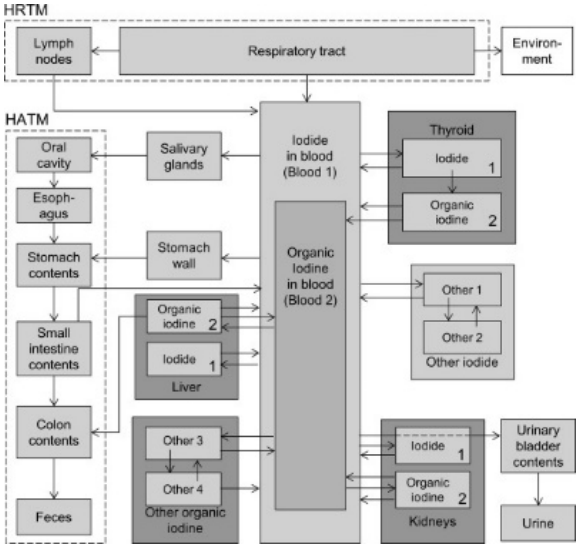
Objectives and Expected Outcomes

- Objectives and Strategy
  - Investigate existing methodology of ITB
  - Review efficacy of ITB
  - **Suggest alternative method** that is less reliant on expert judgement and based on technical results

- Procedures and Expected Outcomes
  - Utilize existing literature to construct alternative method for determination of efficacy of ITB
  - Utilize MACCS output to help determine efficacy
  - **Develop toolkit to determine efficacy**
  - **Build a sample problem and perform an application study**

Investigation and Review of Existing Methodology of ITB

- Iodine biokinetic model to determine the effectiveness of ITB



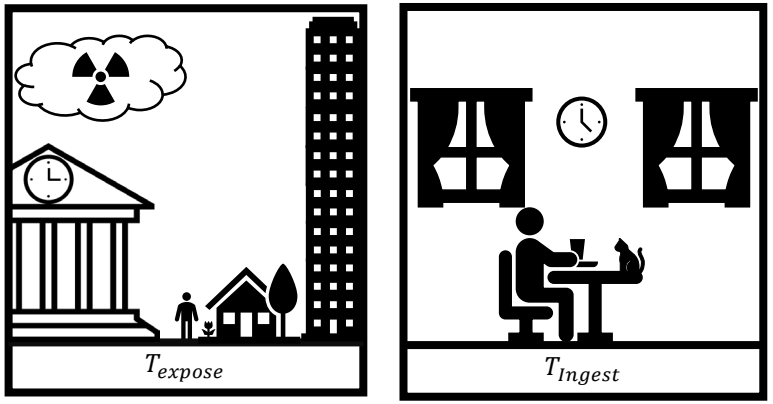
Iodine Biokinetic Model

- Factors that contribute to the efficacy of ITB
  - Time of administration of KI
  - Degree of pre-existing stable iodine saturation of the thyroid gland
  - Ability of residents to find their KI or to obtain new KI during the emergency
- Difficult to pinpoint the efficacy of ITB as a fixed value due to the variability of these factors

TE Kwon, Y Chung, WH Ha, YW Jin, **Application of the new ICRP iodine biokinetic model for internal dosimetry in case of thyroid blocking,** *Nucl Eng Technol.* 52(8):1826-1833, 2020.

Alternative Methodology

- Suggest alternative method
  - **Less reliant on expert judgement**
  - Determine efficacy **with technical inputs**
  - **Focus on T_{Admin}** (administration time) **of KI**



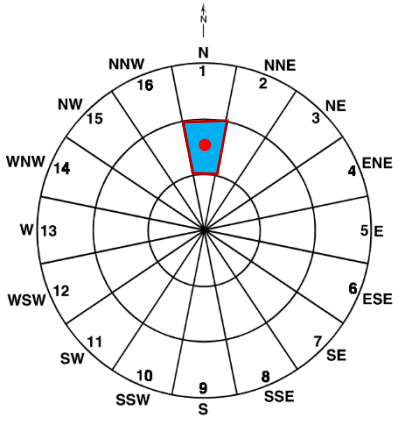
Obtain administration time with the two values:

$$T_{Admin} = T_{Ingest} - T_{Expose}$$

- T_{Admin}: Time (s) in which **KI ingestion occurred** relative to timepoint of radionuclide exposure
- T_{Ingest}: Time (s) in which **KI ingestion occurred** relative to timepoint of initiating event
- T_{Expose}: Time (s) in which **radionuclide exposure occurred** relative to timepoint of initiating event

