Simulations of Rubella Vaccination Strategies in China

Linda Q. Gao
North Central College

Herbert Hethcote
The University of Iowa

February 12, 2009

University of Washington

References

L.Q. Gao and H.W. Hethcote, Simulations of rubella vaccination strategies in China, Mathematical Biosciences 202 (2006) 371-385.

L.Q.Gao and H.W.Hethcote, A mathematical model and projection of various rubella vaccination strategies. Chinese Journal of Vaccines and Immunization 14-3 (2008) 193-197 (in Chinese with English abstract).

Background:

- Rubella: mild childhood infectious disease
- Congenital Rubella Syndrome: severe consequences when pregnant women are infected
- Vaccination status: 1969 – now
- WHO recommendations on Rubella/CRS control

Background :

WHO recommended that “All countries should assess their rubella situation and, if appropriate, make plans for introduction of rubella vaccination and CRS/rubella surveillance.” (Geneva, 2000)

Warning:

"inadequately implemented childhood vaccination runs the risk of altering rubella transmission dynamics and increasing susceptibility in women of child bearing age, thereby increasing the risk of CRS" (Geneva, 2000)

Background: -China

- Rubella vaccination is not mandatory in the national immunization program. MMR is available in some major cities.
- Resources for vaccination are limited.
- Population structure is changing
- Should China vaccinate for rubella? If so, which strategy?

Wannian Su: Rubella in People's Republic of China, Rev. Infect Dis 1985; 7:s72

Table 2. Seropositivity for rubella antibody, by age group, of persons tested in 20 provinces in the People's Republic of China, 1979–1980.

Age (years)	No. of persons tested	Percentage of persons seropositive	Geometric mean titer
<1	766	34.5	40
2	644	41.9	81
3	652	56.9	84
4	698	63.5	81
5	723	73.6	83
6–10	3,422	88.5	71
11–15	2,399	96.0	55
16–20	1,918	96.2	41
21–25	1,624	95.2	38
26–30	1,525	94.6	37
31–40	2,287	96.8	41
Total	16,658	85.6	51

Method:

Use mathematical models and computer simulations to compare various rubella vaccination strategies with consideration of China's changing population structure

- Construct demographical model
- Add epidemiological model

China Demographic Model

- 58 age groups: 0,1,2,...,49, 50-54, 55-59, ..., 75-79, 80-84, 85+

- Interpolate fertility and death rates using 1987 1% sample data (China statistical yearbook 1997, 1990, 2002) 1992 survey and 2000 census data (China Population Information and Research Center)

China Demographic Model

- Derived 1965 age distribution from 1987 age distribution data.
- Used the birth/death rate from 1965-1992 as the scaling factor for fertility and death rate.
- Interpolate fertility and death rate between 1992 and 2000 data.
- Used Leslie matrix population model

Leslie population matrix demographic model

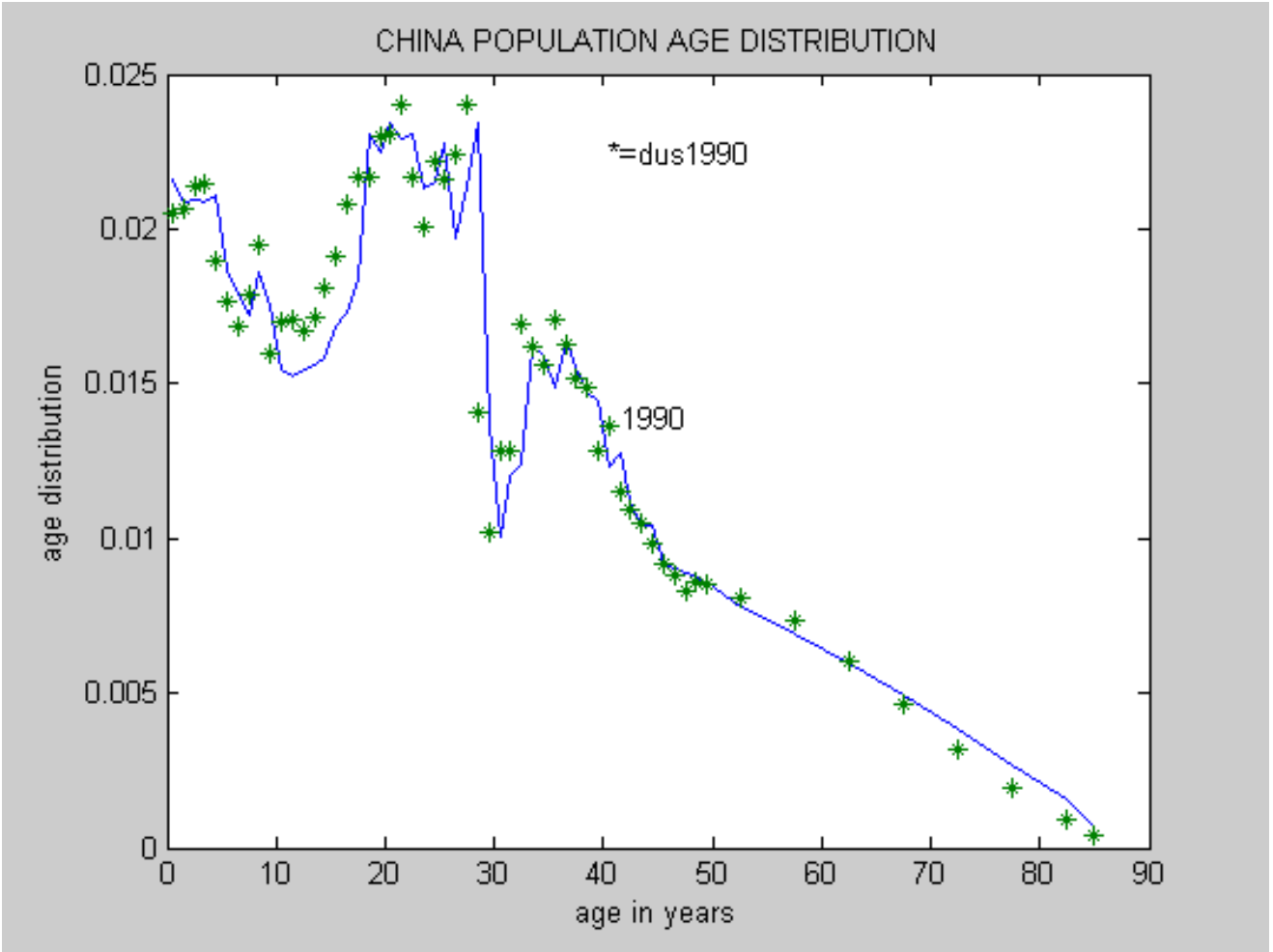
n_i = size of population in age group i

m_i = average birth rate of people in age group i

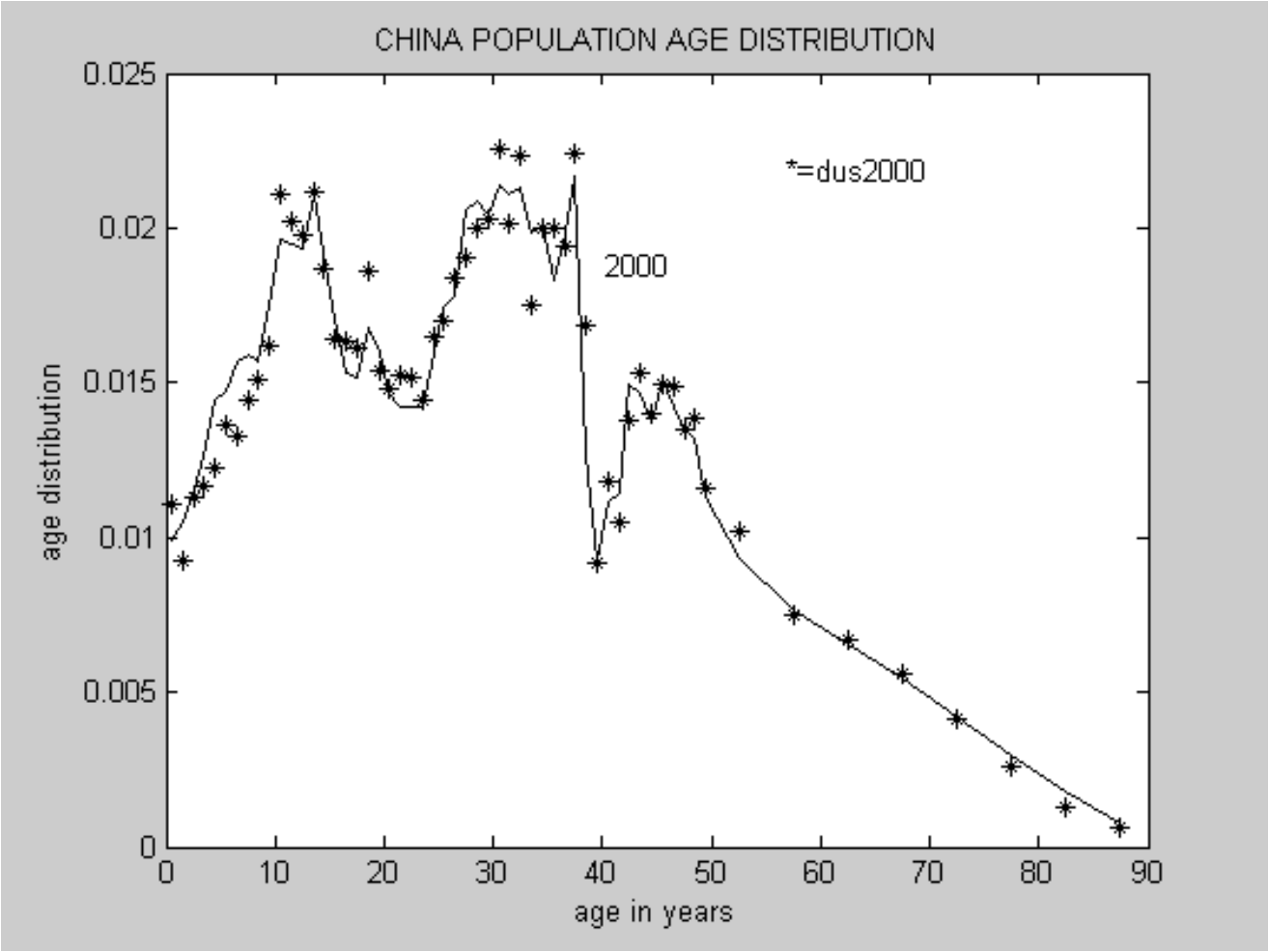
S_i = fraction of those in age group i
who survive to age group i+1

