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The "Ease-of-use" of Vaccines: A Simulation Study of Factors Impacting the Efficiency of the Organisational Models of Vaccination Centers

Massimo Maurici[1], Luca Paulon[1]

[1]Department of Biomedicine and Prevention, University of Rome Tor Vergata

Introduction

With regard to ease-of-use in a vaccination contexts, the World Health Organisation (WHO) calls attention to the fact that "In some situations the time required to prepare a vaccine is critical, such as during campaigns with long lines of waiting clients or during outreach activities. For these situations a vaccine product that is easier to use and takes less time to prepare can be extremely valuable and can help to increase coverage" and also that "... Immunisation programmes may also decide to select products that are similar to those already in use to minimise the burden on health care workers".[1]

Efficiency and management of vaccination is particularly relevant in low-resources settings. For example, regarding meningococcal vaccination, a vaccination point of dispensing (POD) could be called on to reach a coverage target in a short span of time (e.g two-three weeks).[2] This target could be reached, for instance, in a organisational setting in which only a single specific vaccine (such as during an epidemic vaccination campaign) is offered. Another example would be Italian national immunisation plans which could mandatorily require vaccine coverage for meningococcal vaccination >95% within 2019[3] without allocating more resources and possibly even reducing current resources.

Given that the ease-of-use of a vaccine could be crucial for its impact on the immunisation programme and resources-saving,[1] the problem of quantifying its benefits for a vaccination POD in different scenarios, i.e. target population and specific organisational setting.

Since this problem requires a specific in-depth analysis, it is clear that solving such a thorny topic with the simple tools currently available, or with a common sense approach, would be very difficult. We have therefore resorted to a "simulation optimisation approach".[4-7]

The case study

We focused the study on two kinds of vaccination PODs, dispensing only meningococcal vaccination.

The first, i.e., the ideal vaccination POD, is organised according to recommendations of the WHO[2,8] with one "vaccination team" (i.e., one supervisor, two nurses, three-four record clerks, two-three local community representatives, one technician responsible for the cold chain, and one driver) supported by fundamental logistics, and having a daily goal of 1000 vaccinations (about 300 per working shift).

The second, i.e., the real world vaccination POD, is a limited version of the ideal POD (but closer to a common setting of a vaccination center) in terms of available operators: one supervisor and one security officer are allocated, while nurses (two or three, the exact number to be investigated in the following simulation experiments) have to perform all activities reserved to record clerks, community representatives and technicians which are not available as in the ideal vaccination POD. Such a real world POD organisational model is based upon observations in a real world vaccination setting.

In particular, we measured the efficiency impact of the ease-of-use of specific meningococcal vaccines,[1] namely Nimenrix®[9] and Menveo®,[10] which are available on the market and which can be both used in vaccination PODs in Italy. This because such vaccines are quite different in terms of reconstitution phase as stated in their technical fact sheet (see Figure 1).

This study aims to specifically answer the following questions:

- Given the use of Nimenrix® or Menveo® vaccine, is the vaccination POD under study able to provide up to 300 doses per shift (i.e., to reach the WHO goal)?

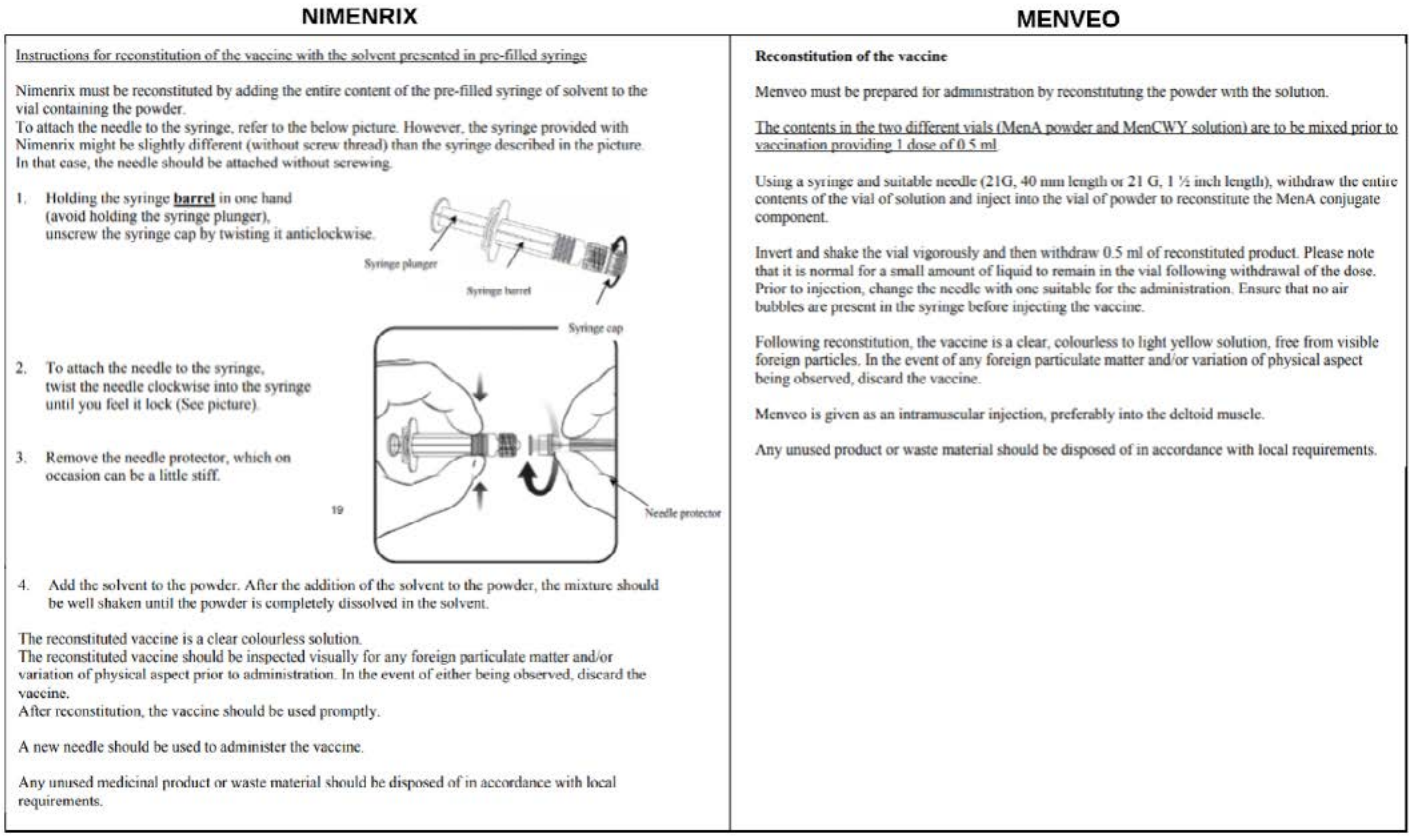
In Italy, the focus on meningococcal vaccination is also motivated by the recent epidemics in Tuscany[13] and the recently approved national immunisation plan of the Ministry of Health "Piano Nazionale Prevenzione Vaccinale"[14] which mandatorily extends coverage of meningococcal vaccination to 12-18 year old cohort. Increasing vaccine coverage to above 95% in 2019 is also an important goal for public health professionals and regulatory agencies in Italy.[3]

