ExpoKids READ ME

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I. ExpoKids Overview

Aggregate exposure, the combined exposures from all pathways to a single chemical, is a critical children's health issue. ExpoKids Version 1.0 is an R-based tool that estimates relative sources of exposure within and across lifestages. The scope of the current version of this tool is limited to estimating average daily dose (ADD) from the oral exposure route for postnatal childhood lifestages (from birth to puberty) and includes adults as a comparator group. To capture potential differences in aggregate exposure at various childhood lifestages compared to those of adults, ExpoKids uses exposure estimates across lifestages generated by the publicly available US EPA's Exposure Factors Interactive Resource for Scenarios Tool (ExpoFIRST). ExpoKids illustrates aggregate oral exposures as average daily doses (ADD) and lifetime average daily doses (LADD) in 5 graphs organized across 7 postnatal and adult lifestages and 10 media. This visualization tool conveys ExpoFIRST findings, from available exposure data, in order to highlight the relative contributions of media and lifestages.

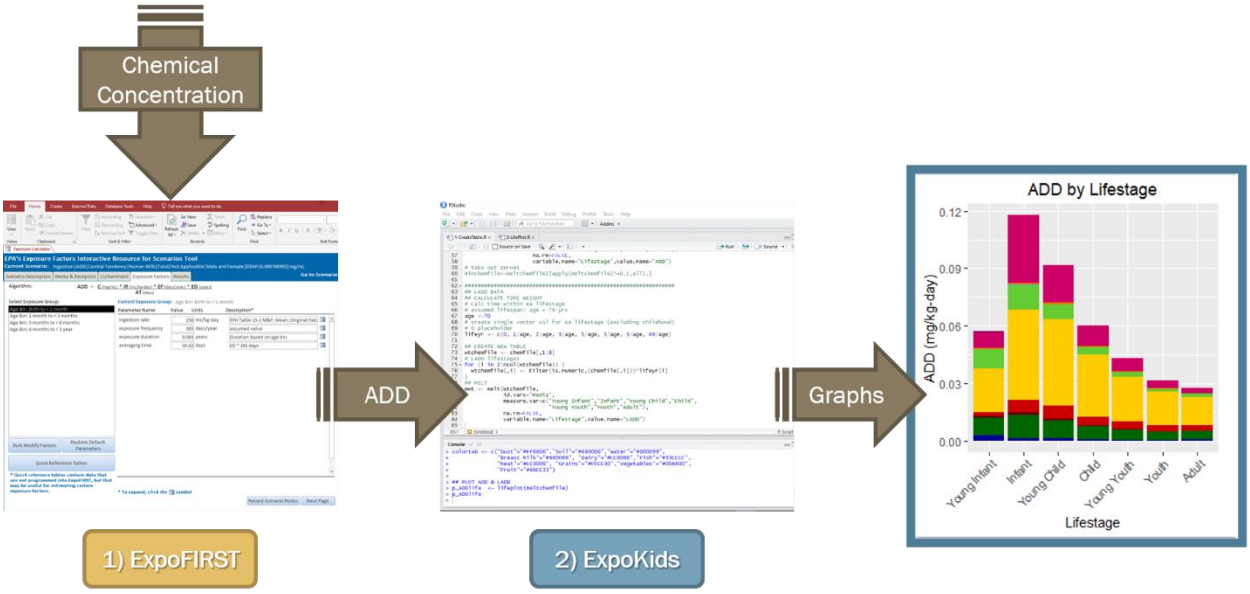
II. ExpoKids Development

The goal of ExpoKids is to illustrate aggregate exposure estimates by lifestage based on exposure factor data in the Exposure Factors Handbook (EFH) used by ExpoFIRST and user-defined concentration data. ExpoKids Version 1.0 characterizes exposure by estimating average daily dose (ADD) values for postnatal only and oral only exposure media with available data.

III. ExpoFIRST and ExpoKids

ExpoFIRST estimates ADDs from ten media (i.e., soil, dust, water, breastmilk, dairy, meat, fish, vegetables, fruit, and grains) [1]. ADD was chosen as the ExpoKids metric to display because it captures typical exposures experienced by average Americans. ExpoFIRST itself does not evaluate aggregate exposure, but rather runs estimates for each medium separately. Subsequently, medium-specific ADD estimates are exported from ExpoFIRST to ExpoKids to develop aggregate exposure graphs (Figure 1).

Figure 1. ExpoKids workflow.