$$\begin{bmatrix} n_1 \\ n_2 \\ n_3 \\ n_4 \\ \\ n_k \end{bmatrix} = \begin{bmatrix} m_1 & m_2 & m_3 & \ldots & m_k \\ S_1 & 0 & 0 & & 0 \\ 0 & S_2 & 0 & & 0 \\ 0 & 0 & S_3 & & 0 \\ & & & & \\ 0 & 0 & 0 & S_{k-1} & 0 \end{bmatrix} \begin{bmatrix} n_1 \\ n_2 \\ n_3 \\ n_4 \\ \\ n_k \end{bmatrix}$$

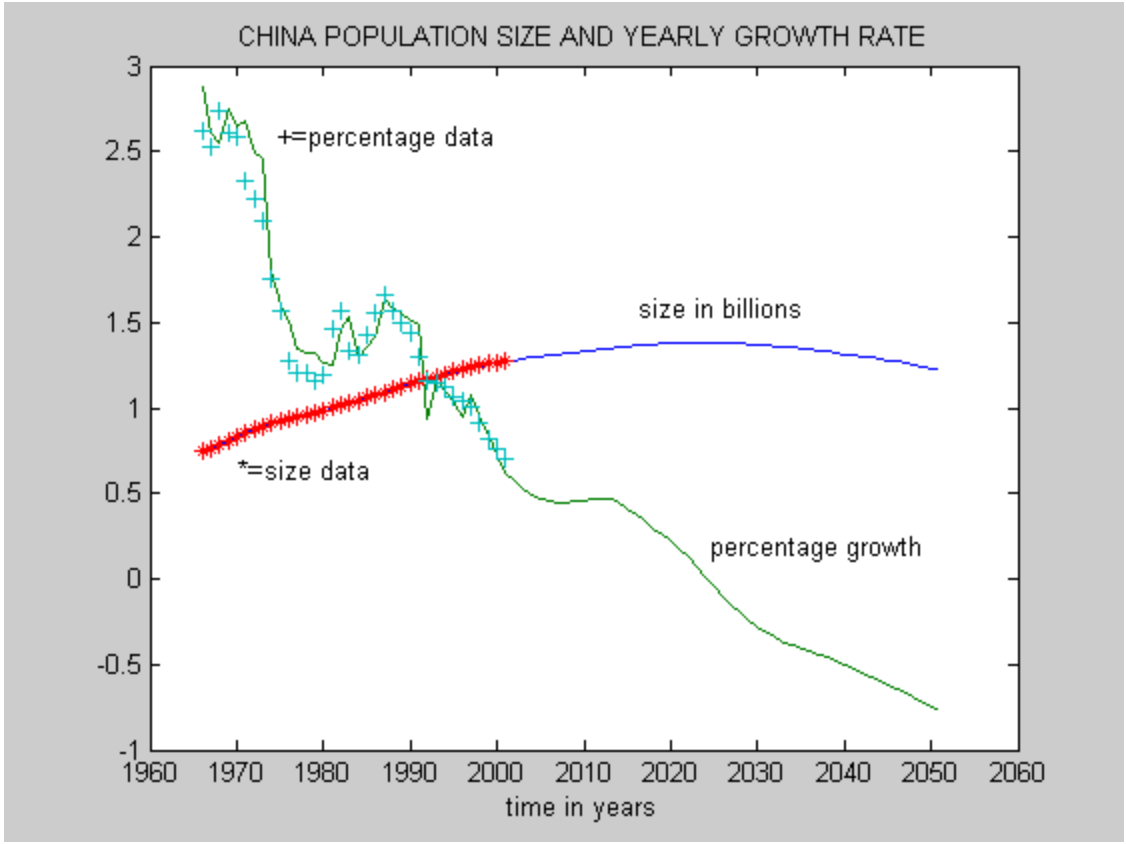
1990: the model and the data



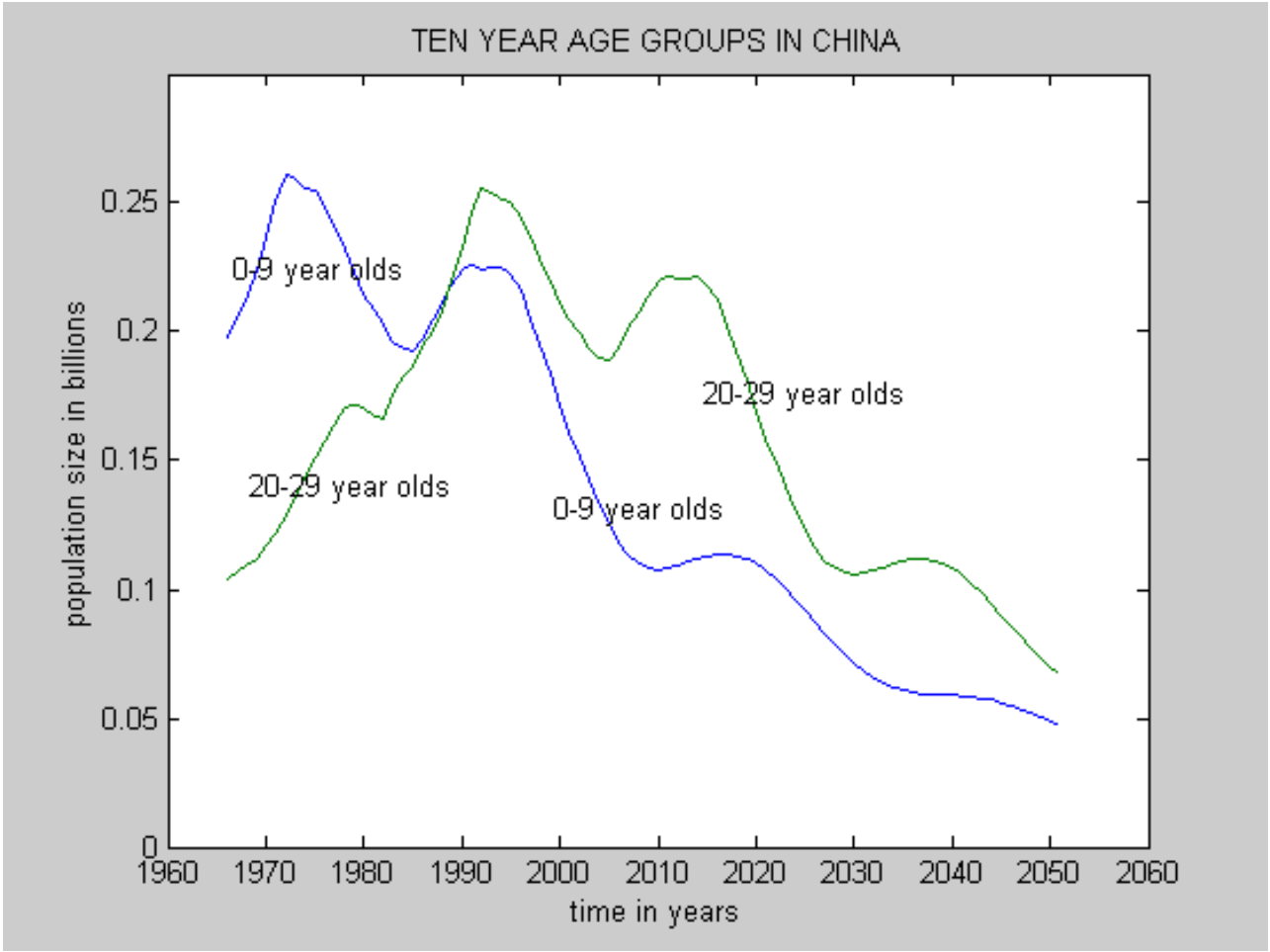
