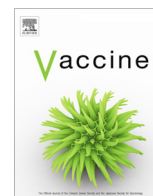




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Review

Preventing infectious diseases for healthy ageing: The VITAL public-private partnership project



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ARTICLE INFO

Article history:

Received 19 March 2020

Received in revised form 1 July 2020

Accepted 3 July 2020

Available online 24 July 2020

Keywords:

Elderly

Immuno-senescence

Infectious diseases

Public health

Public-private partnership

Vaccine

ABSTRACT

Prevention of infectious diseases through immunisation of the growing ageing adult population is essential to improve healthy ageing. However, many licenced and recommended vaccines for this age group show signs of waning of the protective effect due to declining immune responses (immuno-senescence) and decreasing vaccine uptake. Today's major challenge is to improve vaccine effectiveness and uptake and to deploy efficient vaccination strategies for this age group. The Vaccines and Infectious diseases in the Ageing population (VITAL) project, with partners from 17 academic & research groups and public institutes as well as seven industry collaborators, aims to address this challenge. The ambition is to provide evidence-based knowledge to local decision makers. Using a holistic and multidisciplinary approach and novel analytical methods, VITAL will provide tools that allow the development of targeted immunisation programs for ageing adults in European countries. The project is based on four pillars focussing on the assessment of the burden of vaccine-preventable diseases in ageing adults, the dissection of the mechanisms underlying immuno-senescence, the analysis of the clinical and economic public health impact of vaccination strategies and the development of educational resources for healthcare professionals. By the end of the project, a clear, detailed, and integrated program should be available for implementing a consistent, affordable, and sustainable vaccination strategy for ageing adults with regular evaluations of its impact over time.

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1. Introduction

Due to the increase in life expectancy and the persistently low fertility rate, the older population in Europe is proportionally and in absolute terms expanding every year [1]. The group of 65+ represents today on average around 20% of the total European population or 101,5 million persons. Life expectancy at that age is on average 21.5 years for women and 18.2 years for men. During the coming 15 years, this group will linearly increase by 0,43%

per year, moving to 26,5% of the total population. Especially the group of 85+ will heavily boom (now 2.5% of the total population but they may reach up to 4,1% in 2035) [2], which will shift the moment at which aging adults start dying at a higher rate, which is currently at the age of 75 [3]. Those people at an older age mainly die of three causes, accounting for 85% of them: cardiovascular disease, cancer, and respiratory system diseases [4]. Although infection constitutes only a secondary cause of death in that group, happening mainly during the winter periods because of influenza infection and pneumonia disease [5], it is a major threat for aging adults in cluster environments like rest homes or health care facilities. People from that age group arriving in hospitals with a secondary diagnosis of infection monopolize the beds for a long

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period, recover badly and remain weak when leaving the health care facility. This results in a long-term poor overall health condition with a high cost for society. We experience that situation at the extreme now with the COVID epidemics where a sudden increase in mortality caused by the infection has become an urgent societal problem that needs to be solved rapidly [6]. The Sars-Cov-2 virus not only causes major healthcare challenges, but also impacts overall societal functioning [7]. Identification of the individuals most at risk and development of vaccination strategies to prevent the most vulnerable group are urgently needed at this time.

So healthcare systems will have to deal with increasing numbers of ageing adults with severe infections, not only because of the higher number of individuals living longer but also because of the decline in their immune response, called immunosenescence [8], which makes them more vulnerable to pathogens [9]. Ageing adults may thereby also become a new source of infection. However, an effective medical act to safeguard individuals and populations against infectious diseases is vaccination, which has proven its effectiveness in children and young adults for decades with the eradication of smallpox, a strong step towards eradication of polio, and the elimination in many places of infectious diseases such as mumps, measles, diphtheria or whooping cough [10].

The ambition is to achieve a similar level of infectious disease control in ageing adults. This would be fundamental for enhancing healthy ageing [11]. However, many recommended vaccines for ageing adults do not maintain an effective and/or sustained immune response, as is the case for influenza, pneumococcal disease or pertussis, for example [12,13]. This has consequences for the individual and their surroundings. Therefore, there is a need to better understand the aetiology of the major infectious diseases affecting this population [14]. There is also a need to decipher the mechanisms underlying immuno-senescence, which should lead to improved vaccine effectiveness and to the development of more efficient vaccination strategies for this age group (whom to vaccinate, when, where, how frequently, and at what price). Finally, there is a need to provide dedicated educational programs to healthcare professionals (HCPs) [15]. Over the next decade, local decision makers will need to have a clear view on this healthcare problem, with access to effective tools to manage the growing healthcare burden they need to control.

