

# Consistency check for Age-dependent Reference Intervals

## Installation:

Download the Zip-File from GitHub under [https://github.com/SandraKla/Zlog\\_AdRI](https://github.com/SandraKla/Zlog_AdRI). Unzip the file and set your working direction to the path of the folder. The package shiny must be installed before using the Shiny app.

```
1. if("shiny" %in% rownames(installed.packages())){  
2.   library(shiny)}  
3. else{  
4.   install.packages("shiny")}
```

And then start the app with the following code:

```
1. library(shiny)  
2. runApp("app.R")
```

Or use the function runGitHub() from the package shiny:

```
1. library(shiny)  
2. runGitHub("Zlog_AdRI", "SandraKla")
```

The package DT is downloaded or imported when starting this app. The used R-Version must be  $\geq 3.6.1$ . The package DT must be  $\geq 0.13$  and shiny  $\geq 1.4.0$ .

## Data:

### Preloaded dataset:

The CALIPER-Dataset with age-dependent reference intervals has been preloaded into this Shiny App. For this purpose, the data was brought into the appropriate shape for the analysis from the Supplemental Table from Age-Specific and Sex-Specific Pediatric Reference Intervals for 40 Biochemical Markers.

### New data:

For new data use the CALIPER-Dataset as template with the columns:

1. **CODE:** Name of the analyte ("Calcium")
2. **LABUNIT:** Unit of the analyte ("mmol/L")
3. **SEX:** "M" for male, "F" for female and "AL" for both
4. **UNIT:** Unit of the age range in "year", "month", "week" or "day"
5. **AgeFrom:** Start of the age range
6. **AgeUntil:** End of the age range
7. **LowerLimit:** Start of the reference interval (LL)
8. **UpperLimit:** Start of the reference interval (UL)

## Consistency check for Age-dependent Reference Intervals

### Guide:

**Tool for Plausibility Checks of Reference Interval Limits**

**Upload CSV File:**  
①  No file selected

Settings for the calculation of the zlog-value:  
② ☐ Replacement values for reference limits

**Select the sex:**  
③

Settings for the plot:  
④ **Select the lab parameter:**

⑤ ☐ Logarithmic scale for the x-axis

⑥ **Maximum absolute zlog value:**  
  
3 zlog values above 10 from these lab parameters:  
Direct Bilirubin, Gamma-Glutamyl Transferase,  
Immunoglobulin A

- Upload CSV File:** Upload own datasets with reference intervals
- Replacement values:** If the lower reference limit is zero, it will be set to 0.001 and the upper reference limit to 100 or by the given reference limits.

☒ Replacement values for reference limits  
**Replacement value for the lower reference limit:**  
  
**Replacement value for the upper reference limit:**

- Select the Sex:** Important for the plot
- Select the lab parameter:** Important for the plot
- Logarithmic scale for the x-axis:** Important for the plot
- Maximum zlog value:** Quick determination of very high zlog values

### Determination of the zlog values and analysis:

#### Table:

**Tool for Plausibility Checks of Reference Interval Limits**

**Upload CSV File:**  
 No file selected

Settings for the calculation of the zlog-value:  
☐ Replacement values for reference limits

**Select the sex:**

Settings for the plot:  
**Select the lab parameter:**

☐ Logarithmic scale for the x-axis

**Maximum absolute zlog value:**  
  
3 zlog values above 10 from these lab parameters: Direct Bilirubin,  
Gamma-Glutamyl Transferase, Immunoglobulin A

**Table** **Plot**

This Shiny App computes the zlog values of the preceding and the subsequent age group for each lab parameter. Zlog values far below -1.96 are in blue and far above 1.96 in red. The zlog value should be optimally between -1.96 and 1.96 and values above -4 or 4 should be checked and minimized by adding an additional age group with new calculated reference intervals. For further information please visit our [Website](#).

