

## Sweet Tooth and Heavy Metal Problem A

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## 1 Introduction

## 2 Our Model

## 3 Experimental Results

## 4 Limitations & Future Work

# 1 Introduction

## 2 Our Model

## 3 Experimental Results

## 4 Limitations & Future Work

Some chocolate products may have high levels of heavy metals. Eating contaminated chocolate may lead to the bioaccumulation of the materials in the people who eat the chocolate treats. [5]

# The Questions

- What can be implied about long-term accumulation heavy metals in people who eat contaminated chocolate?
- What happens to children who might consume a large amount of candy at certain times of the year?
- What differences might occur to children who have their consumption periods spaced differently ?

Research indicates that chocolates contain measurable amounts of heavy metals, with lead, cadmium, and nickel being the most significant. These metals are of particular concern due to their potential health risks, while the presence of other metals is generally minimal and not considered significant in most studies. [5]

<b>Chocolate</b>	<b>Cadmium (<math>\mu\text{g/g}</math>)</b>	<b>Lead (<math>\mu\text{g/g}</math>)</b>	<b>Nickel (<math>\mu\text{g/g}</math>)</b>
Candies	0.029–0.429	0.029–0.585	0.049–7.9

**Table 1:** Pb, Cd and Ni concentration in chocolate [6]

These factors stem from the chocolate's production and packaging processes.

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Our intake function must satisfy the following constraints

- ① In the consumption time, the amount is non-zero.
- ② Outside of that region, it is zero since there is no intake.

A simple approach is to use a step function which is not continuous. We utilize the sum of two sigmoid functions

$$\text{intake}(t) = a \cdot \exp\left(\frac{-c(t-s)}{-c(t-s)+1}\right) + a \cdot \exp\left(\frac{c(t-e)}{c(t-e)+1}\right) - a$$

where

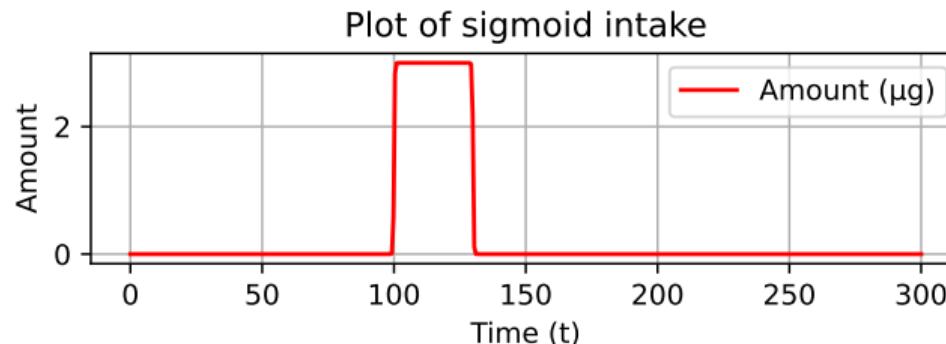
- $a > 0$  is the amount of the intake.
- $c > 0$  is the slope of the sigmoid function.
- $s, e$  respectively be the start and end time of the intake.

## Intake Function. Example

The parameters for the intake function below is shown as

$a$	$c$	$s$	$e$
3	7	100	130

And here is an example figure



The total intake, can be calculated using the integral  $\int_{-\infty}^{\infty} \text{intake}(t) dt$ .

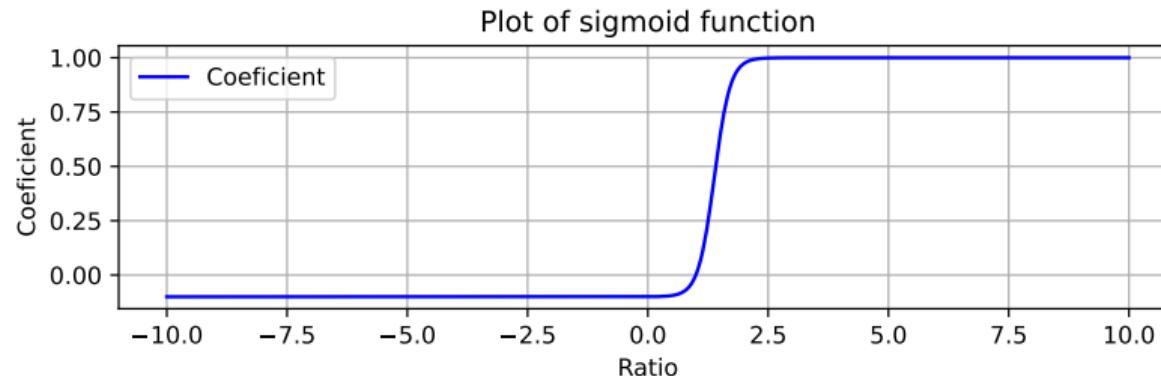
Our research indicates that chemicals in an organ need to stabilize at a specific level, or at most remain within the maximum capacity, termed the equilibrium state [2]. This has inspired us to develop a scaling function to regulate the transfer rate once this equilibrium is reached.

This function meets two conditions: first, in the absence of intake, chemical levels stabilize and do not fall below a certain level; second, if there is intake, the levels rise and eventually stabilize again once intake stops.

We summarize the function's properties

- As the accumulation of nickel in the organ reaches the maximum, or minimum (equilibrium) capacity, it approaches zero.
- As long as the accumulation of nickel in the organ does not lie in the range mentioned above, it stays as a constant rate.

This motivates us to utilize the sigmoid function, which is a continuous version of the step function.



The detailed function is

$$s(x) = a \cdot \exp\left(\frac{c(x-b)}{c(x-b)+1}\right) + k$$

We shall explain the meaning of each parameters

- $c = -6$  is the slope of the function, in which it is parallel to the line  $y = cx$ .
- $a = 1.1$  and  $k = -0.1$  controls the asymptote of the function, which is how we want to scale the parameter.
- $b = -1.38$  is the displacement along the  $x$  axis, which is defined on interest, and is also the inflection point.

The mechanism is straightforward. For  $x \geq b + \alpha$ , where  $\alpha \geq 0$ , we can assume that the transfer rate is scaled approximately to 1, other values of  $x$  will have the transfer rate scaled to 0. This motivates us to use the variable  $x$  as the ratio  $I/I_{\text{base}}$ , where  $I$  is amount of chemical at organ  $I$  and  $I_{\text{base}}$  is the baseline amount of chemical at organ  $I$ .

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**Equilibrium Concentration.** Cadmium always accumulates in the human body at a certain level even when not eating chocolate.

**The influence of nutrients.** The level of nutrient absorption will affect the amount of Cadmium absorbed by that person, specifically as follows:

- ① **Total Ratio Constraint:** The combined influence of Fe, Ca, and Zn is such that when their levels are high, they reduce cadmium absorption significantly. When their levels are low, the absorption of cadmium is higher.
- ② **Baseline Cadmium Intake  $I_0$ :** Without nutrient effects, we assume a baseline cadmium intake per day based on contaminated chocolate consumption.

**Cadmium Absorption Mechanism.** After consuming chocolate, the absorbed amount of cadmium enters the bloodstream. We assume it will accumulate in the blood for 1 day before gradually transferring to other organs — specifically the kidneys, liver, lungs, and bones, as these have the highest concentrations of cadmium accumulation according to statistics. It will then gradually be excreted from the body .

**Transfer Mechanism:** Once cadmium accumulates in the bloodstream, 60% of the accumulated amount transfers to the kidneys, 30% to the liver, 5% to the lungs, and 5% to the bones.

**Transfer Times:** It is assumed that cadmium will completely transfer from the blood to the kidneys, liver, and lungs within 7 days (rapid metabolism), whereas for bones, this transfer period is 30 days (slow metabolism).

**Excretion Rate:** Each organ's half-life is converted to an excretion rate based on the following average half-lives:

- **Kidneys:** Half-life of 10–30 years (average of 20 years = 7,300 days)
- **Liver:** Half-life of 4–15 years (average of 10 years = 3,650 days)
- **Bones:** Half-life of 10–30 years (average of 20 years = 7,300 days)
- **Lungs:** Half-life of 5–10 years (average of 7.5 years = 2,737.5 days)

This system is a closed system, allowing for negligible transfer between organs; however, the total accumulation within the body remains constant. The excreted amounts from each organ will be completely eliminated through urine.

**Equilibrium Concentration.** Baseline blood Cd stabilizes at  $1\mu\text{g}$ , baseline kidneys Cd stabilizes  $15\mu\text{g}$ , baseline liver Cd stabilizes  $1\mu\text{g}$ , baseline bones Cd stabilizes  $0.5\mu\text{g}$ , and baseline lungs Cd stabilizes at  $0.5\mu\text{g}$ .

**Recommended Daily Allowance** (mg/day) for children are:

$$\text{Fe}_{\text{RDA}} = 8.5 \quad (\text{Iron})$$

$$\text{Ca}_{\text{RDA}} = 900 \quad (\text{Calcium})$$

$$\text{Zn}_{\text{RDA}} = 6.5 \quad (\text{Zinc})$$

**The Cadmium absorption rate** into blood for children is 8%:

$$k_{\text{o,b}} = 0.08$$

**Equilibrium Concentration.** Baseline blood Cd stabilizes at  $1\mu\text{g}$ , baseline kidneys Cd stabilizes  $20\mu\text{g}$ , baseline liver Cd stabilizes  $1.5\mu\text{g}$ , baseline bones Cd stabilizes  $1\mu\text{g}$ , and baseline lungs Cd stabilizes at  $0.7\mu\text{g}$ .

**Nutrient average intakes** (mg/day) for adults are:

$$\text{Fe}_{\text{RDA}} = 10.0 \quad (\text{Iron})$$

$$\text{Ca}_{\text{RDA}} = 1000 \quad (\text{Calcium})$$

$$\text{Zn}_{\text{RDA}} = 9.0 \quad (\text{Zinc})$$

**The Cadmium absorption rate** into blood for adults is 5%:

$$k_{\text{o,b}} = 0.05$$

To incorporate these half-lives, we can use the following formula to calculate the **excretion rate** ( $e$ ) for each organ:

$$e = \frac{\ln(2)}{\text{half-life in days}}$$

① **Kidneys**  $e_k$ :

$$e_k = \frac{\ln(2)}{7300} \approx 0.000095$$

② **Liver**  $e_l$ :

$$e_l = \frac{\ln(2)}{3650} \approx 0.00019$$

③ **Bones**  $e_{bo}$ :

$$e_{bo} = \frac{\ln(2)}{7300} \approx 0.000095$$

④ **Lungs**  $e_{lu}$ :

$$e_{lu} = \frac{\ln(2)}{2737.5} \approx 0.000253$$

For each nutrient  $N(t)$  (where  $N$  could be Fe, Ca, or Zn):

$$N(t) = N_{\text{avg}} \times \left(1 + 0.1 \sin\left(\frac{2\pi t}{7}\right)\right)$$

where:

- $N_{\text{RDA}}$ : Recommended daily intake of the nutrient.
- $0.1 \sin\left(\frac{2\pi t}{7}\right)$ : Simulates a weekly fluctuation of  $\pm 10\%$ .

We can define the effective cadmium intake  $I(t)$  as follows:

$$I(t) = I_0(t) \cdot \left( \frac{Ca_{RDA}}{Ca} \right)^2 \cdot \left( \frac{Fe_{RDA}}{Fe} \right)^2 \cdot \left( \frac{Zn_{RDA}}{Zn} \right)^2$$

where:

- $I_0(t)$ : Baseline cadmium intake pattern from chocolate consumption (We assume an intake of  $4.358 \mu\text{g}/\text{day}$  for children, while for adults, it is  $2.725 \mu\text{g}/\text{day}$ ).

We utilize  $I(t)$ , for example,  $Ca < Ca_{RDA}$ , then  $f_{GI-Ca}(Ca) = \left( \frac{Ca_{RDA}}{Ca} \right)^2 > 1$ , otherwise it is less than 1.

The maximum transfer rate  $R$  for each organ can be approximated based on the time needed to transfer the cadmium from the blood:

$$R = \frac{-\ln(0.01)}{\text{time in days}}$$

- For **kidneys, liver, and lungs**:

$$R_{7 \text{ days}} = \frac{-\ln(0.01)}{7} \approx 0.66$$

- For **bones**:

$$R_{30 \text{ days}} = \frac{-\ln(0.01)}{30} \approx 0.154$$

The parameter  $\alpha$  will control how fast the transfer rate approaches its maximum:

- $\alpha_{\text{fast}} = 1$  for the kidneys, liver, and lungs (a relatively quick approach to maximum within the 7-day timeframe).
- $\alpha_{\text{slow}} = 0.1$  for bones (a slower approach, consistent with the 30-day transfer period).