Alternative Methodology

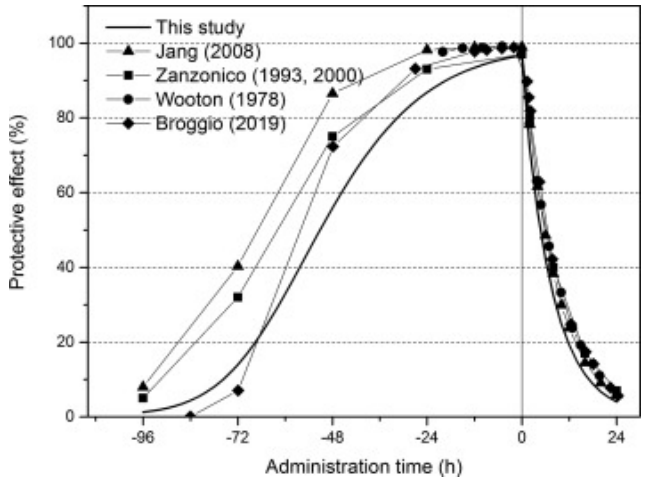
- T_{Ingest}: KI Ingestion time
  - Time point in which KI was consumed
  - **User defined** and dependent on policy & distribution strategy
- T_{Expose}: Exposure time
  - Time point in which radionuclide exposure occurs
  - Assume specific cohort at a specific radial interval was exposed
  - TIMCEN, Time needed for plume to reach the center of a radial interval
  - Obtained from **ATMOS output**



MACCS Polar Coordinate Grid with Selected Radial Interval

Alternative Methodology

- **Determine efficacy based on the updated iodine biokinetic model**
- 1st method: **Lookup table**
  - Hourly breakdown of efficacy vs administration time
  - Values obtained from plot digitizer
- 2nd method: **Fitted equation**
  - Fitted equation based on values obtained from plot digitizer
  - Two parts for positive and negative administration time

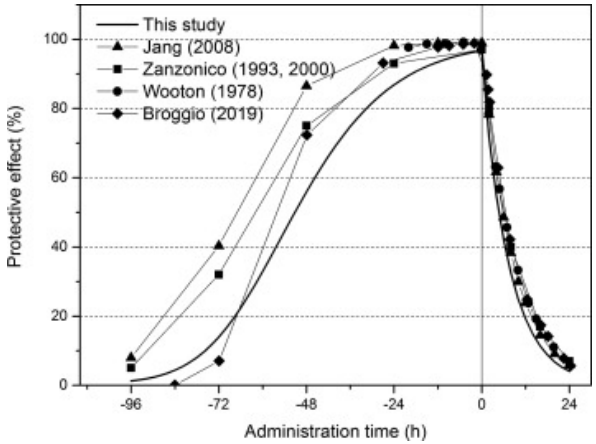


Efficacy Curve based on Administration Time

TE Kwon, Y Chung, WH Ha, YW Jin, **Application of the new ICRP iodine biokinetic model for internal dosimetry in case of thyroid blocking,** *Nucl Eng Technol.* 52(8):1826-1833, 2020.

Alternative Methodology

- Illustration of mentioned process



Plot digitizer

Method 1

Administration time	Protective effect
-96	1.22
-95	1.37
-94	1.51
-93	1.66
-92	1.87
…	…
…	…
20	6.76
21	6.11
22	5.18
23	4.6
24	3.95

