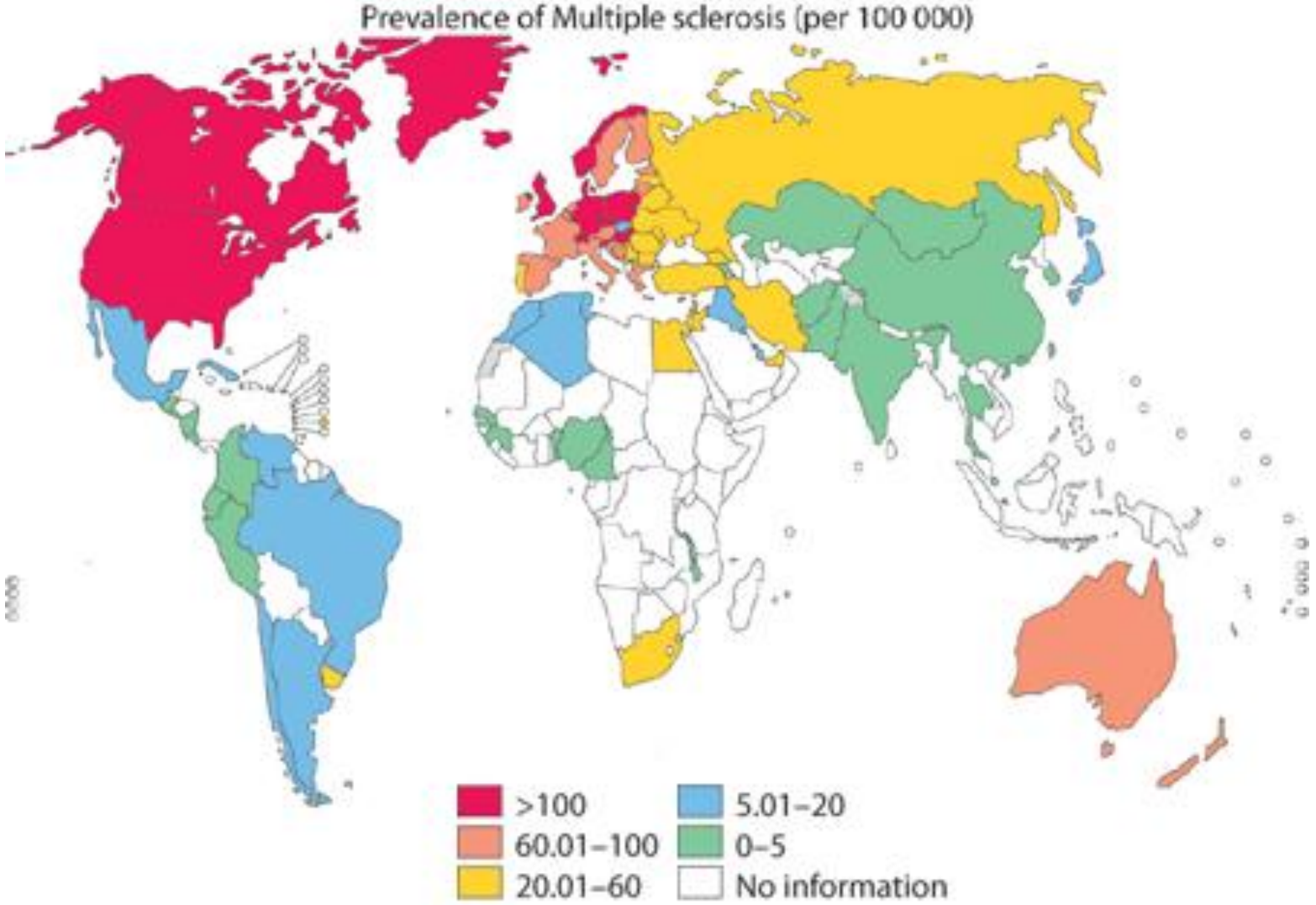
# Epidemiology of Multiple Sclerosis

(The Faroe islands story)

# What is multiple sclerosis?

- “Multiple sclerosis is a chronic demyelinting, inflammatory and degenerative disorder of the central nervous system, and is the most common disabling nervous system disease among young adults”- ( Pugliatti 2006 )
- Etiology (or cause) is not known. Theories are:
  1. Autoimmune disease
  2. Infectious disease

# Worldwide prevalence



# Patterns in Multiple Sclerosis

- Age: Migration studies show that the disease is acquired after the age of 15
- Sex: The disease is more common on females
- Race: white people are more susceptible
- Geography: the further away from the equator, the higher the risk
- Genetics: a 35% chance of getting the disease if the your monozygotic twin sibling has it.

# Forming a theory about disease spread

- Genetics (monozygotic twins)
- Autoimmune disease and hygiene hypothesis (>15 age of susceptibility)
- Epstein-Barr virus and mononucleosis
- Faroe Islands ( disease introduced by British troops in WW II )

# Epstein-Barr Virus

- 50% of children get infected and do not develop any symptoms
- If infected in adolescence, probably will develop infectious mononucleosis
- Mononucleosis highly correlated with MS
- More than 90% of adults have EBV
- Infection occurs through saliva (kissing disease)

# Faroe Islands

- Background: Atlantic islands, part of Denmark
- WW II: British troops occupied the island during 1941-1945
- MS non-existent prior to occupation
- MS incidence rate spikes 1941-1953
- Today: one of the highest incidence rates worldwide

# Kurtzke's theory

- Kurtzke studied for several decades the MS epidemic that occurred in the Faroe Islands.
- Kurtzke proposes that the disease is spread through an infective agent.
- PMSA: most infected are asymptomatic, and transmit the disease passively.

# Kurtzke's theory

- CNMS: a small proportion develop the clinical symptoms (i.e. MS).
- Infectives age: 11-28 (28 is the average disease onset age).
- Exposure: two years to become infective.

# One Strain with childhood Immunity (Model Assumptions 1)

- Kutzke divides the population into three age groups:
  1. Group 0 with age < 11
  2. Group 1 with 11 < age < 27
  3. Group 2 with 27 < age < 48.
- Uniform age distribution is assumed.