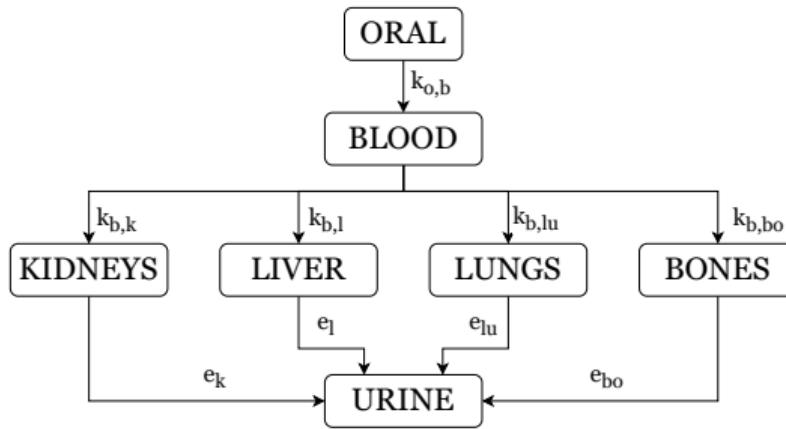
Each transfer rate function will use the total transfer rate  $R$  for each group of organs and scale it according to the specified proportions (60% to kidneys, 30% to liver, 5% to bones, and 5% to lungs). The transfer rates will be time-dependent and increase gradually after the first day.

$$k_{b,k}(t) = \begin{cases} 0.6 \cdot R_{7 \text{ days}} \cdot (1 - e^{-\alpha_{\text{fast}} \cdot (t-1)}), & \text{if } t > 1 \\ 0, & \text{otherwise} \end{cases}$$

$$k_{b,l}(t) = \begin{cases} 0.3 \cdot R_{7 \text{ days}} \cdot (1 - e^{-\alpha_{\text{fast}} \cdot (t-1)}), & \text{if } t > 1 \\ 0, & \text{otherwise} \end{cases}$$

$$k_{b,lu}(t) = \begin{cases} 0.05 \cdot R_{7 \text{ days}} \cdot (1 - e^{-\alpha_{\text{fast}} \cdot (t-1)}), & \text{if } t > 1 \\ 0, & \text{otherwise} \end{cases}$$

$$k_{b,bo}(t) = \begin{cases} 0.05 \cdot R_{30 \text{ days}} \cdot (1 - e^{-\alpha_{\text{slow}} \cdot (t-1)}), & \text{if } t > 1 \\ 0, & \text{otherwise} \end{cases}$$



The figure illustrates the transfer rates of Cadmium (Cd) between compartments, with some rates. After oral intake, the substance enters the blood and then distributes to the kidneys, liver, lungs, and bones. Each organ stores and processes the substance, then excretes it into urine at different rates, ultimately leading to its removal from the body. Each rate constant ( $k$  or  $e$ ) represents the rate of transfer between compartments, highlighting both the distribution and excretion dynamics in the body.

## Blood Compartment:

If  $t \leq 1$ :

$$\frac{dB}{dt} = \text{intake}$$

If  $t > 1$ :

$$\frac{dB}{dt} = \text{intake} - (k_{b,k} + k_{b,l} + k_{b,bo} + k_{b,lu}) \cdot B$$

Transfer rate  $k_{b,k}, k_{b,l}, k_{b,bo}, k_{b,lu}$  is scaled using the scaling function  $s(x)$  above with  $x = B/\text{baseline}_{\text{blood}}$ .

## Total Cadmium Accumulation:

$$\text{Total Cadmium} = B + K + L + Bo + Lu$$

**Kidneys:**

$$\frac{dK}{dt} = k_{b,k} \cdot B - e_k \cdot L$$

**Liver:**

$$\frac{dL}{dt} = k_{b,l} \cdot B - e_l \cdot K$$

**Bones:**

$$\frac{dBo}{dt} = k_{b,bo} \cdot B - e_{bo} \cdot Bo$$

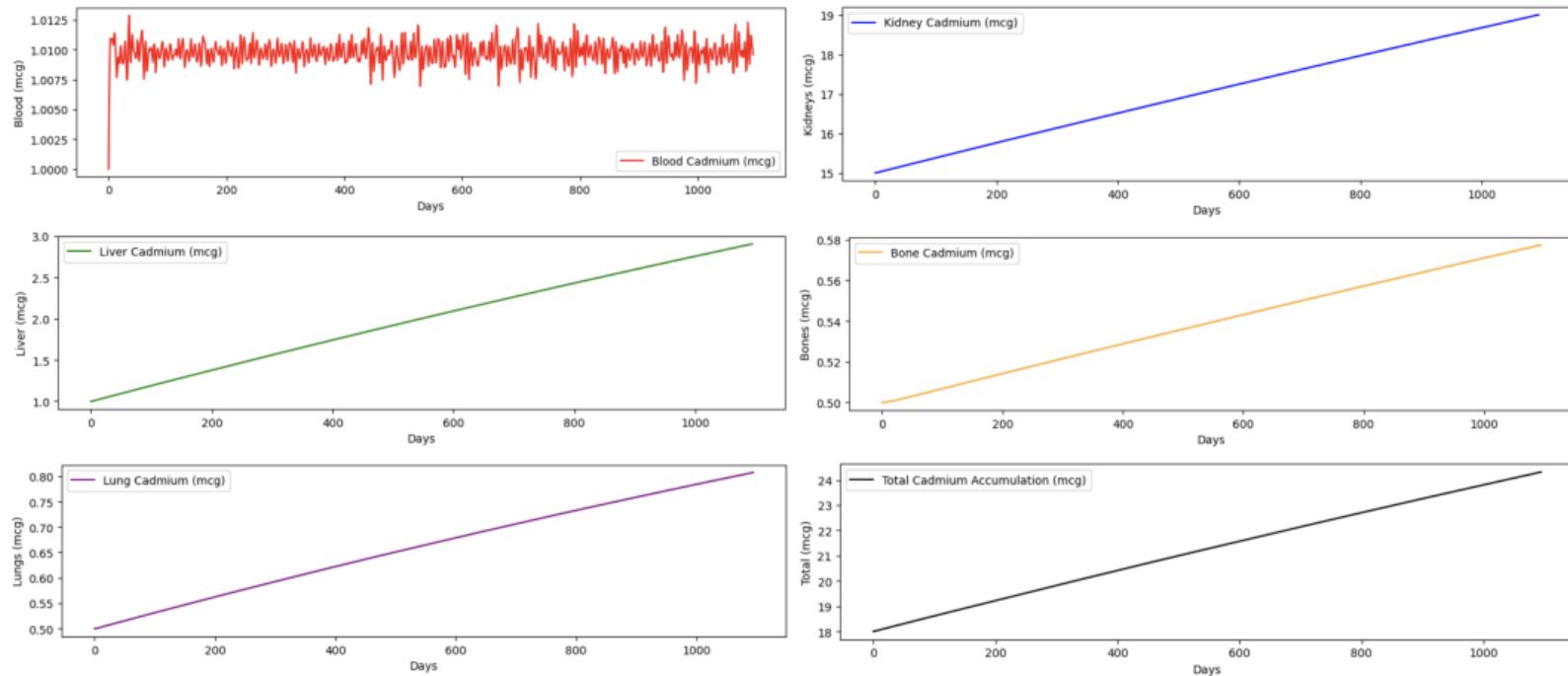
**Lungs:**

$$\frac{dLu}{dt} = k_{b,lu} \cdot B - e_{lu} \cdot Lu$$

Where each transfer rate  $k_{b,k}$ ,  $k_{b,l}$ ,  $k_{b,bo}$ ,  $k_{b,lu}$  is scaled using the scaling function  $s(x)$  above with  $x = B/\text{baseline}_{\text{blood}}$ .

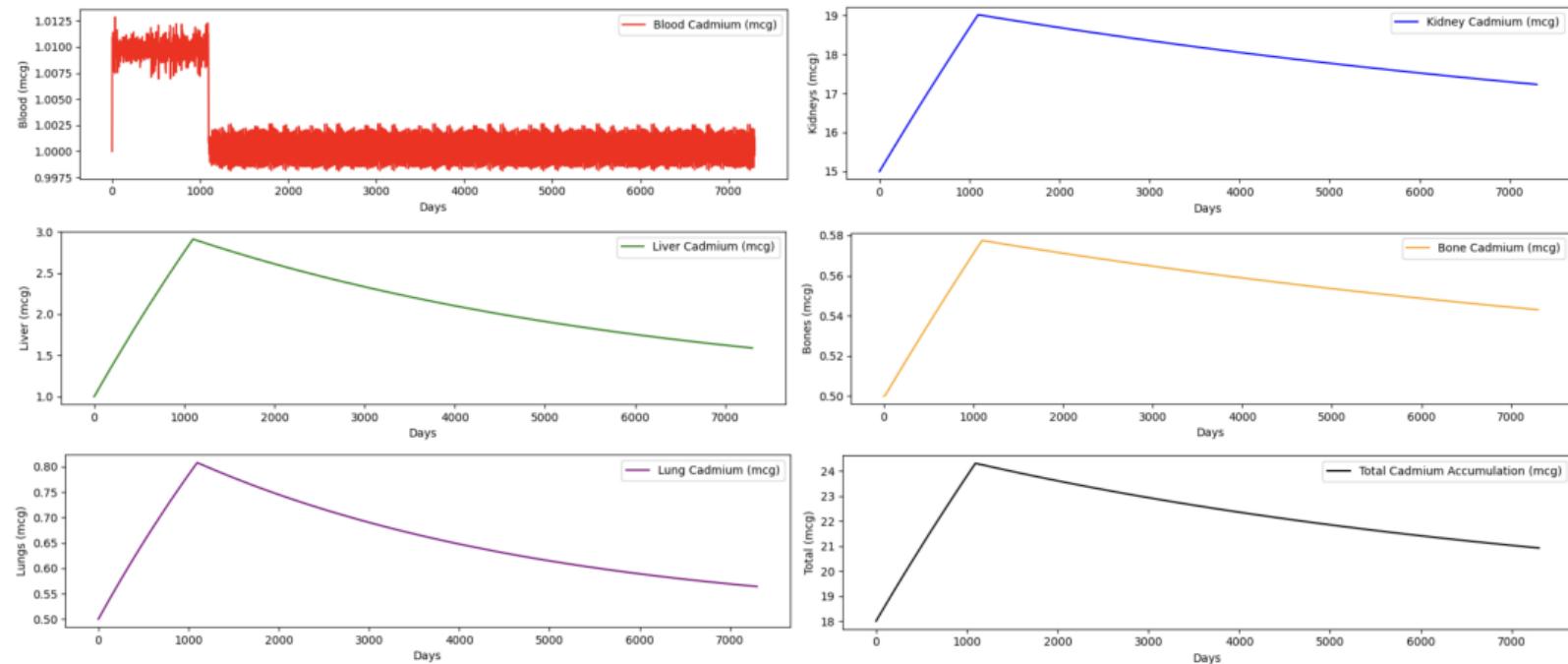
# Cadmium Model. Continuous And Multiple Times Intake For Children

Children eat contaminated chocolate with an average of about  $4.358 \mu\text{g}$  of Cadmium daily for 3 years.



# Cadmium Model. Continuous And Multiple Times Intake For Children

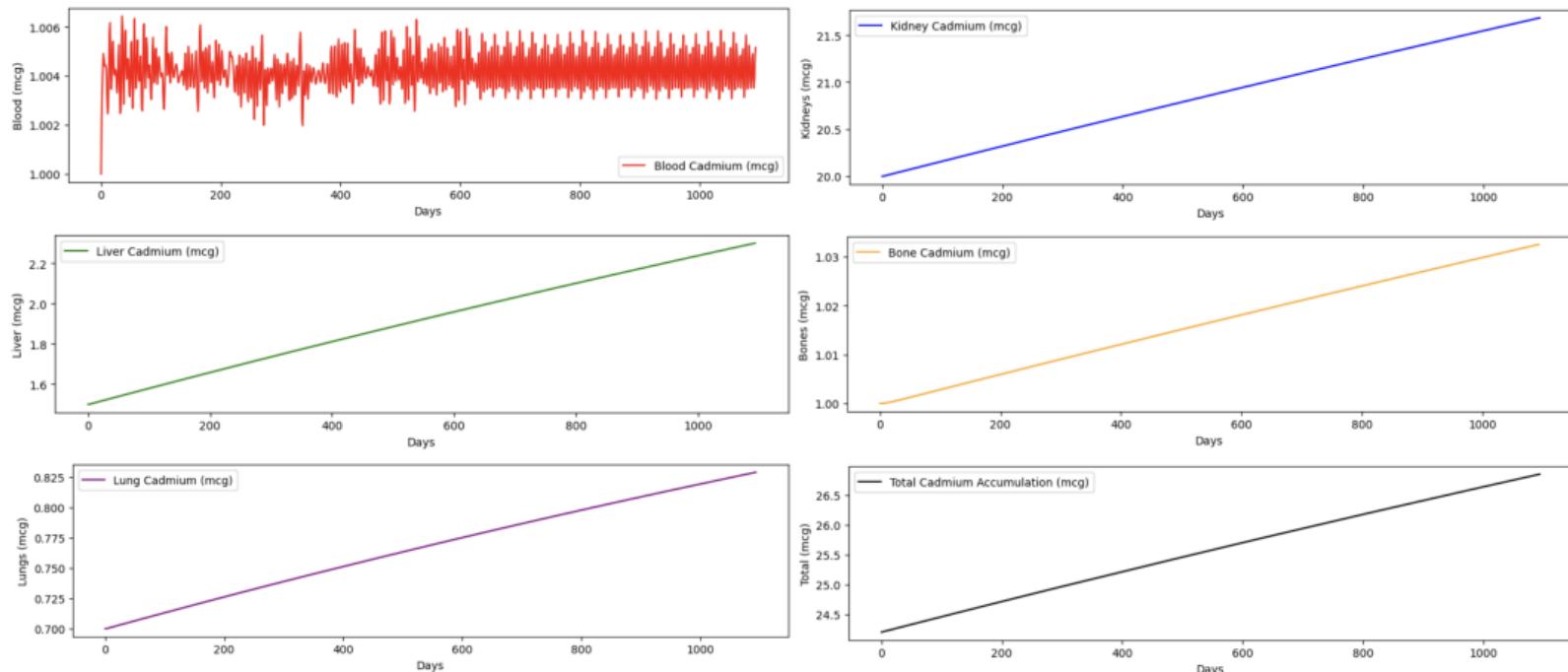
Children eat contaminated chocolate with an average of about  $4.358 \mu\text{g}$  of Cadmium daily for the first 3 years and then do not eat chocolate again in a 20-year period.



- **Organ-Specific Accumulation Rates:** The kidneys and liver show the most significant accumulation, while the bones and lungs accumulate cadmium at a slower rate.
- **Effect of Continuous Intake:** Regular chocolate consumption resulted in a consistent upward trend across all organs and the total accumulation with a negligible amount of cadmium excretion during this period because the excretion time of Cd in the organs is very long.
- **Long-Term Excretion Observation:** The second plot over a 20-year period shows that it takes a very long time for the cadmium accumulation in each organ, as well as the total amount in the body, to decrease by approximately half.

