

# Global Burden of Disease

2023-08-16

Data source: <https://vizhub.healthdata.org/gbd-results/>

## Modeling the global burden of diseases

Objectives: I did some brainstorming and defined some objectives of the analysis a priori in “20230815\_globalHealth.docx” At this point I would generally state the objective as: Can we find some factors/interventions associated with certain diseases/countries that could be applied to other diseases/countries to lower death rates, or that need to be avoided in other diseases/countries to avoid rising death rates? These factors would not necessarily be within the GBD data. For example, I might find that disease X decreased in countries A,B,C from year 19XX, but remained stable in countries D,E. I could then try to research what happened in A,B,C, but not D,E around this time.

[Another simple question to start off with would be: Which disease has a high death rate but also examples (e.g. certain countries, age groups, sex) where it has already declined a lot?]

Change log: In the first version some locations were represented by multiple ‘regions’; here I use data in which only one classification of 21 mutually exclusive regions is used

## Clean and load libraries

```
rm(list=ls())  
cat('\014')
```

```
graphics.off()

wd= getwd()

library('rjags')
library('tidyverse')
library('data.table')
library('gplots')
library('stringr')
library('reshape2')
library('zoo')
library('ggpubr')
library('ggnewscale')
library('dtw') #time series clustering
library('formatR')
source('./DBDA2E-utilities_mod.R') #modified to fit markdown
```

## Data import and cleaning

Obtain a file that contains all years only for “Tuberculosis”, “HIV/AIDS”, “Zika virus”  
(see ‘readme’ for exact parameter specifications)

```
allTime_HTZ_Deaths = read.csv("./20230823_Deaths_HTZ_21reg_MF_5year/IHME-GBD_2019_DATA-afd4b08e-1.csv",
  stringsAsFactors = TRUE) #HTZ= 'Tuberculosis', 'HIV/AIDS', 'Zika virus'
# limit to metric== 'Percent' and remove 'Number'
allTime_HTZ_Deaths = allTime_HTZ_Deaths[allTime_HTZ_Deaths$metric ==
  "Percent", ]

allTime_HTZ_PrevInci = read.csv("./20230907_PrevInci_HTZ_21reg_MF_5year/IHME-GBD_2019_DATA-cacc055a-1.csv",
  stringsAsFactors = TRUE)

allTime_HTZ = rbind.data.frame(allTime_HTZ_Deaths,
  allTime_HTZ_PrevInci)
```

Check data for completeness

```
unique(allTime_HTZ$age)
```

```
## [1] 95+ years 0-6 days 7-27 days 28-364 days 1-4 years 5-9 years
## [7] 10-14 years 15-19 years 20-24 years 25-29 years 30-34 years 35-39 years
## [13] 40-44 years 45-49 years 50-54 years 55-59 years 60-64 years 65-69 years
## [19] 70-74 years 75-79 years 80-84 85-89 90-94
## 23 Levels: 0-6 days 1-4 years 10-14 years 15-19 years ... 95+ years
```

Apparently the “age” column has entry “80-84” instead of “80-84 years” and two other such cases. -> Correct them.

```
levels(allTime_HTZ$age)[levels(allTime_HTZ$age)=='80-84'] = '80-84 years'
levels(allTime_HTZ$age)[levels(allTime_HTZ$age)=='85-89'] = '85-89 years'
levels(allTime_HTZ$age)[levels(allTime_HTZ$age)=='90-94'] = '90-94 years'
levels(allTime_HTZ$age)
```

```
## [1] "0-6 days"      "1-4 years"      "10-14 years"    "15-19 years"    "20-24 years"
## [6] "25-29 years"    "28-364 days"    "30-34 years"    "35-39 years"    "40-44 years"
## [11] "45-49 years"    "5-9 years"      "50-54 years"    "55-59 years"    "60-64 years"
## [16] "65-69 years"    "7-27 days"      "70-74 years"    "75-79 years"    "80-84 years"
## [21] "85-89 years"    "90-94 years"    "95+ years"
```

Not all ages are in 5-year intervals -> remove the ones that are not

```
unique(allTime_HTZ$age[ str_detect(allTime_HTZ$age, '[0-9]+--[0-9]+ years') ] ) #check
```

```
## [1] 1-4 years  5-9 years  10-14 years 15-19 years 20-24 years 25-29 years
## [7] 30-34 years 35-39 years 40-44 years 45-49 years 50-54 years 55-59 years
## [13] 60-64 years 65-69 years 70-74 years 75-79 years 80-84 years 85-89 years
## [19] 90-94 years
## 23 Levels: 0-6 days 1-4 years 10-14 years 15-19 years ... 95+ years
```

```
allTime_HTZ= allTime_HTZ[ str_detect(allTime_HTZ$age, '[0-9]+--[0-9]+ years'), ]
```

All location - cause combinations should have 30 years -> check that this is the case

```
cause_location_tab= allTime_HTZ %>%
  filter(measure=='Deaths' & sex=='Male' & age=='30-34 years' ) %>%
  group_by(cause,location) %>%
  summarise(count= n_distinct(year),.groups='drop')

all(cause_location_tab$count == 30)
```

```
## [1] TRUE
```

Apparently causes which do not have any deaths do not list the “Deaths” measure -> remove causes for which not all three measures are listed

```
incomplete_causes= c()
for (ca in unique(allTime_HTZ$cause)){
  len= length(unique(allTime_HTZ$measure[allTime_HTZ$cause==ca]))
  if(len != 3){
    incomplete_causes= c(incomplete_causes,ca)
  }
}
allTime_HTZ= allTime_HTZ[! allTime_HTZ$cause %in% incomplete_causes,]

dim(allTime_HTZ)
```

```
## [1] 215460      10
```

```
str(allTime_HTZ)
```

```
## 'data.frame': 215460 obs. of 10 variables:
## $ measure : Factor w/ 3 levels "Deaths","Incidence",...: 1 1 1 1 1 1 1 1 1 1 ...
## $ location: Factor w/ 21 levels "Andean Latin America",...: 4 4 4 4 4 4 4 4 4 4 ...
```

```
## $ sex      : Factor w/ 2 levels "Female","Male": 2 1 2 1 2 1 2 1 2 1 ...
## $ age      : Factor w/ 23 levels "0-6 days","1-4 years",...: 2 2 12 12 3 3 4 4 5 5 ...
## $ cause    : Factor w/ 3 levels "HIV/AIDS","Tuberculosis",...: 3 3 3 3 3 3 3 3 3 3 ...
## $ metric   : Factor w/ 2 levels "Number","Percent": 2 2 2 2 2 2 2 2 2 2 ...
## $ year     : int   1991 1991 1991 1991 1991 1991 1991 1991 1991 1991 ...
## $ val      : num   0 0 0 0 0 0 0 0 0 0 ...
## $ upper    : num   0 0 0 0 0 0 0 0 0 0 ...
## $ lower    : num   0 0 0 0 0 0 0 0 0 0 ...
```

Check the cleaned data once more.

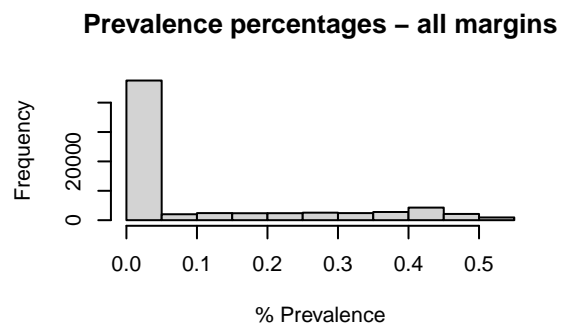
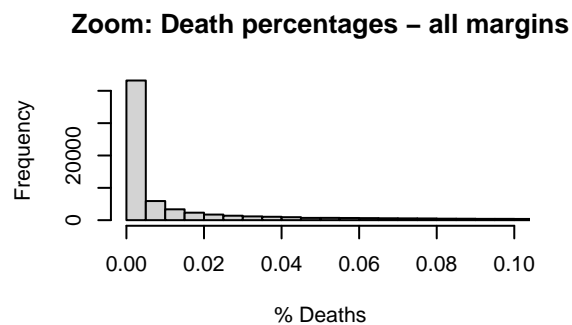
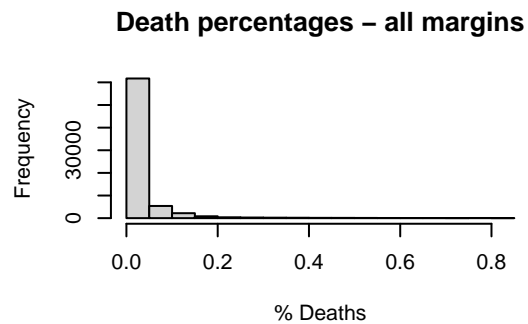
```
head(allTime_HTZ)
```

```
##      measure      location    sex      age      cause  metric year val upper
## 19 Deaths Central Asia   Male   1-4 years Zika virus Percent 1991  0      0
## 20 Deaths Central Asia Female 1-4 years Zika virus Percent 1991  0      0
## 23 Deaths Central Asia   Male   5-9 years Zika virus Percent 1991  0      0
## 24 Deaths Central Asia Female 5-9 years Zika virus Percent 1991  0      0
## 27 Deaths Central Asia   Male 10-14 years Zika virus Percent 1991  0      0
## 28 Deaths Central Asia Female 10-14 years Zika virus Percent 1991  0      0
##      lower
## 19      0
## 20      0
## 23      0
## 24      0
## 27      0
## 28      0
```

## Overview of death and prevalence rates

Display as counts over the various locations, sex, age groups, causes and years

```
par(mfrow = c(3, 1))
hist(allTime_HTZ$val[allTime_HTZ$measure == "Deaths"],
     main = "Death percentages - all margins", xlab = "% Deaths")
hist(allTime_HTZ$val[allTime_HTZ$measure == "Deaths"],
     xlim = c(0, 0.1), breaks = 200, main = "Zoom: Death percentages - all margins",
     xlab = "% Deaths")
hist(allTime_HTZ$val[allTime_HTZ$measure == "Prevalence"],
     main = "Prevalence percentages - all margins",
     xlab = "% Prevalence")
```



```
par(mfrow = c(1, 1))
```

Non-zero death rates for the selected causes are apparently mainly in the region  $< 0.01\%$ ; much higher prevalence rates ( $\sim 0.4\%$ ) are observed.

## Age- & sex- independent analysis

Simplify data: Average percentages over all age groups for location-cause-year combination

```
allTime_HTZ_asi= data.frame( allTime_HTZ %>%      #asi= age-, sex- independent
  group_by(measure,location,cause,year) %>%
  summarize(val= mean(val),.groups='drop') )
head(allTime_HTZ_asi)
```

```
##   measure      location  cause year      val
```

```
## 1 Deaths Andean Latin America HIV/AIDS 1990 0.004760393
## 2 Deaths Andean Latin America HIV/AIDS 1991 0.005558544
## 3 Deaths Andean Latin America HIV/AIDS 1992 0.006581146
## 4 Deaths Andean Latin America HIV/AIDS 1993 0.007625122
## 5 Deaths Andean Latin America HIV/AIDS 1994 0.008771679
## 6 Deaths Andean Latin America HIV/AIDS 1995 0.009228276
```