# One Strain with childhood Immunity (Model Assumptions 2)

- Group 0 when exposed acquire life-long immunity .
- Group 1 is the only group that has infective individuals.
- Group 2 can become infected and develop MS.
- MS develops only in a small percentage of the infected individuals.

# One Strain Disease Compartments

$S_0$ Susceptible individuals between 0 and 11 years of age

$M_0$ Immune individuals between 0 and 11 years of age

$S_1$ Susceptible individuals between 11 and 28 years of age

$M_1$ Immune individuals between 11 and 28 years of age

$E_1$ Exposed individuals between 11 and 28 years of age

$I_1$ Infective individuals between 11 and 28 years of age

$S_2$ Susceptible individuals between 28 and 48 years of age

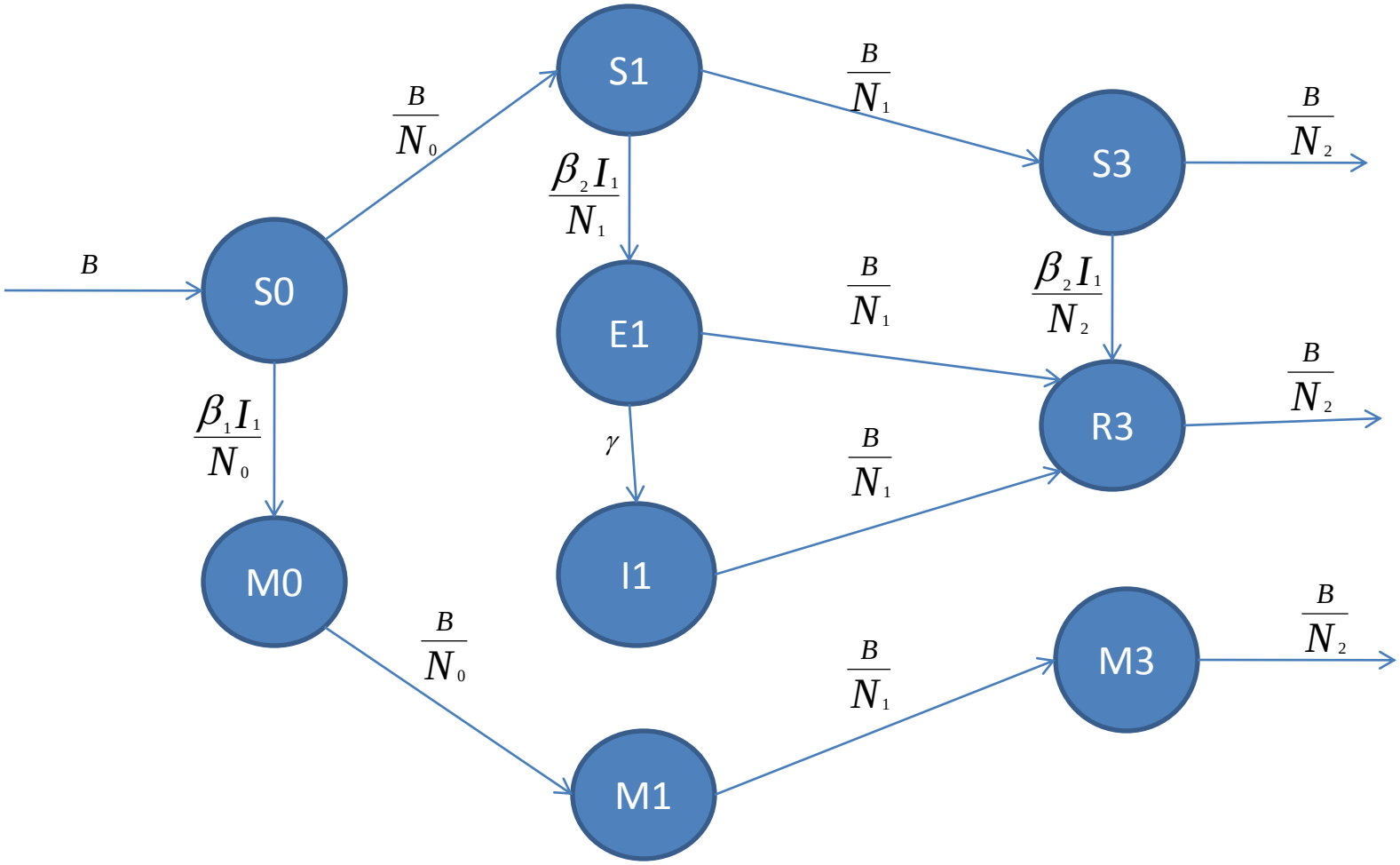
$M_2$ Immune individuals between 28 and 48 years of age