To meet this need, a holistic research project, called VITAL (Vaccines and Infectious diseases in the Ageing population), was initiated in early 2019. The program was approved in 2018 by the Innovative Medicines Initiative (IMI2-2014-20 Horizon) and is funded by the European Commission and the European pharmaceutical industry for a total budget of 12.6 million euros over a period of five years [16]. In this article, we present and discuss the objectives and the scope of the program, showing the rationale of this need.

2. What is VITAL?

VITAL is a public-private consortium that brings together a group of scientists with expertise in different domains of immunology, virology, clinical, epidemiology, health economics, communication, and education (website: <https://VITAL-IMI.eu>). Table 1 shows the different participants to the study that comprises 17 public partners from 11 countries in Europe (ten academic & research groups, four public health institutes, and three small to medium-sized enterprises) together with seven biopharmaceutical companies (EFPIA partners).

VITAL aims to evaluate the location and the magnitude of the infection problem in the ageing population. The knowledge gained

Table 1

List of the participants to the VITAL study, split by academic and EFPIA partners.

Academic	EFPIA partners
Universitair Medisch Centrum Utrecht, the Netherlands	GlaxoSmithKline Biologicals SA
Rijksinstituut voor Volksgezondheid en Milieu, the Netherlands	Pfizer limited
P95 cvba, Belgium	Sanofi Pasteur SA
Academisch Ziekenhuis Groningen, the Netherlands	MSD
Folkehelseinstituttet, Norway	Janssen Vaccines & Prevention BV
Institut National de la Santé et de la Recherche Medicale, France	Biomerieux SA
Statens Serum Institut, Denmark	Vaccines Europe (EFPIA)
Universitaet Innsbruck, Austria	
Imperial College of Science Technology and Medicine, UK	
Centre National de la Recherche Scientifique, France	
Istituto Superiore di Sanita, Italy	
Fundacion para el fomento de la Investigacion Sanitaria y Biomedico de la Comunitat Valenciana, Spain	
Syreon Kutato Intezet Korlatolt Felelossegu Tarsasag, Hungary	
Universita degli Studi di Ferrara, Italy	
Université Jean Monnet Saint-Etienne, France	
Mihaljiovic Jovan, Serbia	

should enable to develop methods to reduce and control the infections. Different intervention options will be analysed and compared, such as better quarantine of infected persons, improved hygiene measures, more intensive use of disinfectants on critical places, but a special focus of the project will be on vaccination. The different options will be tested for their economic viability (cost and health gain) compared with the current total national management of infectious diseases that includes prevention as well as treatment. By evaluating the ageing immune response in depth, VITAL will help elucidate the main causes of immune waning and adjust vaccination strategies to tackle the resulting sub-optimal responses to vaccines. VITAL's mission extends beyond the research domain by developing better communication tools to inform doctors and help them to apply the strategic recommendations in their medical practice. Moreover, it will set up post-surveillance monitoring to follow the implementation of these strategies.

The VITAL project has been structured into four research domains, called work packages (WP): epidemiology (WP1), clinical immunology research (WP2), health economics (WP3) and communication (WP4). Each WP has a list of tasks to fulfil within the initial 5-year timeframe (2019–2023) (see Table 2). The specific objectives of each WP and their respective tasks are detailed below in the next chapters.

The project also builds upon the experience and outcomes of previous and current Europe-sponsored projects including:

- I-MOVE (Influenza Monitoring Vaccine Effectiveness) [17] and I-MOVE+ (Integrated Monitoring of Vaccines) [18]: the data collection of WP1 in retrospective databases in specific regions on influenza disease will be rechecked for validity with I-MOVE data.
- ADVANCE (Accelerated Development of VAccine beNefit-risk Collaboration in Europe) [19]: this program allows access to many different databases in Europe that can be consulted to test the research protocol developed in WP1.
- DRIVE (Development of Robust and Innovative Vaccine Effectiveness) [20]: the project will help to populate specific values for the assessment of vaccines in the economic models that will be developed in WP3.

Table 2
Defining the different tasks to be performed by Work Package, when, and by whom.

