



UNIVERSIDAD
POLITECNICA
DE VALENCIA



Ciudad Politécnica
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Pertinence of a change in the meningococcal C vaccine schedule in the Community of Valencia. Agent-based modeling.

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- **Instituto Universitario de Investigación (Decree 128/2005, Jul 25th, 2005, DOGV Aug 2nd/2005)**

- Located at the Universitat Politècnica de Valéncia in the Polytechnic City of Innovation
- 50 researchers
- Most of them are professors at the UPV (grade, masters, doctoral)

- **Multidisciplinary Mathematics**

- Main goal: knowledge transfer to the social environment by means of training/research relationships with industry, administration, institutions and public services
- Introduction of mathematical models
- Interaction with researchers of other areas



Recent years partners

University Institute of Multidisciplinary Mathematics

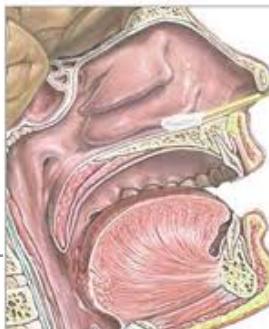


- Departamento de Urología del Hospital La Fe
- Unidad de Deshabituación Tabáquica del Hospital Arnau de Vilanova (Valencia)
- Servicio de Salud Infantil y de la Mujer de la Dirección General de Salud Pública de la Conselleria de Sanitat
- Área de vacunas del Centro Superior de Investigación en Salud Pública (CSISP)
- Instituto de Salud Carlos III
- Laboratorios Baxter
- Unidad de Conductas Adictivas de Catarroja (Valencia)
- Departamento de Motores Térmicos de la UPV

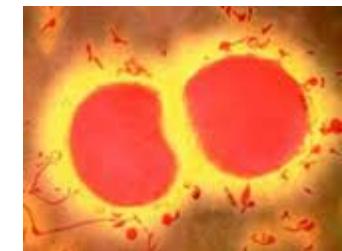
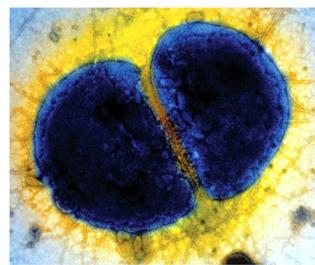


Meningitis: What is this?

- *It is an infection of the brain and spinal cord and can even infect the blood*
- *Before 1990 the main cause was the bacterium *Haemophilus influenzae*: (almost completely eradicated by the Hib vaccine)*
- *Nowadays the main cause of Meningitis is the bacterium *Neisseria meningitidis*:*
 - Transmitted exclusively among humans, mainly during adolescence
 - Carriers: May be infected; Healthy carriers transmit the bacteria
 - It is treated with specific antibiotics
 - Even properly treated, there is up to 10% of mortality and 10% of survivors have sequelae



A sterile swab is passed gently through the nostril and into the nasopharynx



Meningococcal C: Incidence, serogroups and vaccines

- *Low protection levels in adolescence increases the transmission to children under one year old, who may get infected more easily.*
- *The main serogroups are A, B, W135, C, Y, ...*
- *We are interested in serogroup C, the responsible of meningococcal C.*
- *Several types of vaccines:*
 - Simple polysaccharides against serogroups A and C
 - Simple polysaccharides against serogroups A, C, Y and W135
 - *Meningococcal serogroup C conjugate (MCC) vaccine*
 - There is still no vaccine against serogroup B



Vaccination campaigns in CV

- *In 1997, 85% of population between 18 months and 19 years of age was immunized with the bivalent polysaccharide vaccine A + C.*
- *From 2000 the **Conjugate Vaccine C** is used in campaigns with different strategies:*
 - In 2001, it was incorporated at vaccination schedule of children under 6 months of age and 1 dose for children between 1 and 6 years old.
 - ***In 2002, this dose was extended to 19 years old.***
 - In 2006 is fixed the **current vaccination schedule** with three doses: **2, 6 and 18 months of age**