$R_2$ Infected individuals between 28 and 48 years of age

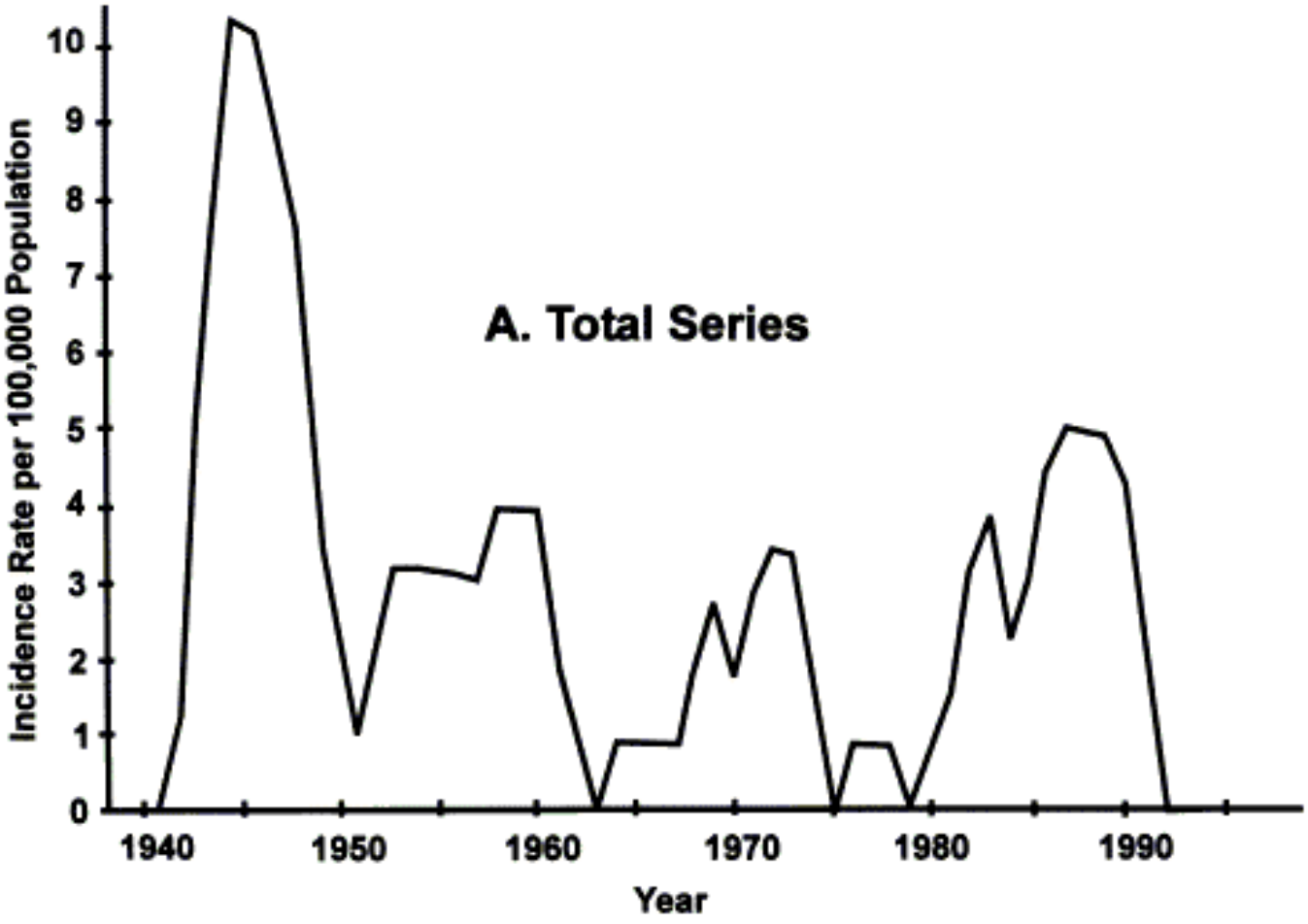
# Parameters

| | |
|---|---|
| $N_0$ | Population size between 0 and 11 years of age |
| $N_1$ | Population size between 11 and 28 years of age |
| $N_2$ | Population size between 28 and 48 years of age |
| $\beta_1$ | Rate of infection in between ages 0 and 11 |
| $\beta_2$ | Rate of infection in between ages 11 and 48 |
| $\gamma$ | Rate of change from exposed to infective |