More in general, according to WHO "Meningitis remains a universal public health challenge in countries around the world - cases and outbreaks are highly dreaded. The global number of deaths due to meningitis was estimated at 380,000 annually. Meningitis is an epidemic-prone disease, and as such deserves special attention given the potentially major impact on health systems, the economy and society as a whole due to the disruptive nature of meningitis outbreaks which are costly and challenging to control".[15]

Materials and Methods

The study adopts a quantitative research methodology supported by a simulation approach.

We identified three main steps for solving the simulation problem.



NIMENRIX

Instructions for reconstitution of the vaccine with the solvent presented in pre-filled syringe

Nimenrix must be reconstituted by adding the entire content of the pre-filled syringe of solvent to the vial containing the powder.
To attach the needle to the syringe, refer to the below picture. However, the syringe provided with Nimenrix might be slightly different (without screw thread) than the syringe described in the picture. In that case, the needle should be attached without screwing.

1. Holding the syringe **barrel** in one hand (avoid holding the syringe plunger), unscrew the syringe cap by twisting it anticlockwise.

Syringe plunger
Syringe barrel

2. To attach the needle to the syringe, twist the needle clockwise into the syringe until you feel it lock (See picture).

Syringe cap

3. Remove the needle protector, which on occasion can be a little stiff.

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Needle protector

4. Add the solvent to the powder. After the addition of the solvent to the powder, the mixture should be well shaken until the powder is completely dissolved in the solvent.

The reconstituted vaccine is a clear colourless solution.
The reconstituted vaccine should be inspected visually for any foreign particulate matter and/or variation of physical aspect prior to administration. In the event of either being observed, discard the vaccine.
After reconstitution, the vaccine should be used promptly.

A new needle should be used to administer the vaccine.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

MENVEO

Reconstitution of the vaccine

Menveo must be prepared for administration by reconstituting the powder with the solution.

The contents in the two different vials (MenA powder and MenCWY solution) are to be mixed prior to vaccination providing 1 dose of 0.5 ml

Using a syringe and suitable needle (21G, 40 mm length or 21 G, 1 ½ inch length), withdraw the entire contents of the vial of solution and inject into the vial of powder to reconstitute the MenA conjugate component.

Invert and shake the vial vigorously and then withdraw 0.5 ml of reconstituted product. Please note that it is normal for a small amount of liquid to remain in the vial following withdrawal of the dose. Prior to injection, change the needle with one suitable for the administration. Ensure that no air bubbles are present in the syringe before injecting the vaccine.

Following reconstitution, the vaccine is a clear, colourless to light yellow solution, free from visible foreign particles. In the event of any foreign particulate matter and/or variation of physical aspect being observed, discard the vaccine.

Menveo is given as an intramuscular injection, preferably into the deltoid muscle.

Any unused product or waste material should be disposed of in accordance with local requirements.

Figure 1. Nimenrix® vs Menveo® reconstitution. Details are extracted from the leaflets published by the European Medicine Agency website.[11,12]

- **Step 1 (feasibility of the simulation)** consists of an agile iterative prototyping of the conceptual model and simulator of the vaccination POD. Proofs of concept (POC) of the simulator are implemented by using specialised simulation software in order to define, as fast as possible, the required time and costs for performing as fast as possible;
- **Step 2 (implementation)** and
- **Step 3 (application)** of the simulation.

The modelling process requires the collaboration between subject matter experts (e.g., medical doctors) and modeling experts (e.g., mathematical engineers) in order to accurately answer the specific questions under investigation by estimating relevant key performance indicators (KPI) of the vaccination POD (Figure 2 and Figure 3).

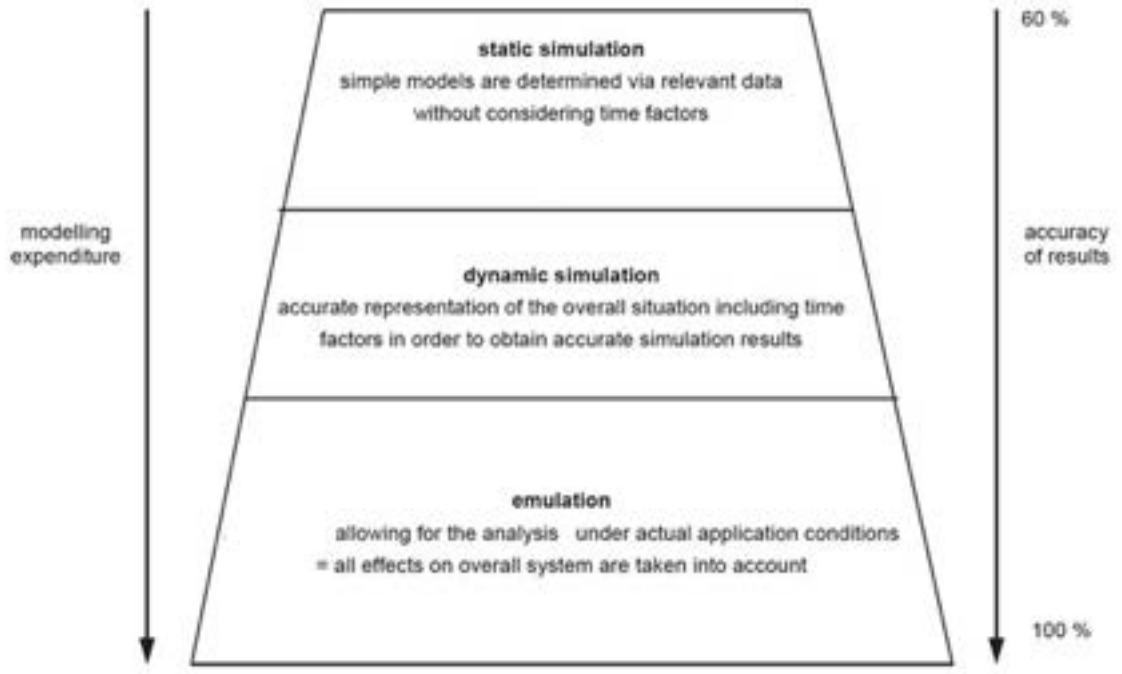


Figure 2. Accuracy of results (adaptation from).[16]