Recent studies on the protection of MCC-vaccine

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- *Recent studies on the MCC-vaccination have determined that levels of protection provided by this vaccine are lower than expected, in particular, in toddlers (young children).*
- *Doctors conjecture that, in 5 – 10 years, there will be an increase of cases in children younger than a year because the herd immunity provided among the adolescents by the current vaccination schedule will disappear.*





- *The Joint Committee on Vaccination and Immunization of DH has recommended in January 2012 a change in the vaccination schedule for UK:*
 - ✓ An adolescent dose of MCC-vaccine should be introduced and a dose in infants should be removed.
 - ✓ This change needs to ensure that coverage is high enough to maintain the herd immunity.
- In Spain, the Grupo de Trabajo MENCC 2012 recently recommended a new the vaccination schedule 2 months, 12 months and 12 years old.
 - ✓ In both cases, the new schedule will start in Jan 2014.
 - ✓ Any of these recommendations are based on mathematical modelling study.

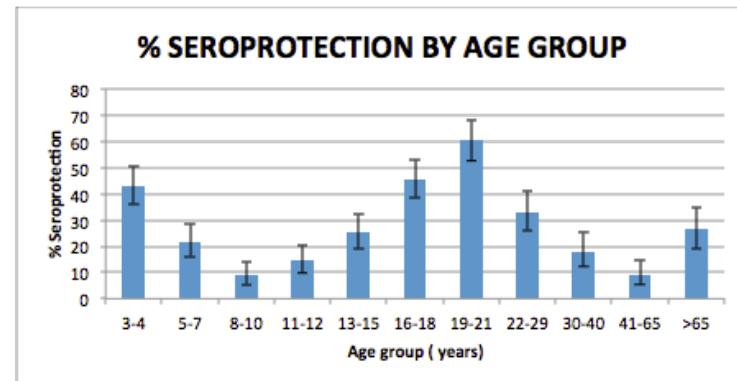
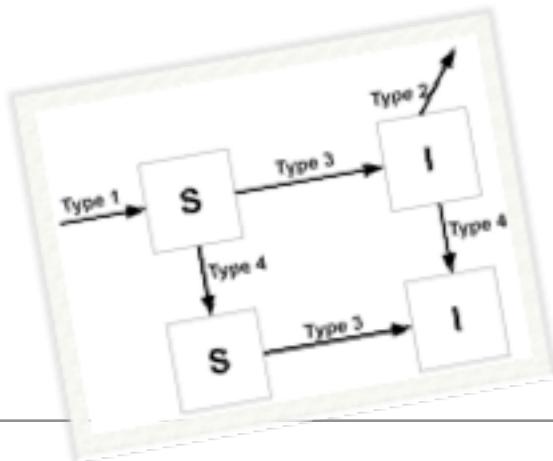


Our objective is to support the schedule change with a mathematical model.



How to state the model: Data hunt

- *There are no data of carriers, only data of cases (currently, very few). The period of carriage is very short and it is difficult to “count” carriers.*
- *We cannot assume a stationary situation because few years ago, in Spain, serogroup B was substituted partially by serogroup C.*
- *Then, typical SIS (continuous susceptible-infected-susceptible) models can not be proposed due to the lack of proper data.*