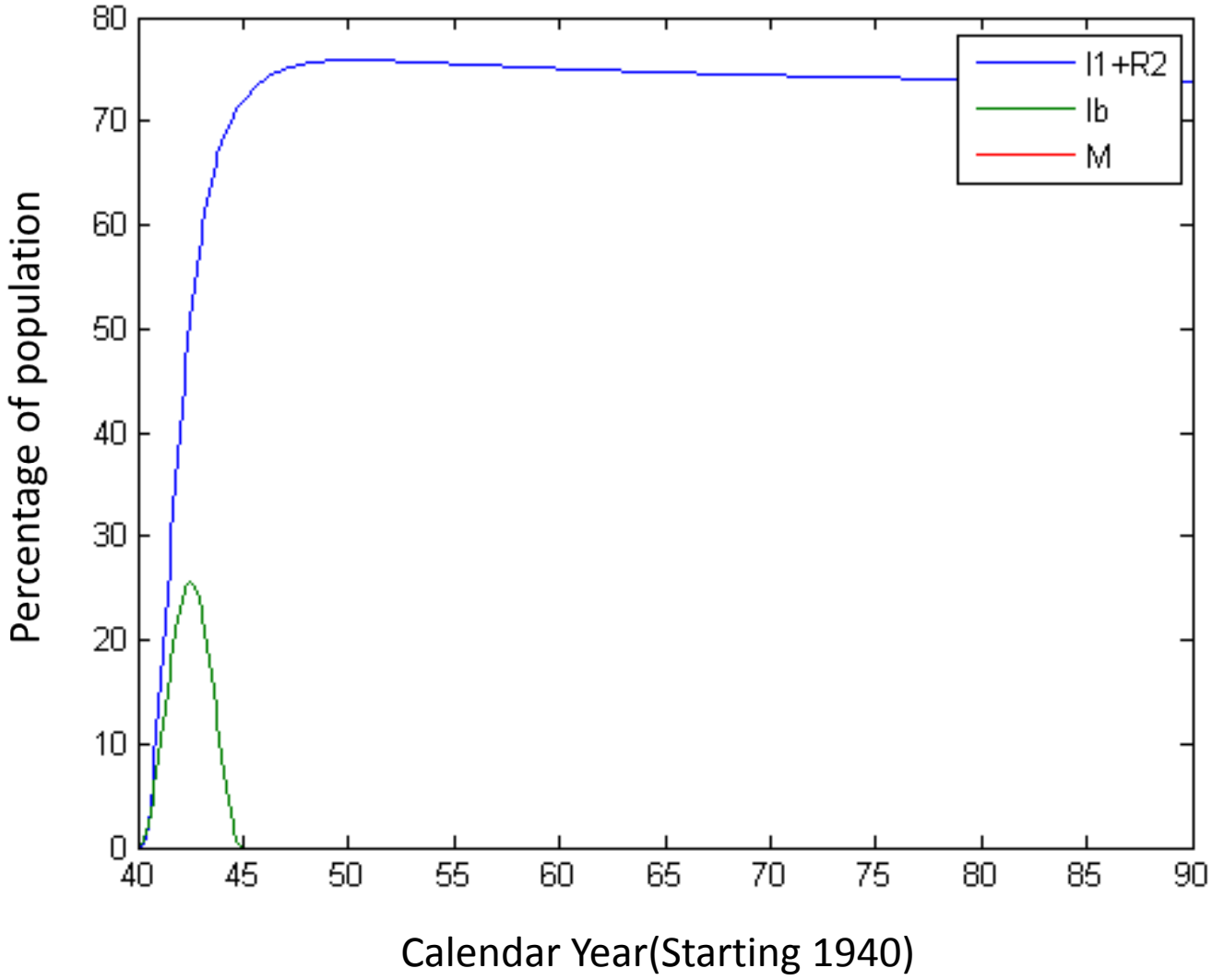
# One Strain with childhood Immunity



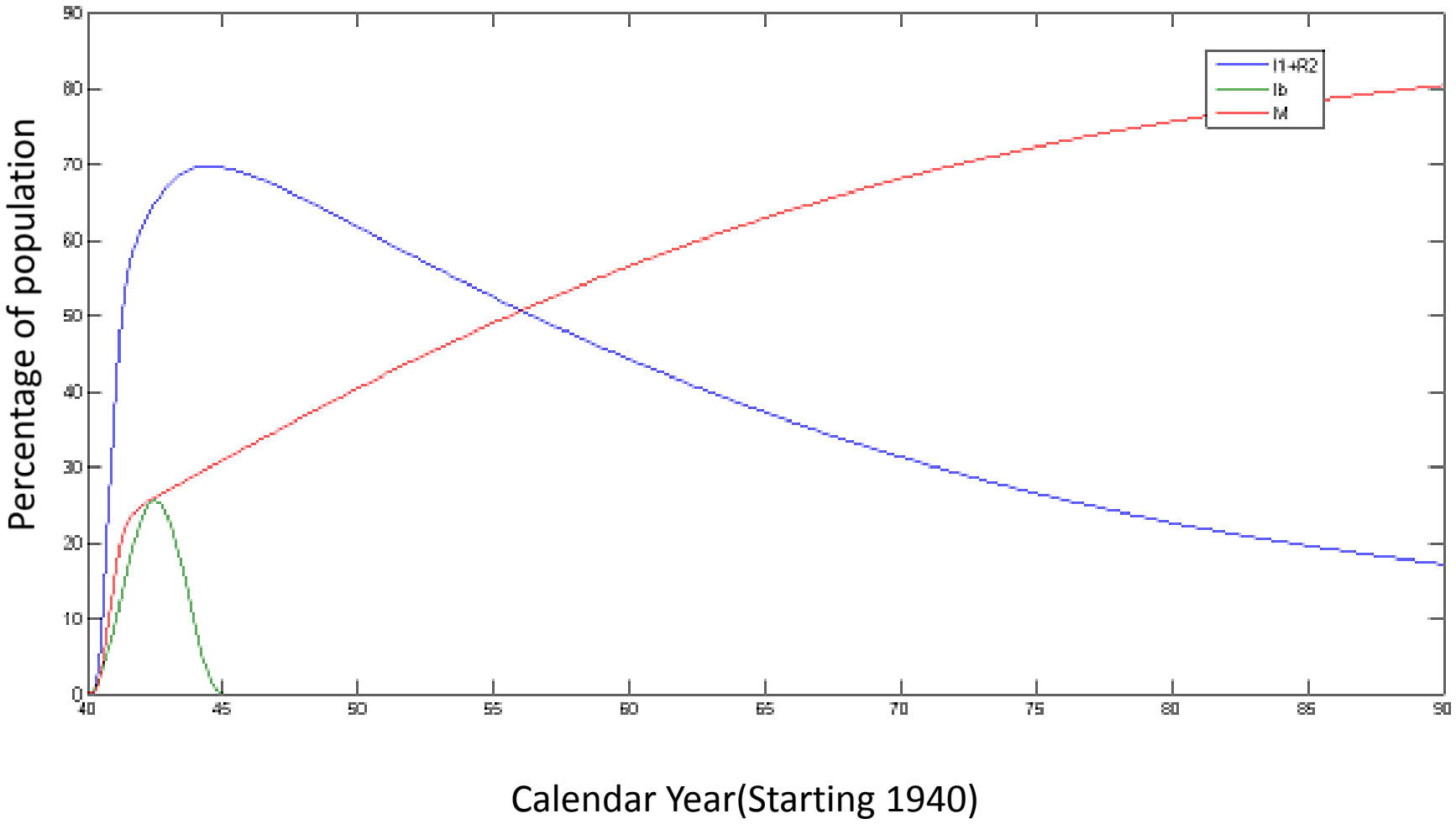
# Faroe Islands MS incidence rate 41-93 (Kurtzke 2001)