2000: the model vs. data



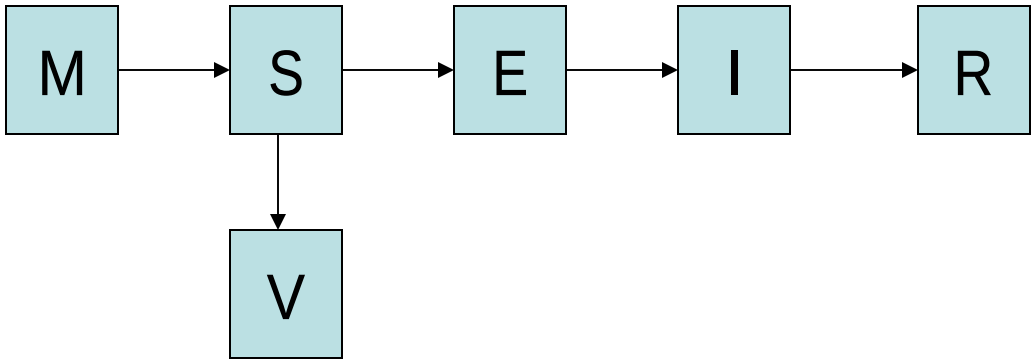
Growth rate with the size



The changing age structure of the population:



The epidemiological model:



M: passively immune

S: susceptible

E: exposed (latent)

I: infective

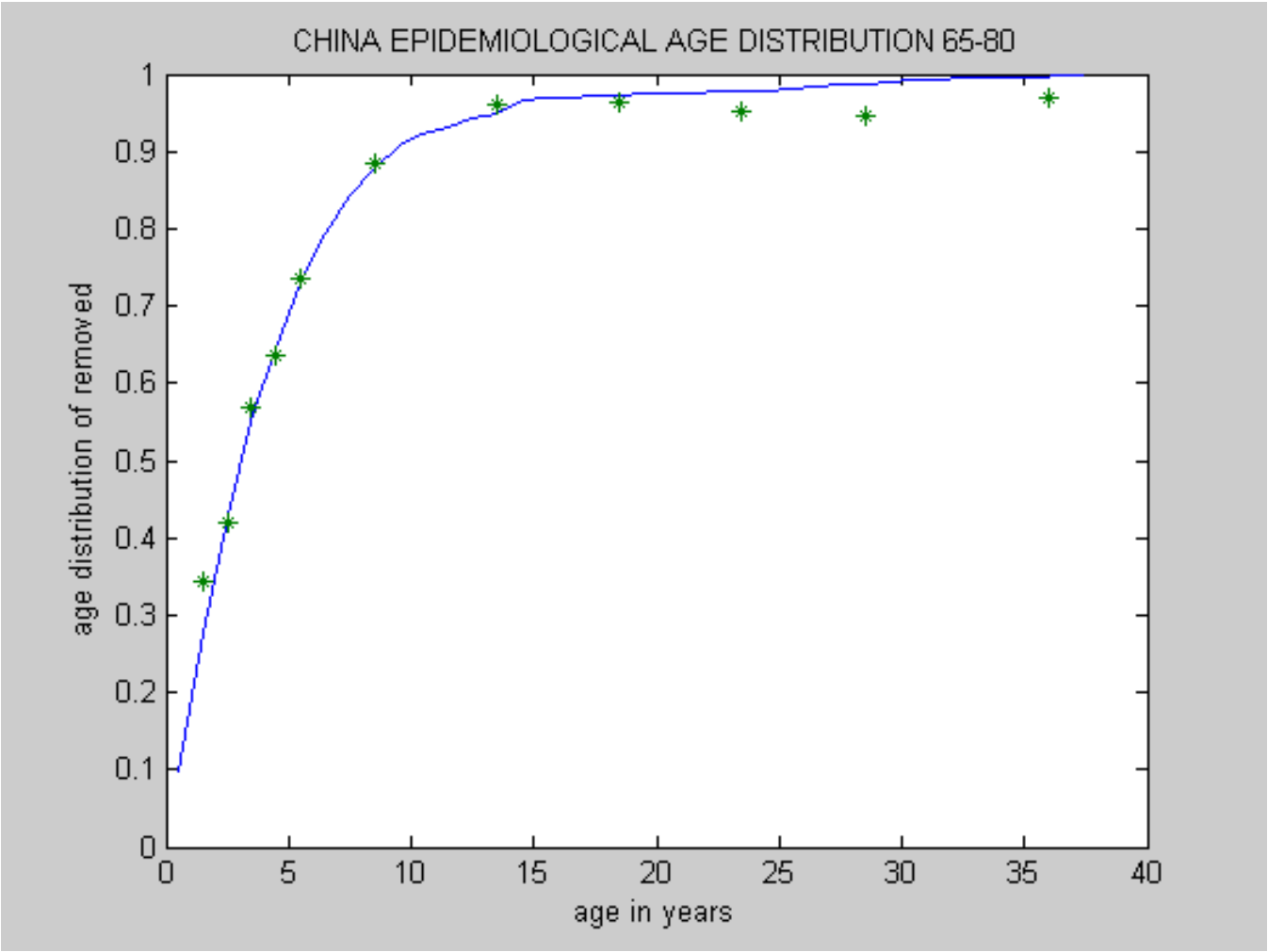
R: recovered with immunity

V: vaccinated

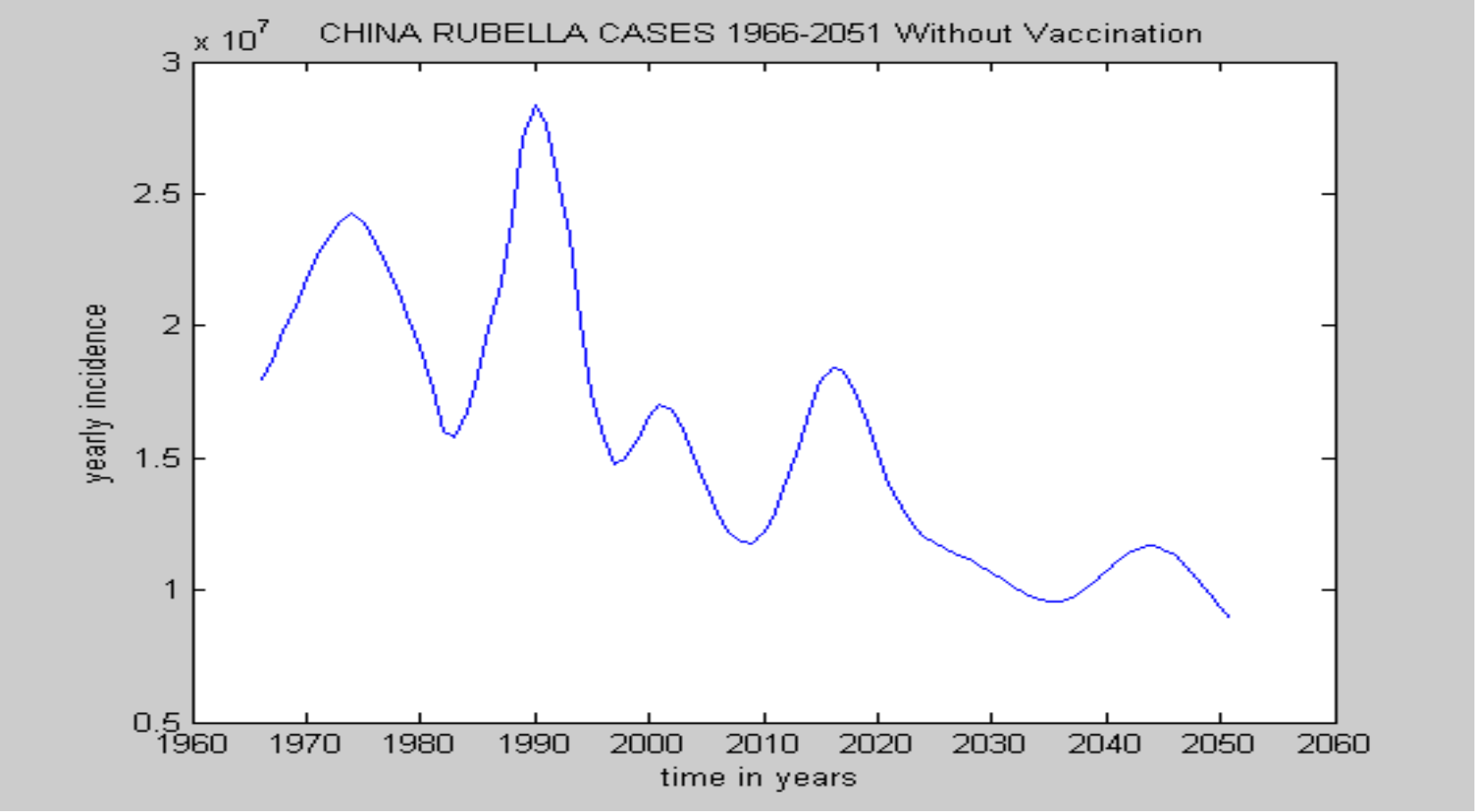
Parameter values:

- average passive immunity period is 6 months (182.5 days)
- average latent period is 10 days
- average infectious period is 12 days
- force of infection values: .20 for 0, .24 for 1-4, .27 for 5-9, .15 for 10-14, .10 for 15-49, .04 for 50-64, .03 for 65+

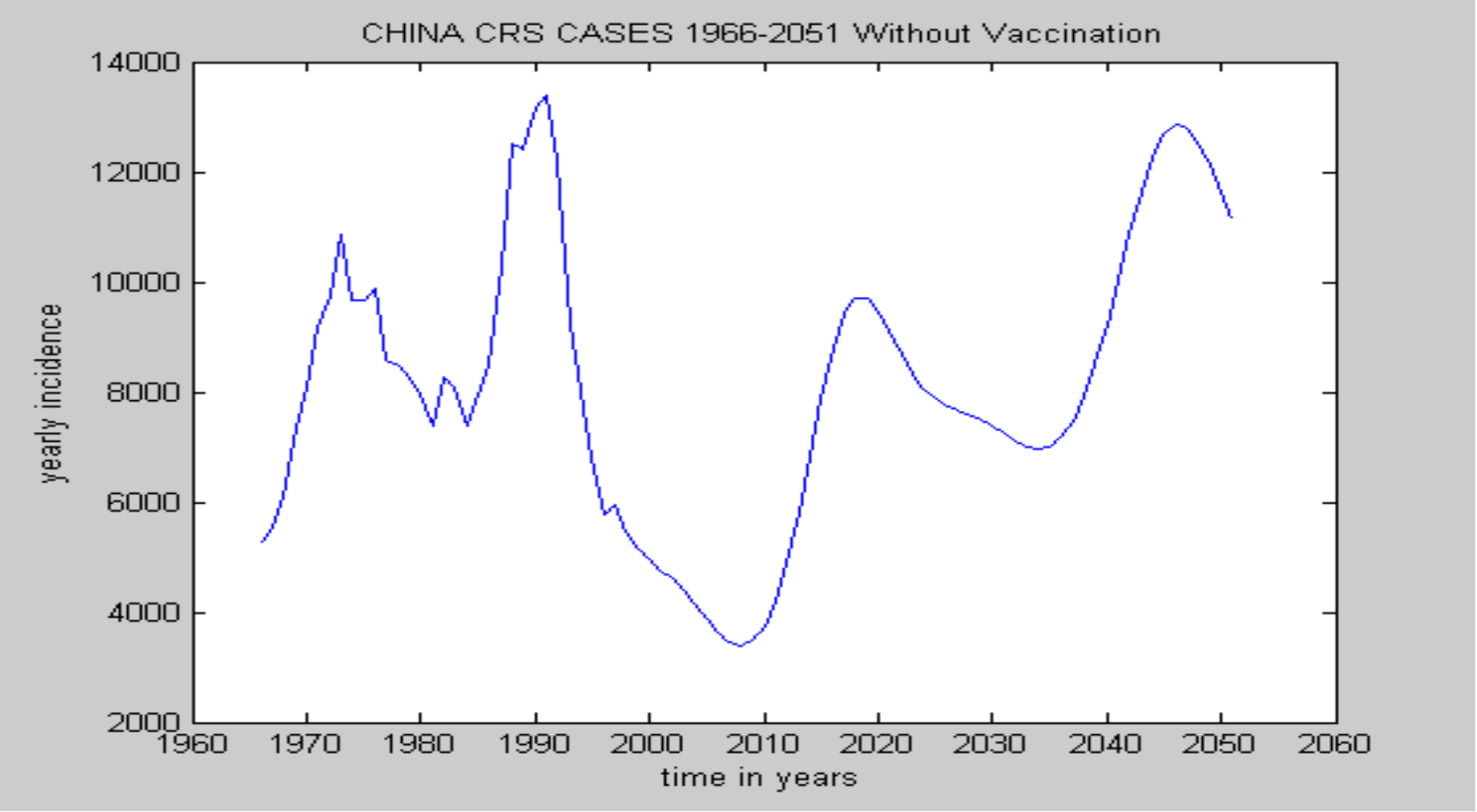
Seropositivity: the model vs. data (with no vaccination)



Rubella cases: no vaccination



CRS cases: no vaccination



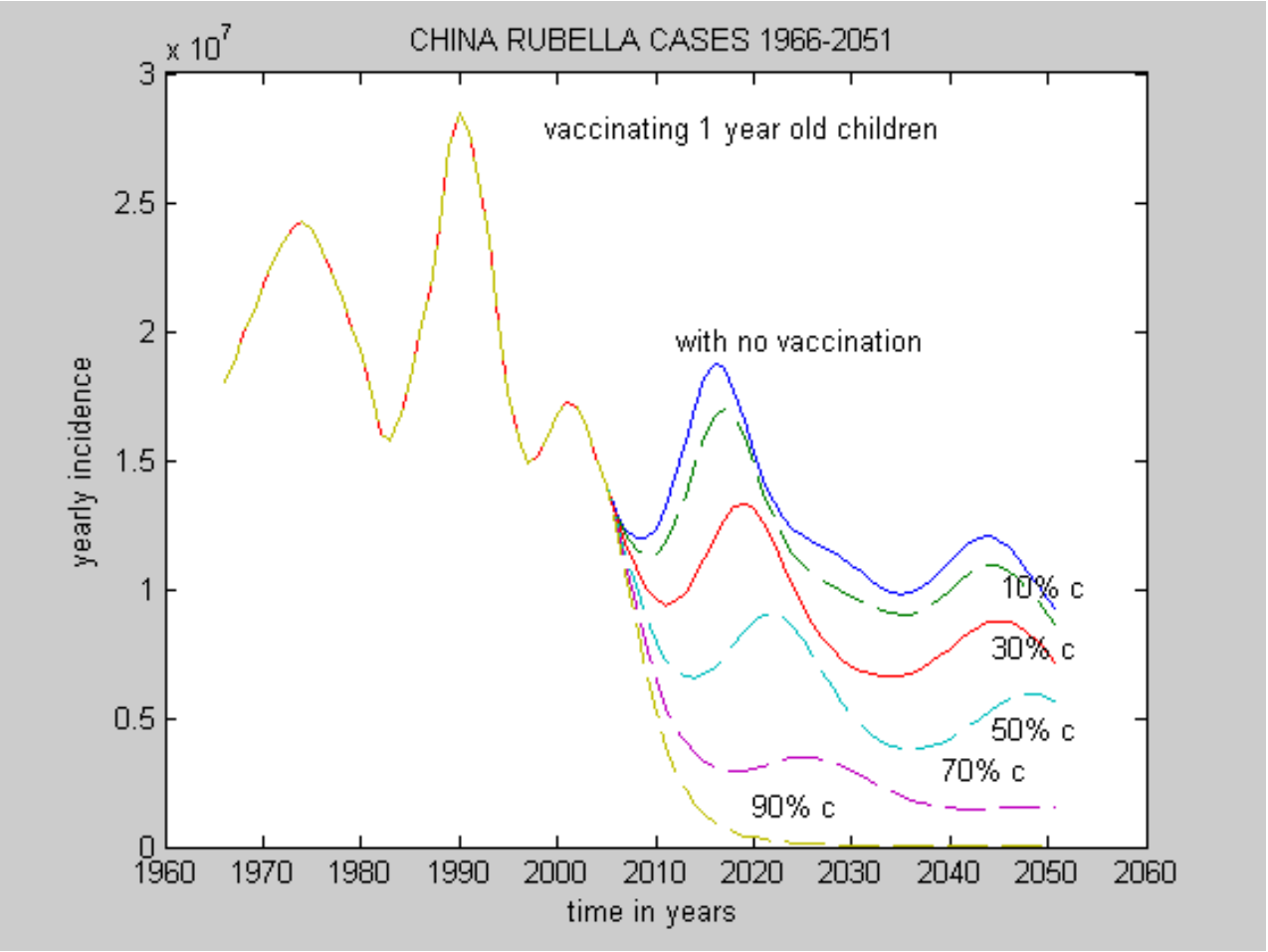
Why ?