Stating the model: Data hunt



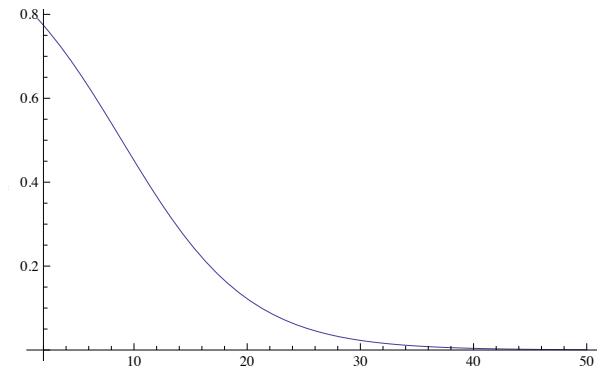
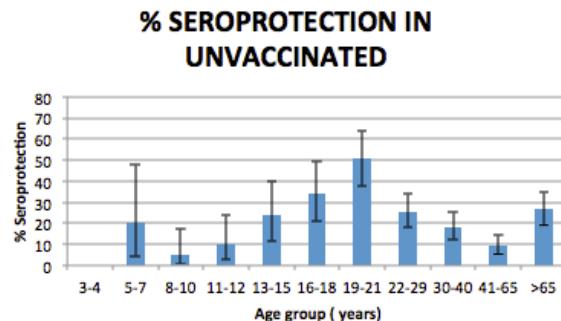
- Most of data in the recent literature are based on analysis of the Serum Bactericidal Activity (SBA) in blood.
- SBA is related to the immunity against meningococcal disease (SBA >1/8), not with the carriage state.
- The studies analysing SBA in blood samples give a general trend about the population protection against meningococcal