# Absence of immunity



# Immunity acquired in childhood

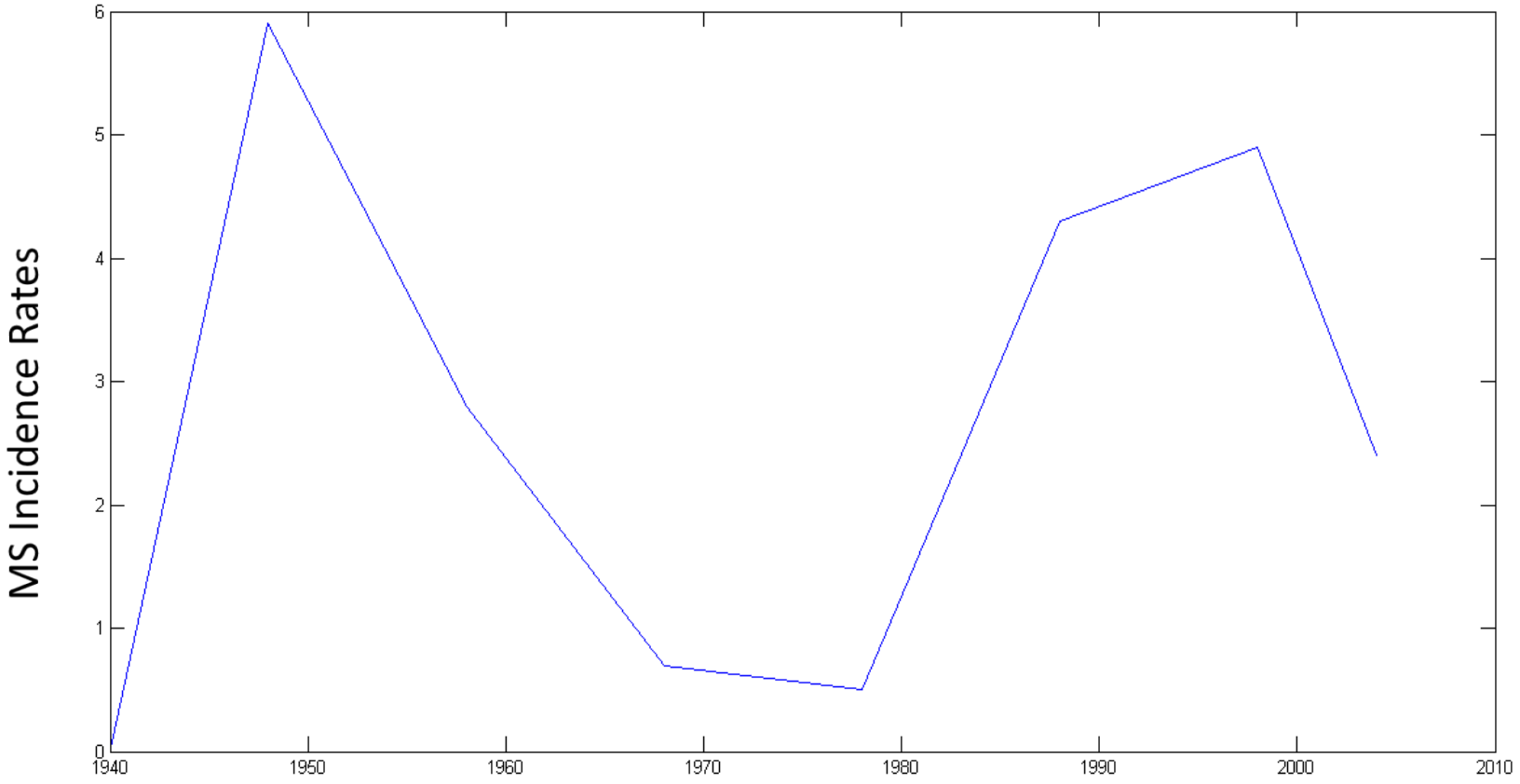


# Problems with this model

- Poul Joensen reports in 2011 the following MS incidence rates from 1943-1952, in Faroe islands, with two peaks:

| Period | 1943-1952 | 1953-1962 | 1963-1972 | 1973-1982 | 1983-1992 | 1992-2002 | 2003-2007 | 1943-2007 |
|---|---|---|---|---|---|---|---|---|
| Mean Age | 32 | 27 | 26 | 34 | 33 | 37 | 38 | 30 |
| Incidence Rate per 100,000 | 5.9 | 2.8 | 0.7 | 0.5 | 4.3 | 4.9 | 2.4 | 2.7 |

# Poul Joensen MS Incidence Rates in Faroe Islands 1943-2007



# Two Strains Theory

- There are two strains of the transmissible agent.
- One strain has a higher infectivity than the other, and a shorter period of infection.
- Both strains induce cross immunity on infecting children (age < 11), and on recovery.
- There are only two age cohorts: (group 0 of age < 11, and group 1 of age > 11)

# Two Strains Disease Compartments

$S_0$ Susceptible individuals between 0 and 11 years of age

$M_0$ Immune individuals between 0 and 11 years of age

$S_1$ Susceptible individuals older than 11 years of age

$M_1$ Immune individuals older than 11 years of age

$E_{11}$ Strain 1 exposed individuals older than 11 years of age

$I_{11}$ Strain 1 infective individuals older than 11 years of age

$E_{12}$ Strain 2 exposed individuals older than 11 years of age

$I_{12}$ Strain 2 infective individuals older than 11 years of age

$R_2$ Recovered individuals older than 11 years of age

# Two Strains Parameters

| | |
|---|---|
| $N_0$ | Population size between 0 and 11 years of age |
| $N_1$ | Population size between 11 and 48 years of age |
| $N$ | Population size between 0 and 48 years of age |
| $\beta_{11}$ | Rate of infection with strain 1 for age < 11 |
| $\beta_{21}$ | Rate of infection with strain 1 for age > 11 |
| $\gamma_1$ | Rate of change from strain 1 exposed to strain 1 infective |
| $\beta_{12}$ | Rate of infection with strain 2 for age < 11 |
| $\beta_{22}$ | Rate of infection with strain 2 for age > 11 |
| $\gamma_2$ | Rate of change from strain 2 exposed to strain 2 infective |