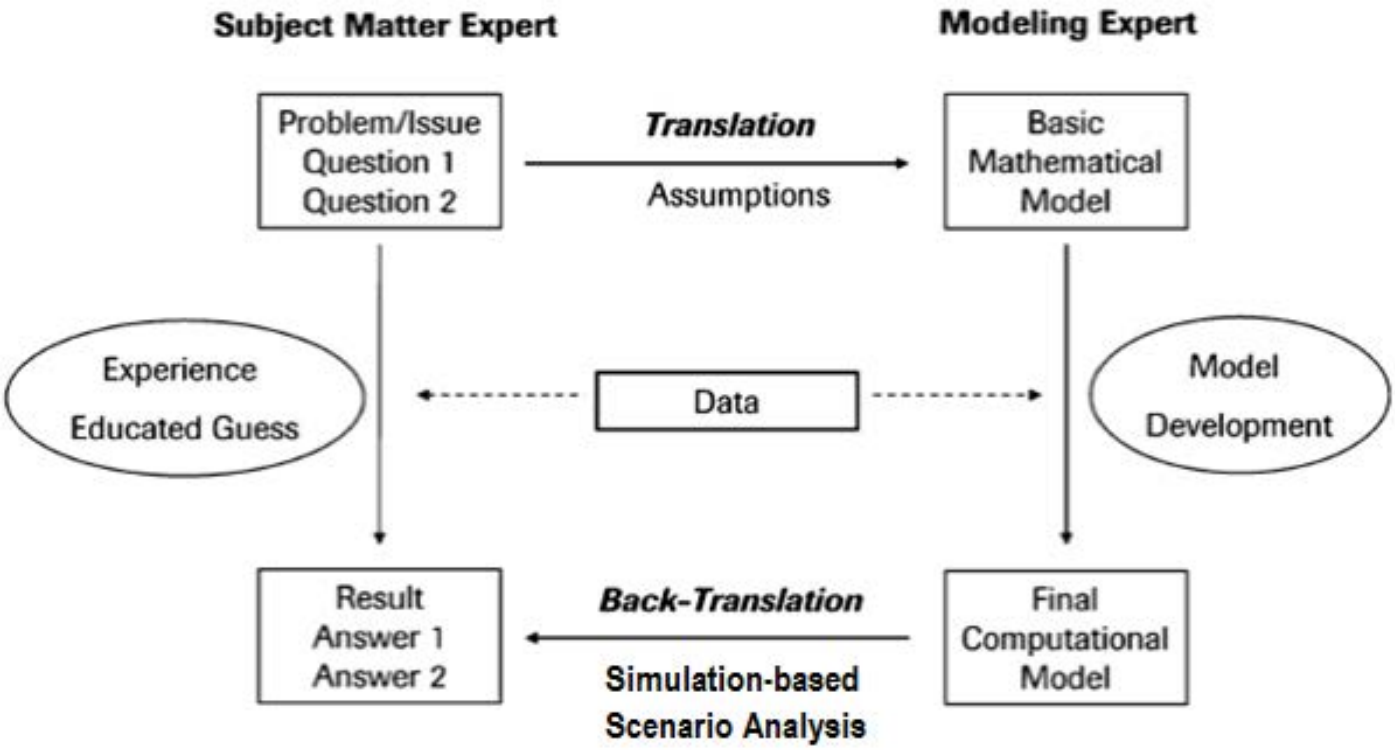


Figure 3. Modeling process (adaptation from).[17]

Conceptual model of the vaccination POD

A top-down method is used to construct the conceptual model of the vaccination POD. Areas and zones of the vaccination POD are identified from WHO guidelines (Figure 4).[2,8]

Next, parameters characterising each area and zone both in terms of activities, materials and resources, including relevant parameters assessing the goal under study, are proposed, discussed, chosen and are quantified by the modelers. These decisions are not only based on the simple choices of the modelers but also on various documents (including mandatory parameters such as "daily session duration") and direct observations.

Some initial assumptions were necessary to better define the model's needs (see "Notes" in Figure 5).

Simulation model of the vaccination POD

The discrete-event simulation (DES) of the vaccination POD, i.e., the simulator (see Figure 6), is implemented in Simio version 10 (build 168.16501), an integrated development environment for realising general-purpose simulations.[18]

Verification of the simulator (i.e., the process of confirming that the simulation is correctly implemented with respect to the conceptual model) and validation of the simulator (i.e., checking the accuracy of the computational model's representation of the real system) were performed by comparing their results with the WHO indications, field observation (Figure 7), and results obtained by another independent implementation in R (https://www.r-project.org/).

The figure 7 shows the results obtained from several observations in a real vaccination setting. These data (not published), derived from a recent degree thesis (which the authors co-tutored),[19] have provided the crucial measure (in terms of KPI) we used to compare data we adopted in simulation model (particularly "in a real world setting").

Simulation Experiments

Given a target population to cover, such a simulator is used to perform several scenario analyses (i.e. experiments for testing different settings and targets), including simulation optimisation of the vaccination session (particularly its duration) and response sensitivity analysis based on linear regression to relate experiment responses (i.e. time to target) to specific input parameters of interest (i.e. vaccine administration time and vaccine reconstitution time).

Fixed parameters (which are the same for all vaccination POD scenarios under investigation in the following) are:

- shift duration (380 minutes);
- session duration (340 minutes, vaccinations starting 10 minutes after the beginning of the shift);

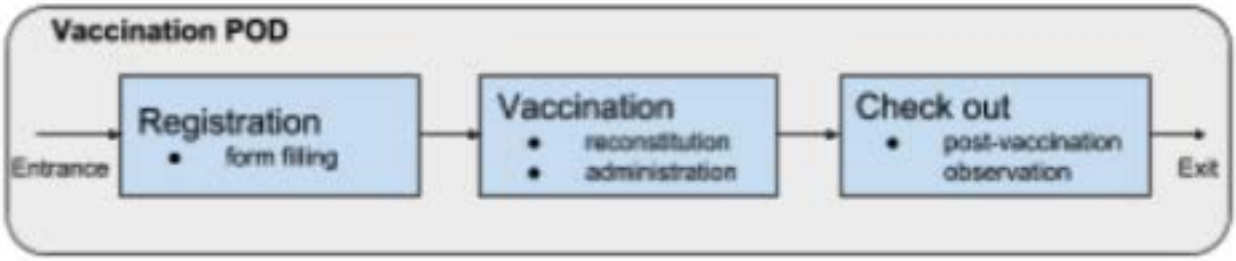


Figure 4. Conceptual model of the vaccination POD.