C, but they are not comparable and do not allow a quantification of the lose of the protection over the time.
- In 2011, supported by THIS research project doctors in the CSISP and Health Institute Carlos III have measured the SBA in 1800 individuals of different ages (older than 3 years old) in Community of Valencia (SBA-CV data).



Stating the model: Data hunt

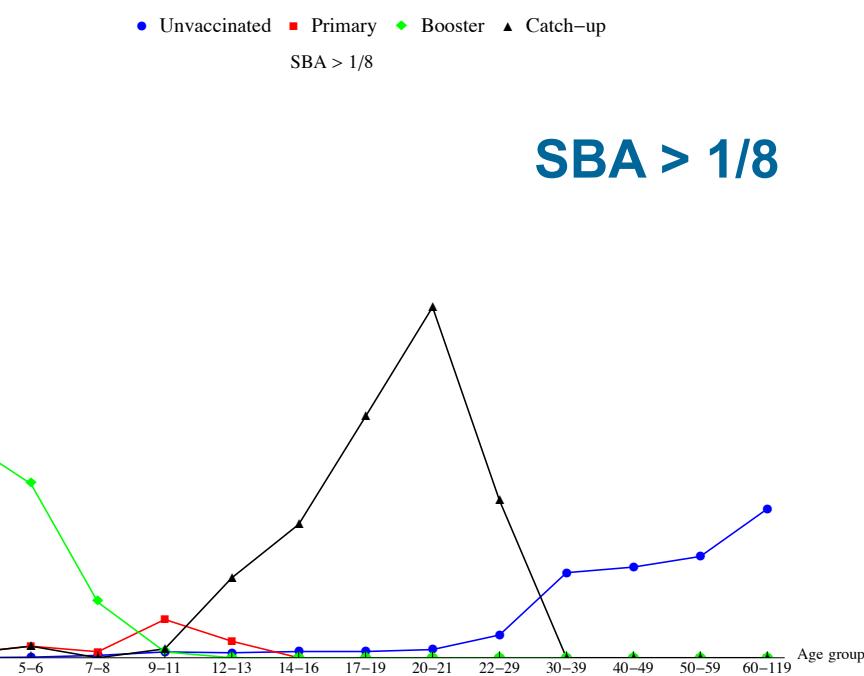
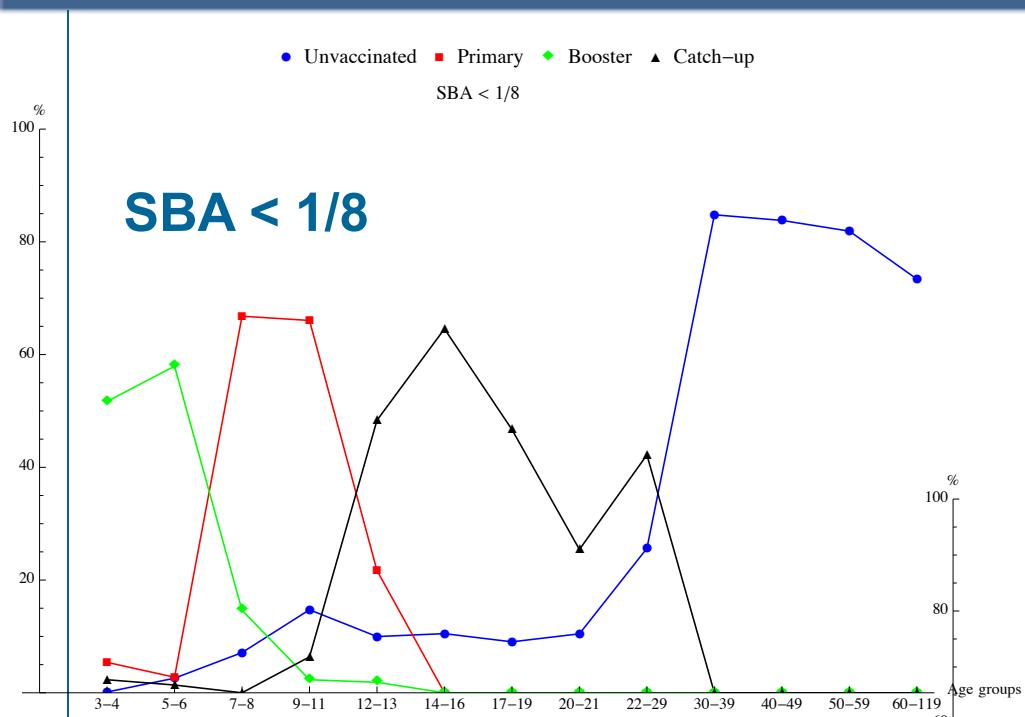