Number	Tasks	Lead	2019	2020	2021	2022	2023
WP1							
1.1a	Methods of measuring disease burden	RIVM	X				
1.1b	Data sources of the different infections to be studied	RIVM	X				
1.1c	Feasibility of data collection in retrospective data-bases	P95	X				
1.2a	Protocol development retrospective study	P95		X			
1.2b	Protocol development prospective study on QALY-measurement	Sanofi		X			
1.3a	Implementation of retrospective data collection in two pilot regions, Valencia & Denmark	Fisabio/SSI			X		
1.3b	Implementation of prospective data collection in different centres in Europe	P95			X		
1.4	Assess the transferability of the protocols in other regions in Europe	P95				X	
1.5	Database development	P95				X	
1.6	Assessment of the analysis of the database evaluating the epidemiologic immuno-senescence score	P95					X
WP2							
2.1a	Protocol development with approval for testing the immunology response to two vaccine (flu & PCV) across 3 age-groups	RIVM	X				
2.1b	Start the enrollment and vaccination of flu vaccine with collection of samples and data	RIVM	X				
2.1c	Prepare and develop the data repository	RIVM	X				
2.1d	Start and collect samples and data of PCV-vaccination	RIVM		X			
2.2a	Analyse the adaptive immune parameters	RIVM		X	X		
2.2b	In-depth analysis of responsiveness (mucosal, innate and adaptive immune profile)	RIVM			X	X	X
2.2c	Data analysis to assess differences	RIVM			X	X	X
2.3a	Identify biomarkers associated with aging	RIVM		X	X		
2.3b	Identify biomarkers associated with vaccination and frailty	RIVM				X	X
2.3c	Identify biomarkers predicting vaccination response in the presence/absence of inflammation	RIVM				X	X
WP3							
3.1	Literature review on models infections in aging adults	Mihaljovic	X				
3.2	Review of measuring heterogeneity in aging adults	Academisch Ziekenhuis Groningen	X				
3.3	Patient flow in health care using appropriate software	Syreon	X				
3.4	Economic evaluation of different prevention methods on infectious disease in aging adults	RIVM	X				
3.5a	Summary of the gap analysis of the first 4 projects	Academisch Ziekenhuis Groningen		X			
3.5b	Contact matrix assessment in aging adults	Universiteit Hasselt		X			
3.5c	QTwIST-application in data-base of Valencia	GSK-Fisabio		X			
3.6	Development of a simple model evaluation for different infections in aging adults	Academisch Ziekenhuis Groningen		X			
3.7	Assessment of developing advanced epidemiologic models	RIVM			X		
3.8	Assessment of different options in the economic evaluations (optimisation and SAM modeling)	Academisch Ziekenhuis Groningen/GSK				X	
3.9	Transferability of the programs across different regions	Academic Ziekenhuis Groningen					X
WP4							
4.1a	Focus groups of aging adults in 4 countries (Ndl, Fr, It, Hu) on content and networking	RIVM	X				
4.1b	Literature review on educational material of HCP	RIVM	X	X			
4.1c	Focus groups of HCPs on preferences of education	RIVM		X			
4.1d	Framework development of educational instruments to be accessible to HCPs	RIVM		X			
4.2a	Inventory of health care networks around aging adults creating a sustainable network	RIVM		X			
4.2b	Mapping existing courses and needs	RIVM			X		
4.3a	Develop and deliver training	RIVM			X	X	
4.3b	Ensure sustainability and transferability	RIVM					X

impacted tasks by COVID-19 epidemic; WP: Work Package; RIVM: Rijksinstituut voor Volksgezondheid en Milieu; P95: Excellence in Pharmacovigilance and Epidemiology; SSI: Statens Serum Institut, Denmark

- RESCEU (Respiratory Syncytial Virus consortium in EUrope) [21] and PERISCOPE (Pertussis Correlates of Protection Europe) [22]: will allow to use their simple models for the economic assessment of RSV and pertussis vaccines in ageing adults (WP3). In addition, immune signatures identified within the VITAL project could be validated for prediction of vaccine response in the Periscope project.
- COMBACTE (Combatting Antibiotic Resistance in Europe) [23]: will give access to critical information about AMR that will be used in WP3 for the economic evaluations of the specific infections that show AMR reduction through vaccination.
- MARK-AGE (European Study to Establish Biomarkers of Human Ageing) [24]: the project should help to confirm the findings from the VITAL clinical immunology research program.
- EuroMomo (European Mortality Monitoring) [25]: it is essential for the economic assessment of ageing adults to have data on their causes of mortality. Having access to reliable sources of information on this critical parameter of mortality should strengthen the economic analyses on preventative interventions in ageing adults (WP3).