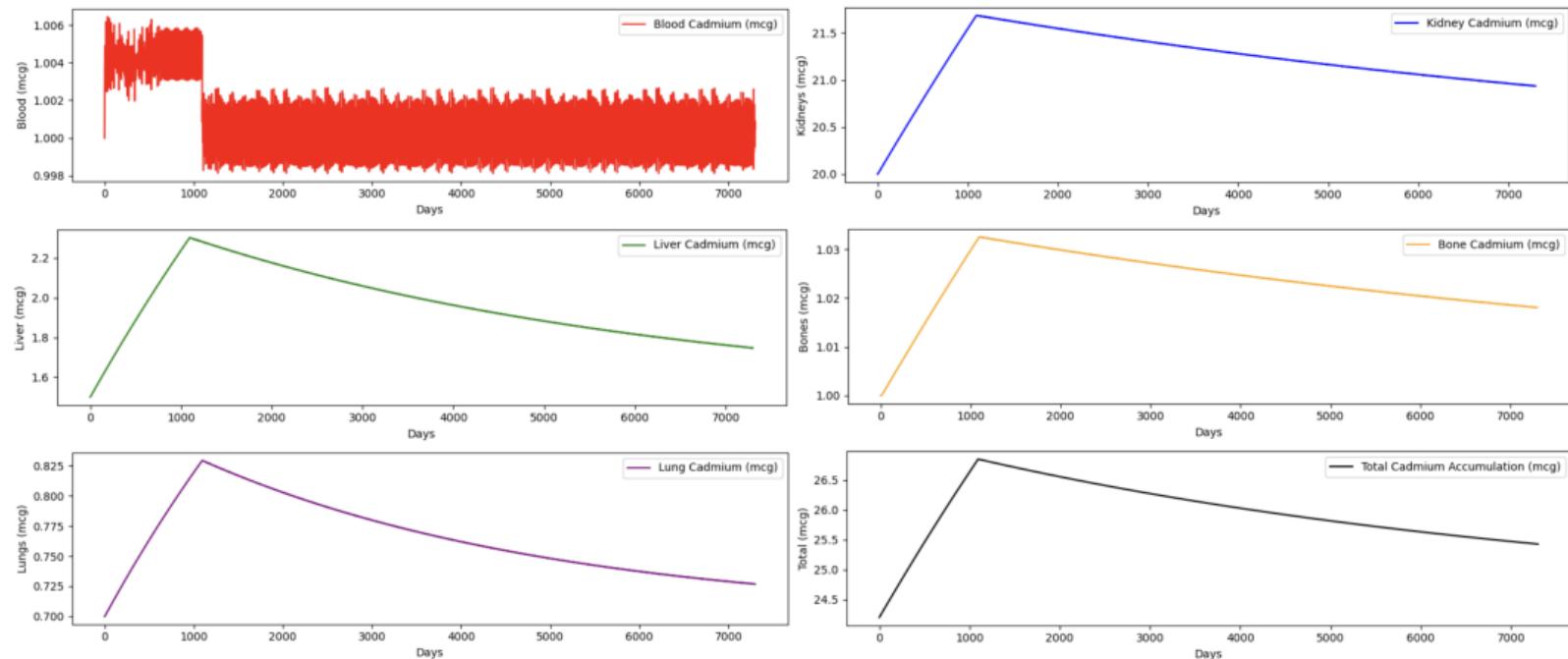
# Cadmium Model. Continuous And Multiple Times Intake For Adults

Adults eat contaminated chocolate with an average of about  $2.725 \mu\text{g}$  of Cadmium daily for 3 years.



# Cadmium Model. Continuous And Multiple Times Intake For Adults

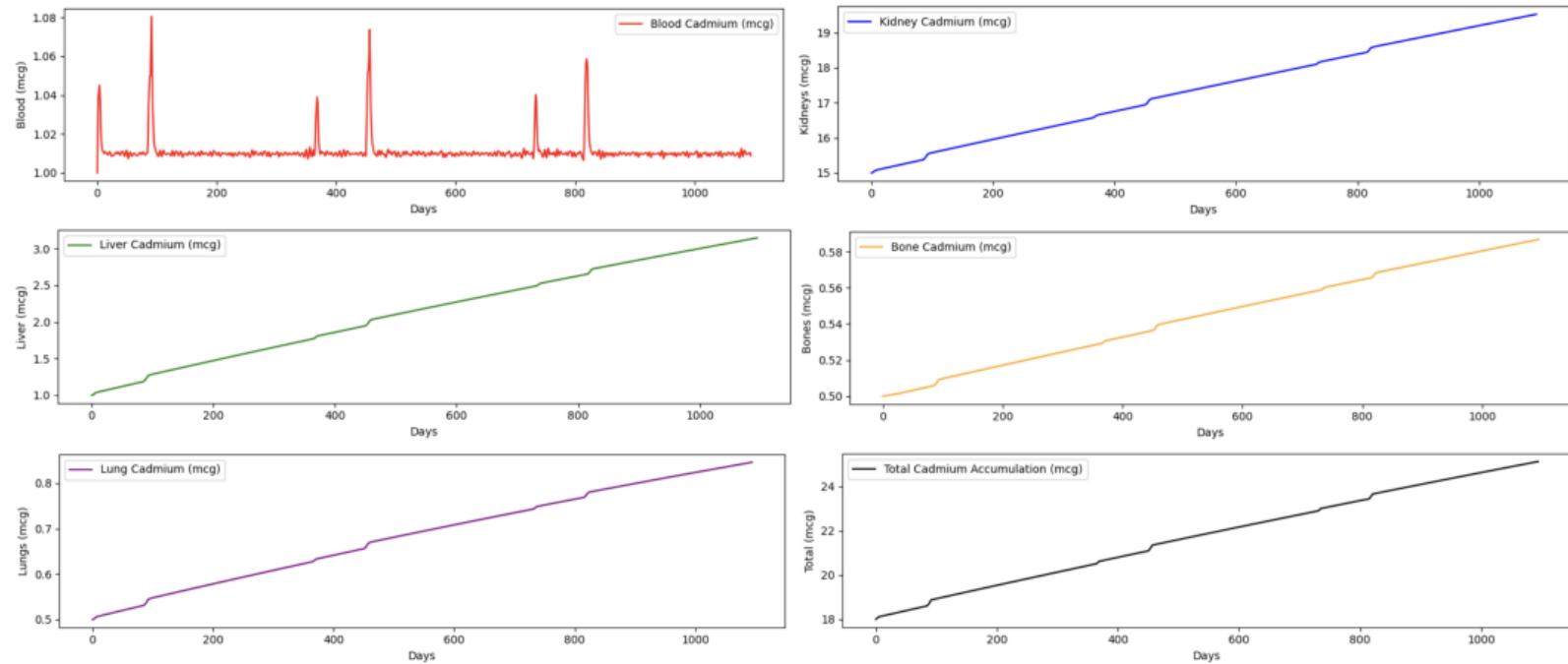
Adults eat contaminated chocolate with an average of about  $2.725 \mu\text{g}$  of Cadmium daily for the first 3 years and then do not eat chocolate again in a 20-year period.



- **Adult Cadmium Accumulation Pattern:** In the case of adults, we assume they consume less chocolate than children. However, similar to the case with children, cadmium primarily accumulates in the kidneys and liver.
- **Impact of Continuous Daily Intake:** Daily chocolate consumption leads to a continuous increase in cadmium accumulation in the body over time, as the elimination rate is very slow compared to the intake rate.
- **Comparison of Long-Term Accumulation in Adults and Children:** With continuous consumption over a 3-year period followed by cessation, although children have a higher base intake, the total cadmium accumulation in their bodies is lower than in adults. This is because, over many years, adults have accumulated a significantly higher baseline level of cadmium in their organs compared to children.

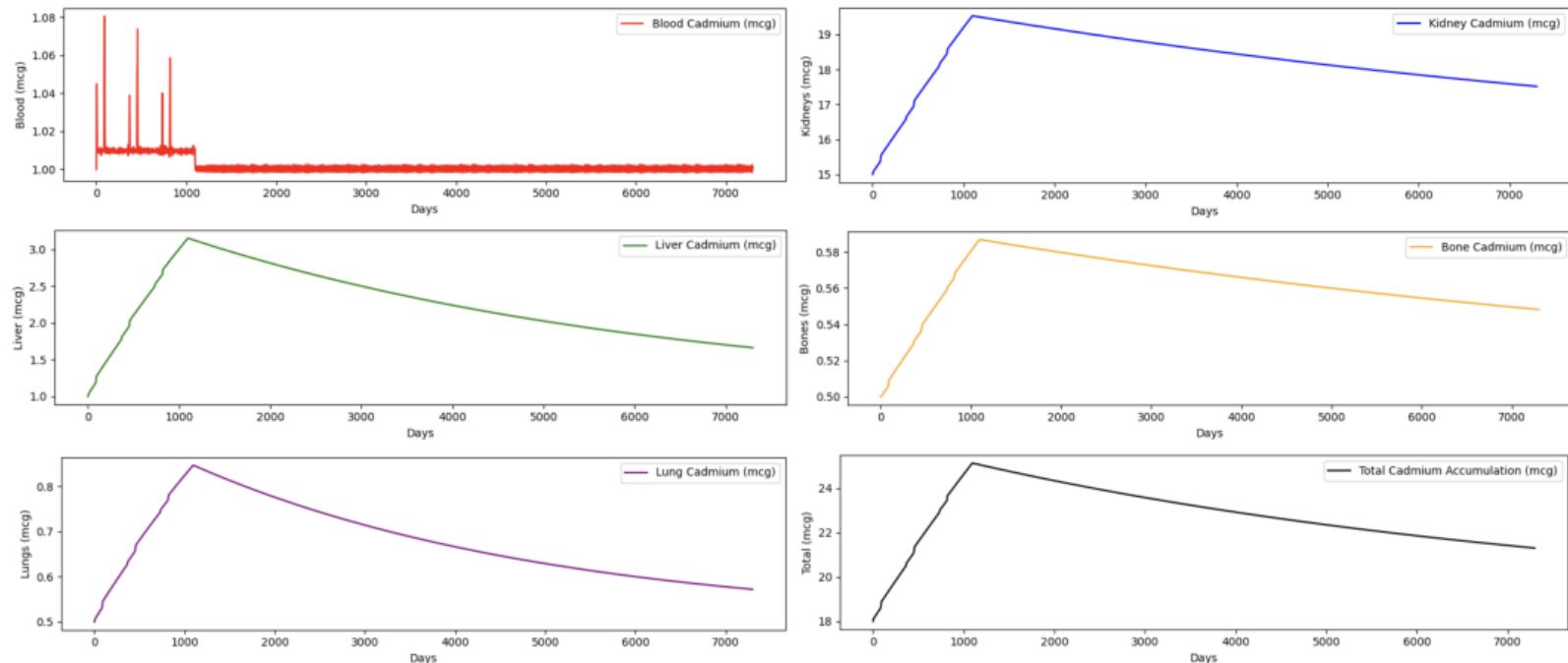
# Cadmium Model. Children Whose Birthday is Close to the Holiday Period

Children consume contaminated chocolate daily, averaging  $4.358 \mu\text{g}$  of cadmium for 3 years. Intake increases to 5 times the daily average on birthdays and 3 times during a five-day holiday period 3 months before each birthday.



# Cadmium Model. Children Whose Birthday is Close to the Holiday Period

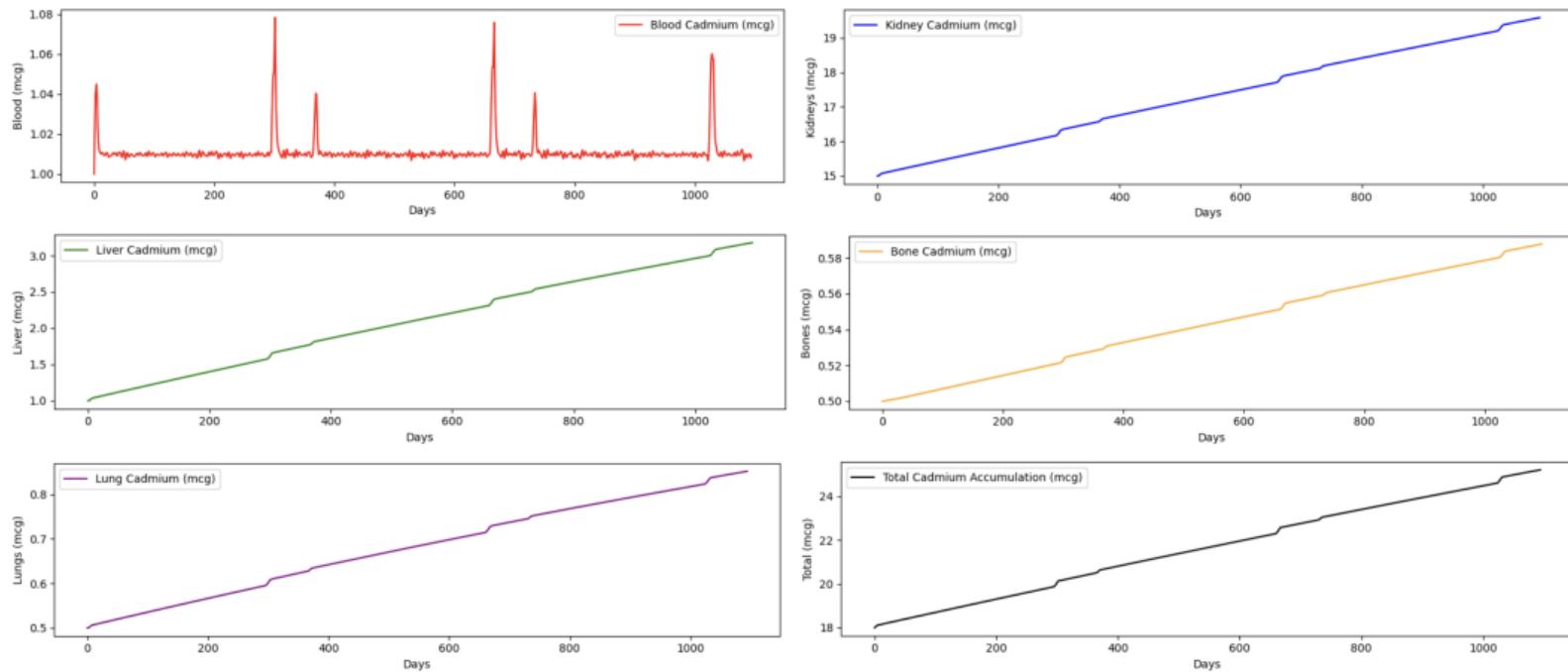
Children consume contaminated chocolate daily, averaging  $4.358 \mu\text{g}$  of cadmium for 3 years, with intake spiking fivefold on birthdays and threefold during a 5-day holiday period 3 months prior. Consumption then ceases. The plot covers 20 years.