- *With these SBA-CV data and some papers we are able to know*
 - *The seroprotection map in 2011 (initial condition of our model)*
 - *Seroprotection of unvaccinated individuals (natural protection)*
 - *Seroprotection evolution of vaccinated individuals depending on the way they were vaccinated (primary, booster or catch-up) and age*



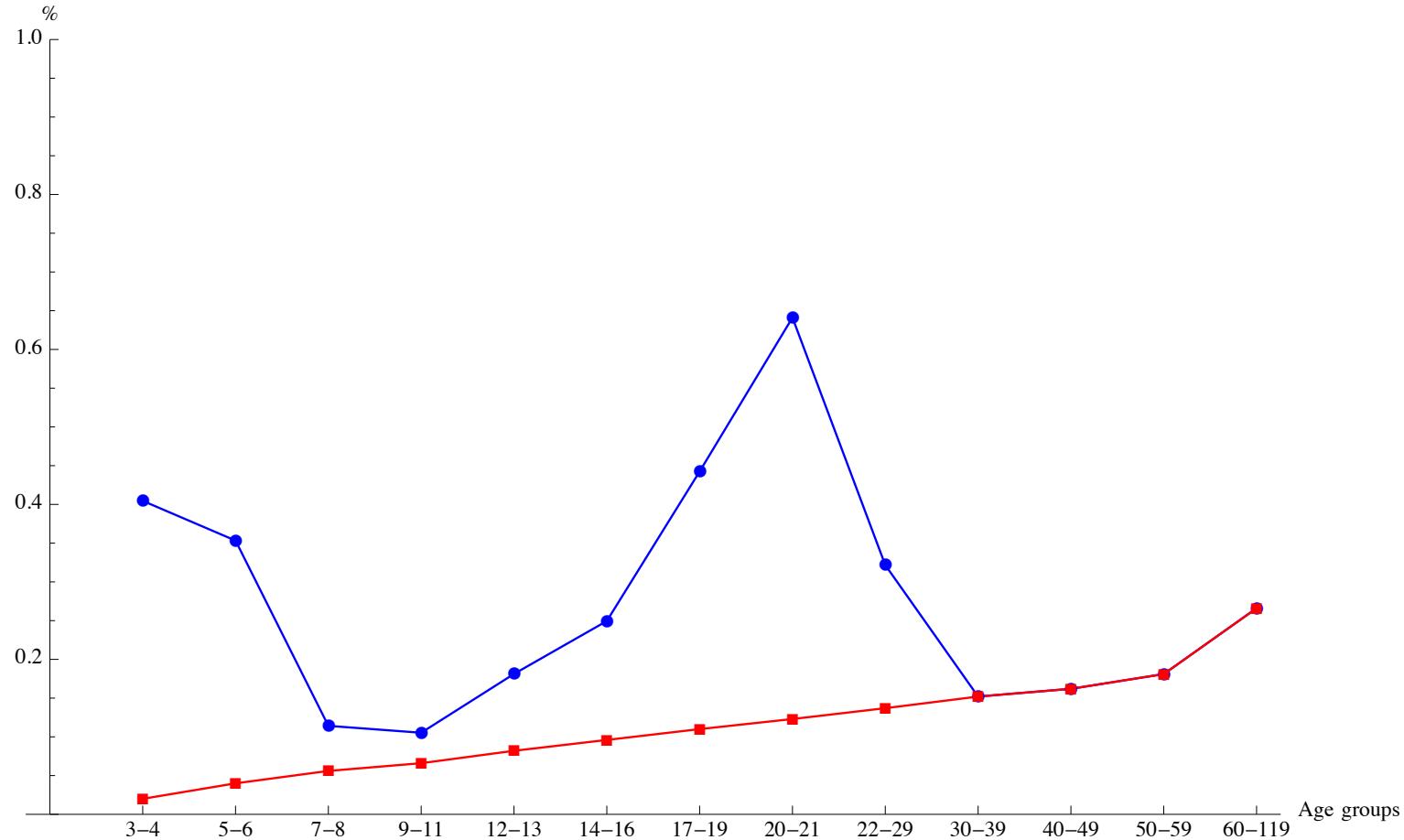
Initial seroprotection and vaccination per age group

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Initial (global) protection and natural protection