- Changing demographics => average age of infection increases => more rubella in pregnant women.
- Average CRS in 2020-2050 is over two times the level in 2005
- Thus maintaining current policy will lead to more CRS

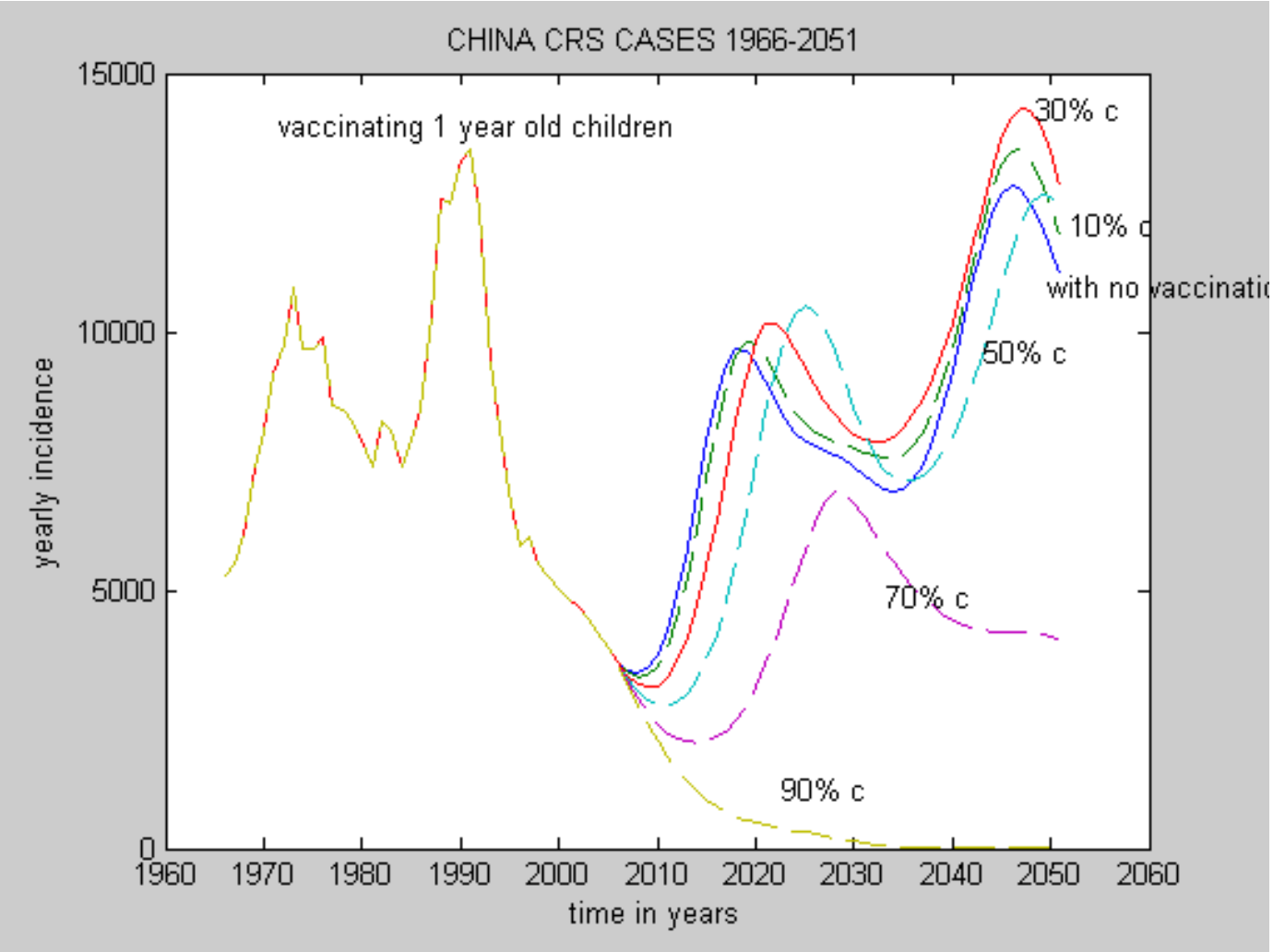
Vaccination Strategies

- Routine vaccination: 1 year old children
- Routine vaccination: 12 year old girls
- Mass campaign: 2-14 year old children
- Mass campaign: 2-14 year old girls
- Mass campaign: 15-40 year old women
- Combinations of above

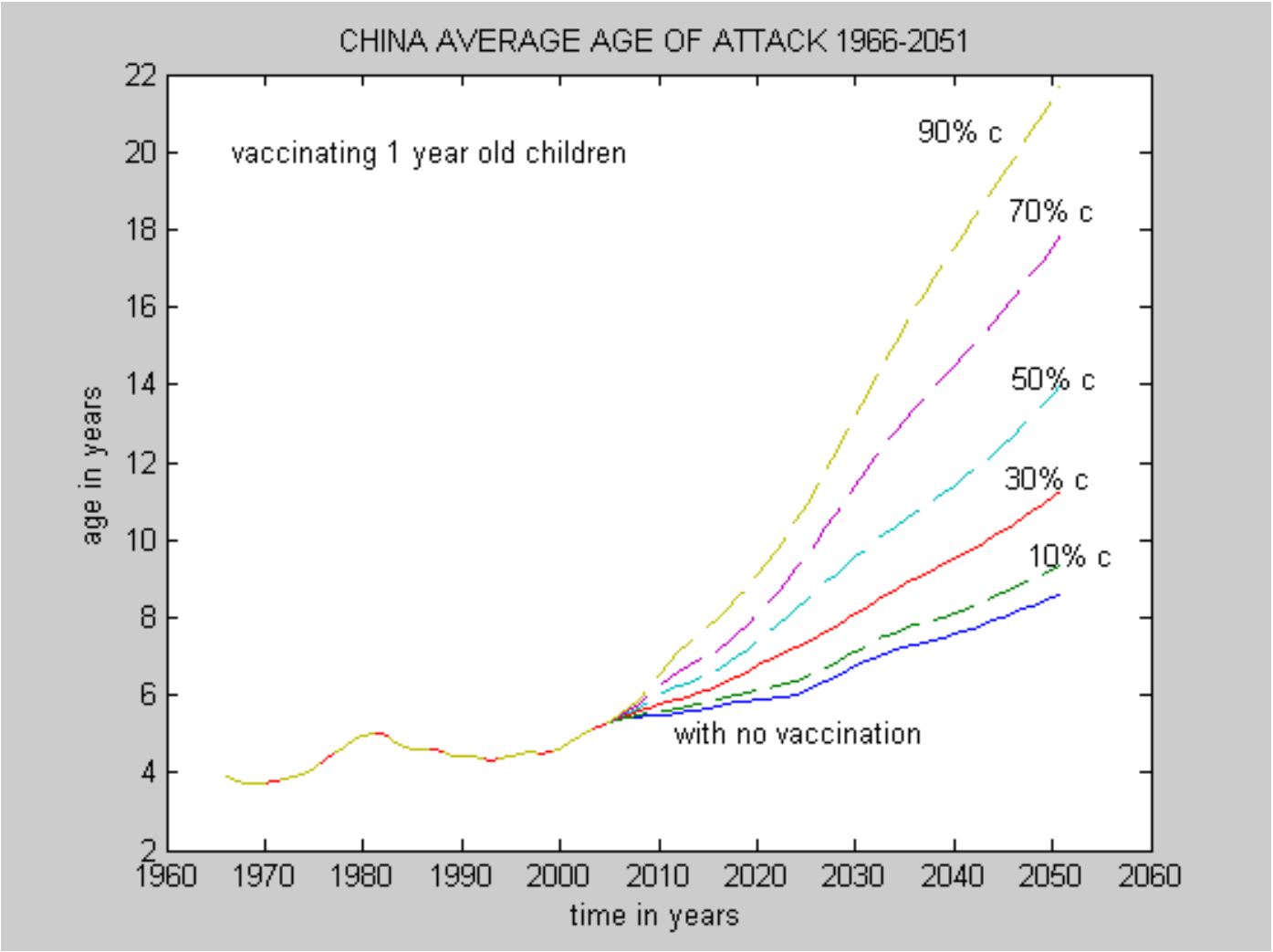
Rubella cases:



CRS cases:


CHINA CRS CASES 1966-2051
vaccinating 1 year old children
30% c
10% c
with no vaccinati
50% c
70% c
90% c
yearly incidence
time in years
15000
10000
5000
0
1960
1970
1980
1990
2000
2010
2020
2030
2040
2050
2060