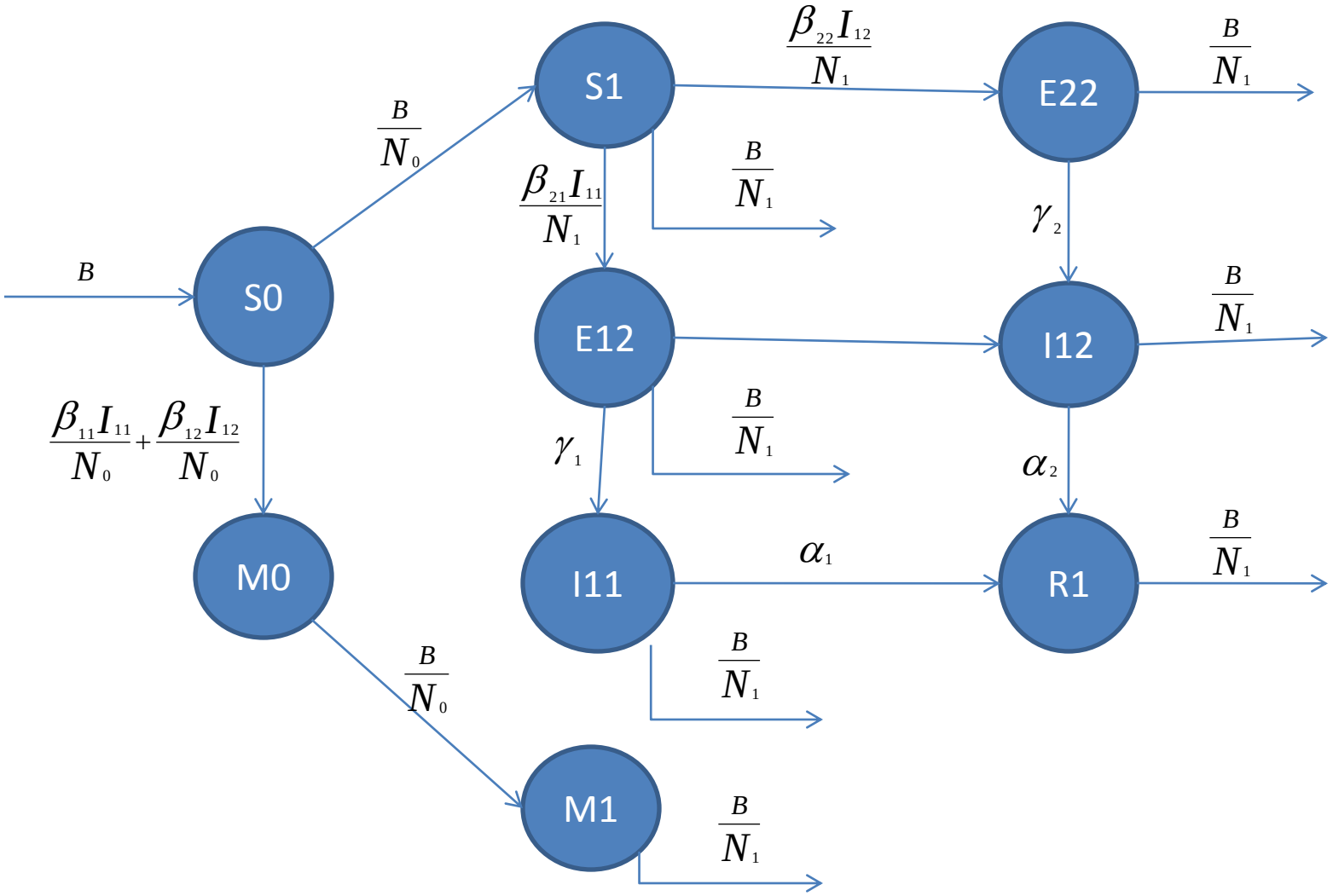
# Two Strains Parameters

$\alpha_1$ Rate of recovery from infection with strain 1

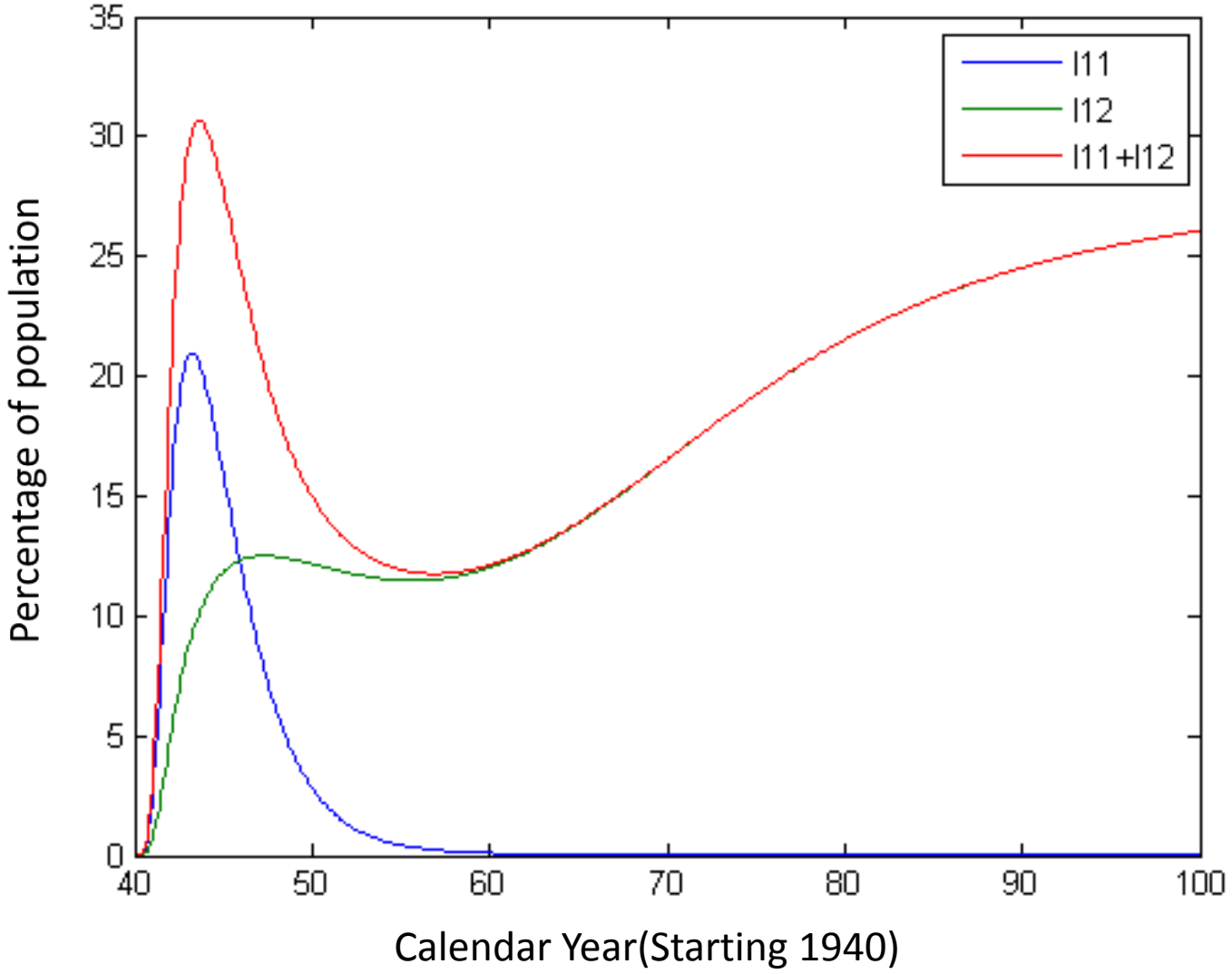
$\alpha_2$ Rate of recovery from infection with strain 2