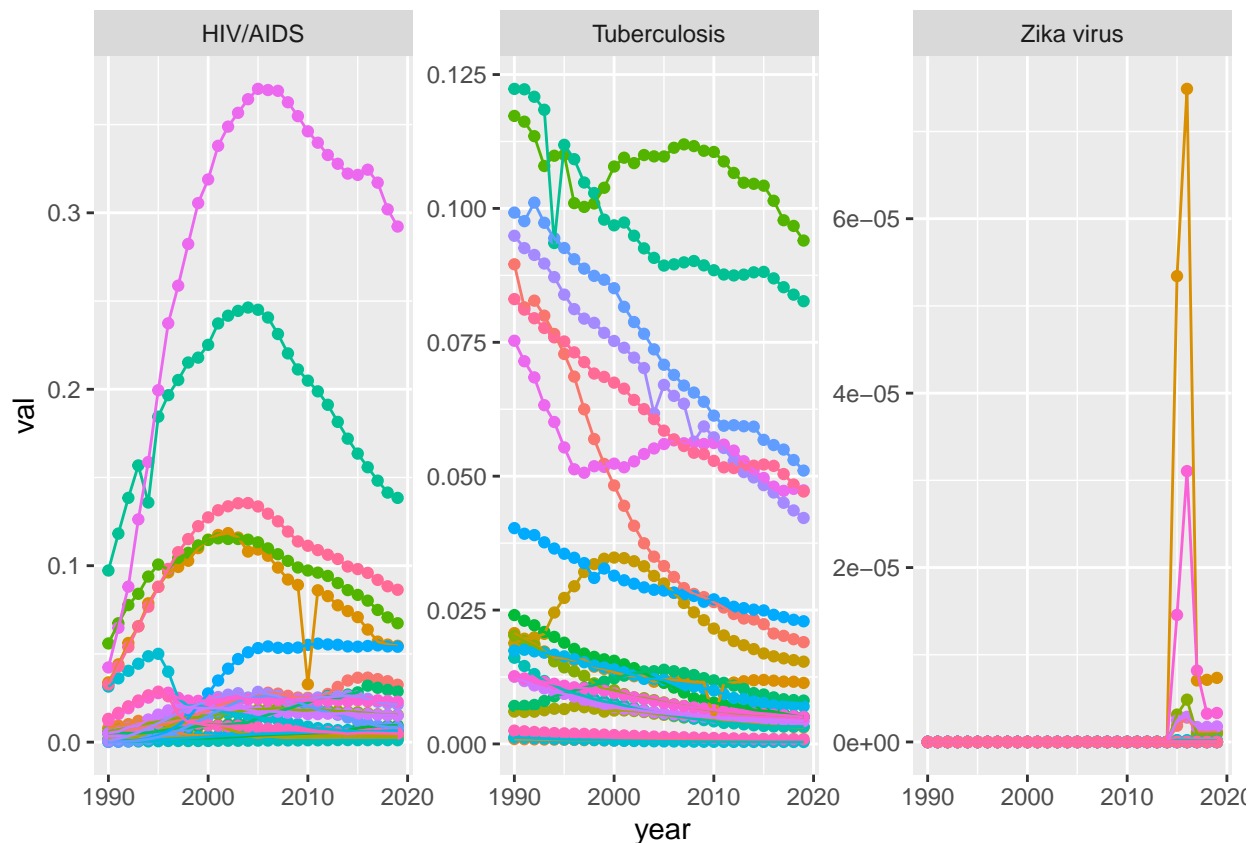
```
dim(allTime_HTZ_asi)
```

```
## [1] 5670    5
```

Visualize death rates

```
allTime_HTZ_asi_D= allTime_HTZ_asi %>%
  filter(measure=='Deaths')

ggplot(data=allTime_HTZ_asi_D,mapping=aes(x=year,y=val,group=location,color=location))+
  geom_point()+
  geom_line()+
  facet_wrap(~cause,scales='free_y')+
  guides(color='none')
```



First impression:

- For countries with highest HIV/AIDS death rates: HIV/AIDS death rates rises till about year 2000-2005, then steady decline

- some HIV outliers that need to be investigated: data entry error or really some factor that lowered death rates
- In most countries, tuberculosis is steadily declining, but in some there appears to be outbreak
- Zika is only observed in recent years and has high death rates only in few locations

Are there locations that did not have any Zika case?

```
allTime_HTZ_asi_D_sums= allTime_HTZ_asi_D %>%
  group_by(location,cause) %>%
  summarize(sumPerc= sum(val),.groups='drop')

allTime_HTZ_asi_D_sums[allTime_HTZ_asi_D_sums$sumPerc==0,]
```

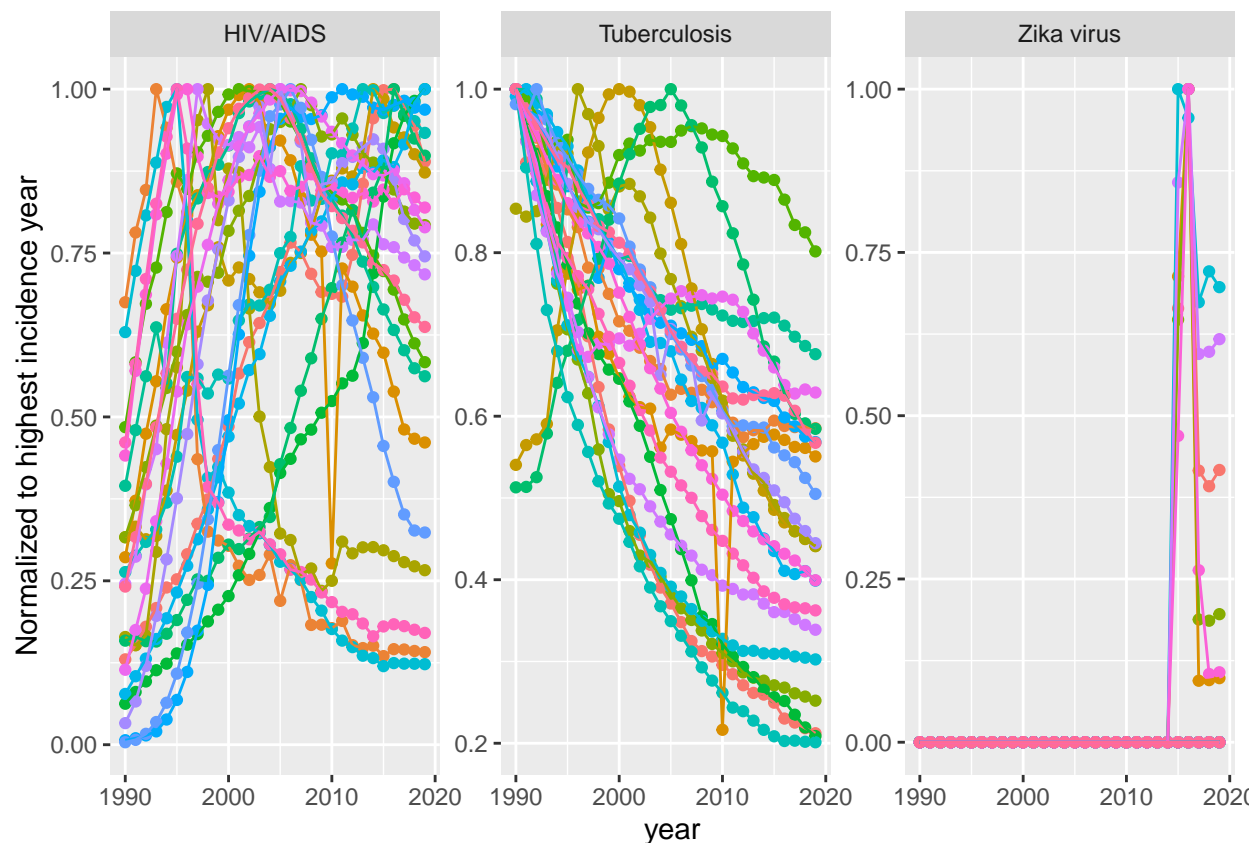
```
## # A tibble: 15 x 3
##   location      cause      sumPerc
##   <fct>         <fct>      <dbl>
## 1 Australasia   Zika virus    0
## 2 Central Asia   Zika virus    0
## 3 Central Europe Zika virus    0
## 4 Central Sub-Saharan Africa Zika virus    0
## 5 East Asia      Zika virus    0
## 6 Eastern Europe Zika virus    0
## 7 Eastern Sub-Saharan Africa Zika virus    0
## 8 High-income Asia Pacific Zika virus    0
## 9 North Africa and Middle East Zika virus    0
## 10 Oceania       Zika virus    0
## 11 South Asia     Zika virus    0
## 12 Southeast Asia Zika virus    0
## 13 Southern Sub-Saharan Africa Zika virus    0
## 14 Western Europe Zika virus    0
## 15 Western Sub-Saharan Africa Zika virus    0
```

15 locations did not have any case of Zika

Normalize to max. percentages to get a clearer picture of dynamics in low incidence locations

```
allTime_HTZ_asi_D_norm = allTime_HTZ_asi_D %>%
  group_by(location, cause) %>%
  mutate(val_maxNorm = val/ifelse(max(val) > 0, max(val),
    1)) %>%
  ungroup()

ggplot(data = allTime_HTZ_asi_D_norm, mapping = aes(x = year,
  y = val_maxNorm, group = location, color = location)) +
  geom_point() + geom_line() + scale_y_continuous(name = "Normalized to highest incidence year") +
  facet_wrap(~cause, scales = "free_y") + guides(color = "none")
```




---

[ To be added: Outlier investigation For some points it is obvious that they are outliers as they break the otherwise “smooth appearance” of the curve; In most cases these may just be data entry problems, but in some something might have occurred that lead to a vastly different death rate. To find outliers, check the deviation of each actual point from the average of two points to the left and two to the right.

```
r a= c(2,0,1,2,6)
zoo::rollapply(a,width=5,FUN=function(x){mean(c(x[1],x[2],x[4],x[5]))},align='center')
## [1] 2.5 ]
```

---

The time behavior of death rates for HIV/AIDS and Tuberculosis differs widely between locations; 1. I will first summarize curves into a few parameters. This will facilitate comparison and processing more data 2. I will cluster curves based on the full data

Questions:

- How do death rates relate to prevalence/incidence rate of the same disease at the same location?
- Do countries within the same region behave similarly? Which are outliers?
- Can I find common features among groups with similar curves?

## Two-line model

Fit a “two-line model” with linear combination of increasing and a decreasing slope. Both assume 0th-order kinetics; increase starts (from baseline value) at the first time point (1990); decrease can start at any time point from 1990. See “20230905\_twoLine\_model.html/.Rmd” for evaluation of the model.

Fit parameters  $b_0$  (baseline at 1990),  $b_1$  (increasing slope),  $b_2$  (decreasing slope) and  $t_0$  (time point at which



decrease starts) via a Bayesian model. Report b1 and b2 if they are part of the best model (i.e. better than the model where at least one of them is excluded); report t0 if b2 is part of the best model.

$$\mu(t) = b_0 + b_1 * t, t < t_0$$

$$\mu(t) = b_0 + b_1 * t + b_2 * t, t \geq t_0$$

Due to its special nature (only very recent appearance; only in few locations) ignore Zika from this point on.

```
source("./20230912_twoLine_inclFac_fit.R")

allTime_HT_asi = allTime_HTZ_asi[allTime_HTZ_asi$cause %in%
  c("HIV/AIDS", "Tuberculosis"), ]
# allTime_HT_asi_D=
# allTime_HT_asi[allTime_HT_asi$measure=='Deaths',]
groupedDF = allTime_HT_asi %>%
  group_by(location, cause, measure) %>%
  summarize(n(), .groups = "drop")
dim(groupedDF) #126 combinations

## [1] 126 4

head(allTime_HT_asi)

##   measure      location      cause year      val
## 1 Deaths Andean Latin America HIV/AIDS 1990 0.004760393
## 2 Deaths Andean Latin America HIV/AIDS 1991 0.005558544
## 3 Deaths Andean Latin America HIV/AIDS 1992 0.006581146
## 4 Deaths Andean Latin America HIV/AIDS 1993 0.007625122
## 5 Deaths Andean Latin America HIV/AIDS 1994 0.008771679
## 6 Deaths Andean Latin America HIV/AIDS 1995 0.009228276

# groupedDF= groupedDF[groupedDF$location %in%
# c('Andean Latin America', 'Eastern
# Europe', 'South Asia'),] ### only temporary

if (!file.exists("./20230914_MCMCcoefs.csv")) {
  # execute only if not yet done
  MCMCcoefs_DF = data.frame(matrix(NA, nrow = dim(groupedDF)[1],
    ncol = 7))
  colnames(MCMCcoefs_DF) = c("location", "cause",
    "measure", "b0_median", "b1_median", "b2_median",
    "t_inflec_median")
  MCMCcoefs_DF$location <- factor(MCMCcoefs_DF$location,
    levels = levels(groupedDF$location))
  MCMCcoefs_DF$cause <- factor(MCMCcoefs_DF$cause,
    levels = levels(groupedDF$cause))
  MCMCcoefs_DF$measure <- factor(MCMCcoefs_DF$measure,
    levels = levels(groupedDF$measure))

  for (i in 1:dim(groupedDF)[1]) {
    print(paste(i, "of", dim(groupedDF)[1]))
    currDF = allTime_HT_asi[allTime_HT_asi$location ==
```

```

        groupedDF$location[i] & allTime_HT_asi$cause ==
        groupedDF$cause[i] & allTime_HT_asi$measure ==
        groupedDF$measure[i], ]
mcmcDF_orig = twoLine_fit(t = currDF$year,
                          y = currDF$val)

# There are two coefficients (b1, b2)
# that each can either be present of
# absent as indicated by indicator
# factors
mcmcDF_orig$iF1 = factor(mcmcDF_orig$iF1, levels = c(0,
1)) #to make sure both levels are listed even if only one observed
mcmcDF_orig$iF2 = factor(mcmcDF_orig$iF2, levels = c(0,
1))
tab2Way = data.table(table(cbind.data.frame(iF1 = mcmcDF_orig$iF1,
iF2 = mcmcDF_orig$iF2)))
# find the most frequent combination of
# indicator factors -> the best model
iF1_best = tab2Way$iF1[tab2Way$N == max(tab2Way$N)]
iF2_best = tab2Way$iF2[tab2Way$N == max(tab2Way$N)]

# Reduce to MCMC output of the best model
mcmcDF = mcmcDF_orig[mcmcDF_orig$iF1 == iF1_best &
mcmcDF_orig$iF2 == iF2_best, ]
if (iF1_best == 0 | iF2_best == 0) {
  mcmcDF$t0 = NA
}

# Analysis could be extended by cases
# cross-informing each other (e.g.
# countries from same region)

MCMCcoefs_DF$location[i] = groupedDF$location[i]
MCMCcoefs_DF$cause[i] = groupedDF$cause[i]
MCMCcoefs_DF$measure[i] = groupedDF$measure[i]
MCMCcoefs_DF$b0_median[i] = median(mcmcDF$b0)
MCMCcoefs_DF$b1_median[i] = median(mcmcDF$b1)
MCMCcoefs_DF$b2_median[i] = median(mcmcDF$b2)
MCMCcoefs_DF$t_inflec_median[i] = median(mcmcDF$t0) #may be NA
}

# write output so you do not need to run this
# code every time
write.csv(MCMCcoefs_DF, "./20230914_MCMCcoefs.csv",
row.names = FALSE)
} else {
  MCMCcoefs_DF = read.csv("./20230914_MCMCcoefs.csv",
stringsAsFactors = TRUE)
}
str(MCMCcoefs_DF)

## 'data.frame': 126 obs. of 7 variables:
## $ location : Factor w/ 21 levels "Andean Latin America",...: 1 1 1 1 1 1 2 2 2 2 ...