Plot digitizer

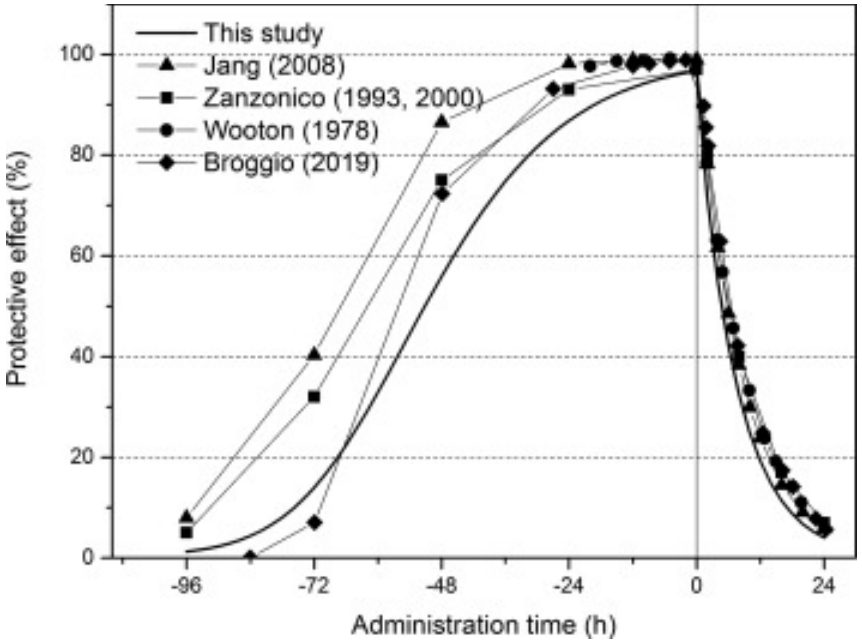
Method 2

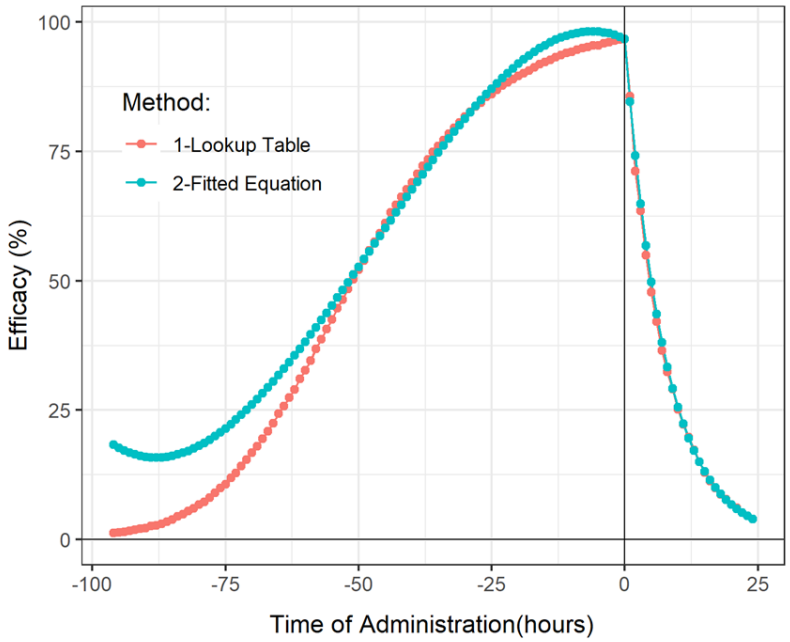
$$\varepsilon_{KI} = -0.0003T_{Admin}^{3} - 0.0424T_{Admin}^{2} - 0.4892T_{Admin} + 96.7, \quad when\ \mathrm{T_{Admin}} < 0$$

$$\varepsilon_{KI} = 96.7\exp(-0.133\ T_{Admin}), \quad when\ T_{Admin} \geq 0$$

Verification

- Illustration of method and difference



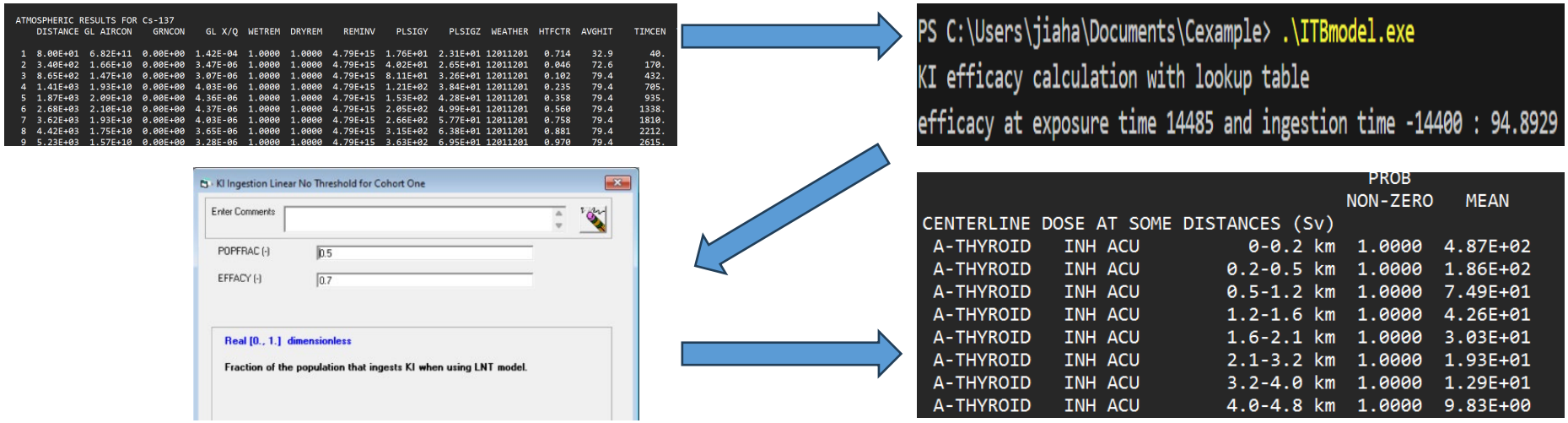


Efficacy Curve based on Administration Time

- Method 1: **More accurate**
- Method 2: **Easier to implement in calculation**

Workflow Demonstration

- Workflow of alternative method with MACCS
  1. Run MACCS with desired inputs without KI ingestion model
  2. Calculate administration time
  3. Estimate efficacy based on administration time
  4. Compute radiation dose of cohort with KI efficacy