- **Cadmium Spikes Due to Intake Events:** In the case of children who consume chocolate continuously and eat more during birthdays and holiday periods, especially when these events are close together, cadmium intake into the bloodstream spikes during these occasions and subsequently distributes to various organs.
- **Slow Excretion and Continuous Accumulation:** However, because the excretion rate of cadmium from these organs is very slow, only a negligible amount is eliminated before new intake occurs. Consequently, the overall cadmium accumulation in the body continues to increase steadily.
- **Long-Term Cadmium Decline After Intake Stops:** Assuming we consume chocolate in this manner for three years and then stop, the 20-year plot shows that it takes a very long time for the accumulated cadmium levels to decrease by nearly half.

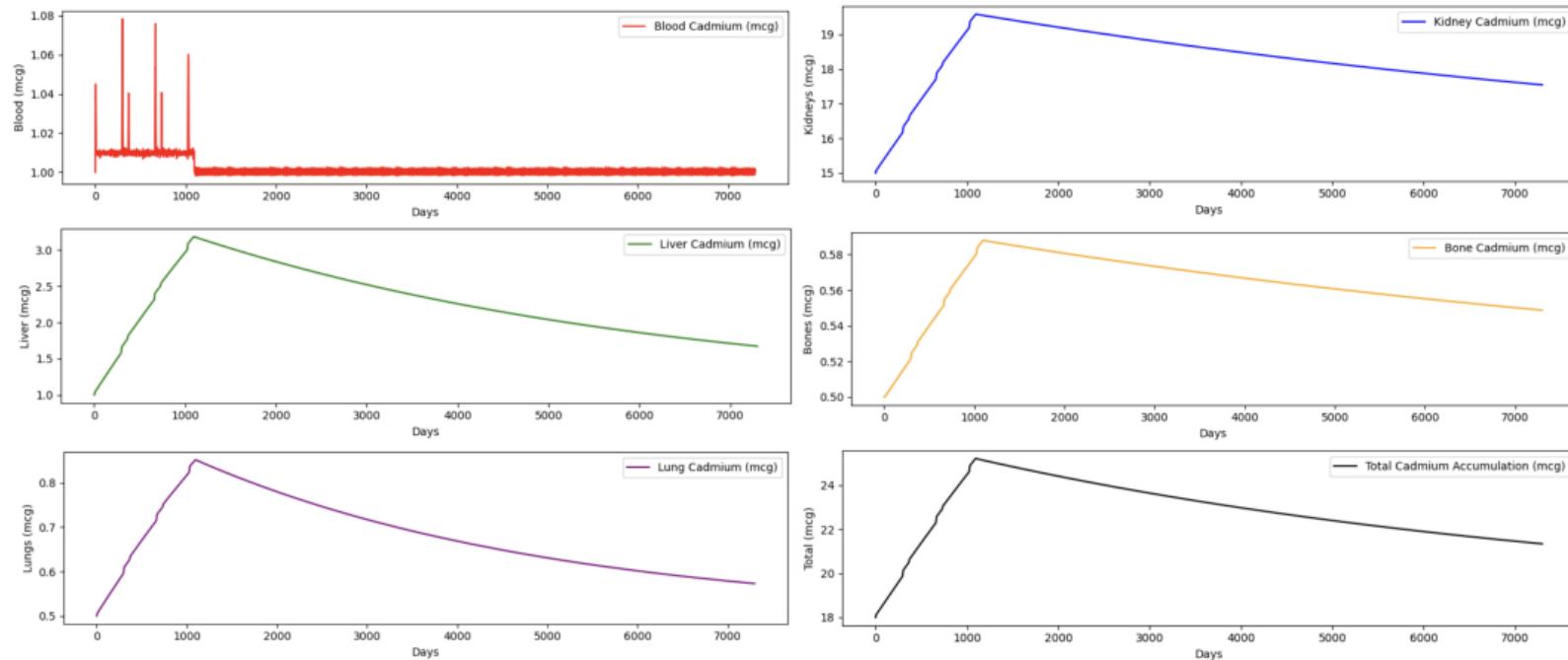
# Cadmium Model. Children Whose Birthday is far Away From the Holiday Period

Children consume contaminated chocolate daily, averaging  $4.358 \mu\text{g}$  of cadmium for 3 years. Intake increases to 5 times the daily average on birthdays and 3 times during a five-day holiday period 10 months before each birthday.



# Cadmium Model. Children Whose Birthday is far Away From the Holiday Period

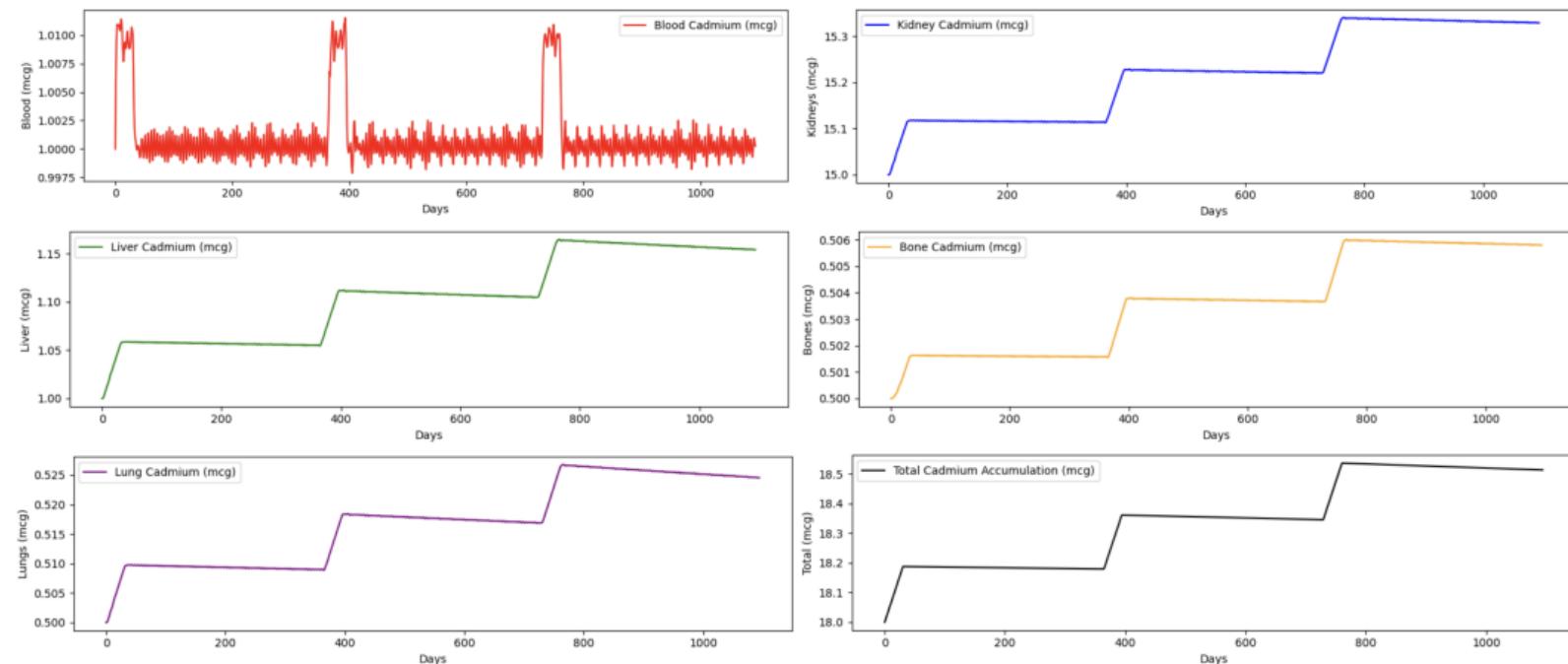
Children consume contaminated chocolate daily, averaging  $4.358 \mu\text{g}$  of cadmium for 3 years, with intake spiking fivefold on birthdays and threefold during a 5-day holiday period 10 months prior. Consumption then ceases. The plot covers 20 years.



- **Cadmium Spikes with Distant Intake Events:** Similarly, in the case where birthdays and holiday periods are further apart, cadmium intake in the bloodstream still spikes during these two occasions. Although the events are spaced farther apart, this interval is still too short relative to the slow excretion rate, resulting in only a negligible amount being eliminated before new cadmium intake occurs. As a result, the overall cadmium levels in the body continue to increase steadily.
- **Similarity in Accumulation Patterns:** In both cases, whether birthdays are close to or far from the holiday period, the shapes of the graphs in each scenario are relatively similar. The only difference is the timing of the intake spikes, while the overall pattern remains alike. This is because the excretion rate is so low that it's challenging to observe any significant difference between the two intake instances.

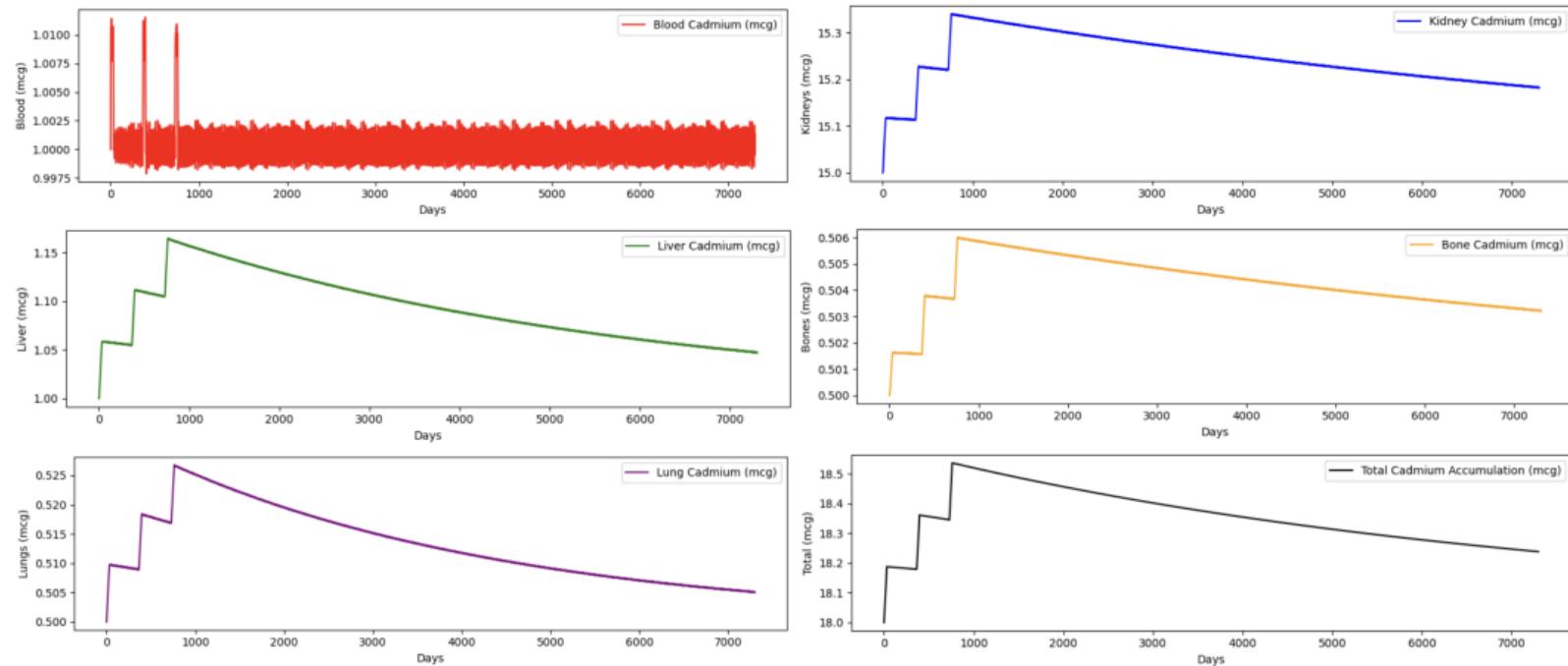
# Cadmium Model. Children Consume Chocolate Over a Long Period After a Holiday

Children only consume contaminated chocolate daily for a period of 30 days after the holiday period with an average daily intake of  $4.358 \mu\text{g}$  in 3 years.