```

```
## $ cause      : Factor w/ 2 levels "HIV/AIDS","Tuberculosis": 1 1 1 2 2 2 1 1 1 2 ...
## $ measure    : Factor w/ 3 levels "Deaths","Incidence",...: 1 2 3 1 2 3 1 2 3 1 ...
## $ b0_median  : num  0.005725 0.000013 0.00029 0.076575 0.000394 ...
## $ b1_median  : num  1.12e-03 4.84e-07 5.62e-05 0.00 0.00 ...
## $ b2_median  : num  0.00 0.00 0.00 -2.46e-03 -1.13e-05 ...
## $ t_inflec_median: num  NA NA NA NA NA NA NA NA NA NA ...
```

```
dim(MCMCcoefs_DF)
```

```
## [1] 126 7
```

Looking at the estimated coefficients

```
print(paste("Estimates for", dim(MCMCcoefs_DF)[1],
"settings."))
```

```
## [1] "Estimates for 126 settings."
```

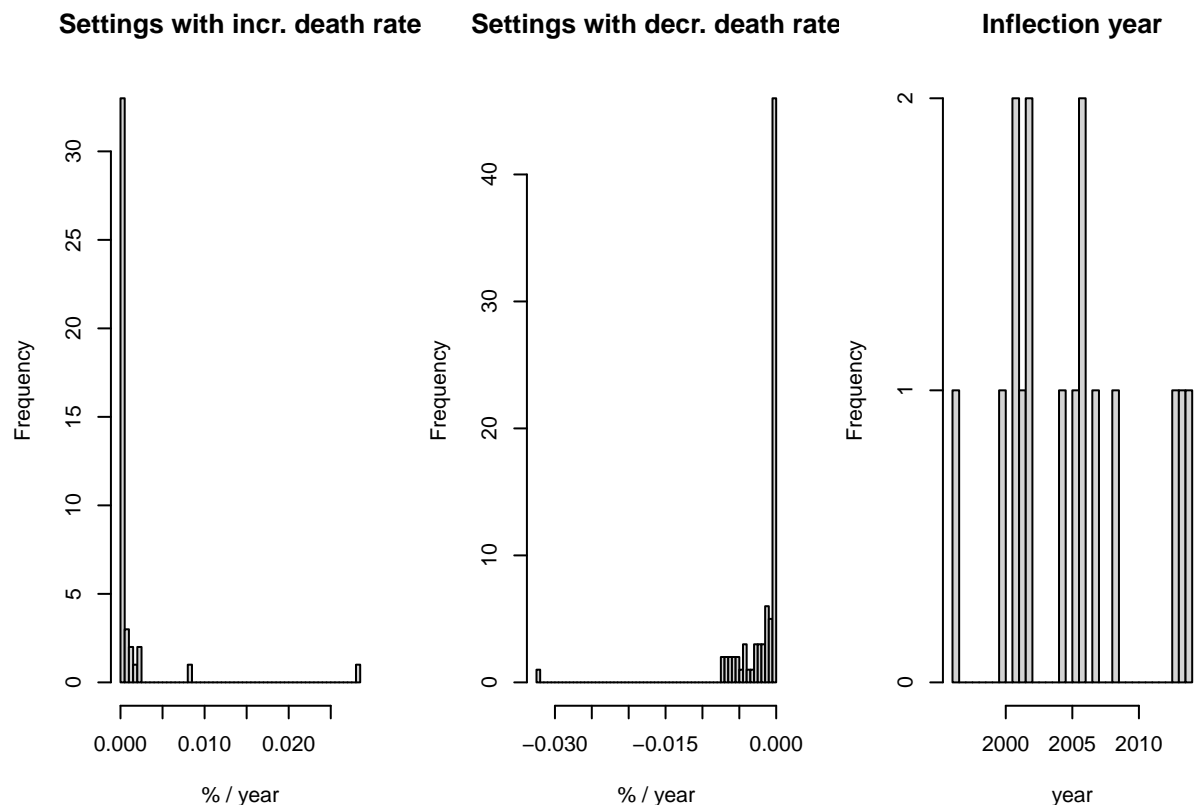
```
print(paste(sum(MCMCcoefs_DF$b1_median > 0), "with increase in death rate."))
```

```
## [1] "43 with increase in death rate."
```

```
print(paste(sum(MCMCcoefs_DF$b2_median < 0), "with decrease in death rate."))
```

```
## [1] "83 with decrease in death rate."
```

```
par(mfrow = c(1, 3))
hist(MCMCcoefs_DF$b1_median[MCMCcoefs_DF$b1_median >
0], breaks = 50, main = "Settings with incr. death rate",
xlab = "% / year")
hist(MCMCcoefs_DF$b2_median[MCMCcoefs_DF$b2_median <
0], breaks = 50, main = "Settings with decr. death rate",
xlab = "% / year")
hist(MCMCcoefs_DF$t_inflec_median, breaks = 50, main = "Inflection year",
xlab = "year")
```



[to do: change from % to cases/10 000]

```
#
#out.width=c('500px','300px','500px')
#out.width=c('100%','100%','100%')
#R, fig.width=10, fig.height=7

MCMCcoefs_DF$b0_median= as.numeric(MCMCcoefs_DF$b0_median)
MCMCcoefs_DF$b1_median= as.numeric(MCMCcoefs_DF$b1_median)
MCMCcoefs_DF$b2_median= as.numeric(MCMCcoefs_DF$b2_median)
MCMCcoefs_DF$t_inflec_median= as.numeric(MCMCcoefs_DF$t_inflec_median)
str(MCMCcoefs_DF)

## 'data.frame': 126 obs. of 7 variables:
## $ location : Factor w/ 21 levels "Andean Latin America",...: 1 1 1 1 1 1 2 2 2 2 ...
## $ cause : Factor w/ 2 levels "HIV/AIDS","Tuberculosis": 1 1 1 2 2 2 1 1 1 2 ...
## $ measure : Factor w/ 3 levels "Deaths","Incidence",...: 1 2 3 1 2 3 1 2 3 1 ...
## $ b0_median : num 0.005725 0.000013 0.00029 0.076575 0.000394 ...
## $ b1_median : num 1.12e-03 4.84e-07 5.62e-05 0.00 0.00 ...
## $ b2_median : num 0.00 0.00 0.00 -2.46e-03 -1.13e-05 ...
## $ t_inflec_median: num NA NA NA NA NA NA NA NA NA NA ...

ggplot(data=allTime_HT_asi[ allTime_HT_asi$cause=='HIV/AIDS', ],
  mapping=aes(x=year,y=val,group=measure,color=measure))+
  geom_line()+
  ggtitle('HIV/AIDS')+
```

```

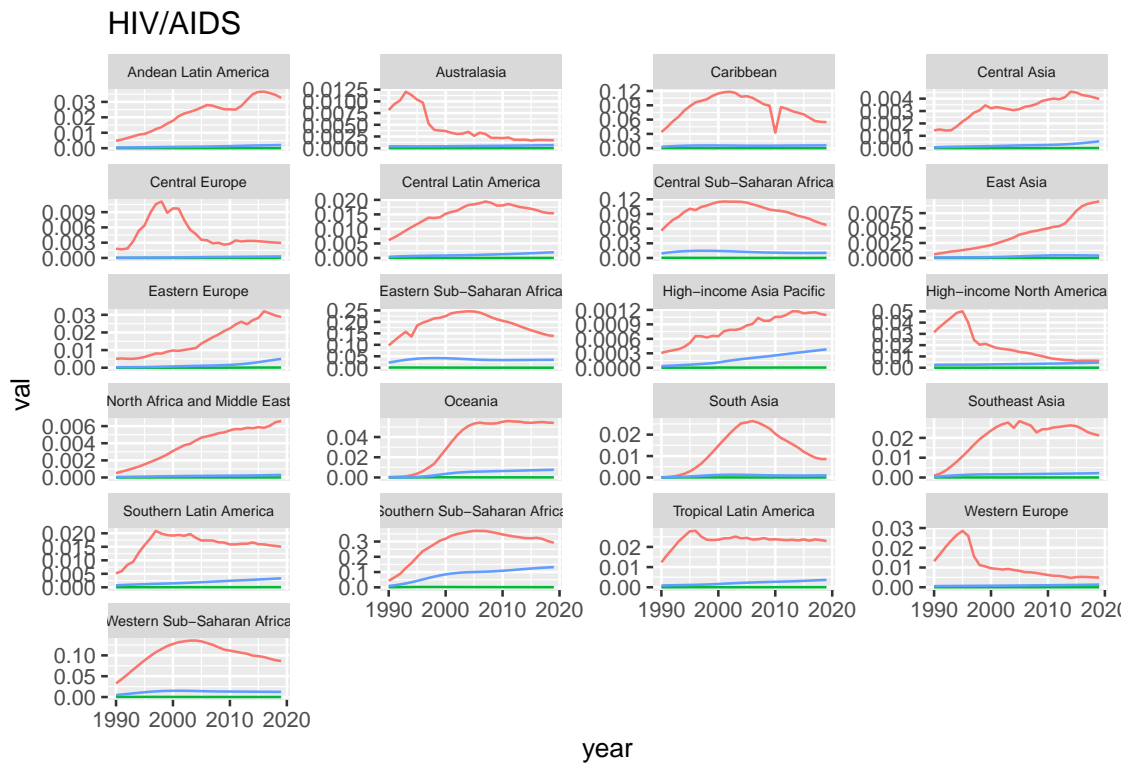
guides(color="none")+
facet_wrap(vars(location),ncol=4,scales='free_y')+ #look at both fixed and free y
theme(strip.text.x=element_text(size=6))

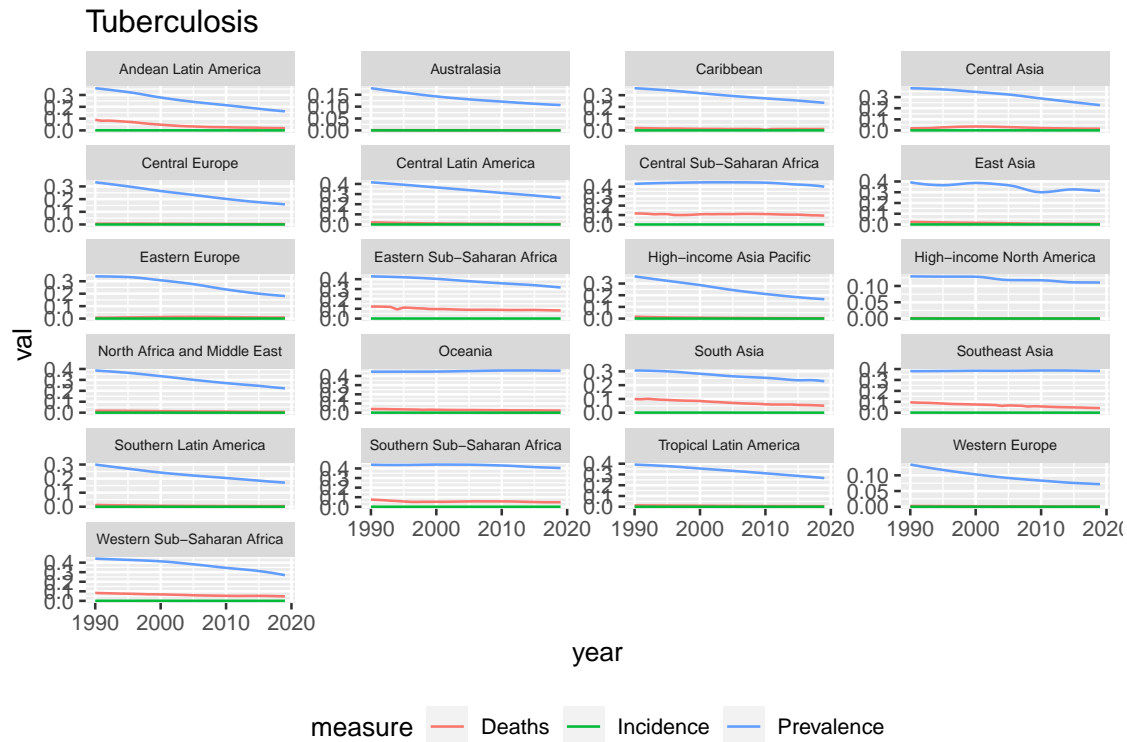
# leg= ggpubr::get_legend(ggplot(data=allTime_HT_asi[ allTime_HT_asi$cause=='HIV/AIDS', ],
#                               mapping=aes(x=year,y=val,group=measure,color=measure))+
#                               geom_line())

ggplot(data=allTime_HT_asi[ allTime_HT_asi$cause=='Tuberculosis', ],
       mapping=aes(x=year,y=val,group=measure,color=measure))+
geom_line()+
ggtitle('Tuberculosis')+
#guides(color="none")+
facet_wrap(vars(location),ncol=4,scales='free_y')+ # look at both fixed and free y
theme(strip.text.x=element_text(size=6),legend.position = 'bottom')

# leg= ggpubr::get_legend(ggplot(data=allTime_HT_asi[ allTime_HT_asi$cause=='HIV/AIDS', ],
#                               mapping=aes(x=year,y=val,group=measure,color=measure))+
#                               geom_line() )
# as_ggplot(leg)