Workflow of Alternative Method

Workflow Demonstration

- Workflow
  - Step 1: Single plume release without evacuation

ATMOSPHERIC RESULTS FOR I-131

	DISTANCE	GL AIRCON	GRNCON	GL X/Q	WETREM	DRYREM	REMINV	PLSIGY	PLSIGZ	WEATHER	HTFCTR	AVGHIT	TIMCEN
1	8.00E+01	2.30E+14	0.00E+00	3.92E-04	1.0000	1.0000	5.89E+17	1.76E+01	2.31E+01	12011201	1.000	0.0	40.
2	3.40E+02	8.80E+13	0.00E+00	1.50E-04	1.0000	1.0000	5.89E+17	4.02E+01	2.65E+01	12011201	1.000	0.0	170.
3	8.65E+02	3.55E+13	0.00E+00	6.03E-05	1.0000	1.0000	5.88E+17	8.11E+01	3.26E+01	12011201	1.000	0.0	432.
4	1.41E+03	2.02E+13	0.00E+00	3.43E-05	1.0000	1.0000	5.88E+17	1.21E+02	3.84E+01	12011201	1.000	0.0	705.
5	1.87E+03	1.43E+13	0.00E+00	2.43E-05	1.0000	1.0000	5.88E+17	1.53E+02	4.28E+01	12011201	1.000	0.0	935.
6	2.68E+03	9.12E+12	0.00E+00	1.55E-05	1.0000	1.0000	5.88E+17	2.05E+02	4.99E+01	12011201	1.000	0.0	1338.
7	3.62E+03	6.10E+12	0.00E+00	1.04E-05	1.0000	1.0000	5.88E+17	2.66E+02	5.77E+01	12011201	1.000	0.0	1810.

    - Population located at radial interval 5 will have a time of exposure at 935s

  - Step 2: By assuming ingestion time as zero, administration time will be equal to -935s

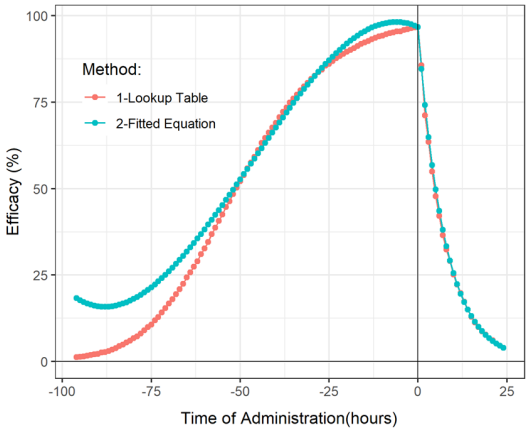
$$T_{Admin} = T_{Ingest} - T_{Expose}$$

    - Ingestion time can be varied (User input of suggested method)
    - Ingestion at zero seconds: Ingestion before plume arrival (i.e. exposure)

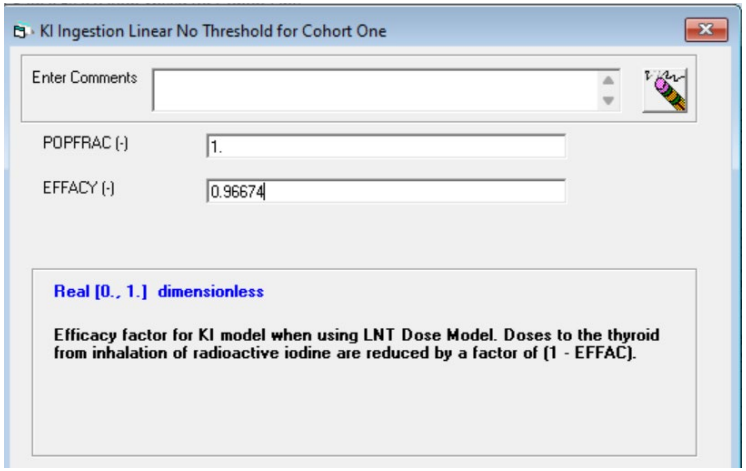
Workflow Demonstration

- Step 3: Efficacy calculated to be 96.67%

```
PS C:\Users\jiaha\Documents\Cexample> .\ITBmodel.exe
KI efficacy calculation with lookup table
efficacy at exposure time 935 and ingestion time 0 :  96.674
```