Area	Zone	Parameters				
		Name	Type	Values	Unit of measure	Range
		number of vaccination sessions	Input	positive integers		1;15
		session duration	Input	positive reals	minutes	330;340;350
		target population (ie, users) to be vaccinated	Input	positive integers		280:300;280x15;300x15
		user's waiting time	Output	positive reals	minutes	-
		user's time in system	Output	positive reals		-
		number of doses administered	Output	positive integers		-
		vaccination coverage	Output	[0,100] %		-
		number of doses used	Output	positive integers		-
		percentage of vaccine utilization	Output	[0,100] %		-
		number of health staff - supervisor	Input	positive integers		1
		number of health staff - nurses	Input	positive integers		1-4
		number of security officers				1
		number of voluenteers	Input	positive integers		0-4
		health staff utilization	Output	[0,100] %		-
Entry & Registration Area	Entrance	time between arrivals	Input	positive reals	minutes	(note 1)
		entrance capacity	Input	positive integers		1 (note 2)
		user's health status	Input/Output	{0=bad,1=good}		1 (note 3)
		entrance lenght of time	Input/Output	positive reals	minutes	not relevant
	Waiting	work-in-progress (WIP) at the waiting zone	Output	positive integers		- (note 4)
		waiting capacity	Input	positive integers		300 (note 5)
		waiting lenght of time	Output	positive reals	minutes	-
	Registration	WIP at the registration zone	Output	positive integers		- (note 4)
		registration capacity	Input	positive integers		1-4 (note 5bis)
		registration lenght of time	Output	positive reals	minutes	-
Clinical Area	Sorting	WIP at the sorting zone	Input/Output	positive integers		0 (note 4)
		sorting capacity	Input	positive integers		300 (note 5)
		sorting lenght of time	Output	positive reals	minutes	-
	Vaccination	WIP at the vaccination zone	Output	positive integers		- (note 4)
		vaccination capacity	Input	positive integers		1-4
		mix of vaccine products per session	Input	[0,100] %		Nimenrix 100%; Menveo 100% (note 6)
		vaccine reconstitution lenght of time	Input/Output	positive reals	minutes	Nimenrix 0,833+/- 17%; Menveo 1,15+/- 17% (note 7)
		number of reconstitution errors	Output	0 or positive integers		0
		vaccination administration lenght of time	Input/Output	positive reals	minutes	0,5 +/-0,166 (note 8)
First-aid & Discharge Area	Check out	WIP at the check-out zone	Output	positive integers		- (note 4)
		check-out capacity	Input	positive integers		300 (note 5)
		check-out lenght of time	Output	positive reals	minutes	-
	Exit	number of users	Output	positive integers		-
		number of vaccinated users = number of administered doses	Output	0 or positive integers		-
NOTES	note 1: we assume no delay between patient arrival (all target patient are ready to enter into vaccination POD)					
	note 2: we assume that patient entered into vaccination POD one by one					
	note 3: we assume that all patient are in good halth status					
	note 4: the output value is a control variable: If it's value is different from 0 it means that some people are not scheduled for next vaccination session					
	note 5: we assume that non-clinical activities are optimized at the highest level of efficiency					
	note 6: in our experiments we assumed the single utilization of one type of vaccine per session					
	note 7: range and statistic distribution come out from 2 videos observation					
	note 8: this value and its distribution came out from interviews with medical doctor and direct observation in in a real vaccination setting					

Figure 5. Relevant indicators defined by the modelers and their ranges.

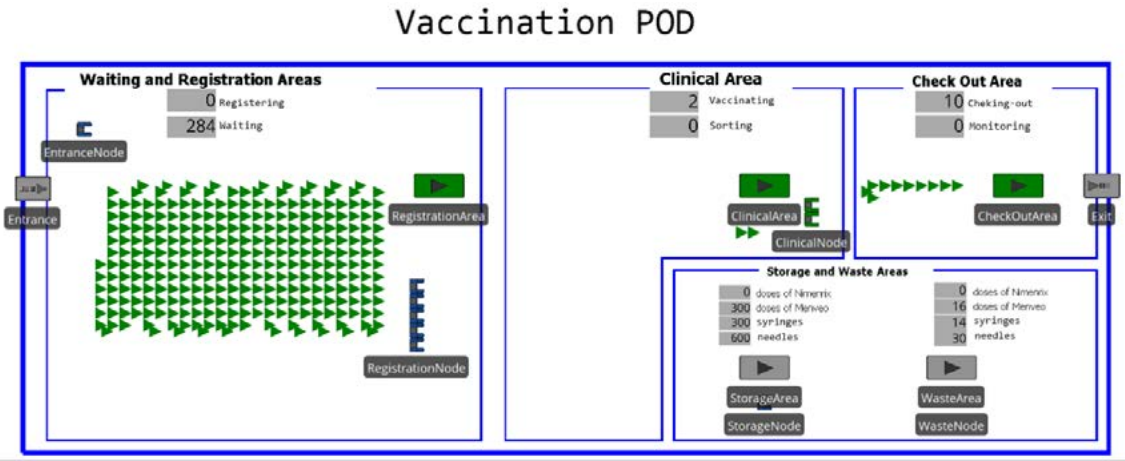
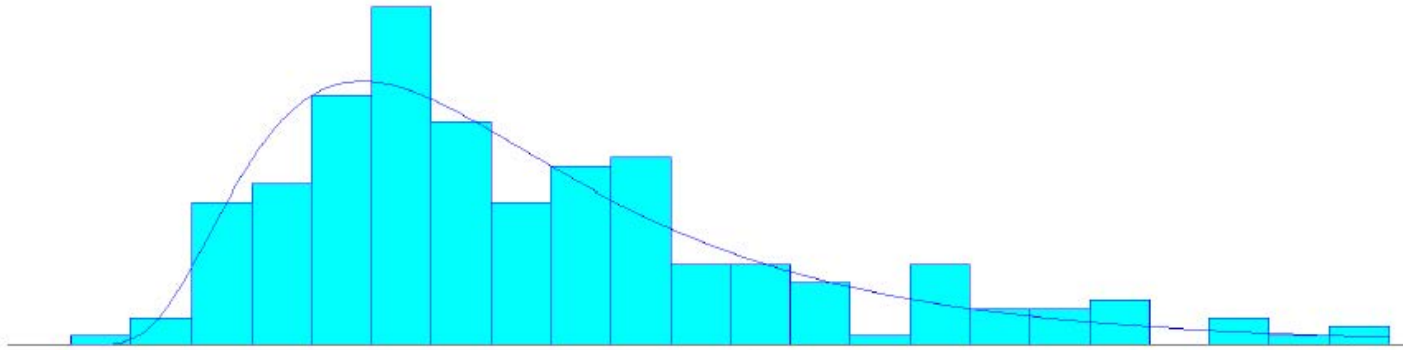