```





Observations:

HIV/AIDS:

*in the countries with high death rates (Sub-Saharan Africa, Caribbean, Oceania), there is an inflection point ~2000-2005; from this point on, rates decrease in Sub-Saharan Africa and Caribbean and are stable in Oceania the death rate is above prevalence in all regions -> this needs to be clarified: how can more people die from a disease than have the disease?; how were prevalence data collected? the dynamics in lower death rate regions, vary but most seem to have an inflection point within the 1990-2019 period; in regions with very low death rate, the death rate is still rising (e.g. Central Asia, Western Europe) prevalence is generally rising or stable; incidences are close to 0 everywhere*

Tuberculosis:

*the dynamics are quite different from HIV/AIDS prevalence is higher than death rate in all regions prevalence is generally declining or stable death rate is generally declining from first recording on \*there appears to be pos. correlation between prevalence and death rate, but with exceptions (e.g. countries with high prevalence and very low deaths) -> follow up on*

---

How meaningful are prevalence (and incidence) rates? Possible scenarios:

*prevalence is tested in random sample; death rates should also be from random samples or all deaths recorded all serious cases of the disease (the ones that may lead to death) are recorded -> probably true for countries with decent healthcare system \*for each death it is determined if it was due to the cause of interest -> depends on environment (e.g. autopsies at unknown cause of death?) and disease manifestation (obvious signs of the disease?)*

---

## Summary of dynamics

Summarize the dynamics via coefficients  $b_0$  (level around 1990),  $b_1$  (increase rate),  $b_2$  (decline rate) and  $t_0$  (inflection point)

```
MCMCcoefs_DF$loc_cause = paste(MCMCcoefs_DF$location,
  MCMCcoefs_DF$cause, sep = ", ")
str(MCMCcoefs_DF)
```

```
## 'data.frame': 126 obs. of 8 variables:
## $ location : Factor w/ 21 levels "Andean Latin America",...: 1 1 1 1 1 1 2 2 2 2 ...
## $ cause : Factor w/ 2 levels "HIV/AIDS","Tuberculosis": 1 1 1 2 2 2 1 1 1 2 ...
## $ measure : Factor w/ 3 levels "Deaths","Incidence",...: 1 2 3 1 2 3 1 2 3 1 ...
## $ b0_median : num 0.005725 0.000013 0.00029 0.076575 0.000394 ...
## $ b1_median : num 1.12e-03 4.84e-07 5.62e-05 0.00 0.00 ...
## $ b2_median : num 0.00 0.00 0.00 -2.46e-03 -1.13e-05 ...
## $ t_inflec_median: num NA NA NA NA NA NA NA NA NA NA ...
## $ loc_cause : chr "Andean Latin America, HIV/AIDS" "Andean Latin America, HIV/AIDS" "Andean L
```

```
# pivot:
MCMCcoefs_wide = pivot_wider(data = MCMCcoefs_DF, id_cols = c("loc_cause",
  "location", "cause"), names_from = c("measure"),
  values_from = c("b0_median", "b1_median", "b2_median",
    "t_inflec_median"))

# manually sorted:
MCMCcoefs_DF_NA = MCMCcoefs_wide[is.na(MCMCcoefs_wide$t_inflec_median_Deaths),
  ] #no inflection point
MCMCcoefs_DF_noNA = MCMCcoefs_wide[!is.na(MCMCcoefs_wide$t_inflec_median_Deaths),
  ] #with inflection point

# out of the data that do not have inflection
# year, get the ones that have decline
MCMCcoefs_DF_NA_decl = MCMCcoefs_DF_NA[MCMCcoefs_DF_NA$b2_median_Deaths !=
  0, ]
MCMCcoefs_DF_NA_nodecl = MCMCcoefs_DF_NA[MCMCcoefs_DF_NA$b2_median_Deaths ==
  0, ]

# sort data with declining death rate (but no
# inflection) by decline of death rate
ord1 = order(MCMCcoefs_DF_NA_decl$b2_median_Deaths)
# sort data with inflection by inflection year
ord2 = order(MCMCcoefs_DF_noNA$t_inflec_median_Deaths) +
  max(c(0, ord1)) #start after ord1
# sort data without declining death rate by
# increase in death rate
ord3 = order(MCMCcoefs_DF_NA_nodecl$b1_median_Deaths) +
  max(c(0, ord2)) #start after ord2

# order factor levels of 'loc_cause'
MCMCcoefs_patchw = rbind.data.frame(MCMCcoefs_DF_NA_decl,
  MCMCcoefs_DF_noNA, MCMCcoefs_DF_NA_nodecl)
ord = c(ord1, ord2, ord3)
MCMCcoefs_patchw$loc_cause = factor(MCMCcoefs_patchw$loc_cause,
  ordered = TRUE, levels = MCMCcoefs_patchw$loc_cause[ord])

DrD_melt = melt(MCMCcoefs_patchw, id.vars = c("loc_cause",
  "location", "cause"), measure.vars = c("b0_median_Deaths",
```

```

    "b1_median_Deaths", "b2_median_Deaths", "t_inflec_median_Deaths",
    "b0_median_Prevalence", "b1_median_Prevalence",
    "b2_median_Prevalence"))
# drop Incidence (very
# low): 'b0_median_Incidence',
# 'b1_median_Incidence', 'b2_median_Incidence', 't_inflec_median_Incidence'
# drop inflection of prevalence (very few
# observed): , 't_inflec_median_Prevalence'
str(DrD_melt)

```

```

## 'data.frame':   294 obs. of  5 variables:
## $ loc_cause: Ord.factor w/ 42 levels "Andean Latin America, Tuberculosis"<...: 1 16 23 18 8 20 12 4 ...
## $ location : Factor w/ 21 levels "Andean Latin America",...: 1 2 2 3 4 5 6 7 8 10 ...
## $ cause     : Factor w/ 2 levels "HIV/AIDS","Tuberculosis": 2 1 2 2 2 2 2 2 2 ...
## $ variable  : Factor w/ 7 levels "b0_median_Deaths",...: 1 1 1 1 1 1 1 1 1 ...
## $ value     : num  0.076575 0.00822 0.000799 0.016243 0.028248 ...

```

```

DrD_melt$coefType = rep("rate", dim(DrD_melt)[1])
DrD_melt$coefType[DrD_melt$variable %in% c("b0_median_Deaths",
    "b0_median_Prevalence", "b0_median_Incidence")] = "basel."
DrD_melt$coefType[DrD_melt$variable %in% c("t_inflec_median_Deaths",
    "t_inflec_median_Prevalence", "t_inflec_median_Incidence")] = "year"
head(DrD_melt)

```

```

##           loc_cause           location      cause
## 1 Andean Latin America, Tuberculosis Andean Latin America Tuberculosis
## 2           Australasia, HIV/AIDS           Australasia      HIV/AIDS
## 3           Australasia, Tuberculosis           Australasia Tuberculosis
## 4           Caribbean, Tuberculosis           Caribbean Tuberculosis
## 5           Central Asia, Tuberculosis           Central Asia Tuberculosis
## 6           Central Europe, Tuberculosis           Central Europe Tuberculosis
##           variable      value coefType
## 1 b0_median_Deaths 0.0765746093   basel.
## 2 b0_median_Deaths 0.0082204252   basel.
## 3 b0_median_Deaths 0.0007991389   basel.
## 4 b0_median_Deaths 0.0162433765   basel.
## 5 b0_median_Deaths 0.0282482063   basel.
## 6 b0_median_Deaths 0.0063972962   basel.