● Protected ■ Natural protection



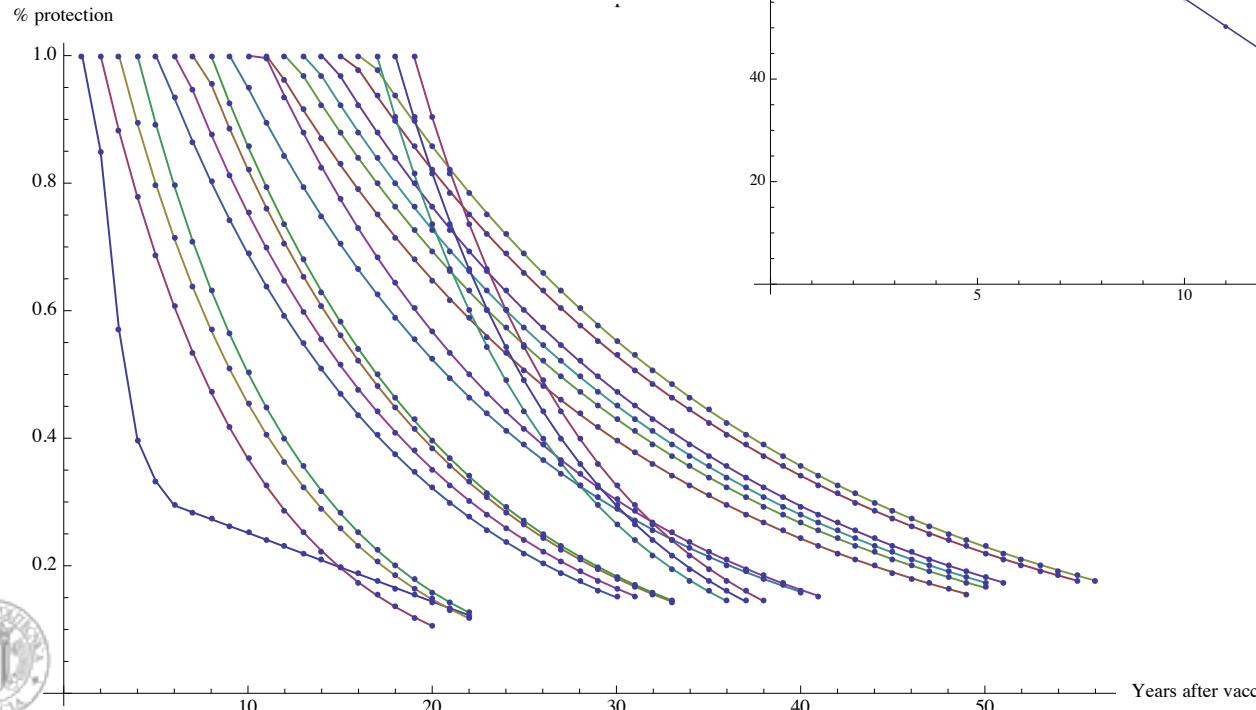
Seroprotection over the time

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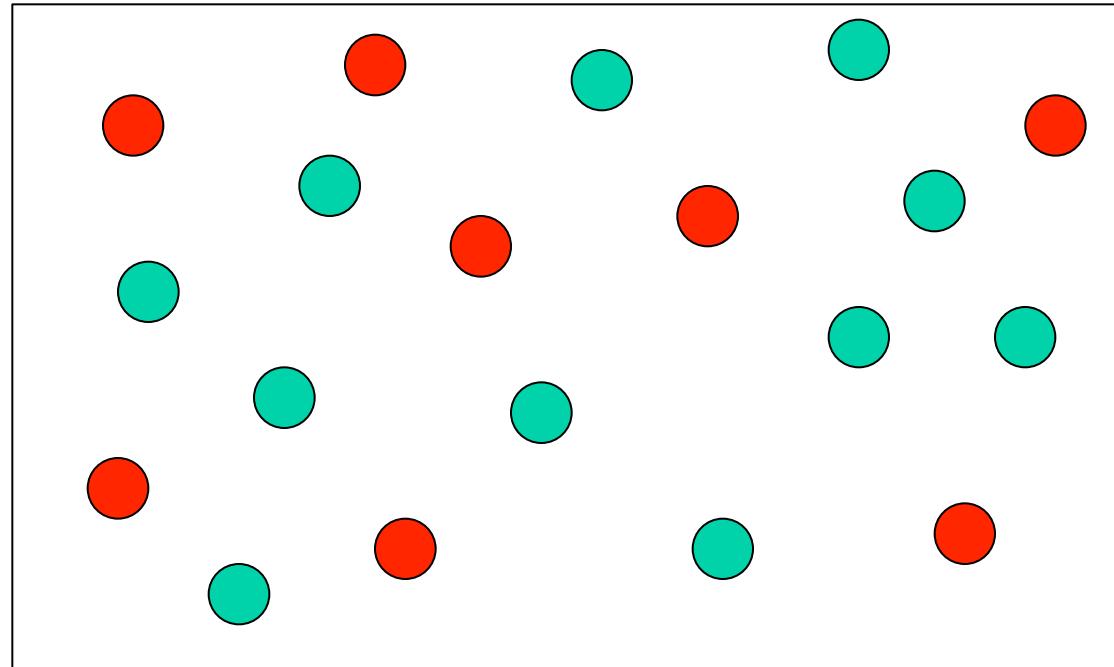
Primary