Figure 6. Simulator of the vaccination POD (at the beginning of simulation). Patients are represented by green triangles. Spatial dimension are not considered assuming rapid movements of people (both patients and operators).



Distribution Summary

Distribution: Lognormal
Expression: 1.5 + LOGN(7.85, 4.85)
Square Error: 0.004920

Chi Square Test
Number of intervals = 12
Degrees of freedom = 9
Test Statistic = 12.4
Corresponding p-value = 0.206

Data Summary

Number of Data Points = 240
Min Data Value = 2
Max Data Value = 23
Sample Mean = 9.26
Sample Std Dev = 4.25

Histogram Summary

Histogram Range = 1.5 to 23.5
Number of Intervals = 22

Figure 7. Overall registration and vaccination length of time (in minutes) observed during a study[19] in a vaccination POD of the National Health Service in Rome (one-week, February, 2018) during ordinary vaccination sessions (i.e., in a non-epidemic condition).

- administration length of time (described by a uniform distribution in the range of 20 and 40 seconds), and
- reconstitution length of time (described by a triangular distribution in the range of 50 and 70 seconds with a 60 median, and a triangular distribution in the range of 69 and 97 seconds with an 83 median, for Nimenrix® and Menveo®, respectively).

"Control variables" (controls), i.e., parameters which change over different scenarios hereafter shown, are:

- the target population per session (300 or 280 people);
- the registration area capacity (three or four for the ideal vaccination POD, and two or three, i.e., equal to the clinical area capacity, for the real world vaccination POD);
- the clinical area capacity (two or three) and
- the adopted meningococcal vaccine (Nimenrix® or Menveo®).

The simulated vaccination team, which differs from ideal and real world PODs, is composed of:

- one supervisor;
- one security officer;
- community representatives in a number equal to the registration area capacity or zero for the ideal and real world vaccination PODs, respectively;
- record clerks in a number equal to the registration area capacity or zero for the ideal and real world vaccination POD, respectively;
- nurses in a number equal to the clinical area capacity;
- technicians in a number equal to one or zero for the ideal and real world vaccination PODs, respectively.

Results

By using two instances of the simulator, the ideal vaccination POD and the real vaccination POD defined in the introduction of the case-study have been tested together (Figure 8).

The simulator of the ideal vaccination POD provides the following responses:

- O (output patients) is the number of vaccinated people;
- T2T (time to target) measures the time between the beginning of the vaccination session to when all the target population is covered (0 otherwise);
- FT (free time percentage) measures the ratio between the time remaining at the end of session after the T2T, and the session duration.

In the simulation of the real vaccination POD, the responses O_real, T2T_real and FT_real have the same meaning as O, T2T and FT for the ideal vaccination POD, respectively.

Having fixed exactly the same relevant parameters for both vaccination POD (as described in more in detail in the previous section, e.g., the shift duration to 380 minutes) and by varying the target population per session as control variables, the number

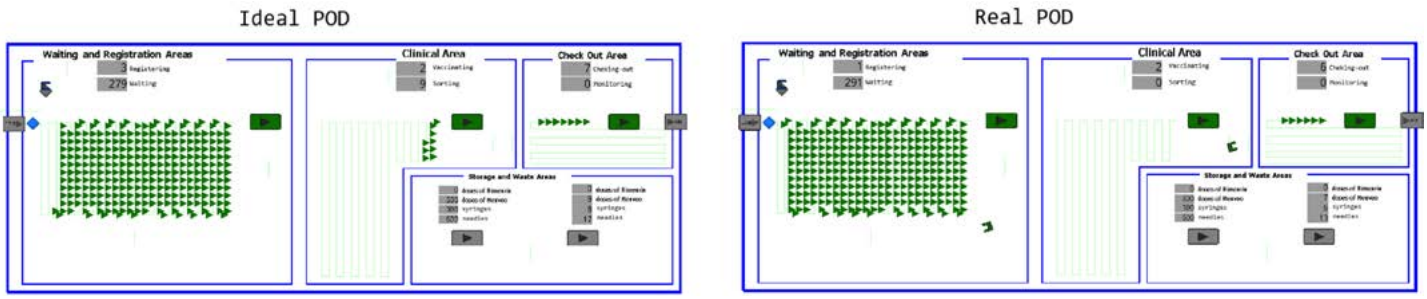


Figure 8. Ideal vaccination POD (left) and real vaccination POD (right) under investigation at the same time (i.e., per single scenario).

Scenario		Replications		Session - Controls	Registration Area - Controls	Clinical Area - Controls	Responses					
	Name	Required	Completed	targetPopulationPerSession	RegistrationAreaCapacity	ClinicalAreaCapacity	O	T2T (Minutes)	FT	O_real	T2T_real (Minutes)	FT_real
☑	Nimenrix-Scenario02-300	100	100 of 100	300	3	2	300	225.989	33.5328	300	300.356	11.6601
☑	Menveo-Scenario02-300	100	100 of 100	300	3	2	300	283.504	16.6164	280.46	0	0
☑	Nimenrix-Scenario02-280	100	100 of 100	280	3	2	280	210.987	37.945	280	280.348	17.5447
☑	Menveo-Scenario02-280	100	100 of 100	280	3	2	280	264.657	22.1596	280	334.101	1.73495
☑	Nimenrix-Scenario03-300	100	100 of 100	300	4	3	300	151.166	55.5393	300	200.551	41.0144
☑	Menveo-Scenario03-300	100	100 of 100	300	4	3	300	189.708	44.2036	300	238.887	29.7392

Figure 9. Definitive scenario analysis of the Ideal (first three responses columns) and Real (last three responses columns) vaccination POD.

of vaccinators (i.e. the clinical area capacity) and the presence or absence of supporting personnel (i.e. the registration capacity which characterises the ideal and real world setting, respectively), there are six analysed vaccination scenarios (Figure 9). Furthermore, due to the randomicity of the parameters vaccine reconstitution and administration length of times, 100 simulation replications per simulation scenario were executed.