```

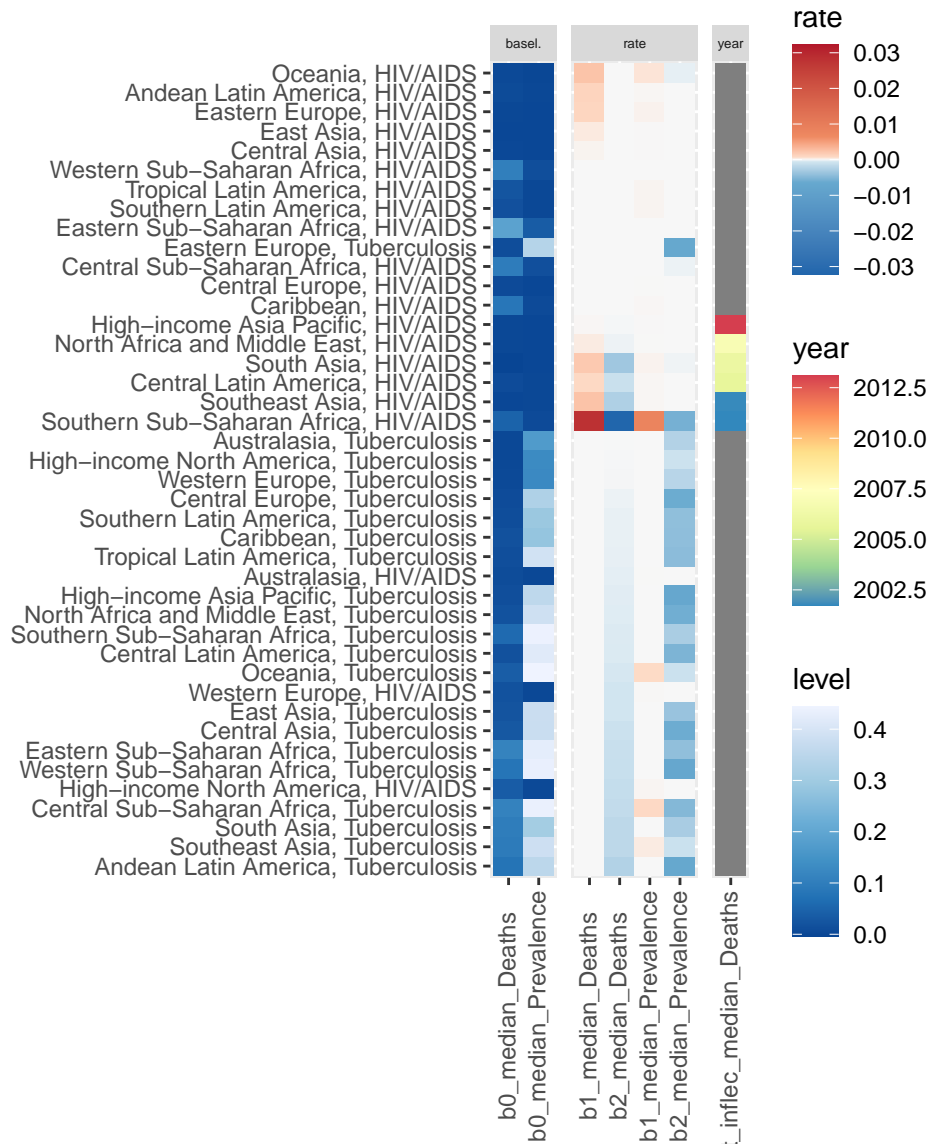
```

ggplot() + geom_tile(data = DrD_melt[DrD_melt$coefType ==
    "rate", ], aes(x = variable, y = loc_cause, fill = value)) +
    scale_fill_distiller(type = "seq", palette = "RdBu",
        limits = c(-max(abs(DrD_melt$value[DrD_melt$coefType ==
            "rate"])) , max(abs(DrD_melt$value[DrD_melt$coefType ==
            "rate"]))), values = c(0, 0.4, 0.49, 0.5,
            0.51, 0.6, 1), guide = guide_colorbar(title.position = "top"),
        name = "rate") + ggnewscale::new_scale_fill() +
    geom_tile(data = DrD_melt[DrD_melt$coefType ==
        "basel.", ], aes(x = variable, y = loc_cause,
            fill = value)) + scale_fill_distiller(type = "seq",
        palette = "Blues", guide = guide_colorbar(title.position = "top"),
        name = "level") + ggnewscale::new_scale_fill() +

```



```
geom_tile(data = DrD_melt[DrD_melt$coefType ==
  "year", ], aes(x = variable, y = loc_cause,
  fill = value)) + scale_fill_distiller(type = "div",
  palette = "Spectral", guide = guide_colorbar(title.position = "top"),
  name = "year") + facet_grid(. ~ coefType, scales = "free_x",
  space = "free_x") + theme(axis.text.x = element_text(angle = 90,
  vjust = 0.4), axis.title.y = element_blank(), axis.title.x = element_blank(),
  strip.text.x = element_text(size = 5))
```



For tuberculosis, most regions show a decrease in death rate that started before 1990. Most of them are associated with decreasing prevalence rate. Central Asia is an exception, where rates increased till around year 2000. HIV/AIDS is divided into clusters with A, inflection point in the 1990ies with little increase beforehand B, inflection from high increase to high decrease coefficient in the 2000ds, C, locations with no change or even increase in deaths. Southern Sub-Saharan Africa stands out with its very high increase, and decrease rate coefficients. Tuberculosis has a much higher baseline prevalence than HIV/AIDS, but baseline deaths are similar.

The strategy for condensing the 30-year behavior into 4 coefficients seems promising. Let's apply it to more causes.

## 10 additional causes

Repeat the same analysis [to do: merge the analyses]

Load data (Download choices similar to above; see 'readme' for details)

```
allTime_10caus_1 = read.csv("./20230911_DeathPrevInci_10caus_21reg_MF_5year/IHME-GBD_2019_DATA-d86a6f40
  stringsAsFactors = TRUE)
allTime_10caus_2 = read.csv("./20230911_DeathPrevInci_10caus_21reg_MF_5year/IHME-GBD_2019_DATA-d86a6f40
  stringsAsFactors = TRUE)
allTime_10caus_3 = read.csv("./20230911_DeathPrevInci_10caus_21reg_MF_5year/IHME-GBD_2019_DATA-d86a6f40
  stringsAsFactors = TRUE)
allTime_10caus = rbind.data.frame(allTime_10caus_1,
  allTime_10caus_2, allTime_10caus_3)
allTime_10caus = allTime_10caus[allTime_10caus$metric ==
  "Percent", ]
unique(allTime_10caus$metric)
```

```
## [1] Percent
## Levels: Percent Rate
```

```
str(allTime_10caus)
```

```
## 'data.frame': 652680 obs. of 10 variables:
## $ measure : Factor w/ 3 levels "Deaths","Prevalence",...: 1 1 1 1 1 1 1 1 1 1 ...
## $ location: Factor w/ 21 levels "Andean Latin America",...: 4 4 4 4 4 4 4 4 4 4 ...
## $ sex : Factor w/ 2 levels "Female","Male": 2 1 2 1 2 1 2 1 2 1 ...
## $ age : Factor w/ 18 levels "1-4 years","10-14 years",...: 1 1 9 9 2 2 3 3 4 4 ...
## $ cause : Factor w/ 10 levels "Diarrheal diseases",...: 9 9 9 9 9 9 9 9 9 9 ...
## $ metric : Factor w/ 2 levels "Percent","Rate": 1 1 1 1 1 1 1 1 1 1 ...
## $ year : int 1991 1991 1991 1991 1991 1991 1991 1991 1991 1991 ...
## $ val : num 0.000919 0.001201 0.002354 0.004431 0.003152 ...
## $ upper : num 0.00127 0.00164 0.00294 0.00552 0.0038 ...
## $ lower : num 0.000541 0.000797 0.001906 0.003651 0.00262 ...
```

```
dim(allTime_10caus)
```

```
## [1] 652680 10
```

Clean

```
unique(allTime_10caus$age) #this indicates entry '80-84' instead of '80-84 years' and two other such c
```

```
## [1] 1-4 years 5-9 years 10-14 years 15-19 years 20-24 years 25-29 years
## [7] 30-34 years 40-44 years 45-49 years 50-54 years 55-59 years 60-64 years
## [13] 65-69 years 70-74 years 75-79 years 80-84 85-89 90-94
## 18 Levels: 1-4 years 10-14 years 15-19 years 20-24 years ... 90-94
```

```

levels(allTime_10caus$age)[levels(allTime_10caus$age) ==
  "80-84"] = "80-84 years"
levels(allTime_10caus$age)[levels(allTime_10caus$age) ==
  "85-89"] = "85-89 years"
levels(allTime_10caus$age)[levels(allTime_10caus$age) ==
  "90-94"] = "90-94 years"
levels(allTime_10caus$age)

## [1] "1-4 years" "10-14 years" "15-19 years" "20-24 years" "25-29 years"
## [6] "30-34 years" "40-44 years" "45-49 years" "5-9 years" "50-54 years"
## [11] "55-59 years" "60-64 years" "65-69 years" "70-74 years" "75-79 years"
## [16] "80-84 years" "85-89 years" "90-94 years"

```

```

# cleaning: remove causes for which not all three
# measures are listed
unique(allTime_10caus$measure[allTime_10caus$cause ==
  "Guinea worm disease"])

```

```

## [1] Prevalence Incidence
## Levels: Deaths Prevalence Incidence

```

```

# apparently causes that does not have any death
# associated do not have Deaths metric
incomplete_causes = c()
for (ca in unique(allTime_10caus$cause)) {
  len = length(unique(allTime_10caus$measure[allTime_10caus$cause ==
    ca]))
  if (len != 3) {
    incomplete_causes = c(incomplete_causes, ca)
  }
}
allTime_10caus = allTime_10caus[!allTime_10caus$cause %in%
  incomplete_causes, ]

```

## Age- & sex- independent analysis

Simplify data: Average percentages over all age groups for location-cause-year combination

```

allTime_10caus_asi= data.frame( allTime_10caus %>% #asi= age-, sex- independent
  group_by(measure,location,cause,year) %>%
  summarize(val= mean(val),.groups='drop') )
head(allTime_10caus_asi)

```

```

##   measure      location      cause year      val
## 1 Deaths Andean Latin America Diarrheal diseases 1990 0.02405603
## 2 Deaths Andean Latin America Diarrheal diseases 1991 0.02565334
## 3 Deaths Andean Latin America Diarrheal diseases 1992 0.02423331
## 4 Deaths Andean Latin America Diarrheal diseases 1993 0.02336296
## 5 Deaths Andean Latin America Diarrheal diseases 1994 0.02210943
## 6 Deaths Andean Latin America Diarrheal diseases 1995 0.02136141

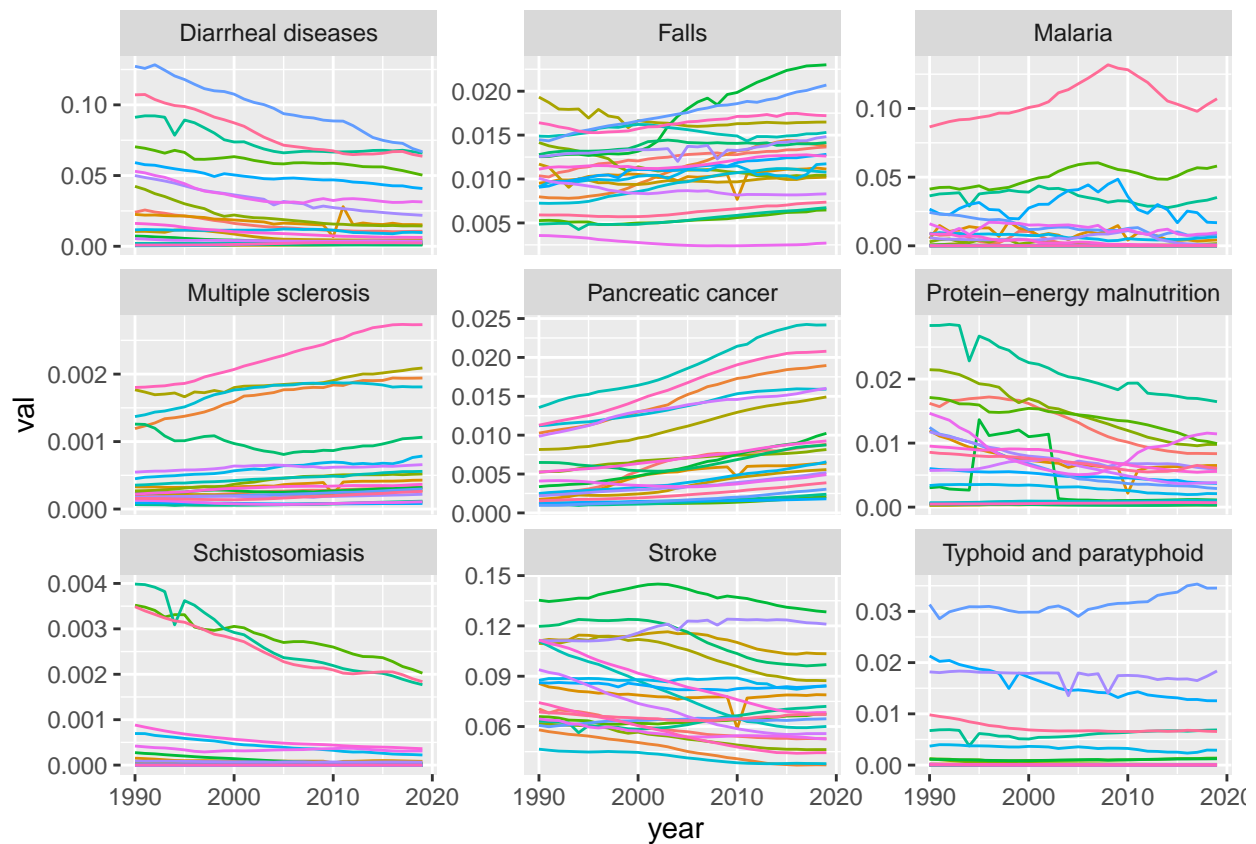
```

```
dim(allTime_10caus_asi)
```

```
## [1] 17010      5
```