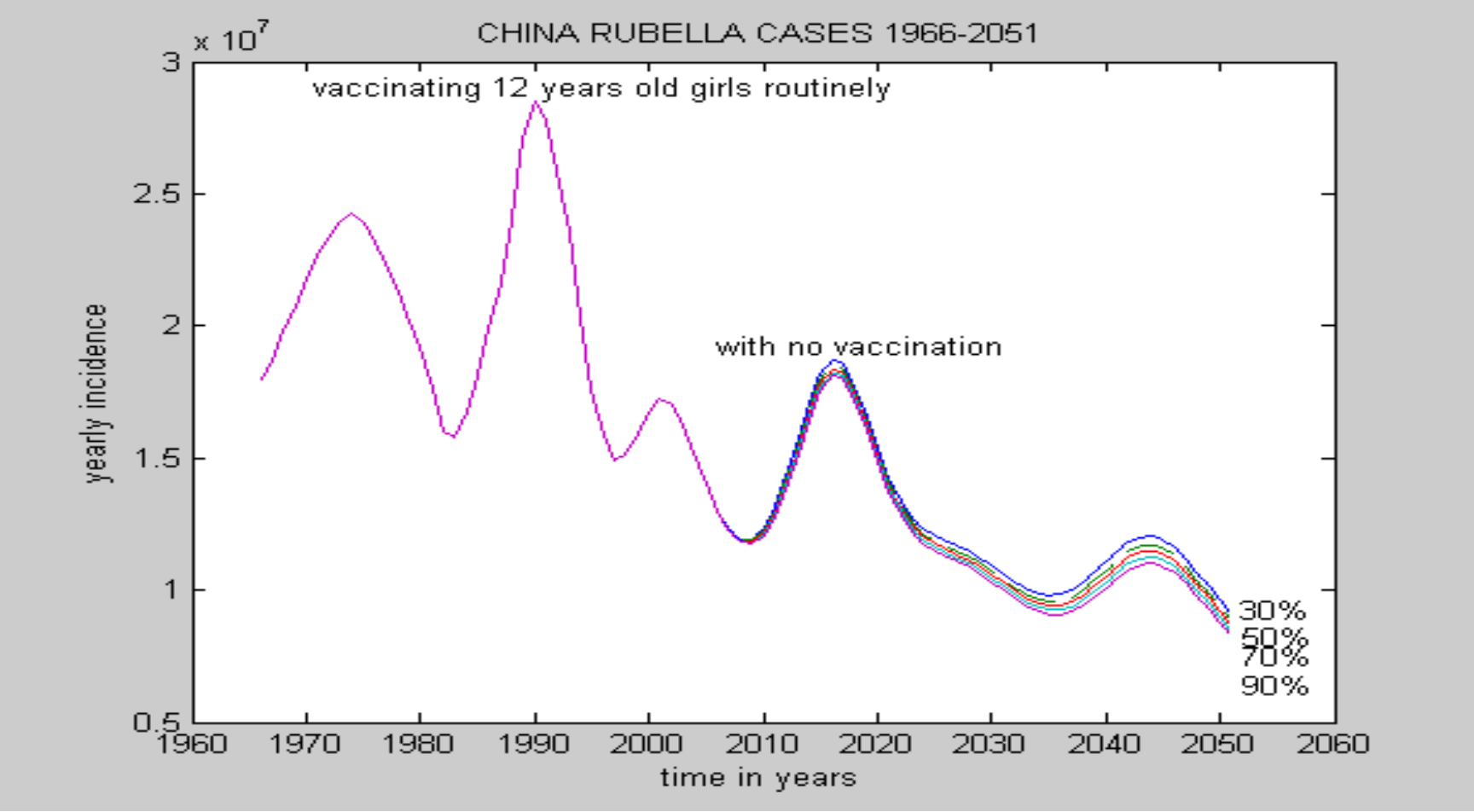
Increasing age of attack:



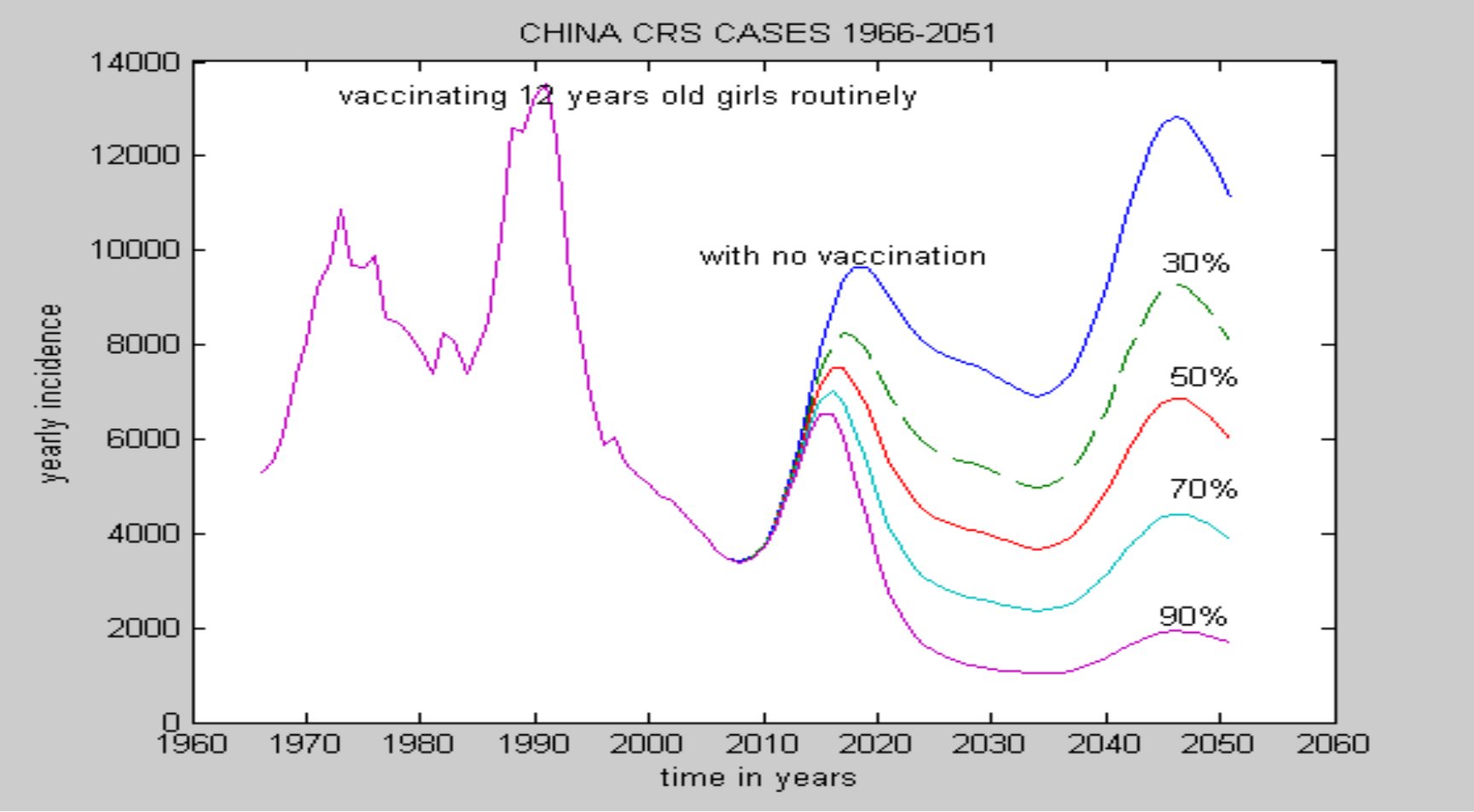
Results from simulations:

- Routine vaccination of 1 year old children causes rubella incidence to decrease
- CRS incidence increases unless 50% or more are vaccinated.
- Rubella and CRS will be eliminated if 80% or more are vaccinated (assuming the current population control policy continues).

Rubella: vaccinate 12 year old girls



CRS:vaccinate 12 years old girls



Observations:

- Routine vaccination of 12 year old girls are effective in reducing CRS cases
- This strategy will never lead to elimination of rubella.