$B$ Birth Rate

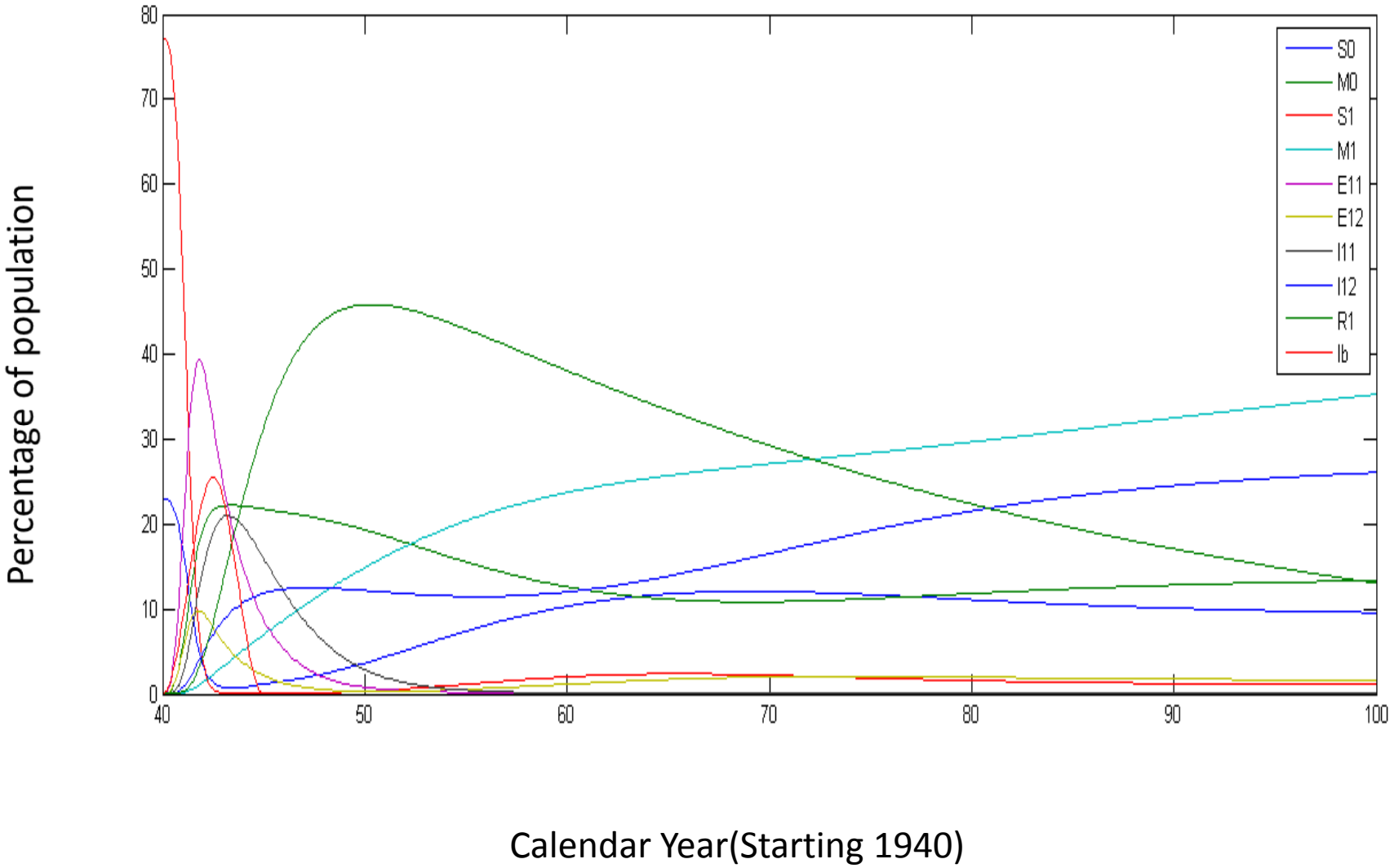
# Two Strains with Cross Immunity



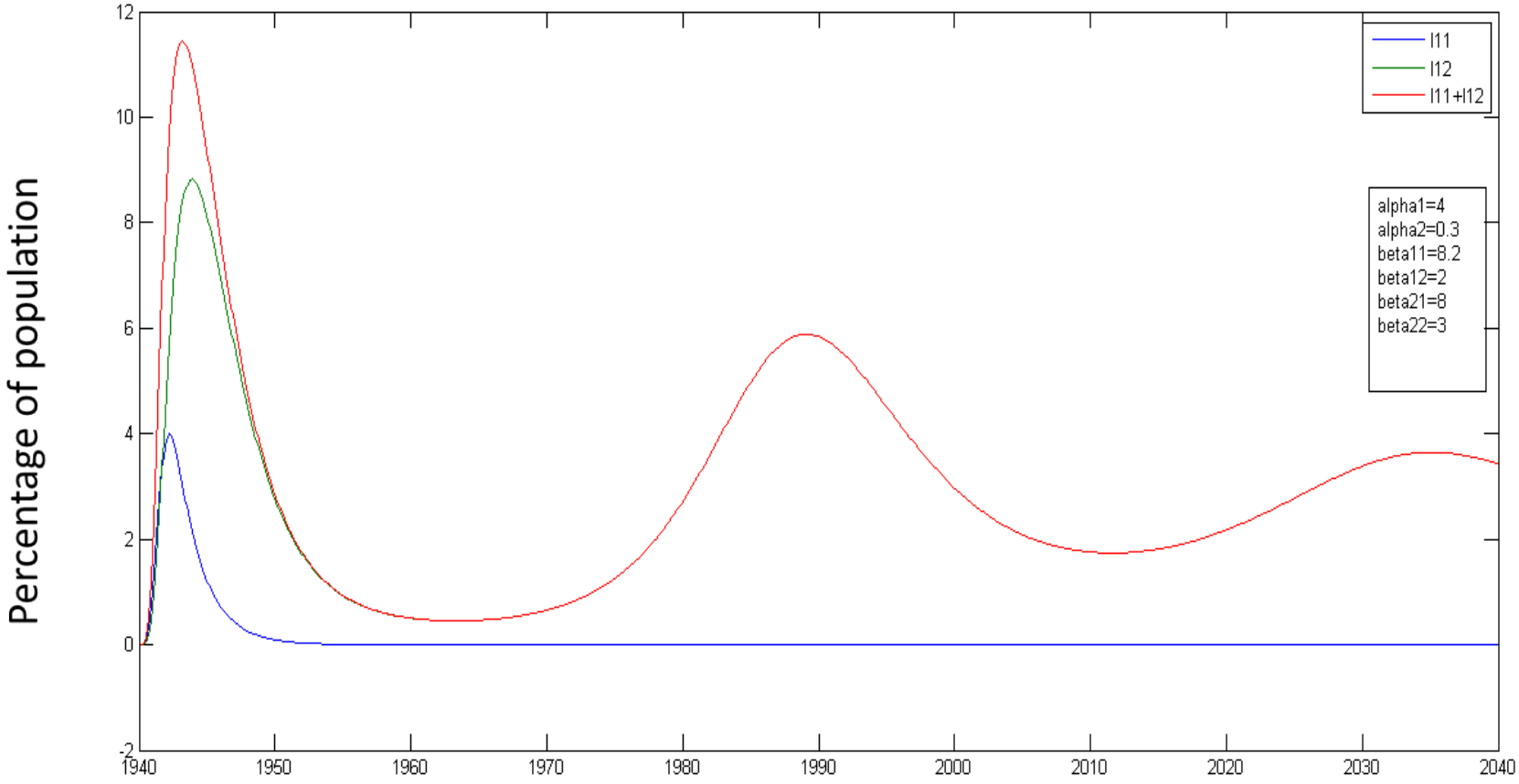
# Infected and at risk of developing MS



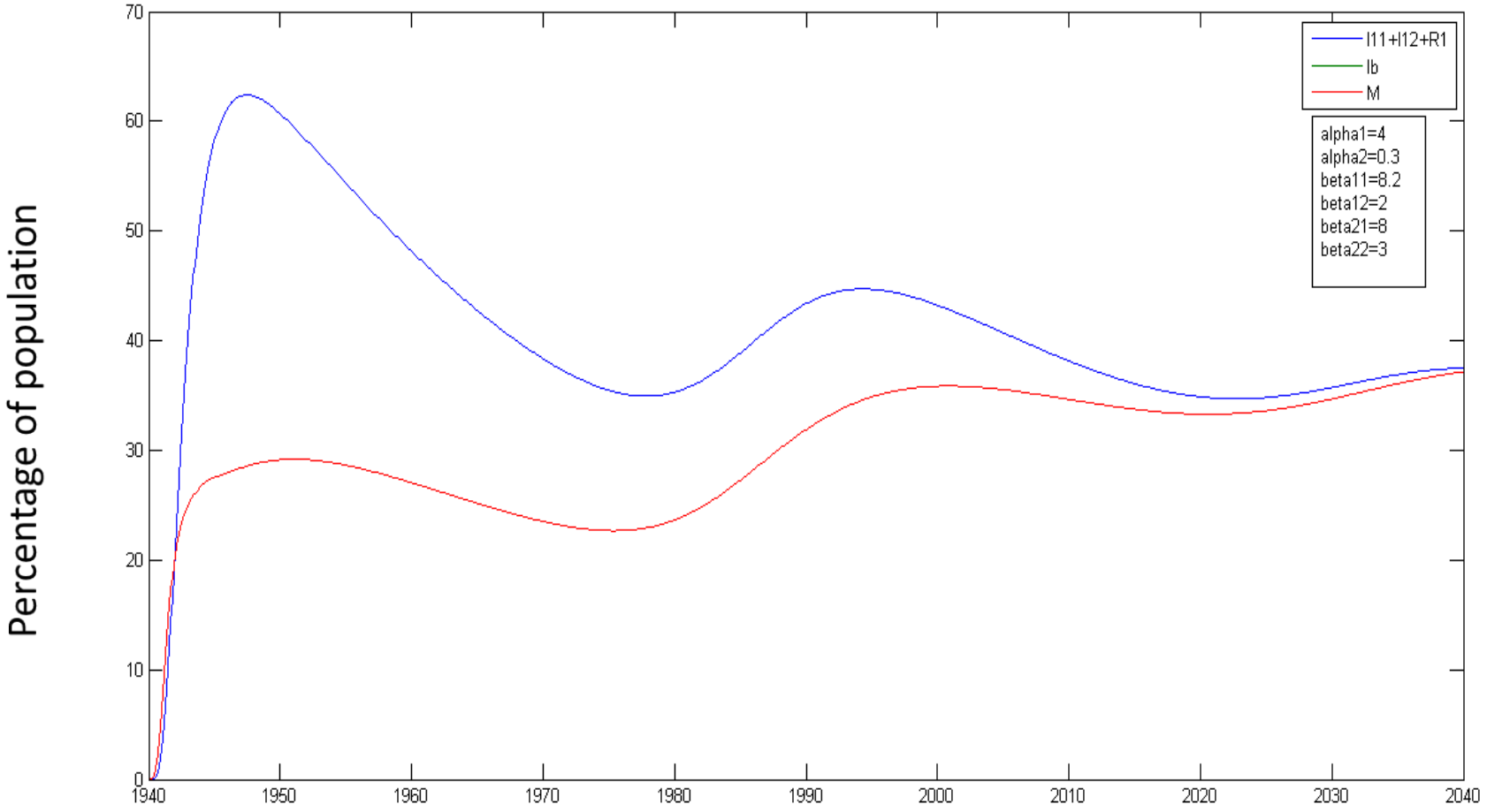
# All compartments



# Infected and at risk of developing MS (The future)



# Infected and at risk of developing MS (The future)



# Discussion

- The two strain model does capture the general features of the disease:
  1. The sharp initial increase (1943-1953)
  2. The sharp decline to small values (1953-1983)
  3. The second peak

# Future Work

- Study the age structure of incidence rates offered by the two strain hypothesis
- Try to fit the model to other available data in the literature

# References


- Multiple sclerosis in the Faroe Islands: an epitome ( Kurtzke and Heltberg-2001 )
- Multiple sclerosis: variation of incidence of onset over time in the Faroe Islands ( Poel Joensen-2011 )
- Environmental Risk Factors for Multiple Sclerosis Part I: The Role of Infection ( Ascherio and Munger-2007)