Visualize data

```
ggplot(data = allTime_10caus_asi[allTime_10caus_asi$measure ==  
  "Deaths", ], mapping = aes(x = year, y = val, group = location,  
  color = location)) + geom_line() + facet_wrap(~cause,  
  scales = "free_y") + guides(color = "none")
```



```
## Two-line model
```

```
groupedDF = allTime_10caus_asi %>%  
  group_by(location, cause, measure) %>%  
  summarize(n(), .groups = "drop")  
dim(groupedDF) #609 combinations
```

```
## [1] 567      4
```

```
head(allTime_10caus_asi)
```

```
## measure      location      cause year      val  
## 1 Deaths Andean Latin America Diarrheal diseases 1990 0.02405603
```

```

## 2 Deaths Andean Latin America Diarrheal diseases 1991 0.02565334
## 3 Deaths Andean Latin America Diarrheal diseases 1992 0.02423331
## 4 Deaths Andean Latin America Diarrheal diseases 1993 0.02336296
## 5 Deaths Andean Latin America Diarrheal diseases 1994 0.02210943
## 6 Deaths Andean Latin America Diarrheal diseases 1995 0.02136141

# groupedDF= groupedDF[groupedDF$location ==
# 'Andean Latin America',] ###, 'Eastern
# Europe', 'South Asia' only temporary

if (!file.exists("./20230914_MCMCcoefs_10caus.csv")) {
  # execute only if not yet done
  MCMCcoefs_DF_10caus = data.frame(matrix(NA, nrow = dim(groupedDF)[1],
    ncol = 7))
  colnames(MCMCcoefs_DF_10caus) = c("location", "cause",
    "measure", "b0_median", "b1_median", "b2_median",
    "t_inflec_median")
  MCMCcoefs_DF_10caus$location <- factor(MCMCcoefs_DF_10caus$location,
    levels = levels(groupedDF$location))
  MCMCcoefs_DF_10caus$cause <- factor(MCMCcoefs_DF_10caus$cause,
    levels = levels(groupedDF$cause))
  MCMCcoefs_DF_10caus$measure <- factor(MCMCcoefs_DF_10caus$measure,
    levels = levels(groupedDF$measure))

  for (i in 1:dim(groupedDF)[1]) {
    print(paste(i, "of", dim(groupedDF)[1]))
    currDF = allTime_10caus_asi[allTime_10caus_asi$location ==
      groupedDF$location[i] & allTime_10caus_asi$cause ==
      groupedDF$cause[i] & allTime_10caus_asi$measure ==
      groupedDF$measure[i], ]
    mcmcDF_orig = twoLine_fit(t = currDF$year,
      y = currDF$val)

    # There are two coefficients (b1, b2)
    # that each can either be present of
    # absent as indicated by indicator
    # factors
    mcmcDF_orig$iF1 = factor(mcmcDF_orig$iF1, levels = c(0,
      1)) #to make sure both levels are listed even if only one observed
    mcmcDF_orig$iF2 = factor(mcmcDF_orig$iF2, levels = c(0,
      1))
    tab2Way = data.table(table(cbind.data.frame(iF1 = mcmcDF_orig$iF1,
      iF2 = mcmcDF_orig$iF2)))
    # find the most frequent combination of
    # indicator factors -> the best model
    iF1_best = tab2Way$iF1[tab2Way$N == max(tab2Way$N)]
    iF2_best = tab2Way$iF2[tab2Way$N == max(tab2Way$N)]

    # Reduce to MCMC output of the best model
    mcmcDF = mcmcDF_orig[mcmcDF_orig$iF1 == iF1_best &
      mcmcDF_orig$iF2 == iF2_best, ]
    if (iF1_best == 0 | iF2_best == 0) {
      mcmcDF$t0 = NA
    }
  }
}

```

```

# Analysis could be extended by cases
# cross-informing each other (e.g.
# countries from same region)

MCMCcoefs_DF_10caus$location[i] = groupedDF$location[i]
MCMCcoefs_DF_10caus$cause[i] = groupedDF$cause[i]
MCMCcoefs_DF_10caus$measure[i] = groupedDF$measure[i]
MCMCcoefs_DF_10caus$b0_median[i] = median(mcmcDF$b0)
MCMCcoefs_DF_10caus$b1_median[i] = median(mcmcDF$b1)
MCMCcoefs_DF_10caus$b2_median[i] = median(mcmcDF$b2)
MCMCcoefs_DF_10caus$t_inflec_median[i] = median(mcmcDF$t0) #may be NA
}

# write output so you do not need to run this
# code every time
write.csv(MCMCcoefs_DF_10caus, "./20230914_MCMCcoefs_10caus.csv",
         row.names = FALSE)
} else {
  MCMCcoefs_DF_10caus = read.csv("./20230914_MCMCcoefs_10caus.csv",
                                stringsAsFactors = TRUE)
}
str(MCMCcoefs_DF_10caus)

```

```

## 'data.frame':   567 obs. of  7 variables:
## $ location      : Factor w/ 21 levels "Andean Latin America",...: 1 1 1 1 1 1 1 1 1 1 ...
## $ cause         : Factor w/ 9 levels "Diarrheal diseases",...: 1 1 1 2 2 2 3 3 3 4 ...
## $ measure       : Factor w/ 3 levels "Deaths","Incidence",...: 1 3 2 1 3 2 1 3 2 1 ...
## $ b0_median     : num  0.0225 0.0162 0.1521 0.0103 0.0501 ...
## $ b1_median     : num  0 0.000347 0.002984 0.000218 0.001114 ...
## $ b2_median     : num -0.000538 -0.000131 -0.001337 -0.000148 -0.000707 ...
## $ t_inflec_median: num  NA 2000 2002 1999 2003 ...

```

```
dim(MCMCcoefs_DF_10caus)
```

```
## [1] 567    7
```

```

MCMCcoefs_DF_10caus$loc_cause = paste(MCMCcoefs_DF_10caus$location,
                                       MCMCcoefs_DF_10caus$cause, sep = ", ")
str(MCMCcoefs_DF_10caus)

```

```

## 'data.frame':   567 obs. of  8 variables:
## $ location      : Factor w/ 21 levels "Andean Latin America",...: 1 1 1 1 1 1 1 1 1 1 ...
## $ cause         : Factor w/ 9 levels "Diarrheal diseases",...: 1 1 1 2 2 2 3 3 3 4 ...
## $ measure       : Factor w/ 3 levels "Deaths","Incidence",...: 1 3 2 1 3 2 1 3 2 1 ...
## $ b0_median     : num  0.0225 0.0162 0.1521 0.0103 0.0501 ...
## $ b1_median     : num  0 0.000347 0.002984 0.000218 0.001114 ...
## $ b2_median     : num -0.000538 -0.000131 -0.001337 -0.000148 -0.000707 ...
## $ t_inflec_median: num  NA 2000 2002 1999 2003 ...
## $ loc_cause     : chr  "Andean Latin America, Diarrheal diseases" "Andean Latin America, Diarrheal

```

```
str(MCMCcoefs_DF)
```

```
## 'data.frame':    126 obs. of  8 variables:
## $ location      : Factor w/ 21 levels "Andean Latin America",...: 1 1 1 1 1 1 2 2 2 2 ...
## $ cause         : Factor w/ 2 levels "HIV/AIDS","Tuberculosis": 1 1 1 2 2 2 1 1 1 2 ...
## $ measure       : Factor w/ 3 levels "Deaths","Incidence",...: 1 2 3 1 2 3 1 2 3 1 ...
## $ b0_median     : num  0.005725 0.000013 0.00029 0.076575 0.000394 ...
## $ b1_median     : num  1.12e-03 4.84e-07 5.62e-05 0.00 0.00 ...
## $ b2_median     : num  0.00 0.00 0.00 -2.46e-03 -1.13e-05 ...
## $ t_inflec_median: num  NA NA NA NA NA NA NA NA NA NA ...
## $ loc_cause      : chr   "Andean Latin America, HIV/AIDS" "Andean Latin America, HIV/AIDS" "Andean L
```

```
# combine with data from HT
```

```
MCMCcoefs_DF_comb = rbind.data.frame(MCMCcoefs_DF,
  MCMCcoefs_DF_10caus)
```

```
# pivot:
```

```
MCMCcoefs_wide = pivot_wider(data = MCMCcoefs_DF_comb,
  id_cols = c("loc_cause", "location", "cause"),
  names_from = c("measure"), values_from = c("b0_median",
    "b1_median", "b2_median", "t_inflec_median"))
```

```
# manually sorted:
```

```
MCMCcoefs_DF_NA = MCMCcoefs_wide[is.na(MCMCcoefs_wide$t_inflec_median_Deaths),
  ] #no inflection point
MCMCcoefs_DF_noNA = MCMCcoefs_wide[!is.na(MCMCcoefs_wide$t_inflec_median_Deaths),
  ] #with inflection point
```

```
# out of the data that do not have inflection
```

```
# year, get the ones that have decline
```

```
MCMCcoefs_DF_NA_decl = MCMCcoefs_DF_NA[MCMCcoefs_DF_NA$b2_median_Deaths !=
  0, ]
```

```
MCMCcoefs_DF_NA_nodecl = MCMCcoefs_DF_NA[MCMCcoefs_DF_NA$b2_median_Deaths ==
  0, ]
```

```
# sort data with declining death rate (but no
```

```
inflection) by decline of death rate
```

```
ord1 = order(MCMCcoefs_DF_NA_decl$b2_median_Deaths)
```

```
# sort data with inflection by inflection year
```

```
ord2 = order(MCMCcoefs_DF_noNA$t_inflec_median_Deaths) +
  max(c(0, ord1)) #start after ord1
```

```
# sort data without declining death rate by
```

```
increase in death rate
```

```
ord3 = order(MCMCcoefs_DF_NA_nodecl$b1_median_Deaths) +
  max(c(0, ord2)) #start after ord2
```

```
# order factor levels of 'loc_cause'
```

```
MCMCcoefs_patchw = rbind.data.frame(MCMCcoefs_DF_NA_decl,
  MCMCcoefs_DF_noNA, MCMCcoefs_DF_NA_nodecl)
```

```
ord = c(ord1, ord2, ord3)
```

```
MCMCcoefs_patchw$loc_cause = factor(MCMCcoefs_patchw$loc_cause,
  ordered = TRUE, levels = MCMCcoefs_patchw$loc_cause[ord])
```

```
DrD_melt = melt(MCMCcoefs_patchw, id.vars = c("loc_cause",
      "location", "cause"), measure.vars = c("b0_median_Deaths",
      "b1_median_Deaths", "b2_median_Deaths", "t_inflec_median_Deaths",
      "b0_median_Prevalence", "b1_median_Prevalence",
      "b2_median_Prevalence"))
# drop Incidence (very
# low): 'b0_median_Incidence',
# 'b1_median_Incidence', 'b2_median_Incidence', 't_inflec_median_Incidence'
# drop inflection of prevalence (very few
# observed): , 't_inflec_median_Prevalence'
str(DrD_melt)
```

```
## 'data.frame': 1617 obs. of 5 variables:
## $ loc_cause: Ord.factor w/ 231 levels "Andean Latin America, Tuberculosis"<...: 1 50 87 55 16 61 34 ...
## $ location : Factor w/ 21 levels "Andean Latin America",...: 1 2 2 3 4 5 6 7 8 10 ...
## $ cause : Factor w/ 11 levels "HIV/AIDS","Tuberculosis",...: 2 1 2 2 2 2 2 2 2 ...
## $ variable : Factor w/ 7 levels "b0_median_Deaths",...: 1 1 1 1 1 1 1 1 1 1 ...
## $ value : num 0.076575 0.00822 0.000799 0.016243 0.028248 ...
```

```
DrD_melt$coefType = rep("rate", dim(DrD_melt)[1])
DrD_melt$coefType[DrD_melt$variable %in% c("b0_median_Deaths",
      "b0_median_Prevalence", "b0_median_Incidence")] = "basel."
DrD_melt$coefType[DrD_melt$variable %in% c("t_inflec_median_Deaths",
      "t_inflec_median_Prevalence", "t_inflec_median_Incidence")] = "year"
head(DrD_melt)
```

```
##           loc_cause           location           cause
## 1 Andean Latin America, Tuberculosis Andean Latin America Tuberculosis
## 2           Australasia, HIV/AIDS           Australasia           HIV/AIDS
## 3           Australasia, Tuberculosis           Australasia Tuberculosis
## 4           Caribbean, Tuberculosis           Caribbean Tuberculosis
## 5           Central Asia, Tuberculosis           Central Asia Tuberculosis
## 6           Central Europe, Tuberculosis           Central Europe Tuberculosis
##           variable           value coefType
## 1 b0_median_Deaths 0.0765746093      basel.
## 2 b0_median_Deaths 0.0082204252      basel.
## 3 b0_median_Deaths 0.0007991389      basel.
## 4 b0_median_Deaths 0.0162433765      basel.
## 5 b0_median_Deaths 0.0282482063      basel.
## 6 b0_median_Deaths 0.0063972962      basel.
```