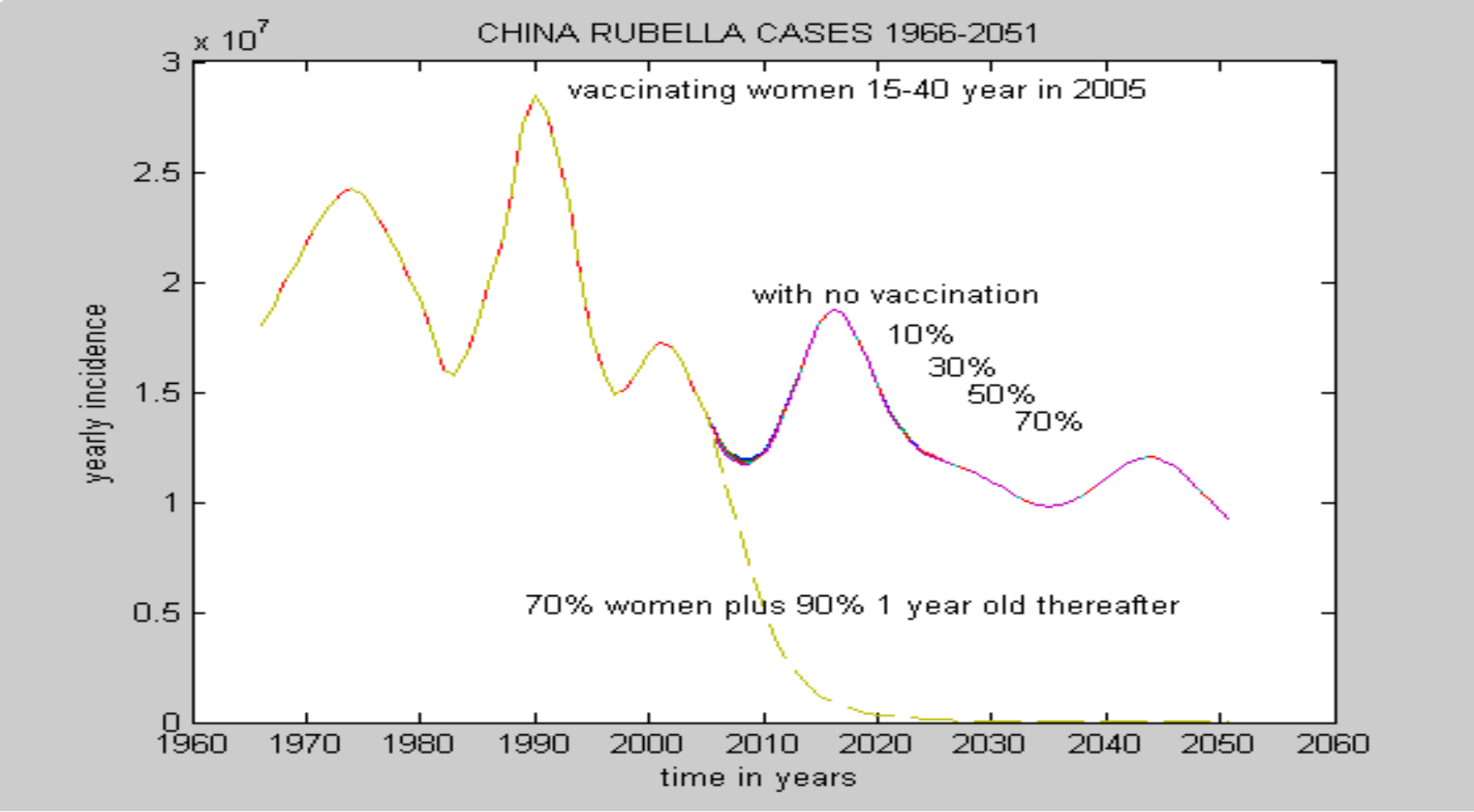
Table 1. Comparison of rubella vaccination strategies in China in 2005 to 2051

mass: 2-14 yr girls	mass: 2-14 yr boys	mass: 15-40 wome	routine: 1 yr old children	routine: 12 yr girls	total CRS Cases 2005-2051	CRS in 2051	# of routine vaccinations	# of mass vaccinations	total # of vaccinations	# of vaccinations per CRS case prevented
90%	90%	60%	90%		2,578	0	596,350,829	395,198,054	991,548,883	2,622
90%		60%	90%		5,515	0	596,350,830	277,610,095	873,960,925	2,329
90%	90%		90%		5,923	0	596,350,828	227,438,932	823,789,760	2,198
		70%	90%		8,173	0	596,350,828	195,718,976	792,069,804	2,126
90%			90%		12,613	0	596,350,830	109,850,973	706,201,803	1,918
			90%		20,757	0	596,350,830	0	596,350,830	1,657
			80%		27,308	1	530,089,627	0	530,089,627	1,500
			70%		100,970	2,247	463,828,423	0	463,828,423	1,658
				90%	117,601	1,722	308,049,970	0	308,049,970	1,171
				80%	147,426	2,837	273,822,196	0	273,822,196	1,174
			60%		276,978	8,139	397,567,219	0	397,567,219	3,831
90%					302,672	11,015	0	109,850,973	109,850,973	1,407
90%	90%				327,554	10,656	0	227,438,932	227,438,932	4,276
		80%			345,807	11,386	0	223,678,829	223,678,829	6,403
		50%			358,881	11,387	0	139,799,268	139,799,268	6,395
			50%		362,752	12,453	331,306,016	0	331,306,016	18,417
			0		380,741	11,389	0	0	0	
			10%		399,712	12,307	66,261,203	0	66,261,203	
			40%		406,976	13,910	265,044,813	0	265,044,813	
			20%		413,971	13,143	132,522,406	0	132,522,406	
			30%		419,181	13,701	198,783,609	0	198,783,609	

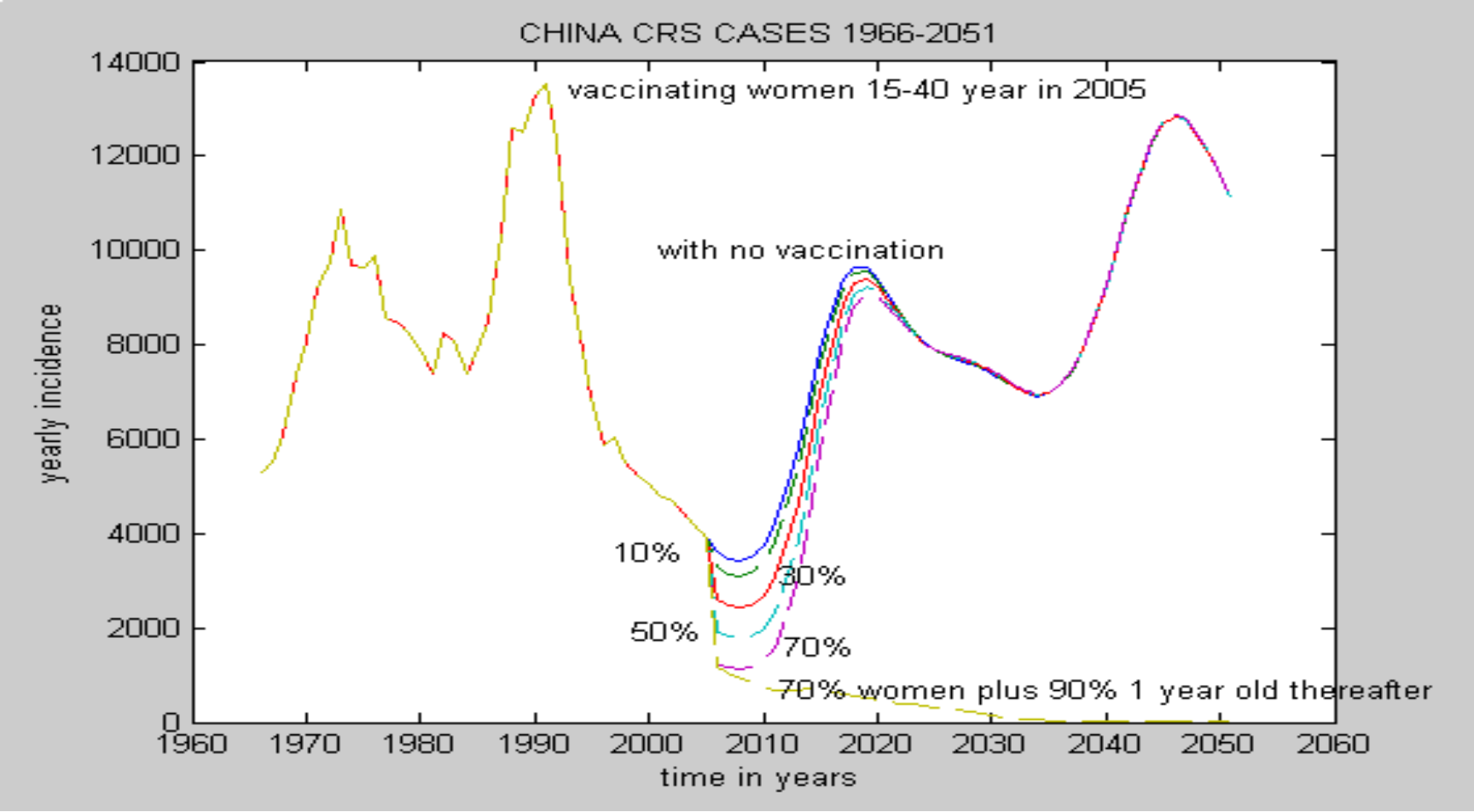
Results from simulations:

- If the achievable vaccination rate is not high, vaccinating 12 year old girls reduces CRS cases by direct protection.
- If the achievable vaccination rate is high, vaccinating 1 year old children is a better strategy that leads to elimination of the disease
- The threshold for switching is about 80%

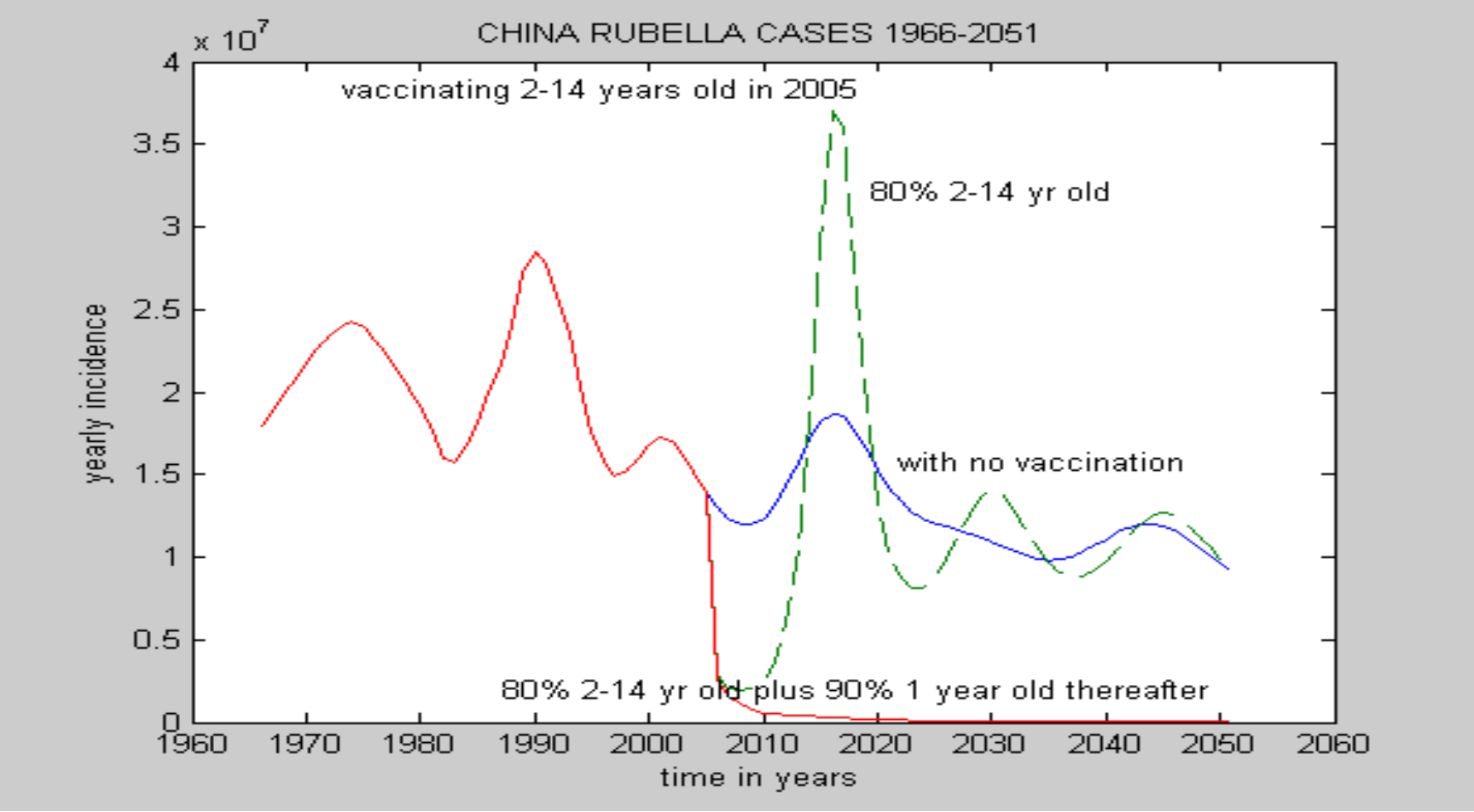
Rubella: 2005 Mass campaign + ...



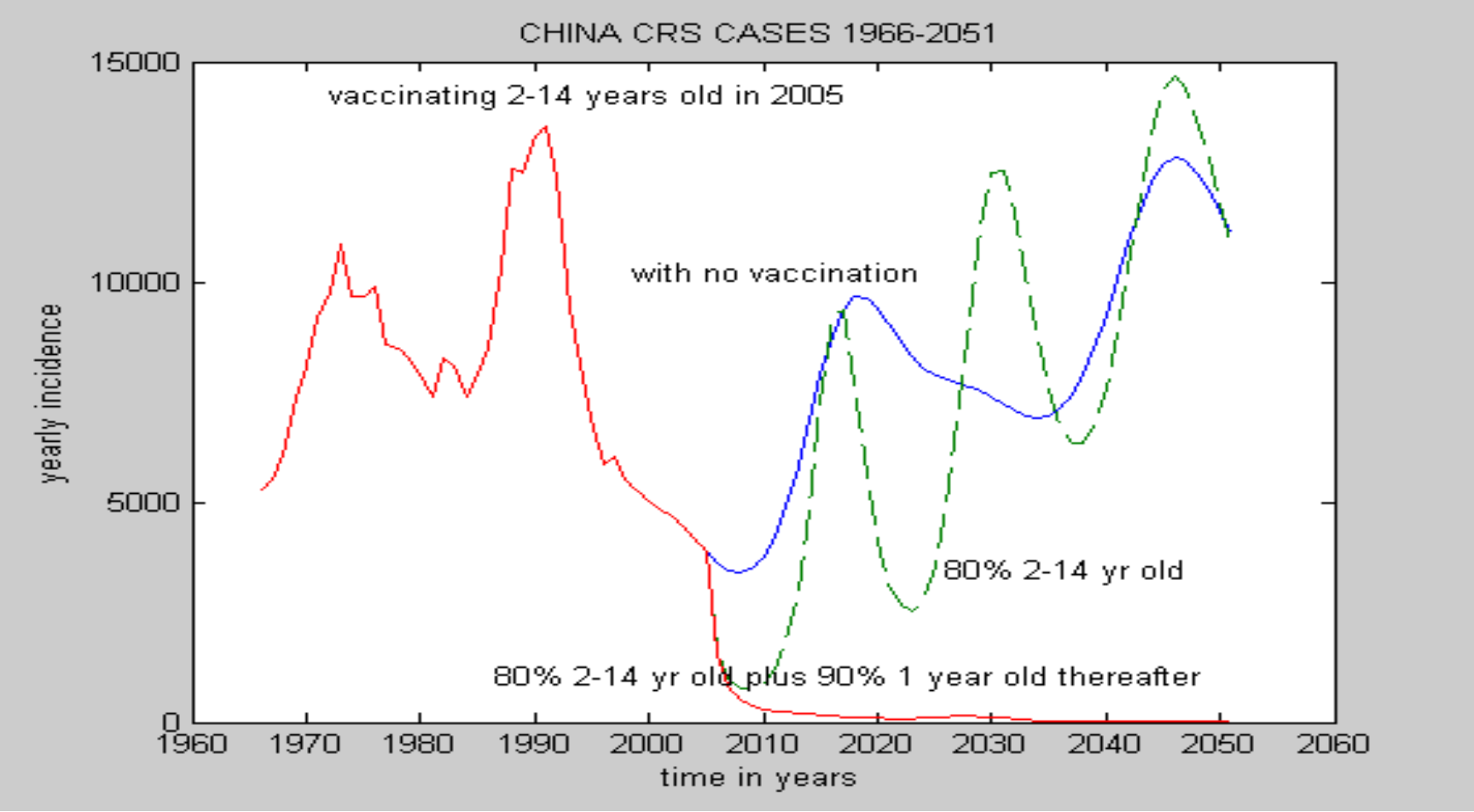
CRS: 2005 mass campaign + ...



Rubella: Campaign vaccination of 2-14 yr olds in 2005



CRS: Campaign vaccination of 2-14 yr olds in 2005



Observations:

- A mass campaign of vaccinating 15-40 year old women can reduce CRS cases during the following 10-20 years.
- A mass campaign of vaccinating 2-14 year old children only can lead to large oscillations in CRS cases with peaks above the no-vaccination levels.

Conclusion (1) :

The changes in demographic structure are altering rubella transmission dynamics. “No vaccination” or “Low coverage infant vaccination” are not good strategies for China.

Conclusion (2):

The best strategy seems to be a combination of initial mass vaccination to provide good short term direct protection plus routine vaccination of at least 80% of 1 year old children to move towards elimination of rubella in China.