The first two scenarios show that with a clinical area capacity of two units, a target population per session of 300 people, as stated by WHO, cannot be served by using the Menveo® vaccine in real world vaccination POD. Thus, the comparison of two vaccines can only be performed by decreasing the target to 280 people. Having established this target, for the real world vaccination POD the average free time percentage (FT_real) is about 17.54% and 1.73% for Nimenrix® and Menveo® respectively (see Figure 9 at column FT_real, scenarios Nimenrix-Scenario02-280 vs Menveo-Scenario02-280). More specifically, the next two figures (Figure 10 and Figure 11) show SMORE (Simio Measure of Risk & Error) plots including FT_real minimum, maximum, mean, median (with upper and lower percentile) and confidence intervals.

Such free time percentages (shown in Figure 10) correspond to an average time to target (T2T_real) of 280.3 and 334.1 minutes when the vaccine is Nimenrix® and Menveo®, respectively (Figure 11). Thus, the time saving can be simply evaluated by difference with the session duration (340 minutes).

By continuing the focus on the scenarios characterised by a target population of 280 people, the sensitivity analysis shows that the relevance of reconstitution phase for having free time, i.e., the impact of the ease-of-use of the vaccine, is 55.72% and 47.76% when the adopted vaccine is Nimenrix® and Menveo®, respectively. The number of vaccinated users (O_real = 280 people in both cases) is less influenced by the reconstitution of Nimenrix® (6.71%) and more sensitive to the reconstitution of Menveo® (36.98%), while the other impact on the covering of the target population derives from the time spent by the vaccinators in the administration of the vaccine (Figure 12).

Results obtained by independent implementation in R (https://www.r-project.org/) showed a good reproducibility of our simulation model, particularly in T2T results (Figure 13).

In sum, according to the above results, it is possible, with some recommendations, to answer positively to the initial questions of the case study:

- vaccination POD should allocate operators as in the ideal setting (according to WHO), or
- real world vaccination POD with fewer operators than in the ideal situation should use the most ease-of-use vaccine, i.e., Nimenrix®, which has lowest reconstitution time.

Discussion

In this study, as we are interested in measuring the impact of the ease-of-use of two different meningococcal vaccines available on the market in Italy, namely Nimenrix® and Menveo®. We compare simulated performance of ideal POD (with a complete vaccination team according to WHO) and real world POD (with a reduced vaccination team) providing only one type of vaccination to predefined target patients (assumed to be present at the beginning of the vaccination and in good health). By adopting a vaccination session, easy under an organisational point of view,

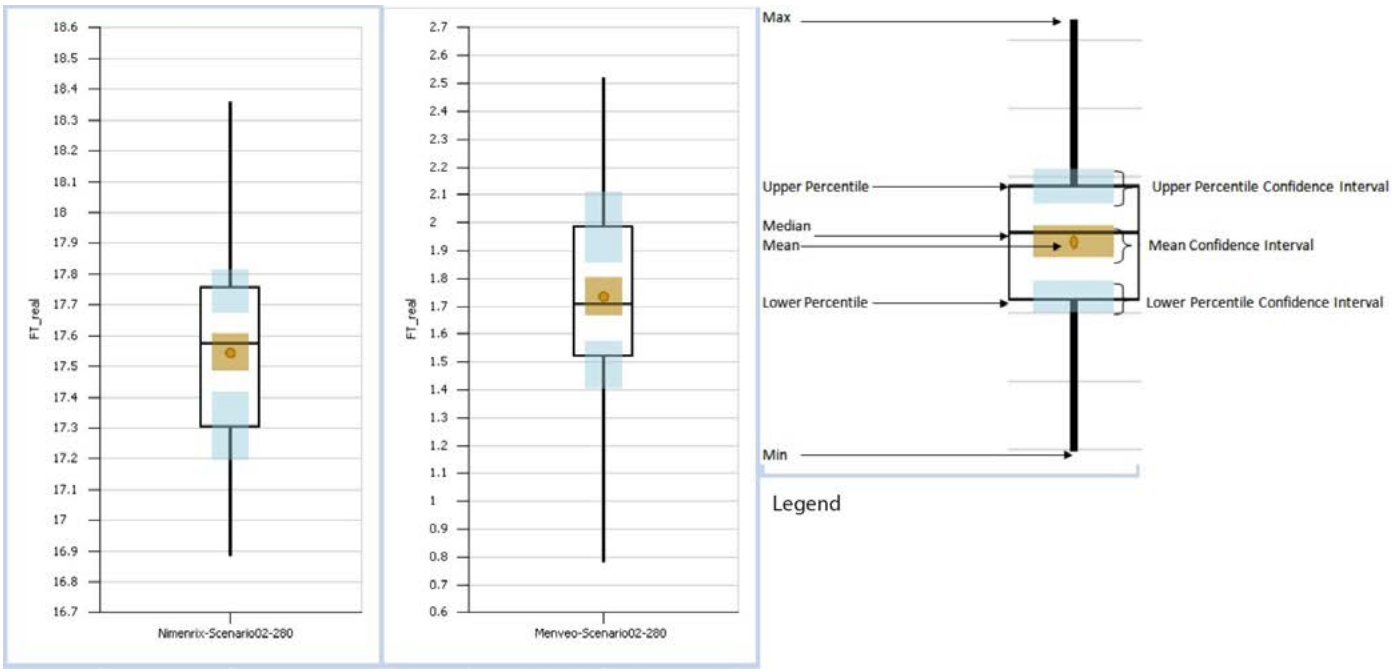


Figure 10. Free time (%) in the real world vaccination POD when the target population is 280 people, the vaccinators are two, and the vaccine used is Nimenrix® and Menveo® respectively.