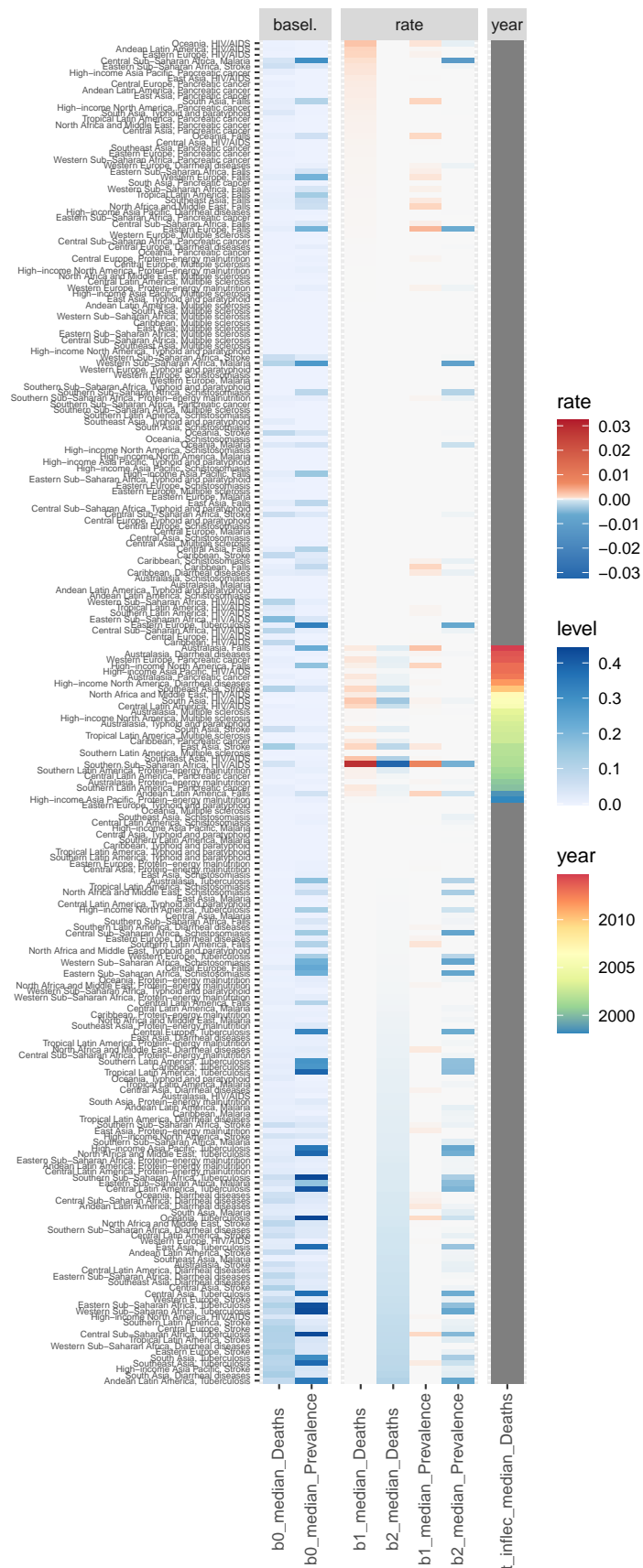
```
ggplot() + geom_tile(data = DrD_melt[DrD_melt$coefType ==
      "rate", ], aes(x = variable, y = loc_cause, fill = value)) +
      scale_fill_distiller(type = "seq", palette = "RdBu",
        limits = c(-max(abs(DrD_melt$value[DrD_melt$coefType ==
          "rate"])) , max(abs(DrD_melt$value[DrD_melt$coefType ==
          "rate"]))), values = c(0, 0.4, 0.49, 0.5,
          0.51, 0.6, 1), guide = guide_colorbar(title.position = "top"),
        name = "rate") + ggnewscale::new_scale_fill() +
      geom_tile(data = DrD_melt[DrD_melt$coefType ==
        "basel.", ], aes(x = variable, y = loc_cause,
          fill = value)) + scale_fill_distiller(type = "seq",
```



```

palette = "Blues", values = seq(1, 0, -0.1), guide = guide_colorbar(title.position = "top"),
name = "level") + ggnewscale::new_scale_fill() +
geom_tile(data = DrD_melt[DrD_melt$coefType ==
  "year", ], aes(x = variable, y = loc_cause,
  fill = value)) + scale_fill_distiller(type = "div",
palette = "Spectral", guide = guide_colorbar(title.position = "top"),
name = "year") + theme(axis.title.x = element_blank(),
axis.text.x = element_text(angle = 90, vjust = 0.4),
axis.title.y = element_blank(), axis.text.y = element_text(size = 5)) +
facet_grid(. ~ coefType, scales = "free_x", space = "free_x")

```



Visual interpretation:

*The heatmap region with increasing deaths is dominated by Pancreatic cancer; however, the highest increase in deaths is due to HIV/AIDS in non-African regions (Oceania, Andean Latin America, Eastern Europe)* There is a relative wide region in which neither increase nor decrease in death rates was identified; Multiple Sclerosis shows a particular clustering in this region -> follow up; among these entries, malaria and stroke have higher baseline values; for essentially all of these entries, there is also no change in prevalence rate *The region with inflection where death rate decreases (this does not necessarily mean the rate is overall negative) is relatively small and with no obvious enrichment of cause or location* There is a large region where deaths are decreasing; there is a clear association between baseline and decrease rate, i.e. settings that start off highest decrease most; as noted above, Tuberculosis has the highest Prevalence baseline and it shows the strongest decrease in prevalence.

## Identification of factors associated with decreasing deaths

I will next use the technique of summarizing time courses into four parameters to learn the factors associated with declining deaths ( $b_2 < 0$ ). I will use a random forest approach. Process the data individually for each age group and sex to have features for classification. Indicate the various categories by which locations can be grouped (e.g. continent, high/low income, ...)

```
# Start with only HIV and Tuberculosis
allTime_HT= allTime_HTZ[allTime_HTZ$cause %in% c('HIV/AIDS','Tuberculosis'),]

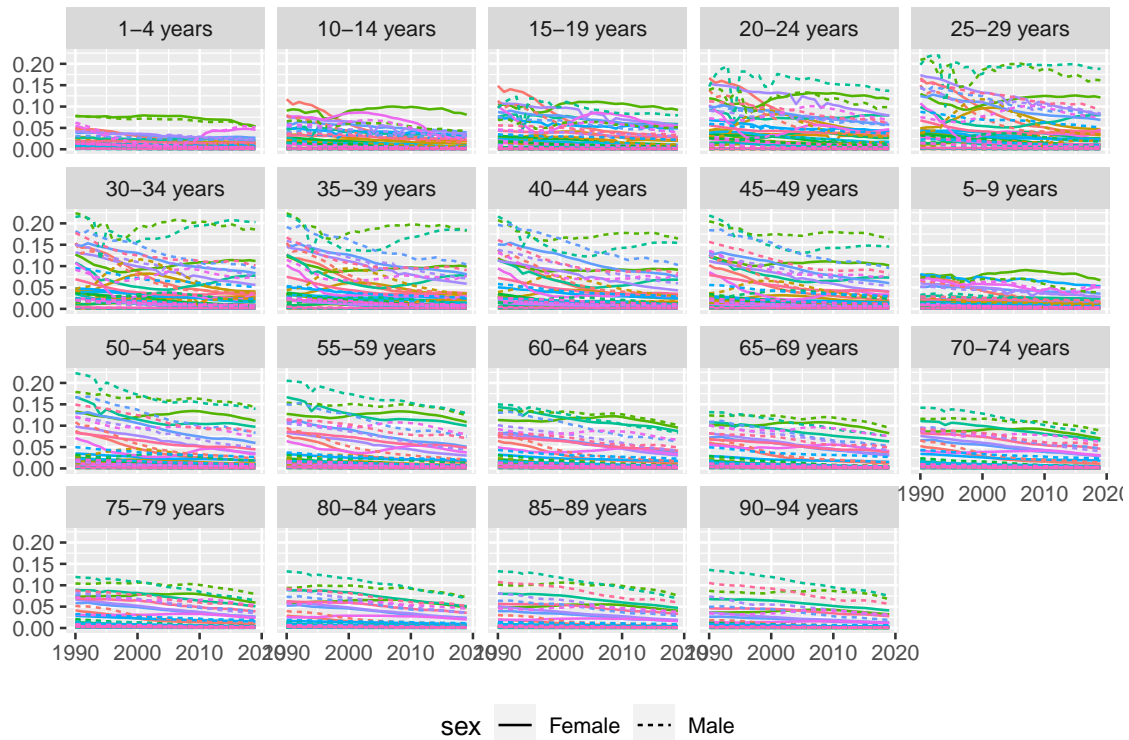
#limit to death rate (not prevalence or incidence)
allTime_HT_D= allTime_HT[allTime_HT$measure=='Deaths',]
head(allTime_HT_D)
```

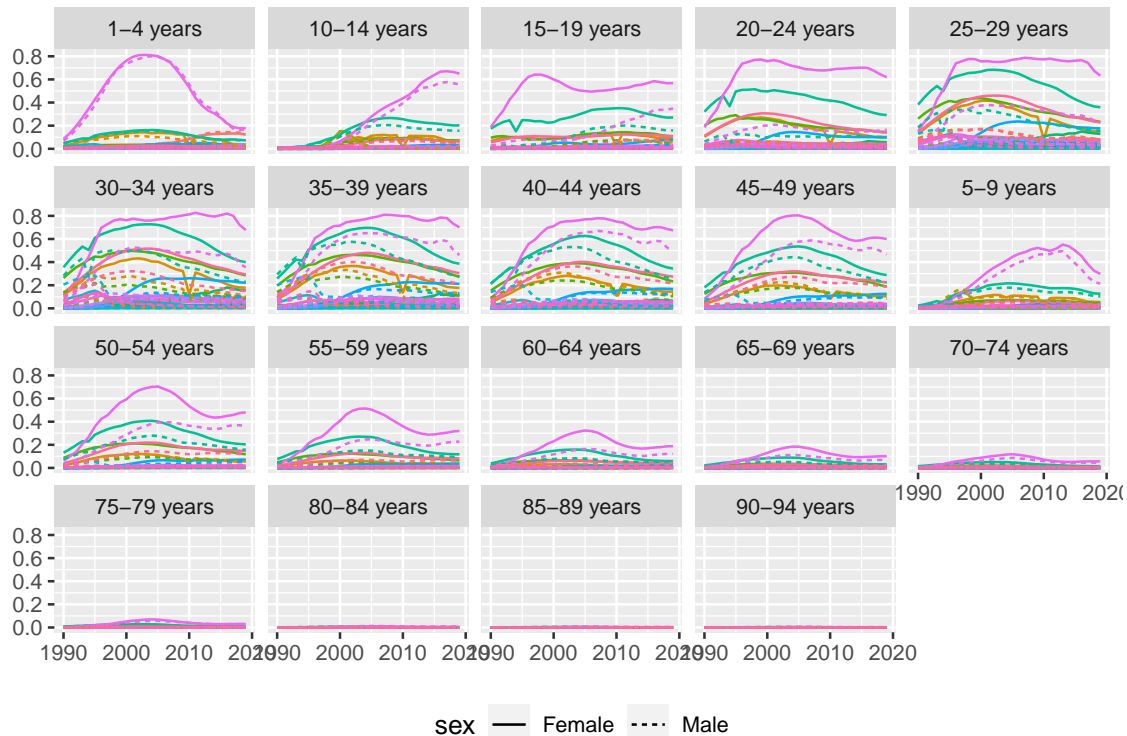
##	measure	location	sex	age	cause	metric
## 103	Deaths	Southern Sub-Saharan Africa	Male	1-4 years	Tuberculosis	Percent
## 104	Deaths	Southern Sub-Saharan Africa	Female	1-4 years	Tuberculosis	Percent
## 107	Deaths	Southern Sub-Saharan Africa	Male	5-9 years	Tuberculosis	Percent
## 108	Deaths	Southern Sub-Saharan Africa	Female	5-9 years	Tuberculosis	Percent
## 111	Deaths	Southern Sub-Saharan Africa	Male	10-14 years	Tuberculosis	Percent
## 112	Deaths	Southern Sub-Saharan Africa	Female	10-14 years	Tuberculosis	Percent
##	year	val	upper	lower		
## 103	1991	0.05828452	0.07584042	0.04230566		
## 104	1991	0.05118780	0.07327022	0.03400883		
## 107	1991	0.06739403	0.08315998	0.05393467		
## 108	1991	0.07159152	0.09918324	0.05226830		
## 111	1991	0.05712411	0.07021589	0.04669703		
## 112	1991	0.07660581	0.10223418	0.06012578		