# Cadmium Model. Children Consume Chocolate Over a Long Period After a Holiday

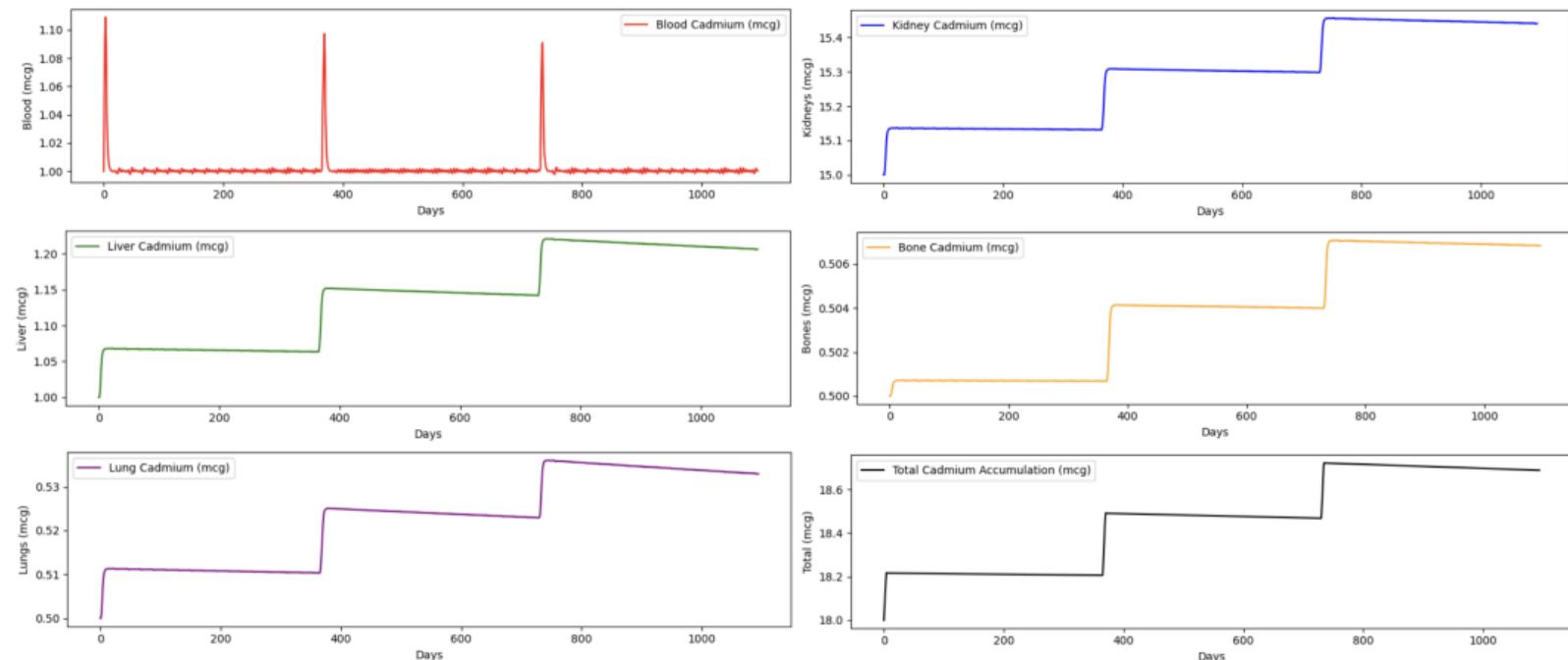
Children only consume contaminated chocolate daily for 30 days following the holiday period, averaging  $4.358 \mu\text{g}$  per day over 3 years, after which consumption ceases. The plot covers 20 years.



- **Cadmium Spikes During Extended Post-Holiday Consumption:** In the case where children consume chocolate only for an extended period after holidays, cadmium intake in the bloodstream spikes during this time and fluctuates around the baseline level at other times.
- **Cadmium Accumulation with Periodic Consumption:** Since they consume chocolate only during a limited period each year, we can observe a slight reduction in cadmium accumulation before new intake occurs.
- **Long-Term Excretion After Intake Cessation:** If children stop consuming chocolate after three years, the graph over a 20-year period will show a noticeable excretion of cadmium from the body.

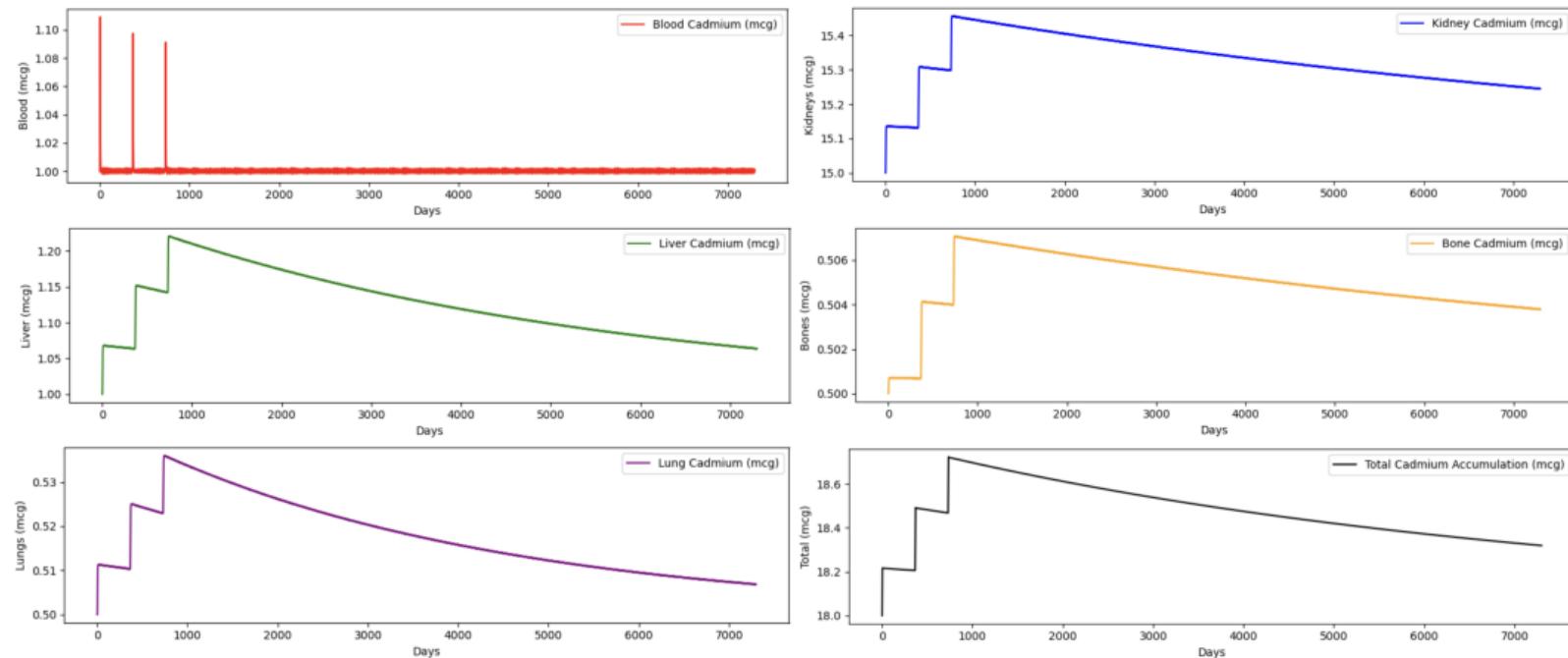
# Cadmium Model. Children Binge on Chocolate During the Holiday

Children only binge on contaminated chocolate daily during a 4-day holiday period, averaging 10 times 4.358  $\mu\text{g}$  per day over three years.



# Cadmium Model. Children Binge on Chocolate During the Holiday

Children only binge on contaminated chocolate daily during a 4-day holiday period, averaging 10 times  $4.358 \mu\text{g}$  per day over three years, after which consumption stops. The plot spans 20 years.



- **Cadmium Spikes During Holiday Consumption Only:** In the case where children consume a large amount of chocolate only during holidays and abstain afterward, cadmium intake in the bloodstream spikes significantly during this period and then gradually distributes to the organs.
- **Periodic Accumulation and Reduction:** Since intake occurs over a short period each year, we can also observe a slight reduction in cadmium accumulation before new intake occurs.
- **Similar Accumulation Patterns Despite Different Intake Durations:** Overall, as the excretion rate is still too slow relative to the annual interval between intakes, the graphs for both cases—whether consuming heavily during holidays or over an extended period afterward—are similar. The only difference is that the intake duration is longer in the case of extended consumption following the holidays.

- **Impact of Low Excretion Rate on Long-Term Cadmium Accumulation:** A key feature of the cadmium accumulation model is the extremely low excretion rate, meaning it takes a very long time for the accumulated cadmium levels in the human body to decrease by half. Therefore, if chocolate consumption is continuous or the intervals between intakes are too short relative to the excretion rate, cadmium accumulation in the body will nearly continuously increase.
- **Fluctuations Due to Nutrient-Influenced Intake:** At certain times and under specific conditions, cadmium accumulation in the bloodstream and organs will fluctuate within a certain range. This fluctuation is due to cadmium intake being influenced by nutrients such as Fe, Ca, and Zn, which follow periodic patterns.
- **Stability of Total Accumulated Cadmium in a Closed System:** Therefore, cadmium levels in organs will adjust to meet the body's needs at that time. However, the total accumulated amount will not fluctuate (this holds true as we assume the system is closed).

# Cadmium Model. The Impact for Different Levels of Consumption

Total Cadmium Accumulation ( $\mu\text{g}$ )	Health Impact
< 50 $\mu\text{g}$	Considered background exposure level in non-exposed populations; no significant health effects observed.
50–200 $\mu\text{g}$	Early signs of kidney dysfunction; increased urinary excretion of proteins indicating renal tubular damage.
200–500 $\mu\text{g}$	Tubular proteinuria indicating more pronounced renal damage; potential onset of bone demineralization.
> 500 $\mu\text{g}$	Severe kidney damage; increased risk of osteoporosis and fractures; potential lung damage; higher risk of cancer.

This table summarizing the health impacts associated with different levels of total cadmium accumulation in the body as a whole shows that as total cadmium accumulation in the body increases, health risks escalate.

## 1 Introduction

## 2 Our Model

2.1. Cadmium Model

2.2. Lead Model

2.3. Nickel Model

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## 4 Limitations & Future Work

**Equilibrium Concentration.** [7] Baseline blood Pb stabilizes at  $0.8\mu\text{g}/\text{dL}$ , baseline bones Pb stabilizes  $2.1\mu\text{g}$ , and baseline soft tissues Pb stabilizes at  $0.3\mu\text{g}$ .

**GI Absorption.** [7] Children absorb 45% of dietary Pb; decreases exponentially to 5% in adults.

## Distribution. [7]

- Pb initially enters blood, then distributes to bones and soft tissues.
- 73% Pb burden in bones during childhood; increases exponentially to 94% in adults.
- Pb resorption from bones accounts for 50% of blood Pb.

## Bone Distribution. [7]

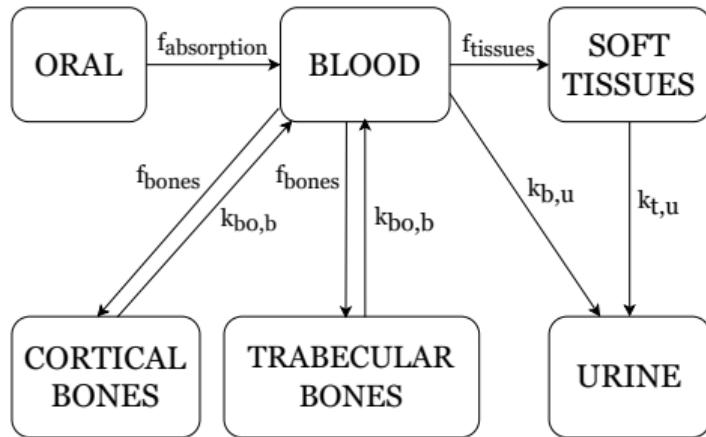
- 80% Pb in cortical bones (half-life: 15 years).
- 20% Pb in trabecular bones (half-life: 3 years).

**Soft Tissue Retention.** Soft tissue half-life: 1 month.

**Blood Dynamics.** Blood Pb half-life: 1 month.

**Excretion. [1]** Proportional to Pb burden:

- Calcium intake < RDA: GI absorption increases.
- Calcium intake  $\geq$  RDA: GI absorption decreases.



The figure illustrates the transfer rates of lead (Pb) between compartments, with some rates ( $f_{absorption}$ ,  $f_{tissues}$ ,  $f_{bones}$ ) depending on age.

Lead enters the bloodstream via gastrointestinal absorption ( $f_{absorption}$ ) and is distributed to soft tissues (liver, kidneys, brain,...) ( $f_{tissues}$ ) or stored in cortical and trabecular bones ( $f_{bones}$ ). Bones release lead back into the blood ( $k_{bo,b}$ ), while excretion occurs directly from blood ( $k_{b,u}$ ) or via soft tissues ( $k_{t,u}$ ) into urine.

Urine merely serves as a pathway for lead excretion, we can exclude it from the model.

$$\begin{cases} GI_{\text{absorption}} &= f_{\text{absorption}}(A) \cdot \left( \frac{Ca_{\text{RDA}}}{Ca} \right)^2 \cdot I \\ \frac{dB}{dt} &= GI_{\text{absorption}} + k_{bo,b}(CB + TB) - (f_{\text{bones}}(A) + f_{\text{tissues}}(A))B - k_{b,u}B \\ \frac{dST}{dt} &= f_{\text{tissues}}(A)B - k_{st,u}ST \\ \frac{dCB}{dt} &= 0.8 \cdot f_{\text{bones}}(A)B - k_{bo,b}CB - k_{cb,u}CB \\ \frac{dT B}{dt} &= 0.2 \cdot f_{\text{bones}}(A)B - k_{bo,b}TB - k_{tb,u}TB \end{cases}$$

$$\begin{cases} f_{\text{absorption}}(A) &= 0.79 \cdot \frac{\exp(-0.0065A^2)}{\exp(-0.0065A^2) + 1} + 0.05 \\ f_{\text{bones}}(A) &= -0.3 \cdot \frac{\exp(-0.006A^2)}{\exp(-0.006A^2) + 1} + 0.94 \\ f_{\text{tissues}}(A) &= 1 - f_{\text{bones}}(A) \end{cases}$$

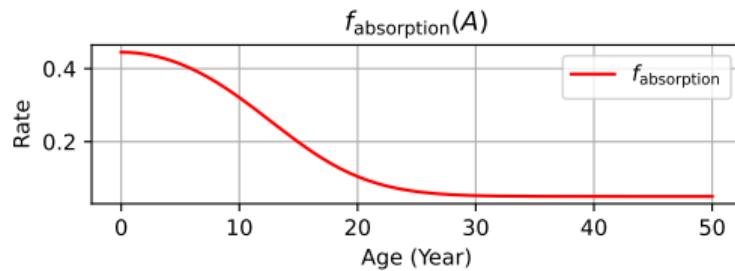


Figure 1:  $f_{\text{absorption}}(A)$  diagram

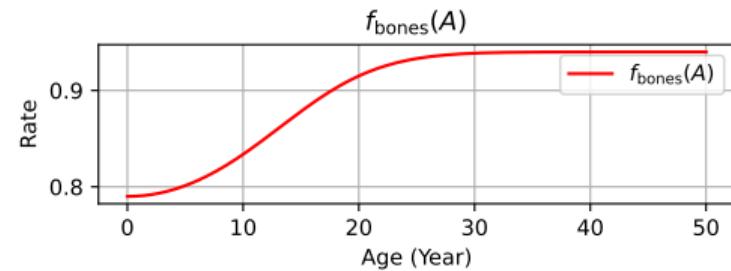


Figure 2:  $f_{\text{bones}}(A)$  diagram

In above, besides transfer rates  $f_{\text{absorption}}(A)$ ,  $f_{\text{bones}}(A)$ ,  $f_{\text{tissues}}(A)$ , we also use constants  $k_{bo,b}$ ,  $k_{b,u}$ ,  $k_{st,u}$ ,  $k_{cd,u}$  and  $k_{tb,u}$ .