Central tendency oral ADDs (mg/kg-day) for the EFH's ten children's age groups and the adult age group ExpoKids can create five unique displays of ADD by lifestage, ADD by media, LADD by lifestage, LADD by media, and percent ADD by lifestage (summarized in Section V - Explanation of Graphs). ADD was estimated in ExpoFIRST for each medium using the following equation [1]:

$$\mathrm{ADD} = \frac{\mathrm{C} \times \mathrm{IR} \times \mathrm{EF} \times \mathrm{ED}}{\mathrm{AT} \times \mathrm{BW}}$$

Above, C = concentration (mg/mL or mg/g), IR = intake rate (mL/kg-day, g/kg-day, or mg/day depending on the medium), EF = exposure frequency (days/year), ED = exposure duration (years), AT = average time (days), and BW = body weight (kg) (US EPA, 2016). Age-specific central tendency estimates (either mean or median, depending on the exposure factor) from the EFH are used for IR, EF, ED, AT, and BW [2]. Chemical concentration (C) is based on literature reported values in the media of interest. ExpoFIRST allows users to define an unlimited number of potential scenarios for various receptor populations and lifestages.

IV. Methods

ExpoKids can create five unique displays of ADD by lifestage, ADD by media, LADD by lifestage, LADD by media, and percent ADD by lifestage (summarized in Section V - Explanation of Graphs). Since the EFH follows the *EPA's Guidance on Selecting Age Groups for Monitoring and Assessing Childhood Exposures to Environmental Contaminants* as available data allows, ExpoKids also follows a similar renaming structure for reorganizing age groups into lifestages [3]. The ingestion pathway, for instance, does not have data for all age groups under 1 year old and the EFH therefore commonly collapses these four age groups into one lifestage, named young infants in ExpoKids. The infant lifestage in ExpoKids treats the 1-3 years old EFH age groups similarly. In other words, eleven ExpoFIRST/EFH age groups were simplified to seven ExpoKids lifestages (Table 1).

Table 1: Default EFH age bins and ExpoKids recategorized lifestages.

	EFH Age Bins	ExpoKids Lifestage	Total Years in Lifestage
Childhood	Birth to < 1 month	Young Infant[1,2]	1
	1 to < 3 months		
	3 to < 6 months		
	6 to < 12 months		
	1 to < 2 years	Infant[1]	2
	2 to < 3 years		
	3 to < 6 years	Young Child	3
	6 to < 11 years	Child	5
	11 to < 16 years	Young Youth	5
	16 to < 21 years	Youth	5
	21 to < 70 years	Adult	49
	Birth to < 70 years	Lifetime	70

[1] The young infant and infant lifestages were the only lifestages to combine multiple age bins.

[2] The young infant lifestage is assumed to be 100% breastfed.

Childhood ADD (defined as the time from birth to less than 21 years old) is also estimated for comparison against adulthood (21 years old to less than 70 years old) and lifetime (birth to less than 70 years old). After the ADD data tables from ExpoFIRST are uploaded into ExpoKids (R package: readxl), the melt function (R package: reshape2)

rearranges the data into a readable format for the statistical program to create stacked bar plots using the ggplot function (R package: tidyverse). The resulting eleven graphs (one all media graph and ten medium specific graphs) display the estimated ADD values by lifestage. LADD values are then estimated by time-weighting each ADD value; in other words, each ADD was multiplied by a ratio of years spent within each lifestage divided by the total lifespan (70 years).

For each medium, ADD per lifestage of interest (ADD_j) is estimated from the age groups using the following equation:

$$\mathrm{ADD_j} = \frac{\sum(\mathrm{ADD_i} \times \mathrm{Y_i})}{\sum \mathrm{Y_i}}$$

in which ADD_i is the ADD value from the ExpoFIRST age group within the relabeled lifestage of interest, Y_i is the length in years of that age group, $\sum Y_i$ is the total number of years in the new lifestage, and i represents the age group within the lifestage being estimated.