- Step 4: Run MACCS again with KI ingestion model and EFFACY set to 0.96674



KI Ingestion Linear No Threshold Form of MACCS

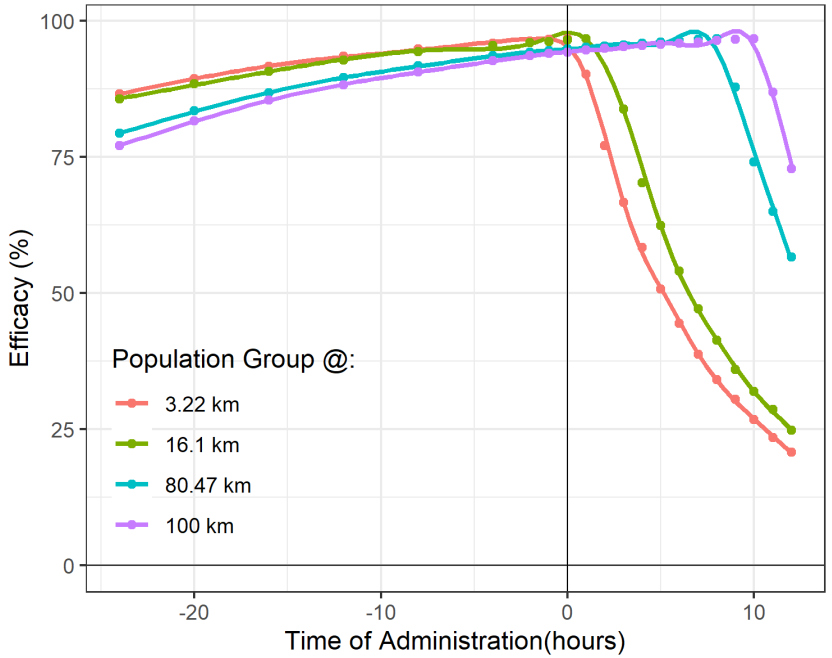
Sample Problem

- Definition of Sample Problem
  - Hypothetical NPP located in Changi, Singapore
  - Release with I-131 and population at different distance
    - 3.22 km, 16.1 km, 80.47km, and 100 km
  - Investigate efficacy for population at different distance based on time of administration
- Step 1: MACCS run without KI model
  - Release occurs at zero seconds

Distance (km)	TIMECEN (s)	TIMECEN (hr)
3.22	1.46E+03	0.41
16.10	6.73E+03	1.87
80.47	2.95E+04	8.19
100	3.64E+04	10.11

Sample Problem

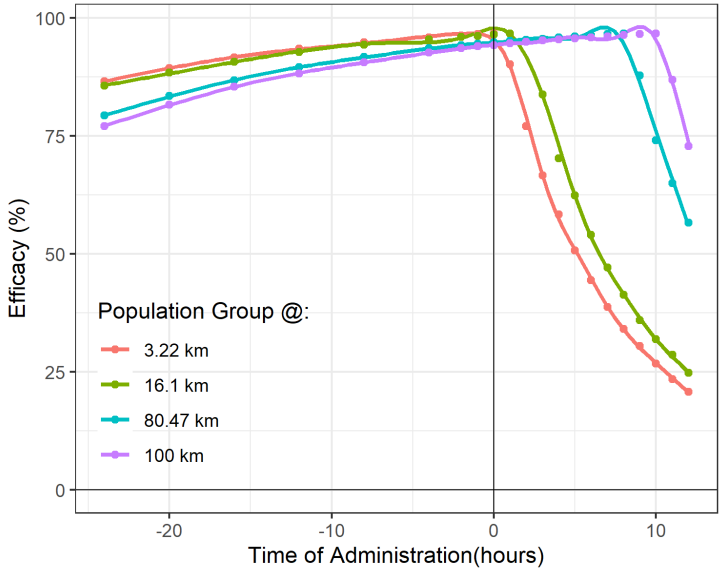
- Step 2 & 3: Calculate **administration time and relevant efficacy** with time of exposure and time of ingestion
  - Plot is obtained by varying time of ingestion
  - More time available after initiating event for optimal efficacy at further distance