Visualize data

```
#Tuberculosis
ggplot(data=allTime_HT_D[allTime_HT_D$cause=='Tuberculosis',],mapping=aes(x=year,y=val,group=interaction(
  #geom_point()+
  geom_line()+
  facet_wrap(~age)+ #,scales='free_y'
  guides(color='none')+
  theme(axis.title=element_blank(),legend.position = 'bottom'))
```

```
ggplot(data=allTime_HT_D[allTime_HT_D$cause=='HIV/AIDS'],mapping=aes(x=year,y=val,group=interaction(los
#geom_point()+
geom_line()+
facet_wrap(~age)+ #,scales='free_y'
guides(color='none')+
theme(axis.title=element_blank(),legend.position = 'bottom')
```





[Change factor order so that years appear consecutively in facet\_wrap]

Visual impression: Tuberculosis: It seems the same locations have highest rates over all age groups; in most of the groups deaths decrease over time; men generally have higher rates; middle aged individuals have higher number of deaths than very young and very old people

HIV/AIDS: frequently increase till ~2005, then decrease similar ordering of countries over age groups Highest rates in middle aged populations Women generally have higher rates than men

!!! Careful with the analysis within age groups: I assume(!) the data give number of deaths per overall population of the location, not percentage within the age group -> you need to consider the demographics of the country [the same problem also applies to sex, but probably much less severely]

```
groupedDF = allTime_HT_D %>%
  group_by(location, cause, measure, sex, age) %>%
  summarize(n(), .groups = "drop")
dim(groupedDF) #1596 combinations
```

```
## [1] 1596    6
```

```
# groupedDF= groupedDF[groupedDF$location ==
# 'Andean Latin America',] ###,'Eastern
# Europe','South Asia' only temporary

if (!file.exists("./20230915_MCMCcoefs_HTsex_age.csv")) {
  # execute only if not yet done
  MCMCcoefs_DF_HTsex_age = data.frame(matrix(NA,
    nrow = dim(groupedDF)[1], ncol = 9))
  colnames(MCMCcoefs_DF_HTsex_age) = c("location",
```

```

    "cause", "measure", "sex", "age", "b0_median",
    "b1_median", "b2_median", "t_inflec_median")
MCMCcoefs_DF_HTsex_age$location <- factor(MCMCcoefs_DF_HTsex_age$location,
    levels = levels(groupedDF$location))
MCMCcoefs_DF_HTsex_age$cause <- factor(MCMCcoefs_DF_HTsex_age$cause,
    levels = levels(groupedDF$cause))
MCMCcoefs_DF_HTsex_age$measure <- factor(MCMCcoefs_DF_HTsex_age$measure,
    levels = levels(groupedDF$measure))
MCMCcoefs_DF_HTsex_age$sex <- factor(MCMCcoefs_DF_HTsex_age$sex,
    levels = levels(groupedDF$sex))
MCMCcoefs_DF_HTsex_age$age <- factor(MCMCcoefs_DF_HTsex_age$age,
    levels = levels(groupedDF$age))

for (i in 1:dim(groupedDF)[1]) {
  print(paste(i, "of", dim(groupedDF)[1]))
  currDF = allTime_HT_D[allTime_HT_D$location ==
    groupedDF$location[i] & allTime_HT_D$cause ==
    groupedDF$cause[i] & allTime_HT_D$measure ==
    groupedDF$measure[i] & allTime_HT_D$sex ==
    groupedDF$sex[i] & allTime_HT_D$age ==
    groupedDF$age[i], ]
  mcmcDF_orig = twoLine_fit(t = currDF$year,
    y = currDF$val)

  # There are two coefficients (b1, b2)
  # that each can either be present of
  # absent as indicated by indicator
  # factors
  mcmcDF_orig$iF1 = factor(mcmcDF_orig$iF1, levels = c(0,
    1)) #to make sure both levels are listed even if only one observed
  mcmcDF_orig$iF2 = factor(mcmcDF_orig$iF2, levels = c(0,
    1))
  tab2Way = data.table(table(cbind.data.frame(iF1 = mcmcDF_orig$iF1,
    iF2 = mcmcDF_orig$iF2)))
  # find the most frequent combination of
  # indicator factors -> the best model
  iF1_best = tab2Way$iF1[tab2Way$N == max(tab2Way$N)]
  iF2_best = tab2Way$iF2[tab2Way$N == max(tab2Way$N)]

  # Reduce to MCMC output of the best model
  mcmcDF = mcmcDF_orig[mcmcDF_orig$iF1 == iF1_best &
    mcmcDF_orig$iF2 == iF2_best, ]
  if (iF1_best == 0 | iF2_best == 0) {
    mcmcDF$t0 = NA
  }

  # Analysis could be extended by cases
  # cross-informing each other (e.g.
  # countries from same region)

  MCMCcoefs_DF_HTsex_age$location[i] = groupedDF$location[i]
  MCMCcoefs_DF_HTsex_age$cause[i] = groupedDF$cause[i]
  MCMCcoefs_DF_HTsex_age$measure[i] = groupedDF$measure[i]

```

```

MCMCcoefs_DF_HTsex_age$sex[i] = groupedDF$sex[i]
MCMCcoefs_DF_HTsex_age$age[i] = groupedDF$age[i]
MCMCcoefs_DF_HTsex_age$b0_median[i] = median(mcmcDF$b0)
MCMCcoefs_DF_HTsex_age$b1_median[i] = median(mcmcDF$b1)
MCMCcoefs_DF_HTsex_age$b2_median[i] = median(mcmcDF$b2)
MCMCcoefs_DF_HTsex_age$t_inflec_median[i] = median(mcmcDF$t0) #may be NA
}

# write output so you do not need to run this
# code every time
write.csv(MCMCcoefs_DF, "./20230915_MCMCcoefs_HTsex_age.csv",
          row.names = FALSE)
} else {
  MCMCcoefs_DF_HTsex_age = read.csv("./20230915_MCMCcoefs_HTsex_age.csv",
                                     stringsAsFactors = TRUE)
}
str(MCMCcoefs_DF_HTsex_age)

```

```

## 'data.frame':   126 obs. of  8 variables:
## $ location      : Factor w/ 21 levels "Andean Latin America",...: 1 1 1 1 1 1 2 2 2 2 ...
## $ cause         : Factor w/ 2 levels "HIV/AIDS","Tuberculosis": 1 1 1 2 2 2 1 1 1 2 ...
## $ measure       : Factor w/ 3 levels "Deaths","Incidence",...: 1 2 3 1 2 3 1 2 3 1 ...
## $ b0_median     : num  0.005725 0.000013 0.00029 0.076575 0.000394 ...
## $ b1_median     : num  1.12e-03 4.84e-07 5.62e-05 0.00 0.00 ...
## $ b2_median     : num  0.00 0.00 0.00 -2.46e-03 -1.13e-05 ...
## $ t_inflec_median: num  NA NA NA NA NA NA NA NA NA NA ...
## $ loc_cause      : Factor w/ 42 levels "Andean Latin America, HIV/AIDS",...: 1 1 1 2 2 2 3 3 3 4 ...

```

```
dim(MCMCcoefs_DF_HTsex_age)
```

```
## [1] 126 8
```

**Below: Work in progress: IGNORE for now!**

```

# allTime_HT_asi[allTime_HT_asi$location=='Eastern Sub-Saharan Africa' &
#               allTime_HT_asi$cause=='HIV/AIDS', ]

```

Work on one cause at a time; start with Tuberculosis most locations decrease steadily, but there seem to be 5 that increase, then decrease Perform clustering at max-normalized data; worry later about differences in absolute percentages

```

# head(allTime_HTZ_asi_D_norm)
#
# allTime_HIV_asi_norm= allTime_HTZ_asi_D_norm[allTime_HTZ_asi_D_norm$cause=='HIV/AIDS',]
# HIV_wide= allTime_HIV_asi_norm %>%
#   mutate(year= as.factor(year)) %>%
#   select(location,year,val)%>%
#   pivot_wider(names_from= year,values_from= val)
#

```

```

# loc_labels= as.character(HIV_wide$location)
# HIV_mtx= as.matrix(HIV_wide[,2:dim(HIV_wide)[2]])
#
# #cluster timecourses
# distMtx= dist(HIV_mtx,method='dtw') #"dynamic time warping"
# hc= hclust(distMtx,method='average') #
# plot(hc) #,labels=loc_labels
#
# #cut into three groups
# dendroInd= cutree(hc,k=3)
# allTime_HIV_asl_norm$dendGrp= dendroInd[match(allTime_HIV_asl_norm$location,loc_labels)]
#
# ggplot(data=allTime_HIV_asl_norm[allTime_HIV_asl_norm$dendGrp ==1,], mapping=aes(x=year,y=val_maxNorm
#   geom_point()+
#   geom_line()+
#   coord_cartesian(ylim=c(0,1)))+
#   theme(axis.title.y= element_text('Normalized to highest incidence year'))
#
# ggplot(data=allTime_HIV_asl_norm[allTime_HIV_asl_norm$dendGrp %in% c(2,3),], mapping=aes(x=year,y=val
#   geom_point()+
#   geom_line()+
#   coord_cartesian(ylim=c(0,1)))+
#   theme(axis.title.y= element_text('Normalized to highest incidence year'))

```

The normalized trajectories for the African locations + Caribbean are very similar

It is interesting to note that some trajectories have a clear turning point, from which on the death percentage decreases; this could be a simple point measure to compare trajectories and answer questions like: *Is turning point present for all countries in a region and does it occur simultaneously* Do different diseases have the a turning point at a similar time (i.e. is turning disease specific or due to change that affects several diseases) \*Does the prevalence/infection rate decline with the disease rate (i.e. was there a reduction in the cause of the disease or did treatment get better?)

## Model1:

Model percent of deaths as a linear function of time, where individual measurements (different locations, genders, ages) are distributed around the mean by a t-distribution; intercept has a uniform prior, slope normal prior with mean 0

Build model1: linear model of percentage vs year using t-distribution on slope

```

# allTime_HTZ$year= allTime_HTZ$year-1990 #Set 1990 as "year 0";
#
# mod1Str='
# model{
#   for(i in 1:Ntotal){ #loop over all observations
#     pc[i] ~ dt(b0[d[i]] + b1[d[i]]*year[i], sigma, nu ) #coefficients specific to disease
#   }
#   for(j in 1:Ndis){
#     b0[j] ~ dunif(1/1000,1000)
#     b1[j] ~ dnorm(0, 2^2) #sd= 1/2
#   }
#   nuMin1 ~ dexp(1/29.0)
#

```



```
# nu= nuMin1 +1
# sigma~ dunif(0,1)
# }'
```

MCMC for posteriors

```
# # data1List= list(
# #   Ntotal= dim(data1)[1],
# #   Ndis= length(unique(data1$cause)),
# #   pc= data1$val, #percentage
# #   d= data1$disFac,
# #   year= data1$year
# # )
#
# redData1List= list(
#   Ntotal= dim(redData)[1],
#   Ndis= length(unique(redData$cause)),
#   pc= redData$val, #percentage
#   d= redData$disFac,
#   year= redData$year
# )
#
# jags1= jags.model(file=textConnection(mod1Str),data=redData1List,n.chains=3)

# cS1= coda.samples(model=jags1,variable.names=c('b0','b1','sigma','nu'),n.iter=10000)

# for(i in 1:length(varnames(cS1))){
#   diagMCMC(codaObject= cS1,parName=varnames(cS1)[i] )
# }
```

This does not produce good coefficient estimates. I probably need a different link function for data that are a percentage.