Code	Sex	Lower Limit	Upper Limit	Prev.lower zlog	Prev.upper zlog	Next.lower zlog	Next.upper zlog	Max.abs.zlog
Direct Bilirubin	AL	5.7	12.1	NA	NA	-12.186	-2.438	12.186
Direct Bilirubin	AL	0.8	5.2	2.152	3.729	-1.96	1.07	3.729
Direct Bilirubin	AL	0.8	3.4	-1.96	3.111	-1.96	3.005	3.111
Direct Bilirubin	AL	0.8	5	-1.96	1.135	-0.348	2.586	2.586
Direct Bilirubin	F	1.7	6.7	-4.114	1.123	-1.642	2.126	4.114
Direct Bilirubin	M	1.9	7.1	-2.291	1.788	NA	NA	2.291
Total Bilirubin	AL	3.3	283.8	NA	NA	-3.207	-0.846	3.207
Total Bilirubin	AL	0.8	11.7	0.111	6.619	-1.96	1.167	6.619
Total Bilirubin	AL	0.8	6.8	-1.96	2.954	-1.96	2.553	2.954
Total Bilirubin	AL	0.8	9.4	-1.96	1.445	-0.761	2.335	2.335
Total Bilirubin	AL	1.7	11.9	-3.478	1.485	-1.96	2.344	3.478
Total Bilirubin	AL	1.7	14.4	-1.96	1.61	NA	NA	1.96
Calcium	AL	2.13	2.74	NA	NA	-0.833	1.322	1.322
Calcium	AL	2.29	2.63	-4.011	3.12	NA	NA	4.011
Carbon Dioxide	AL	5	20	NA	NA	0	2.476	2.476

Table: Dataset with the zlog values

Showing 1 to 15 of 192 entries

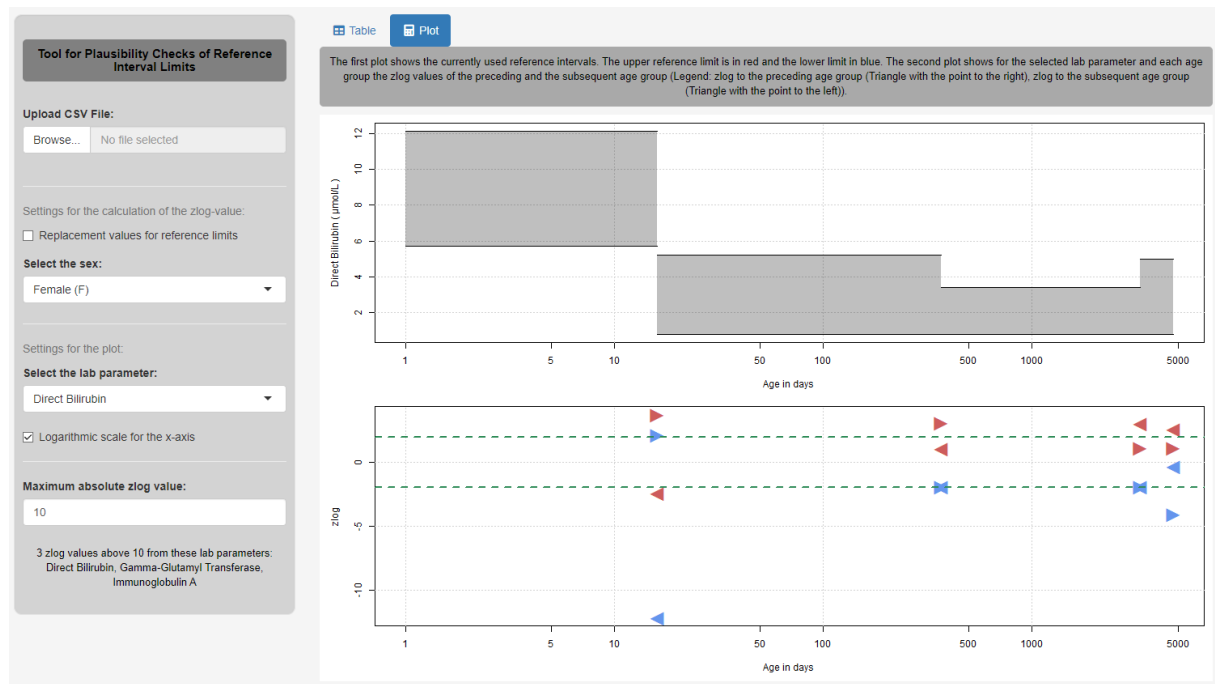
Previous      ...  Next

With the help of the table, find high zlog values and the appropriate laboratory parameters. These can be visualized in step 3. The table shows the zlog values. Zlog values under -1.96 in

## Consistency check for Age-dependent Reference Intervals

blue and above 1.96 in orange. The zlog value should be optimally between 1.96 and -1.96 in white.

Plot:



This Shiny App computes for each lab parameter and each age group the zlog values of the preceding and the subsequent age group. The first plot shows the currently used reference intervals. The second plot shows for the selected lab parameter and each age group the zlog values of the preceding and the subsequent age group (Legend: zlog to the preceding age group (Triangle with the point to the left), zlog to the subsequent age group (Triangle with the point to the right)). The zlog values should be optimally in the middle of the green lines between 1.96 and -1.96.