Efficacy Curve based on Administration Time for Different Population Group

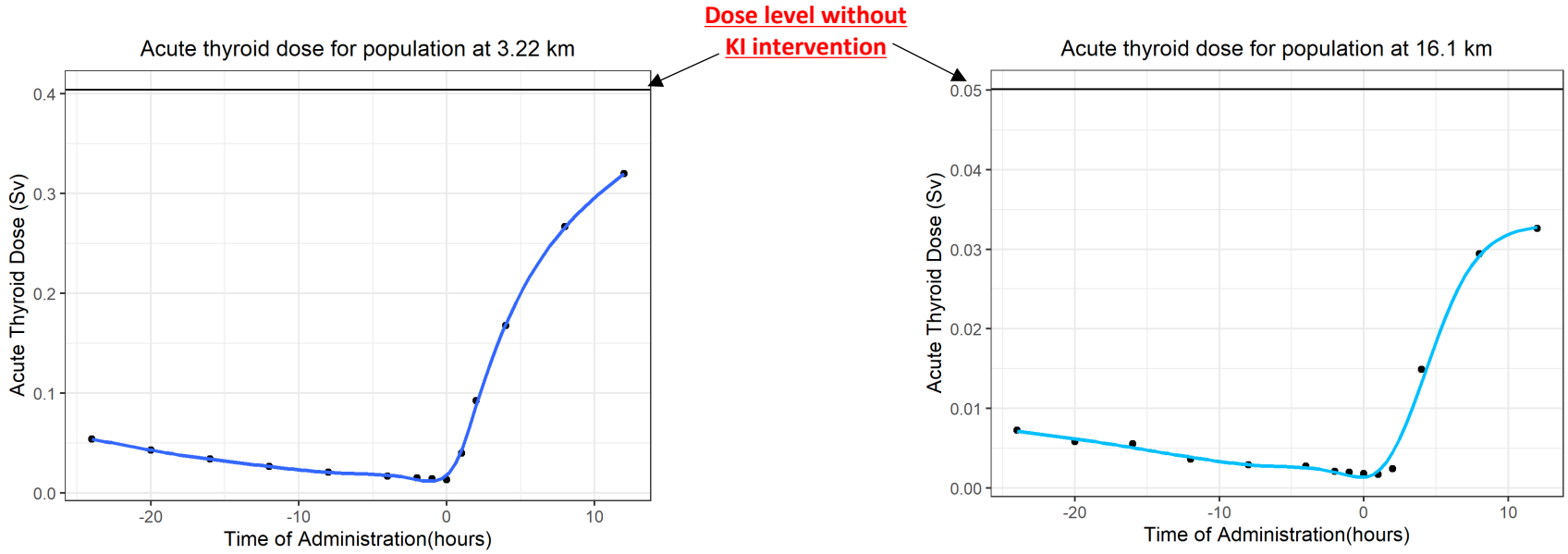
Sample Problem

- Agreed with **WHO recommendation**
  - Optimal period of administration of stable iodine
    - **Less than 24 hours prior to**, and
    - **Up to 2 hours after**, the expected onset of exposure
- To obtain efficacy above 90% it would be better to administer before onset of exposure



Sample Problem

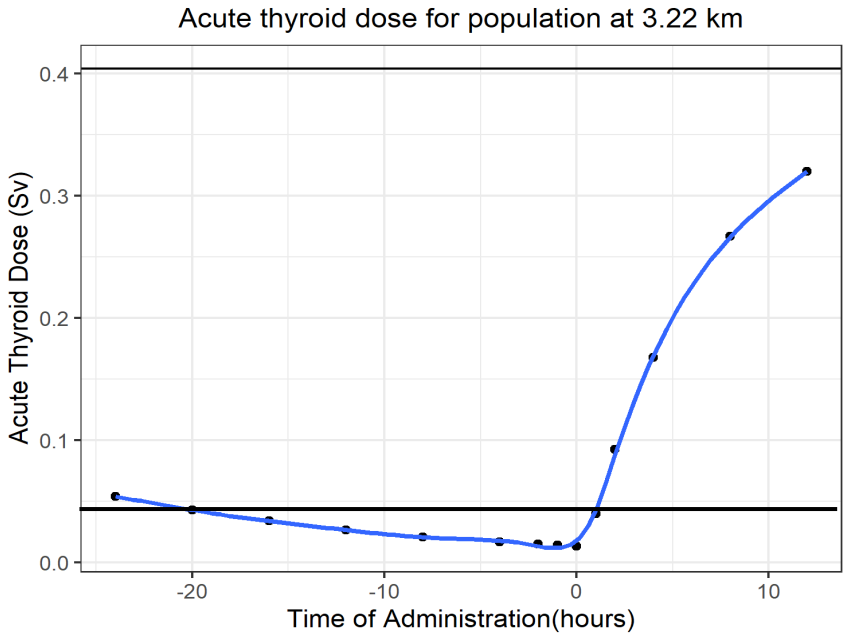
- Step 4. Run MACCS with KI model to estimate dose
  - Focus on two population located at 3.22km and 16.1km
  - KI has a **significant impact** on the thyroid dose regardless of the distance or time of administration



Acute Thyroid Dose for Population at 3.22km & 16.1km against Time of Administration

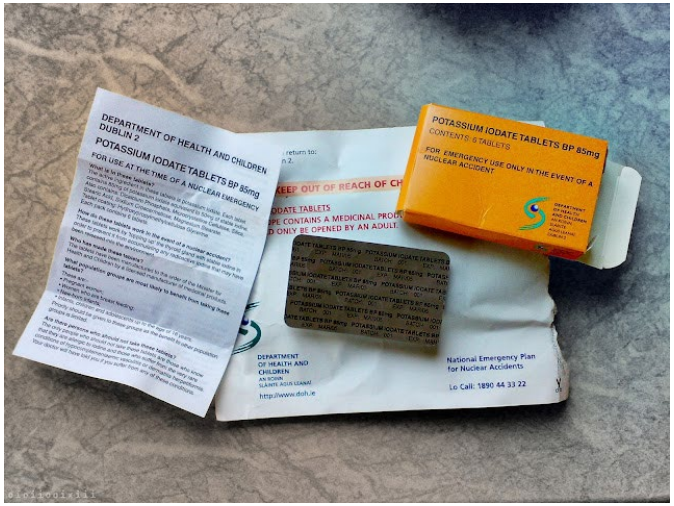
Sample Problem

- Early administration of ITB preferable?
  - Rapidly rising dose level when ITB is applied after the onset of exposure
  - Highlighted importance of early administration
  - Providing the KI tablet 20 hours prior is almost equivalent to giving the tablet 2 hours after exposure