LADD per lifestage ($LADD_j$) of interest for the media is estimated from:

$$\mathrm{LADD_j} = \frac{\mathrm{ADD_j} \times \mathrm{Y_j}}{\mathrm{Lifespan}}$$

ADDs are also converted to percentages to understand the percent contribution of each medium within a lifestage using the following equation:

$$\%\ \mathrm{Lifestage\ Contribution_j} = \frac{\mathrm{ADD_j}}{\sum \mathrm{ADD_j}} \times 100\%$$

V. Getting Started

To run ExpoKids, users must first upload an Excel file with ADD values to the app for the following lifestages:

- Birth to < 1 mo
- 1 mo to < 3 mo
- 3 mo to < 6 mo
- 6 mo to < 1 yr
- 1 yr to < 2 yr
- 2 yr to < 3 yr
- 3 yr to < 6 yr
- 6 yr to < 11 yr
- 11 yr to < 16 yr
- 16 yr to < 21 yr
- 21 yr to < 70 yr

Specifically, ExpoKids was designed to run with EPA's ExpoFIRST. Users are encouraged to run their chemical of interest through ExpoFIRST first to calculate the ADD values (see website for details on ExpoFIRST). Once values are calculated, insert values into the "template.xlsx" file provided on the ExpoKids page and save with the chemical name, adding rows for media types as needed. Alternatively, users may test out ExpoKids with the "sample.xlsx" file (Figure 2).

Figure 2. Sample ADD data table ready to be uploaded into ExpoKids.

Media	Birth to < 1 mo	1 mo to < 3 mo	3 mo to < 6 mo	6 mo to < 1 yr	1 yr to < 2 yr	2 yr to < 3 yr	3 yr to < 6 yr	6 yr to < 11 yr	11 yr to < 16 yr	16 yr to < 21 yr	21 yr to < 70 yr
Time (yrs)	0.083333333	0.166666667	0.25	0.5	1	1	3	5	5	5	49
Dust	0.00E+00	2.12E-05	1.69E-05	1.36E-05	2.19E-05	1.81E-05	1.35E-05	7.87E-06	4.40E-06	3.49E-06	1.53E-06
Soil	0.00E+00	2.54E-08	2.03E-08	1.63E-08	2.19E-08	1.81E-08	1.34E-08	7.86E-09	4.40E-09	3.49E-09	1.22E-09
Water	2.60E-04	2.40E-04	2.60E-04	2.05E-04	1.15E-04	1.15E-04	9.00E-05	7.00E-05	5.00E-05	4.50E-05	6.50E-05
Breast Milk	7.16E-03	6.69E-03	5.25E-03	3.96E-03	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
Dairy	8.65E-04	8.65E-04	8.65E-04	8.65E-04	3.70E-03	3.70E-03	2.05E-03	1.10E-03	7.24E-04	4.37E-04	2.93E-04
Meat	6.24E-05	5.76E-05	6.24E-05	4.92E-05	2.76E-05	2.76E-05	2.16E-05	1.68E-05	1.20E-05	1.08E-05	1.56E-05
Fish	4.24E-07	4.24E-07	4.24E-07	4.24E-07	2.76E-06	2.76E-06	2.54E-06	2.23E-06	1.72E-06	1.59E-06	2.52E-06
Vegetables	2.48E-07	2.48E-07	2.48E-07	2.48E-07	3.12E-07	3.12E-07	1.84E-07	9.20E-08	5.84E-08	3.60E-08	4.42E-08
Fruit	3.91E-05	3.91E-05	3.91E-05	3.91E-05	8.06E-05	8.06E-05	7.81E-05	5.54E-05	4.03E-05	2.97E-05	2.51E-05
Grains	6.48E-05	6.48E-05	6.48E-05	6.48E-05	1.01E-04	1.01E-04	9.80E-05	6.95E-05	5.06E-05	3.73E-05	3.15E-05

To be compatible with ExpoKids, all data tables must have the ExpoFIRST age bins as listed above as columns and the media of interest listed in the rows of the first column. The second row must be the time duration in years of each age group must also stay the same. If desired, users can add or change the media of interest in their own table. Otherwise, users need only change the cells containing the ADD values (highlighted in yellow in Figure 2). The data table should be saved in Microsoft Excel.

Once the data table is ready, the file may be uploaded ExpoKids to start viewing graphs in the side panel. All graphs/tables will automatically update after the file is uploaded.

VI. Tabs

A. ExpoKids Lifestages

View an explanation of the ExpoKids lifestages including how it compares to the Exposure Factors Handbook (EFH) age bins and how many total years are in each lifestage.

B. Uploaded Table

View the uploaded ADD (mg/kg-day) table.

C. Lifestage Tables

View the uploaded table for ExpoKids' reorganized lifestages:

- Young infant
- Infant
- Young child
- Child
- Young youth
- Youth
- Adult
- Lifetime

Two tables are displayed for ADD (mg/kg-day) and for LADD (mg/kg-day).