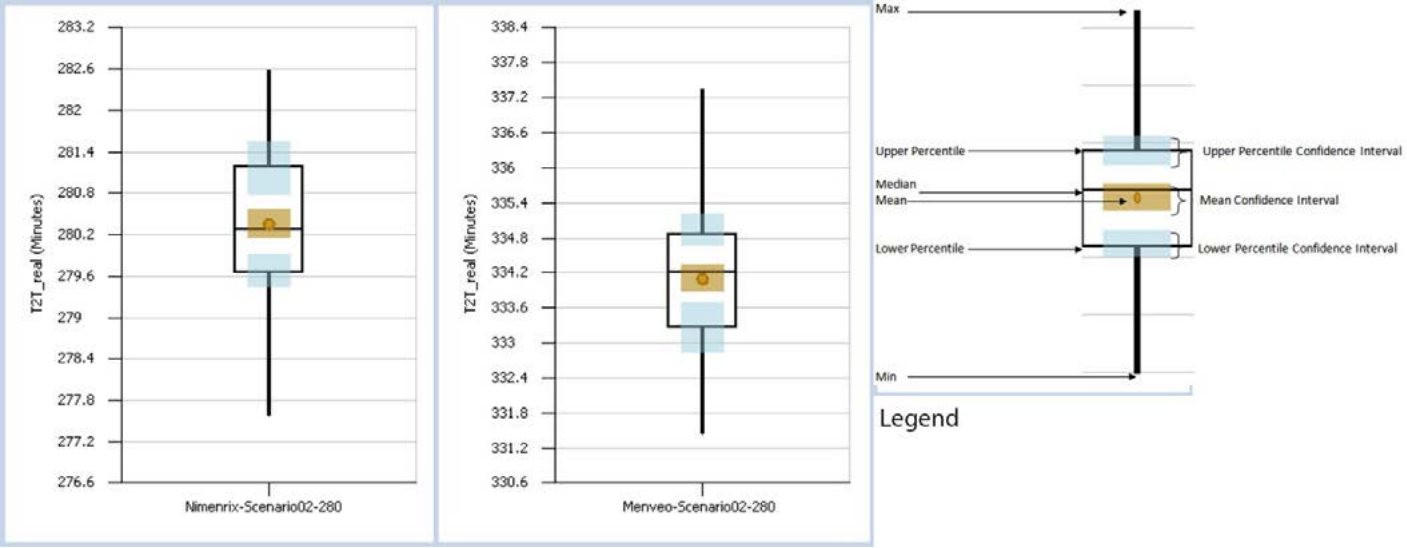


Figure 11. Time to target (minutes) in the real world vaccination POD when the target population is 280 people, the vaccinators are two, and the vaccine used is Nimenrix® and Menveo® respectively.

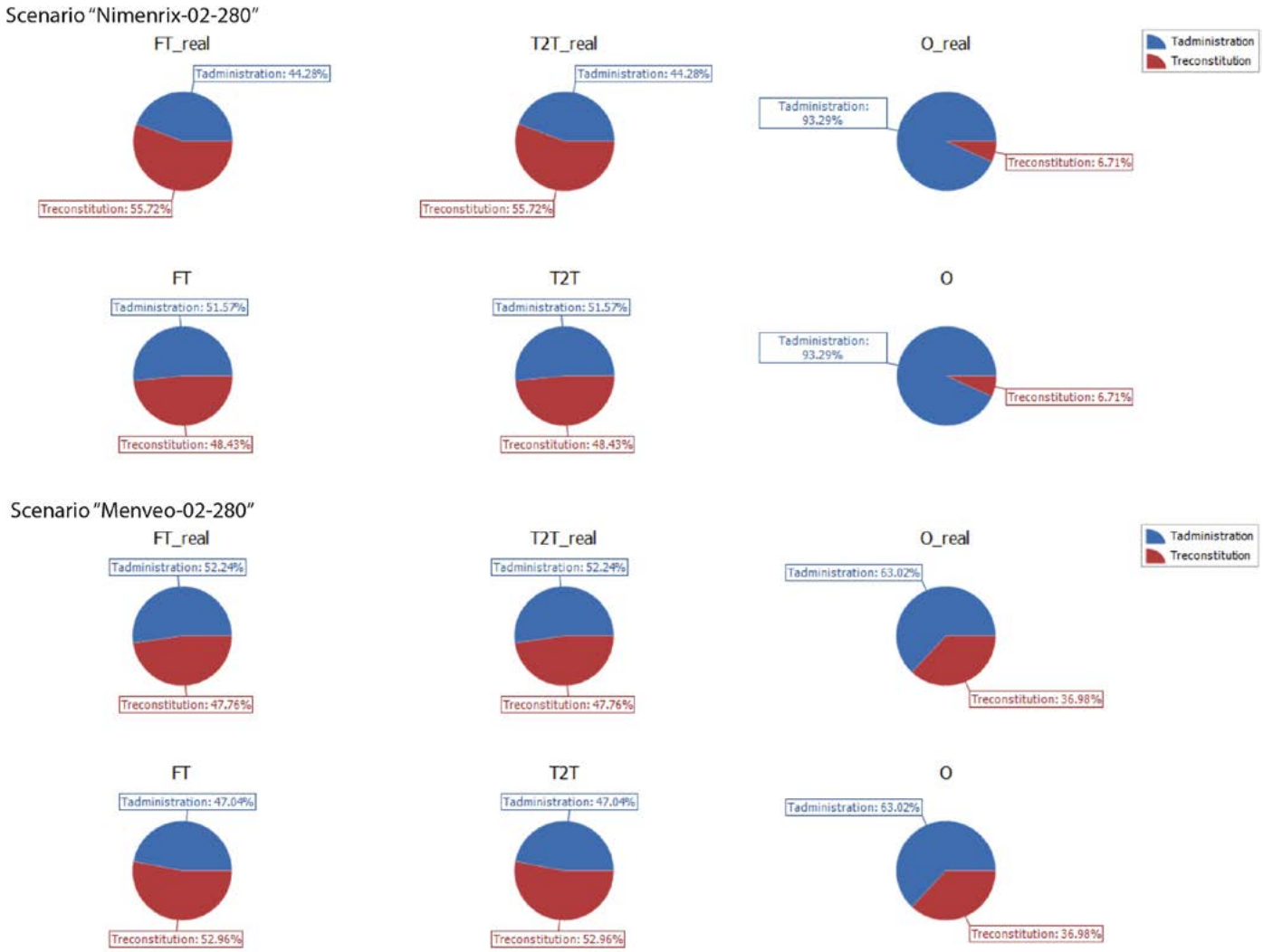


Figure 12. Sensitivity analysis. Weights (%) of the vaccine administration time (i.e., Tadministration) and the vaccine reconstitution time (i.e., Treconstitution) on the defined responses (FT, T2T, O for the ideal vaccination POD, and FT_real, T2T_real, O_real for the real vaccination POD) when the target population is 280 people, the number of vaccinators two, and the adopted vaccine is Nimenrix® (up) and Menveo® (down), respectively.