Booster + catch-up



Stating the model: Agent-based model

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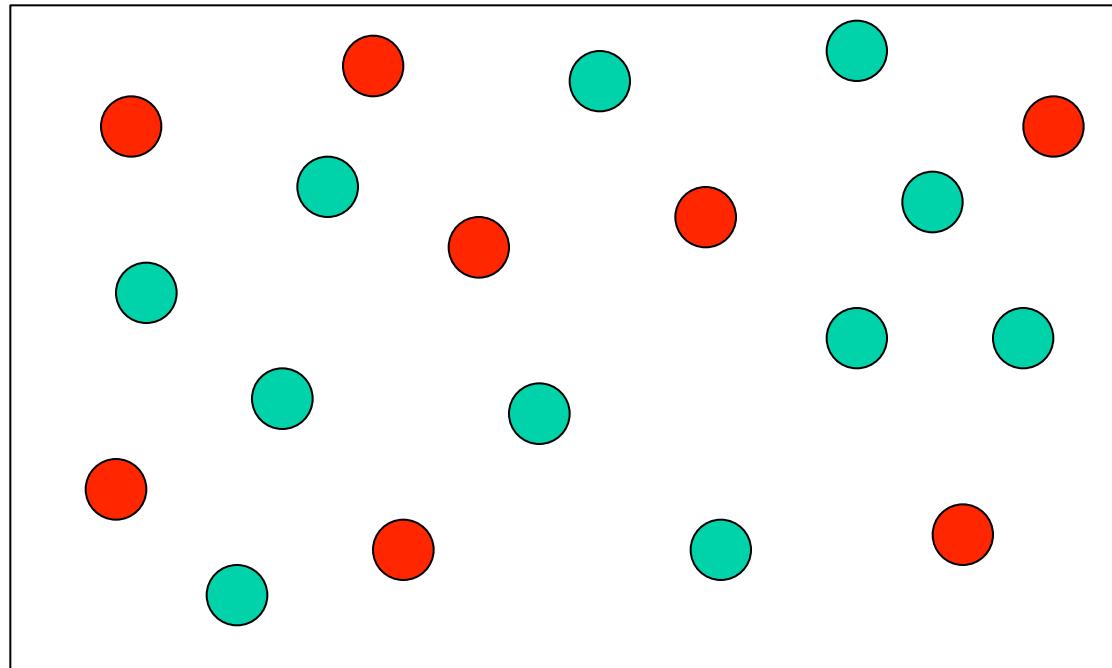


Legend:
Teal circle: $SBA \geq \frac{1}{8}$
Red circle: $SBA < \frac{1}{8}$

*Individuals are represented by points
Around 5,000,000 points (population in CV)
Underlying demographic model*