C. Lifestage Graphs

View graphs for:

- ADD by Lifestage
- LADD by Lifestage

View graphs for:

- ADD Cumulative Percent by Lifestage

D. Media Graphs

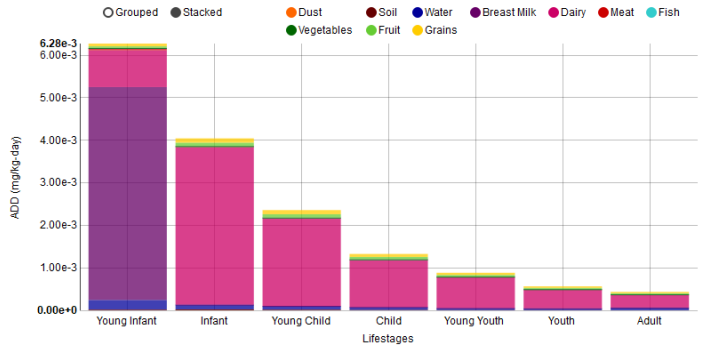
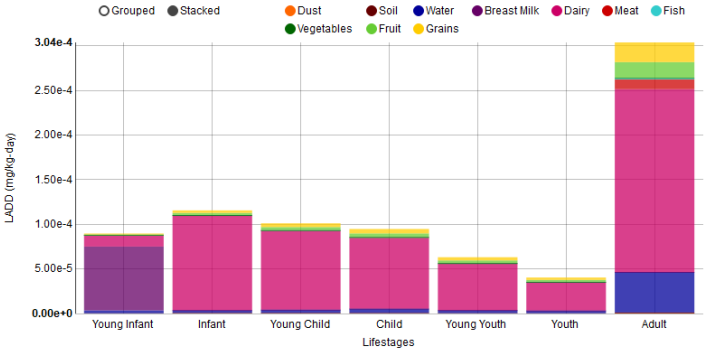
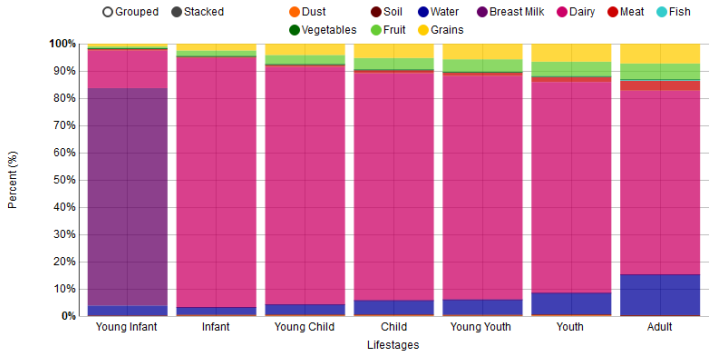
Use the checklist to select individual media groups to display graphs for ADD vs. lifestage and LADD vs. lifestage.

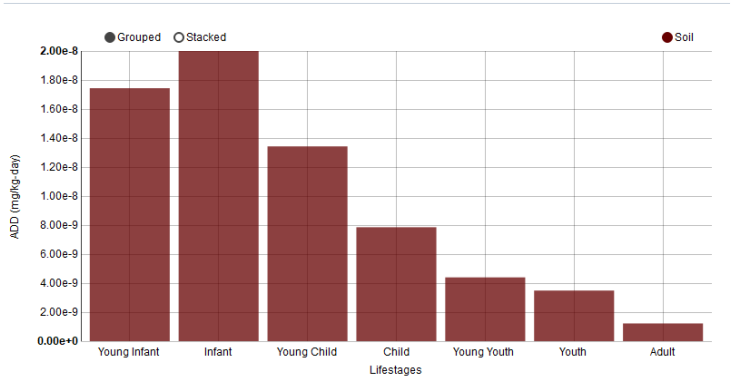
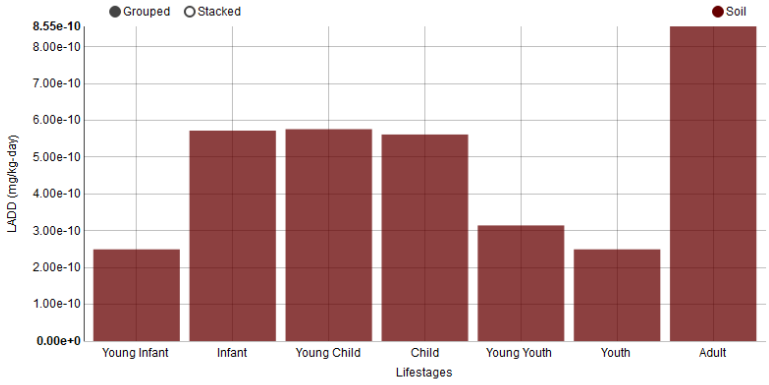
E. Summary Graphs

View the ADD by Lifestage graph and Cumulative Percent by Lifestage graph for childhood, adult, and lifetime.