POD Simulations in R (100 replications)			
POD	**Scenario**	**O**	**T2T (minutes)**
Ideal POD	Nimerix-scenario02-300	300	**226**
	Menveo-scenario02-300	300	**283**
Real POD	Nimerix-scenario02-300	300	**300**
	Menveo-scenario02-300	284	**340**
Ideal POD	Nimerix-scenario02-284	284	**214**
	Menveo-scenario02-284	284	**268**
Real POD	Nimerix-scenario02-284	284	**285**
	Menveo-scenario02-284	284	**340**
Ideal POD	Nimerix-scenario03-300	300	**151**
	Menveo-scenario03-300	300	**189**
Real POD	Nimerix-scenario03-300	300	**201**
	Menveo-scenario03-300	300	**239**

Figure 13. Results given by the R simulator of the vaccination POD.

non-clinical activities of the POD can also be optimised at the highest level of efficiency. This could be considered as a limit of the study. However, if this first impression is exceeded, such an organisational model gives to the vaccination POD the ability to operate efficiently, both in emergency situations as well as under normal conditions, also with relevant time and cost savings by leveraging the ease-of-use of the adopted vaccine. The quality of the service can also be improved more easily by engaging patients and health workers in the study of relevant aspects of the single specific vaccination.[20-21] Due to lack of usable evidence from literature or observable vaccination POD which operate "under the same condition" hypothesised, the results of the study do not take vaccine reconstitution errors or possible vaccination side effects into consideration.[22]

In particular, we evaluated the effects of the advantage given by the reduction of the reconstitution time provided by Nimenrix® during a mono vaccination session in a real world vaccination POD. Having a target of 280 people per session (340 minutes), the ability of the clinical area (i.e., vaccinators) to achieve it is less sensible to the reconstitution of Nimenrix® (6.71%) and more sensible to the reconstitution of Menveo® (36.98%), while for the rest it depends on the time spent in the administration of the vaccine. The resulting average free time percentage is about 17.5% (60 minutes) and 1.7% (6 minutes) for Nimenrix® and Menveo®, respectively. The above percentages are critical to understanding and suggest how to reach the right number of vaccinated patient in a short span of time. The differences that emerged from the sensitivity analysis could be taken into consideration and better investigated in order to offer a more efficient service.

Such a result can be easily applied to obtaining further insights and evaluations (see Figure 14 for some examples of possible economic implications in a real scenario). For example, application to the meningitis epidemics in Tuscany could reveal an overall cost saving of about 24.7 million Euros (including vaccine cost) by using the Nimenrix® vaccine to implement a hypothetical vaccination campaign according to the WHO recommendations.

Although a vaccination POD which provides only one type of vaccination is not frequently to observe in reality, we underline that such a POD can offer valid organisation to be taken into consideration when there is a specific request to reach a vaccination goal, especially in a low setting resources and in a few days/weeks of vaccine sessions (i.e., not only during outbreaks).

	WHO Example - Real settings		**Tuscany Example (>17 y.o.) - Real settings**	
	Scenario "Nimenrix-02-280"	**Scenario "Menveo-02-280"**	**Scenario "Nimenrix-02-280"**	**Scenario "Menveo-02-280"**
estimated population	50.000	50.000	3.173.234	3.173.234
target population (%)	70%	70%	70%	70%
target population	35.000	35.000	2.221.264	2.221.264
goal coverage (%)	100,00%	100,00%	100,00%	100,00%
goal coverage	**35.000**	**35.000**	**2.221.264**	**2.221.264**
number of doses per person	1	1	1	1
number of doses to administer	35.000	35.000	2.221.264	2.221.264
number of doses needed, assuming wastage (~17%)	40.950	40.950	2.598.879	2.598.879
number of doses needed assuming need for a reserve (~25%	**51.597**	**51.597**	**3.274.587**	**3.274.587**
cost of vaccine per dose (euros/dose)	92,00	99,34	92,00	99,34
cost of vaccines (euros)	**4.746.924,00**	**5.125.645,98**	**301.262.012,64**	**325.297.481,91**
campain duration (in days)	15	15	15	15
target population per session	280	280	280	280
number of PODs needed	8,33	8,33	528,87	528,87
time to start the vaccination session (minutes)	10,00	10,00	10,00	10,00
time to target population per session (minutes)	284,24	334,10	284,24	334,10
time after the end of the session, before shift end (minutes)	30,00	30,00	30,00	30,00
number of supervisors	1	1	1	1
cost of supervisor per hour (euros/hour)	48,00	48,00	48,00	48,00
cost of supervisors (euros)	**3.890,92**	**4.489,21**	**3.890,92**	**4.489,21**
number of security officers	1	1	1	1
cost of security officer per hour (euros/hour)	13,71	13,71	13,71	13,71
cost of security officers (euros)	**1.111,34**	**1.282,23**	**1.111,34**	**1.282,23**
nurses	2	2	2	2
cost of nurse per hour (euros/hour)	26,47	26,47	26,47	26,47
cost of nurses (euros)	**4.291,36**	**4.951,23**	**4.291,36**	**4.951,23**
total costs of human resources per POD (euros/POD)	9.293,61	10.722,67	9.293,61	10.722,67
number of PODs	**9**	**9**	**529**	**529**
total costs of human resources (euros)	83.642,53	96.504,03	4.916.322,33	5.672.292,38
total costs (euros)	**4.830.566,53**	**5.222.150,01**	**306.178.334,97**	**330.969.774,30**

Figure 14. Examples of economic implications. In case of meningitis epidemic and according to recommendations by the WHO, operators of each involved vaccination POD can be temporary hired to cover the target population within two weeks from the start of the vaccination campaign. The free time (if any) could be used to close the POD itself in advance for having a cost saving (assuming operator unitary costs per hour).

Our simulation results are confirmed by independent implementation of the simulator.

Future research could consider the simulation of specific vaccination centers in Italy and eventually in other countries as well, also considering different kind of vaccines, and the prototyping of simulation-based decision-support software for vaccination POD decision-makers.

Acronyms

DES = discrete-event simulation
FT = free time percentage
KPI = key performance indicators
O= output patients
POC = Proofs of concept
POD = point of dispensing
T2T = time to target
Tadministration = vaccine administration time
Treconstitution = vaccine reconstitution time
WHO= World Health Organisation

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