All transfer rates are scaled using the scaling function  $s(x)$  as follow

- ① If the transfer rate is multiplied with  $CB$ , then we use the scaling function with  $x = CB/CB_0$ .
- ② If the transfer rate is multiplied with  $TB$ , then we use the scaling function with  $x = TB/TB_0$ .
- ③ If the transfer rate is multiplied with  $CB$ , then we use the scaling function with  $x = B/B_0$ .
- ④ If the transfer rate is multiplied with  $ST$ , then we use the scaling function with  $x = S/ST_0$ .

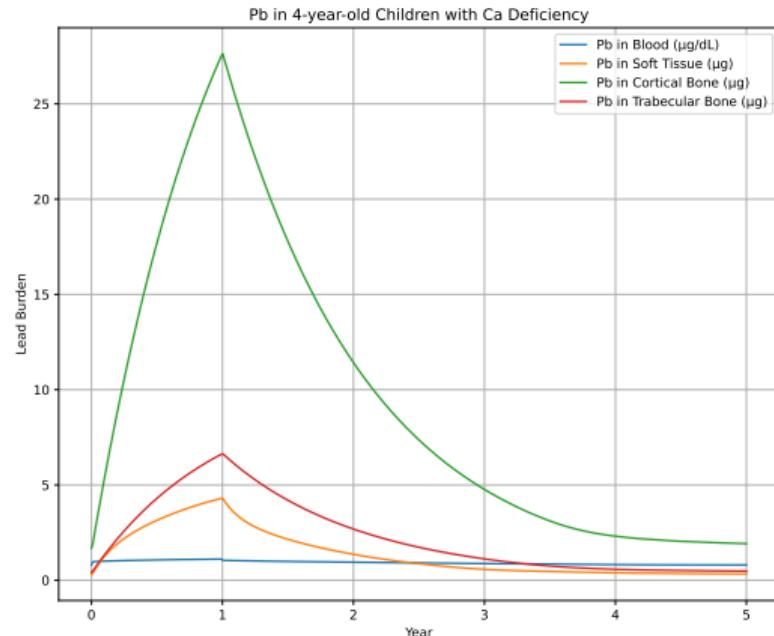
The initial conditions for the model is

Notation	Value	Meaning
$B_0$	0.8	Initial blood Pb ( $\mu\text{g}/\text{dL}$ )
$ST_0$	0.3	Initial Pb in soft tissues ( $\mu\text{g}$ )
$CB_0$	1.68	Initial Pb in cortical bones ( $\mu\text{g}$ )
$TB_0$	0.42	Initial Pb in trabecular bones ( $\mu\text{g}$ )

For the Pb dynamics itself, we have the following rate values

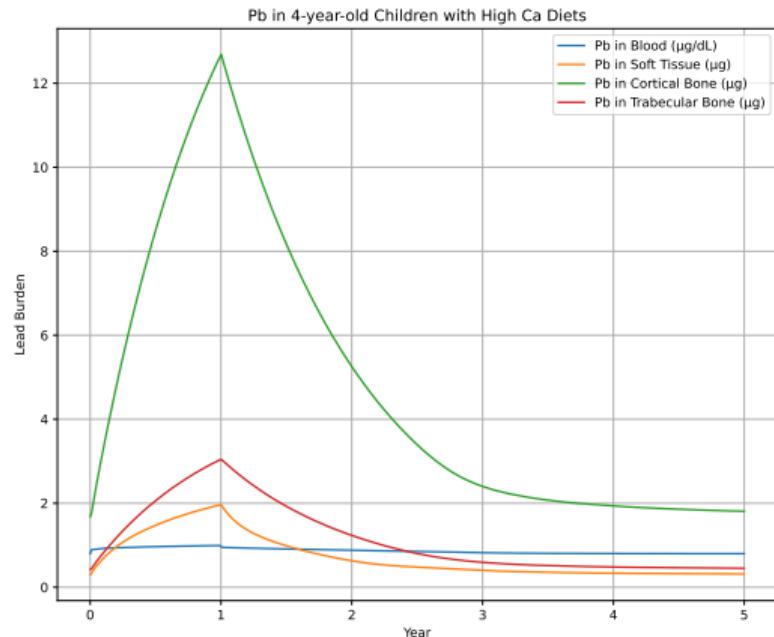
Notation	Calculation	Value	Meaning (day <sup>-1</sup> )
$k_{b,u}$	$\ln(2) / T_{\text{half\_b}}$	$\ln(2) / 30$	Blood lead excretion rate
$k_{st,u}$	$\ln(2) / T_{\text{half\_st}}$	$\ln(2) / 30$	Soft tissue lead excretion rate
$k_{cb,u}$	$\ln(2) / T_{\text{half\_s}}$	$\ln(2) / (15 \times 365)$	Cortical bone lead excretion rate
$k_{tb,u}$	$\ln(2) / T_{\text{half\_c}}$	$\ln(2) / (3 \times 365)$	Trabecular bone lead excretion rate
$k_{bo,b}$		0.01	Rate of Pb resorption from bones to blood

Eating 10g of chocolate contaminated with  $0.3 \mu\text{g/g}$  of lead every day for 1 year, daily Ca intake < RDA.



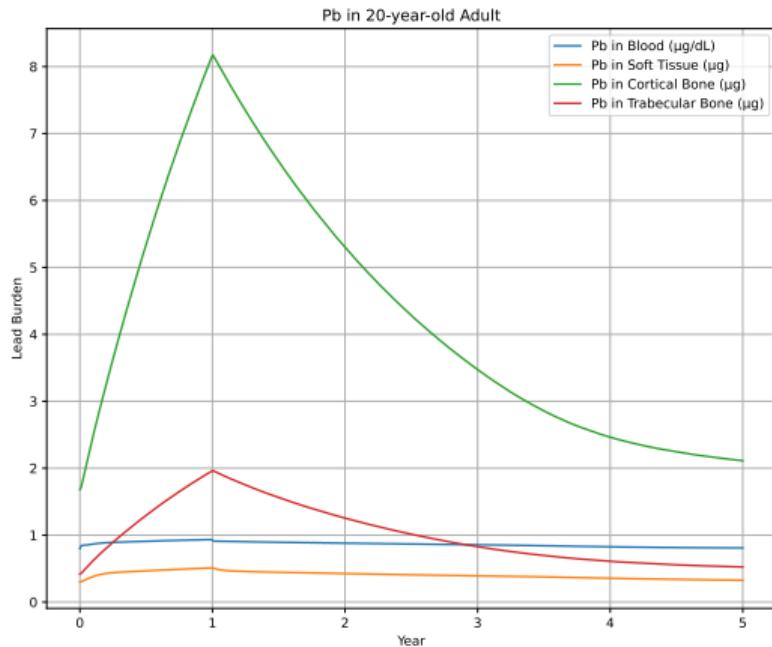
- **Long-term Accumulation:** Blood Pb levels remain relatively low and stable suggesting rapid clearance to other compartments, while bones represent the majority of Pb.
- **Soft Tissue Risk:** Notably, Pb in soft tissues approaching the harmful threshold of  $5 \mu\text{g}$  [8], which is particularly concerning for neurological and organ damage in children.

Eating 10g of chocolate contaminated with  $0.3 \mu\text{g/g}$  of lead every day for 1 year, daily Ca intake < RDA.



- **Reduced Soft Tissue Accumulation:** Pb levels in soft tissues rise slowly and stay well below harmful thresholds, showing calcium's protective effect.
- **Lower Bone Pb Burden:** Cortical and trabecular bones accumulate less Pb compared to the calcium-deficient scenario, reducing long-term release risks.

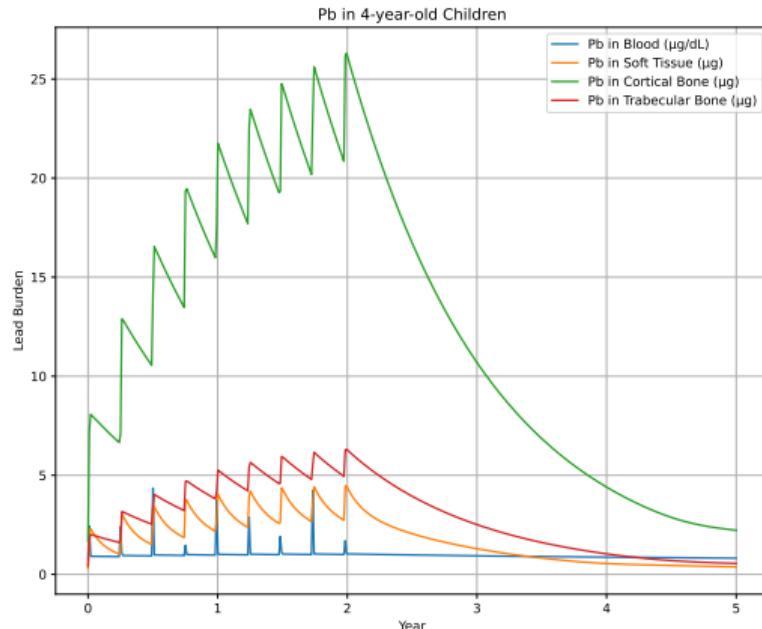
Eating 10g of chocolate contaminated with  $0.3 \mu\text{g/g}$  of lead every day for 1 year, daily Ca intake = RDA



- **Low Soft Tissue Risk:** Due to the significantly reduced Pb absorption rate in adults and high Pb storage in bones, Pb levels in soft tissues remain stable and well below harmful thresholds, minimizing the risk to vulnerable organs.
- **Bone Storage Dominance:** A larger proportion of Pb is stored in cortical and trabecular bones, and Pb remains in bones significantly longer in adults compared to children.

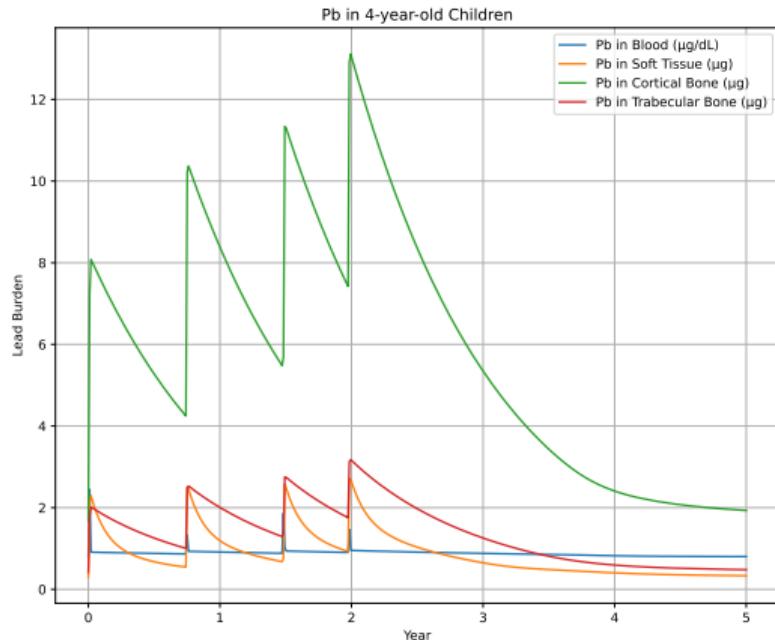
# Lead Model. Children Near Holidays

Eating 250g of chocolate contaminated with  $0.3 \mu\text{g/g}$  of lead in 2 consecutive days, every 3 months in 2 years, daily Ca intake = RDA



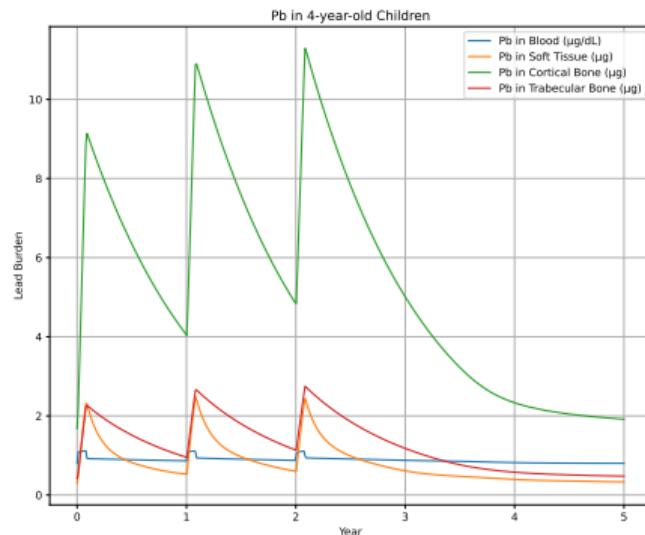
- **Accumulation Trend:** The short intervals between holidays do not allow sufficient time for Pb levels in the body to recover or clear, resulting in a cumulative increase over time.
- **Soft Tissue Risk:** Pb levels in soft tissues steadily rise, approaching the harmful threshold of  $5 \mu\text{g}$ .
- **Dangerous Blood Spikes:** Pb in blood occasionally rises to  $5 \mu\text{g}$  during some holidays due to resorption from bones, posing a significant health risk.