VII. Explanation of Graphs

Table 2: ExpoKids can display different graph types.

Graph Type / Example	Graph Description
ADD by lifestage 	Compares lifestages and media as relative contributors to an individual's lifetime exposure.
LADD by lifestage 	Compares lifestage and media ADD contributions scaled by the number of years an individual spends in each lifestage; time duration within a lifestage is considered.
Cumulative percent 	Converts relative ADD contributions within a lifestage to relative percentages within a lifestage.

ADD by lifestage per exposure pathway 	Focuses on illustrating the relative contribution between lifestages for a specific medium of interest (10 total).
LADD by lifestage per exposure pathway 	Focuses on illustrating the relative contribution between lifestages for a specific medium of interest (10 total).

VIII. Assumptions and Limitations

Limited data constrains the utility of ExpoKids. Inhalation and dermal exposures may play a large role in consumer or residential exposure for some susceptible groups, but these are not specified by ExpoKids. Moreover, the ADD estimation assumed that the media concentrations remain constant over time for all lifestages. This fixed chemical concentration captures only a snapshot of a population's exposure at one point in time; to look at exposure as the population ages, concentration data would need to be collected over time. Similarly, the LADD was estimated separately for each lifestage and therefore, assumed that each lifestage was equivalent to the lifetime. This limitation is inherent to the LADD equation and results in LADDs that do not account for ingestion during other lifestages and, as a result, could underestimate total lifetime exposure. Furthermore, ExpoKids combines the smallest age groups from ExpoFIRST into the young infant and infant lifestages, resulting in a loss of detail for newborn ADD specificity.

ExpoKids also shares limitations from ExpoFIRST. For instance, it calculates point estimates rather than probabilistic distributions. In addition, the effectiveness of ExpoKids relies on the chemical concentration data that users input into ExpoFIRST and its parameters chosen. ExpoFIRST also presently does not have an option to evaluate infant formula consumption; the illustrative case examples thereby assumed that young infants are exclusively breastfed even though supplementing breastmilk with infant formula is commonly practiced in the US and studies have indicated that, at 12 months, only 24% of young infants are breastfed [4]. As a result, ExpoKids overestimates breastmilk consumption and does not represent formula fed infants who would have greater water consumption. No PBPK models are used in ExpoFIRST and accordingly do not allow for estimation of internal dose, if desired. Finally, ExpoFIRST also excludes the prenatal lifestage even though gestation may be a critical window of exposure. However, the gestational lifestage has a number of data gaps that currently makes exposure difficult to estimate [1]. However, by combining the functionality of ExpoFIRST with the visual graphic capabilities of R, ExpoKids facilitates comparisons of aggregate exposure by media both within and across lifestages

IX. References

1. Office of Research and Development (ORD). Exposure Factors Interactive Resource for Scenarios Tool (ExpoFIRST), Version 2.0 [Internet]. US Environmental Protection Agency; 2016. Available from: https://cfpub.epa.gov/ncea/risk/recordisplay.cfm?deid=322489

2. Exposure Factors Handbook: 2011 Edition [Internet]. Washington (DC); 2011 Sep. Report No.: EPA/600/R-090/052F. Available from: https://www.epa.gov/sites/production/files/2015-09/documents/techoverview_efh-complete.pdf

3. Guidance on Selecting Age Groups for Monitoring and Assessing Childhood Exposures to Environmental Contaminants [Internet]. Washington (DC): US Environmental Protection Agency; 2005. Report No.: EPA/630/P-03/003F. Available from: https://www.epa.gov/sites/production/files/2013-09/documents/agegroups.pdf

4. Grummer-Strawn LM, Scanlon KS, Fein SB. Infant feeding and feeding transitions during the first year of life. Pediatrics. 2008 Oct;122 Suppl 2:S36-42.