Application: Distribution

- Assess distribution strategies
  - Debate over the effectiveness of pre-distribution and stockpile distribution strategies
    - **Pre-distribution**: Tablets provided to and self-administered when directed to by appropriate authorities before incident
    - **Stockpile distribution**: Tablets stored in a central stockpile and distribution occurs when directed by appropriate authorities after incident



Pre-distributed Iodine Pills (Photo Credits: RTE Archives)


USA Strategic National Stockpile (Photo Credits: ASPR HHS.gov)

Application: Distribution

- **Alternative methodology with distribution strategy**
  - $T_{Announce}$ (Announcement time): Time (s) when relevant authority announced ingestion of KI tablet relative to timepoint of initiating event
  - T_{Delay} (Ingestion delay time): Time delay (s) to the ingestion of KI tablet relative to the time of announcement for ingestion of KI
  - Incorporate the time delay due to distribution strategy

$$T_{Admin} = T_{Ingest} - T_{Expose}$$

$$T_{Admin} = T_{Announce} + T_{Delay} - T_{Expose}$$

Application: Distribution

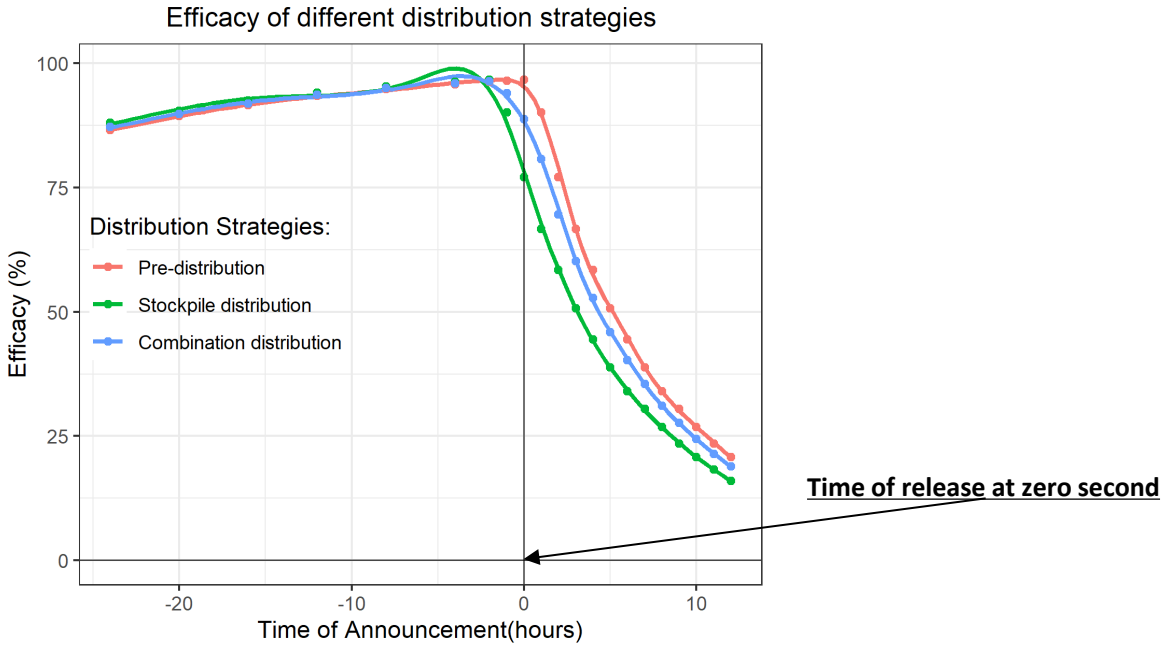
- Time delay for each scenario
  - In **pre-distribution strategy**, time of ingestion will be equal to time of announcement, $\boldsymbol{T_{delay} = 0}$
  - In **stockpile distribution strategy**, time of ingestion will be equal to time of announcement plus time delay due to collection of KI, $\boldsymbol{T_{delay} = 2\ hrs}$
  - Lastly, an **in between scenario** which is a combination of both methods based on 60% retention rate
    - Cohort 1 (60%) with pre-distribution*
    - Cohort 2 (40%) with stockpile distribution

Strategy	Pre-distribution	Combination distribution	Stockpile distribution
T_{delay} (hr)	0	0 (60%) & 2 (40%)	2

*J Astbury, S Horsley, N Gent, **Evaluation of a scheme for the pre-distribution of stable iodine (potassium iodate) to the civilian population residing within the immediate countermeasure zone of a nuclear submarine construction facility,** *Journal of Public Health.* 21 (4), 1999.