Eating 250g of chocolate contaminated with  $0.3 \mu\text{g/g}$  of lead in 2 consecutive days, every 9 months in 2 years, daily Ca intake = RDA



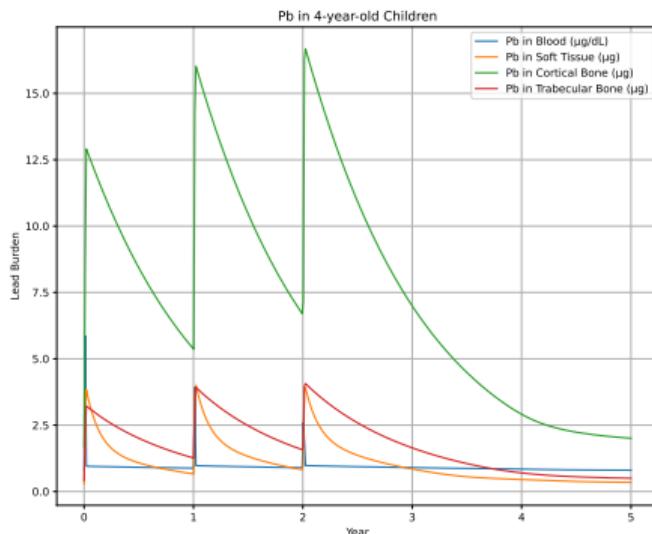
- **Soft Tissue Safety:** With longer intervals between holidays, Pb in soft tissues has sufficient time to clear.
- **Bone Accumulation:** Despite the long intervals, Pb in cortical and trabecular bones shows a gradual accumulation trend due to the long half-life of Pb in these compartments.
- **Blood Pb Levels:** Pb in blood remains below  $2 \mu\text{g}$ , avoiding the dangerous spikes observed in shorter holiday intervals.

Eating 30g of chocolate contaminated with  $0.3 \mu\text{g/g}$  of lead for 30 consecutive days, every year for 3 years, daily Ca intake = RDA



- **Manageable Accumulation:** Pb accumulation in blood and bones remains gradual, and the overall burden after each period stays within a safe range, posing no significant long-term risk.
- **Soft Tissue Recovery:** While Pb levels in soft tissues rise during the 30-day period, the 1-year interval between consumption cycles allows sufficient time for clearance, keeping soft tissue Pb below harmful thresholds.

Eating 300g of chocolate contaminated with  $0.3 \mu\text{g/g}$  of lead for 3 consecutive days, every year for 3 years, daily Ca intake = RDA



- **Binge Effect on Blood and Soft Tissues:** The immediate spike in Pb levels during the holiday sharply elevates blood and soft tissue Pb to near or above harmful thresholds.
- **Recovery Period:** While the 1-year gap allows Pb in soft tissues and blood to clear, the high peaks during each holiday highlight the dangers of binge consumption compared to distributed intake.

## 1 Introduction

## 2 Our Model

2.1. Cadmium Model

2.2. Lead Model

2.3. Nickel Model

## 3 Experimental Results

## 4 Limitations & Future Work

**Equilibrium Concentration.** Baseline blood Ni stabilizes at  $0.006\mu\text{g}/dL$ , baseline bones Pb stabilizes  $0.7\mu\text{g}$ , and baseline soft tissues Pb stabilizes at  $0.3\mu$ . [7]

**GI Absorption.** Both children and adults absorb about 20% – 40% of nickel intake from oral to blood. [7]

**Distribution.** Nickel from blood is distributed to other organs as follow.

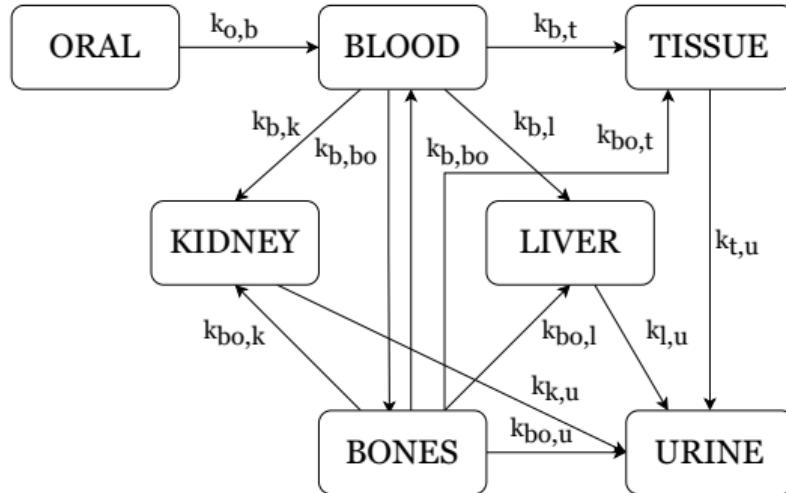
Organ	Nickel Distribution in Children (%)	Nickel Distribution in Adults (%)	Nickel Half-Life (Days)
Liver	5 - 10%	10 - 15%	3 - 7 days
Kidney	15 - 25%	20 - 30%	5 - 10 days
Bone	5 - 10%	10 - 15%	Up to several years
Other Tissues	5 - 15%	10 - 20%	10 - 30 days

Table 2: Nickel Distribution and Half-Life in Organs for Children and Adults. [7]

**Redistribution from Bones.** Nickel in bones is not stored forever in bones, but is also redirected to other organs with the distribution as follow

Organ/Tissue	Potential Redistribution from Bones (% of Released Nickel)	Estimated Excretion Rate of Nickel from Bone (% per year)
Liver	20 - 30%	< 0.5%
Kidney	30 - 40%	< 1%
Blood	10 - 20%	< 0.1%
Other Tissues	10 - 20%	< 0.2%

**Table 3:** Potential Redistribution and Estimated Excretion Rates of Nickel from Bone to Other Organs. [7]



The variable  $k_{i,j}$  on each arrow in the figure shows the ratio of nickel from organ  $i$  transfers to organ  $j$  in one hour.

When nickel enters the body, it first circulates in the blood before distributing to various organs. Studies show it primarily accumulates in the kidneys, liver, bones, and other soft tissues. Nickel stored in the bones does not exit the body directly through urine but instead recirculates to the other locations. [3]

Urine merely serves as a pathway for nickel excretion, we can exclude it from the model.

$$\left\{ \begin{array}{l} \frac{dO}{dt} = I - k_{o,b} \cdot O \\ \frac{dB}{dt} = k_{o,b} \cdot O + k_{bo,b} \cdot Bo - (k_{b,k} + k_{b,l} + k_{b,t} + k_{b,bo}) \cdot B \\ \frac{dK}{dt} = k_{b,k} \cdot B + k_{bo,k} \cdot Bo - k_{k,u} \cdot K \\ \frac{dL}{dt} = k_{b,l} \cdot B + k_{bo,l} \cdot Bo - k_{l,u} \cdot L \\ \frac{dT}{dt} = k_{b,t} \cdot B + k_{bo,t} \cdot Bo - k_{t,u} \cdot T \\ \frac{dBo}{dt} = k_{b,bo} \cdot B - (k_{bo,u} + k_{bo,b} + k_{bo,k} + k_{bo,l} + k_{bo,t}) \cdot Bo \end{array} \right.$$

We use two sigmoid functions - which has the property as the scaling function above - to scale the transfer rates

$$s_1(x) = a_1 \cdot \exp\left(\frac{c_1(x - b_1)}{c_1(x - b_1) + 1}\right) + k_1 \quad \text{and} \quad s_2(x) = a_2 \cdot \exp\left(\frac{c_2(x - b_2)}{c_2(x - b_2) + 1}\right) + k_2$$

Let  $a_{i,j}$  be the constant rate transfer from organ  $i$  to  $j$ , our rate will have three types

- ① If  $i = b$ , which is blood, then  $k_{i,j} = a_{i,j} \cdot s_1(I/I_{\max}) \cdot s_2(B/B_{\min})$ .
- ② If  $j = u$ , which is urine, then  $k_{i,j} = a_{i,j} \cdot s_1(I/I_{\max}) \cdot s_2(I/I_{\min})$ .
- ③ If  $i = bo$ , which is bone, we have  $k_{i,j} = a_{i,j} \cdot s_1(J/J_{\max}) \cdot s_2(Bo/Bo_{\min})$ .
- ④ If  $i = b$  and  $j = bo$ , then it is simply  $k_{i,j} = a_{i,j} \cdot s_2(Bo/Bo_{\min})$ , because we assume that blood has unlimited capacity.

Only when  $i = o$  and  $j = b$ , we have  $k_{i,j} = a_{i,j} \cdot (Fe_{\max}/Fe)^2$ , where  $Fe$  is the constant amount of iron in body at all time. The reason for using such a ratio is explained earlier.

The initial equilibrium value of nickel in blood is  $0.006 \mu\text{g}$ . We have the minimum and maximum capacity ( $\mu\text{g}$ ) of nickel in each organ for children stated as below.[7]

$K_{\min}$	2	$L_{\min}$	1.6	$T_{\min}$	1.2	$Bo_{\min}$	0.7
$K_{\max}$	4	$L_{\max}$	3.2	$T_{\max}$	2.4	$Bo_{\max}$	1.4

The initial equilibrium value of nickel in blood is  $0.048 \mu\text{g}$ . The table below is for adults.[7]

$K_{\min}$	13	$L_{\min}$	8	$T_{\min}$	4.8	$Bo_{\min}$	4.2
$K_{\max}$	26	$L_{\max}$	16	$T_{\max}$	9.6	$Bo_{\max}$	8.4

The distribution of nickel from blood to organs differs for children and adults, which can be described in the following tables. [7]

$a_{b,k}$	0.4	$a_{b,l}$	0.4	$a_{b,t}$	0.1	$a_{b,bo}$	0.12
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The following is the distribution for adults. [7]

$a_{b,k}$	0.5	$a_{b,l}$	0.2	$a_{b,t}$	0.1	$a_{b,bo}$	0.12
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where

- $a_{b,k}$  is the distribution (%) of nickel from blood to kidney in one hour.
- $a_{b,l}$  is the distribution (%) of nickel from the blood to the liver in one hour.
- $a_{b,t}$  is the distribution (%) of nickel from blood to tissue in one hour.
- $a_{b,bo}$  is the distribution (%) of nickel from blood to bones in one hour.

The general formula for calculating the excretion rate is given as follow [4]

$$r = \frac{\ln(2)}{\text{half-life in hours}}$$

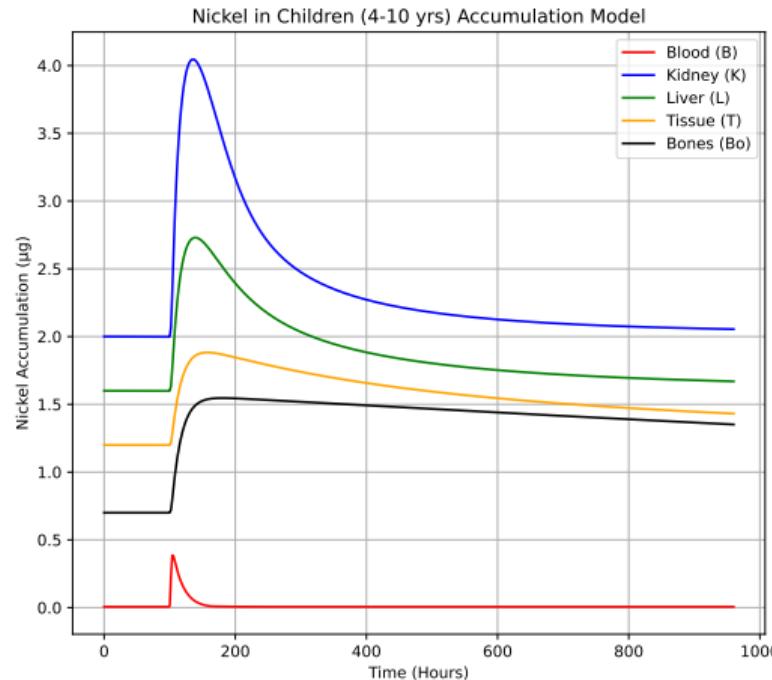
Base on this, we have the following which describes the excretion rates.

$a_{k,u}$	0.006	$a_{l,u}$	0.004	$a_{t,u}$	0.001	$a_{bo,u}$	0.000012
$a_{bo,b}$	0.00001	$a_{bo,k}$	0.0001	$a_{bo,l}$	0.00005	$a_{bo,t}$	0.00002

All values are measured with  $h^{-1}$  unit. The meaning of each notation is as

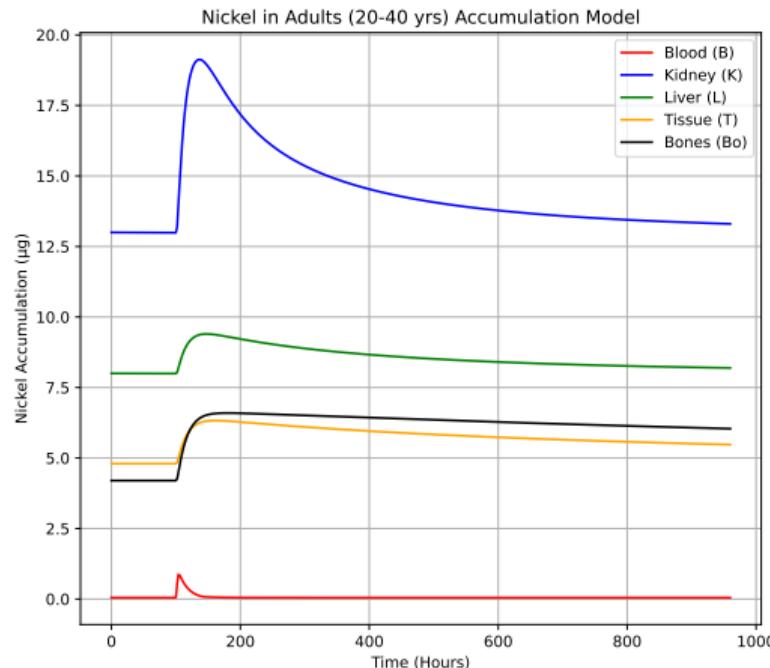
$a_{k,u}$	Excretion rate from kidney to urine	$a_{l,u}$	Excretion rate from liver to urine
$a_{t,u}$	Excretion rate from tissue to urine	$a_{bo,u}$	Excretion rate from bones to urine
$a_{bo,b}$	Redistribution rate from bones to blood	$a_{bo,k}$	Redistribution rate from bones to kidney
$a_{bo,l}$	Redistribution rate from bones to liver	$a_{bo,t}$	Redistribution rate from bones to tissue

In this scenario, the child intake  $3 \mu\text{g}$  in 2 hours, then does not intake any more.