Stating the model: Agent-based model



Legend:
Teal circle: $SBA \geq \frac{1}{8}$
Red circle: $SBA < \frac{1}{8}$

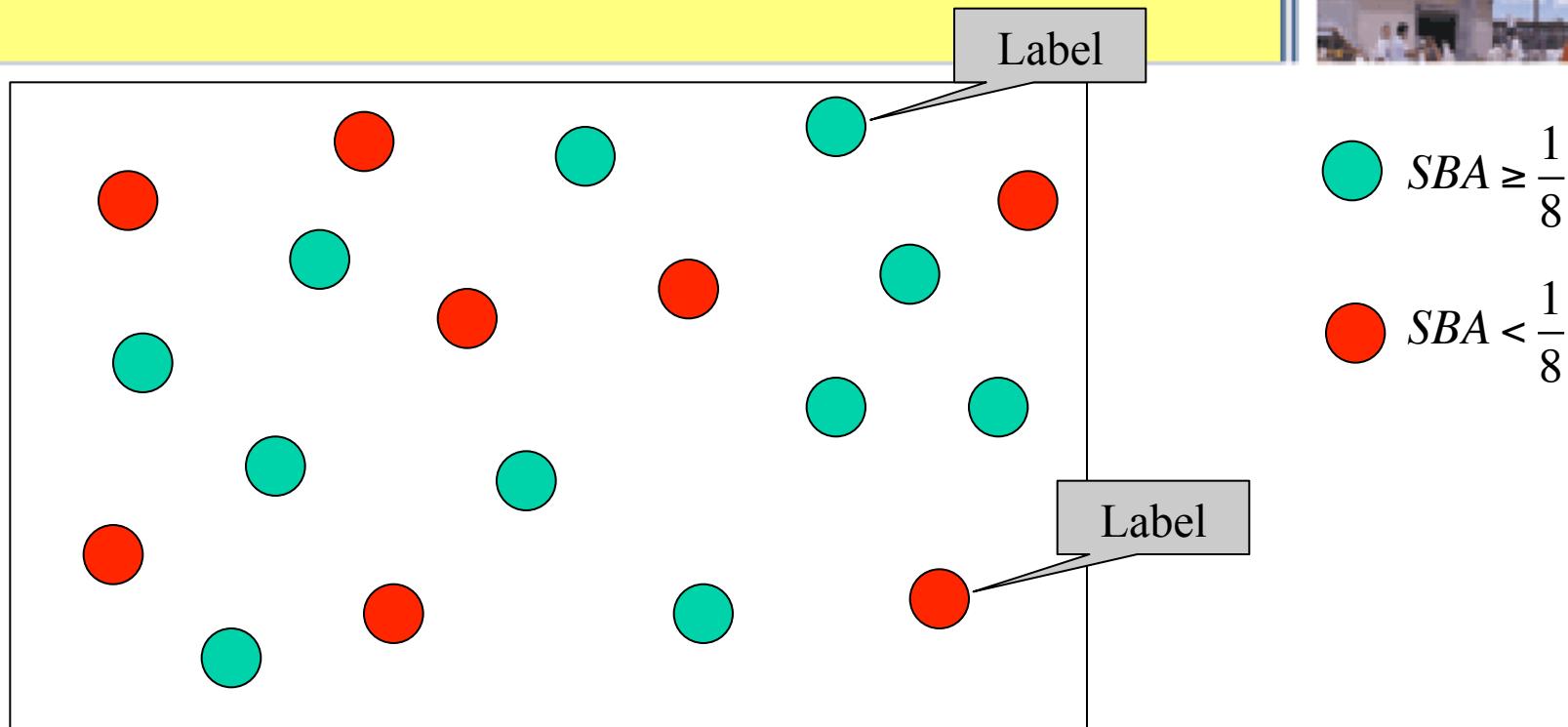
Starting time instant: October 2011

Current vaccination schedule is included into the model:

2, 6 and 18 months old



Stating the model: Agent-based model



Labels

Age (in months)

SBA (<1/8, >1/8)

Type of vaccination: 0 Unvaccinated, 1 Primary, 2 Booster, 3 Catch-up

Age of the last vaccination





Evolution rules (over the time)

- FOR every month t (from Oct 2011 to Jan 2040)
 - FOR every individual i
 - ADD a month to his/her age
 - IF this node i does not die
 - IF this node i has to be vaccinated (following the current schedule)
 - UPDATE the type of vaccination, the age of the last vaccination and the SBA becomes greater than 1/8
 - ELSE UPDATE his/her protection depending on his/her age and age and type of the last vaccination (following the protection graphs)
 - ELSE this node dies, it is “resurrected” as a unprotected unvaccinated newborn





1. *If the current situation does not change ...*

2. *Optimization of the vaccination schedule ...*

- The schedule of paediatric revision in the Spanish region of Valencia at 15 days, 1 month, 2 months, 4 months, 6 months, 12 months, 15 months, 18 months, 6 years, 12 years and 14 years old
- This vaccine cannot be administrated before 2 months, we have combined all the paediatric revision to define all the possible vaccination schedules with 1, 2 and 3 doses, summing up 129 different schedules
- **The best is 2 months, 12 months and 12 years old**

3. *Undesired effects of the schedule change and how to solve them ...*





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