Application: Distribution

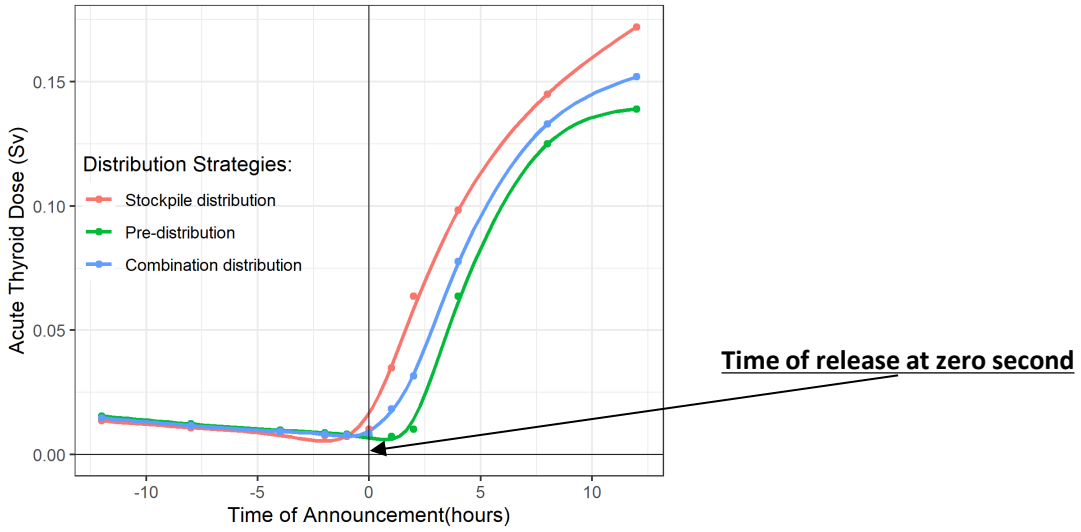
- Impact of distribution strategy
  - Focusing on the population group at 3.22 km
  - Efficacy will be sub-optimal at this distance due to the time delay
  - Pre-distribution should be utilized at close proximity to the NPP



Efficacy of Different Distribution Strategy against Time of Announcement

Application: Distribution

- Preferable strategy?
  - Pre-distribution would be the preferable strategy at 3.22 km
  - Insufficient time to distribute the KI tablet
  - Other strategy will be more viable when there is more lead time
  - Timely activation of KI could be more important than the selection of distribution strategies



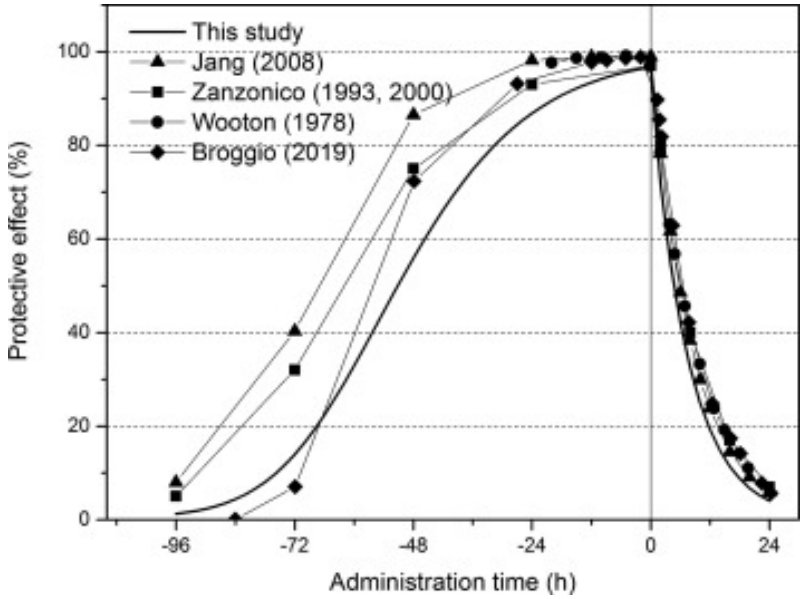
Acute Thyroid Dose of Different Distribution Strategy against Time of Announcement

Advantages & Disadvantages

- Advantages
  - Less reliant on expert judgement
  - Based on technical result from MACCS-ATMOS
  - Require only one new input (ingestion time) which is less abstract compared to efficacy
- Disadvantages
  - Require new user defined input ingestion time
  - Based on TIMCEN that may not be entirely representative of cohort exposure time
  - Not suitable for extended exposure with multiple administration of ITB

Future Work

- Future work:
  - Alternative efficacy curve based on other biokinetic model simulation
  - Incorporate other factors such as pre-existing stable iodine saturation or delay to obtain KI
  - Better incorporation and utilization of technical outputs of MACCS
  - Publication



Conclusion

- Provides an **alternative methodology** to determine the efficacy in Iodine Thyroid Blocking (ITB)
  - **Less reliant on expert judgement**
  - **Determine efficacy with technical rationale**
    - **Calculates efficacy** with **MACCS output (TIMCEN)**, **new input (ingestion time)**, and **efficacy curve from a reference**
    - **Updates MACCS input with calculated efficacy** of KI ingestion
- Showcase of preliminary example and application
  - Method consistent with international recommendation
  - Highlighted importance of early administration of KI
  - Timely activation of KI may be of greater importance than establishing an optimized distribution strategy

Thank you.

ACKNOWLEDGEMENTS

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