- **Kidney accumulation.** Nickel primarily accumulates in the kidneys and is rapidly excreted, peaking around 20 days.
- **Organs excretion.** Other organs excrete nickel at different rates, while bones release it slowly and redistribute it to other tissues, preventing equilibrium.

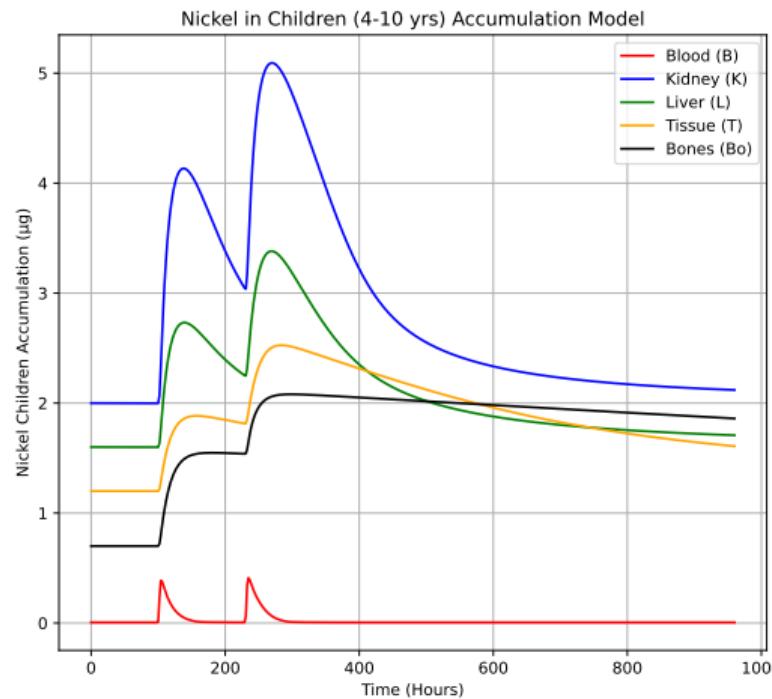
In this scenario, the adult intake  $7 \mu\text{g}$  in 2 hours, then does not intake any more.



- **Distribution.** In adults, a biological mechanism prioritizes nickel distribution to the kidneys, making them the primary storage site.
- **Bones excretion.** Bones retain nickel longer, slowly releasing it and redistributing it to other tissues, which prevents equilibrium in other organs.

## Nickel Model. Multiple Close Intake For Child

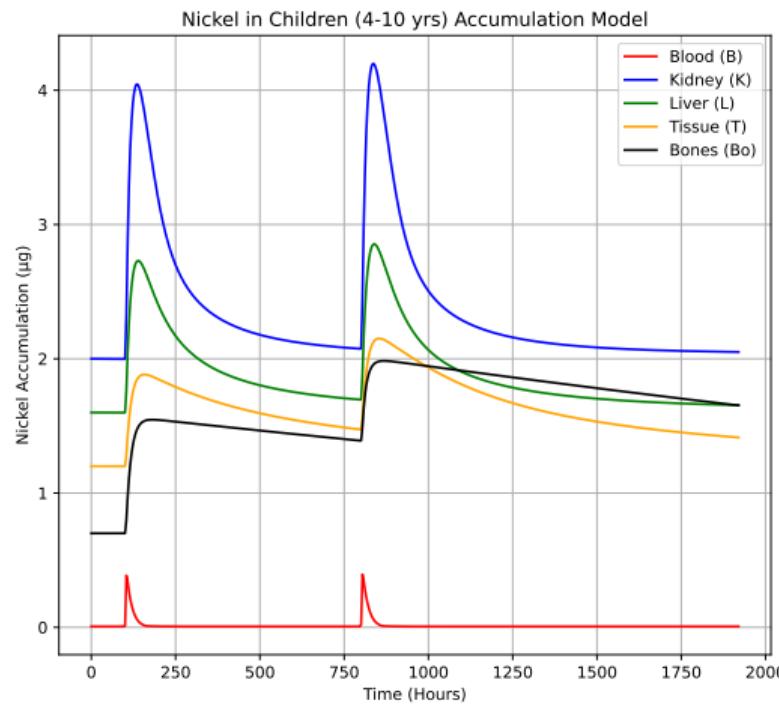
In this scenario, the child consumes 3  $\mu\text{g}$  in 2 hours, from hour 100 to 102, then another 3  $\mu\text{g}$  from hour 230 to 232, and then does not consume any more.



- **Kidney to urine.** Nickel continues to accumulate in the kidneys, limiting sufficient excretion through the urine.
- **Nickel in blood.** Blood does not store nickel permanently due to its rapid excretion rate.

## Nickel Model. Multiple Far Intake for Children

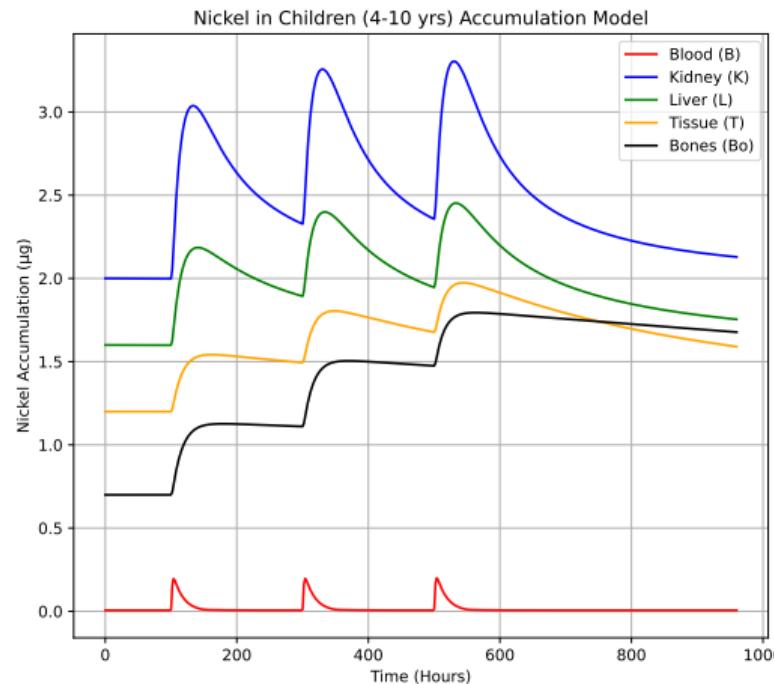
In this scenario, the child intakes 3  $\mu\text{g}$  in 2 hours, from hour 100 to 102, then another 3  $\mu\text{g}$  from hour 800 to 802 (difference in roughly 1 month), then does not intake any more.



- **Periodic.** Most of the nickel in the kidneys is effectively excreted, creating a periodic pattern in the levels of nickel.
- **Increasing.** Nickel accumulates in soft tissues and bones, with previous deposits remaining and gradually increasing with time.

# Nickel Model. Distributed Intake For Children With Multiple Intakes

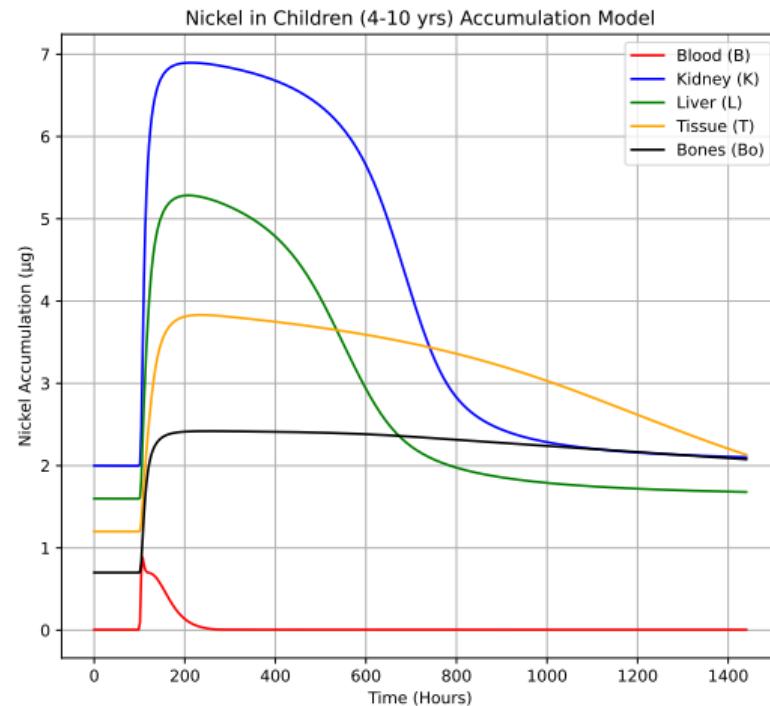
In this scenario, the child intake  $1 \mu\text{g}$  in the following three time periods: 100-101, 300-301 and 500-501, after that, there is no more intake.



- **Stabilize.** With enough time for excretion, nickel accumulation in organs shows a periodic pattern, suggesting a stable condition in children.
- **Bones and tissues.** Nickel continues to build up in bones and soft tissues, as these areas take longer to fully excrete it.

## Nickel Model. Binge Intake For Child

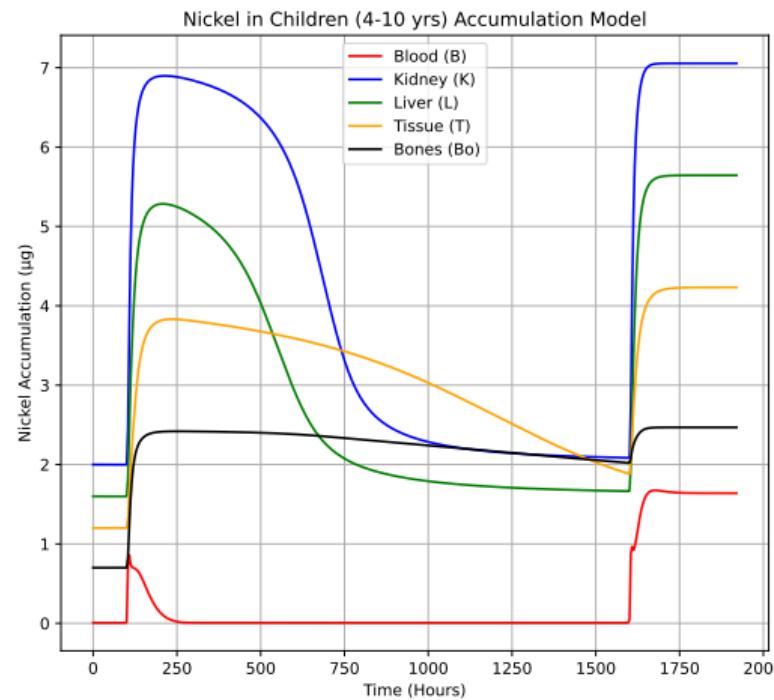
In this scenario, the child intakes  $3.5 \mu\text{g}$  in 4 hours, from hour 100 to 104, then does not intake any more.



- **Large amount.** Children take significantly longer to process large amounts of nickel. Their slower excretion rate allows nickel to accumulate in the body.
- **Health issues.** Prolonged nickel retention can increase the risk of adverse health effects.

# Nickel Model. Binge Intake For Children With Multiple Intakes

In this scenario, the child intakes  $3.5 \mu\text{g}$  in 4 hours, from hour 100 to 104, then another  $3.5 \mu\text{g}$  in 4 hours, from hour 1000 to 1004, after that there is no more intake.



- **Sharp increase.** Initial nickel intake causes a sharp increase in kidney levels. With continued intake, nickel accumulates in all organs, reaching maximum capacity.
- **Maximum capacity.** After reaching capacity, nickel slowly builds up in the blood and other areas. Excretion occurs only after a prolonged period.

1 Introduction

2 Our Model

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What can be implied about the long-term accumulation of heavy metals in the people who eat contaminated chocolate?

The long-term accumulation of heavy metals can occur if intake is regular and exceeds the body's ability to excrete them. In the case of "distributed intake," the heavy metal may remain in the body over time, potentially leading to health issues such as organ damage or toxicity. Continuous exposure to contaminated food sources can exacerbate this accumulation, increasing health risks in the long term.

What happens to children who might consume a large amount of candy at certain times of the year?

If children consume large amounts of candy during specific times (like holidays), as seen in the "close holiday intake" case, the heavy metal content in the body can increase, leading to potential health issues. This happens because the body may not have enough time to excrete the accumulated metals before more are ingested. In this case, an increase in health problems such as poisoning or organ stress could occur.

What difference might happen to children who have their consuming period differently?

Children who have their consuming periods spaced out, as in the "far holiday intake" case, would likely experience less risk of health issues. With a more distributed or controlled intake, the body has time to return to normal and excrete the heavy metals between consumption periods. This could reduce the likelihood of toxicity or long-term damage compared to binge consumption or highly concentrated intake periods.

- 1 Introduction
- 2 Our Model
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Our performance have some limitations:

- **Lack of real life data.** Our models are constructed based on literature reviews, there are no real data for us to verify the correctness of the model.
- **Assumptions.** Assumptions made to simplify calculations may not always hold true in real-world scenarios.
- **Limited generalizability.** These heavy metals are also significantly affected by different routes other than oral, such as Pb through inhalation and Ni through skin absorption.

In the future, to make sure our model works correctly, we can

- **Model Refinement.** Incorporate more accurate data and better assumptions to improve model predictions.
- **Complex Systems Integration.** Integrate more complex interactions and variables to represent real-world scenarios more accurately.
- **Scalability.** Develop models that are more computationally efficient, enabling larger and more complex simulations.

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