3. Key considerations

We'd like to specify upfront some specific issues that need to be tackled in the VITAL WPs:

WP1 is expected to identify the different levels of *heterogeneity* in the health status of the ageing adult population and linking this to their vulnerability to infection [26]. Differences in health status may relate to differences in the potency of immune responses and thereby lead to changes in the protection against infections and the effectiveness of vaccinations [27]. A *Frailty Index* could be a good indicator to capture this heterogeneity as it encompasses many factors associated with biological ageing, including mental, social, and physical impairments [28].

When this heterogeneity and the mechanisms of immuno-senescence will be better understood, we should be able to improve protection against infectious diseases through the development of adult-tailored vaccines and/or vaccination strategies. WP2 is intended to identify (immunological) biomarkers associated with this heterogeneity and the predictive paths that could render new interventions more impactful and efficient. For instance, measuring the status of *inflammageing* (low-grade chronic systemic inflammation that emerges during physiological ageing) could be critical as it may play a role in the diversity of the immune response [29], and could be considered being the action point of the mismatch between chronological and biological ageing [30]. Acquiring more knowledge on the immune decline during life could be insightful for the improvement of healthy ageing. The *pre-ageing period*, defined as the age group 50 to 64, may yield important information for identifying those individuals prone to develop immuno-senescence and those who still can mount successful immune responses [31]. Increasing the body of knowledge on this pre-ageing adult group may reveal whether middle-aged adults would benefit from timely vaccination.

Ageing of the population has implications for the introduction of cost-efficient intervention strategies aimed to prevent infections. Age-related differences in susceptibility to infection or carriage may mean that ageing adults could be important contributors to the *transmission of pathogens*, such as influenza and pneumococci [32,33]. Interactions between ageing, susceptibility to disease transmission and vaccine impact generally affect the economic benefit of vaccines in a nonlinear way. Hence, a framework integrating chrono-biological changes and demograph-

ics to prospectively assess the impact of vaccines in ageing adults using *advanced modelling is needed*. The current management of infectious diseases in ageing adults should be investigated, including both therapeutic options as well as preventive measures, to see how it could be improved [34]. However, the best approach to vaccinate this population should be identified by first considering the way local healthcare is organized. Three geographical/time situations will be evaluated in detail to understand where the *patient flow* starts and ends in relation to infection, contamination and spread in ageing adults, looking at pre-medical, medical, and post-medical conditions.

Finally, to achieve high vaccine coverage, older adults would need to recognize the value of being vaccinated, and understand how and from whom they can obtain information about vaccination. Therefore, in the frame of WP4 *focus-groups* of ageing adults in different countries in Europe as the starting point for developing an education & training program for HCPs who would be trained to meet the need for information, beliefs and attitudes of ageing adults. This would favor behavioral changes leading to increased vaccine uptake in this group [35].

A holistic approach has been developed using a multidisciplinary team of different specialists. The program is conceived in such a way that links have been built between the WPs to facilitate progression from one stage to the next in *a matrix fashion*. This unique form of inter-disciplinary transfer of information will enhance the acquisition of knowledge and stimulate data interpretation to make links between frailty measurement, immune response, immuno-senescence evaluation, epidemiologic immuno-senescence scores, vaccine impact levels, and cost-efficiency.

4. Objectives, challenges and tasks

4.1. WP1: burden of infectious diseases in ageing adults

The aim of WP1 is to evaluate the total burden of infectious diseases in the 50+ age group in different European countries. The selection of that age group has been motivated by the need for understanding the progression of the infection problem with age. WP1 will make use of established datasets addressing the challenges of measuring the burden of vaccine-preventable [VP] infections, such as influenza, pneumococcal disease, zoster, pertussis, tetanus, for example, and potentially vaccine-preventable [PVP] infections, such as respiratory syncytial virus (RSV), norovirus, extra-intestinal pathogenic *Escherichia Coli* (ExPEC), and some others. WP1 tasks consist of reviewing methods and data sources that are available in the EU and to define risk factors on selected infectious diseases in ageing adults (pneumonia caused by *Streptococcus pneumoniae*, RSV, norovirus, ExPEC, *Staphylococcus aureus*) through the identification of gaps. This will help to develop a protocol for collecting pro- and retrospective data on the burden of disease (BoD), risk factors, and co-morbidities on VP and PVP infectious diseases in specific areas. The protocols will be tested in two pilot regions of Valencia (Spain) and Denmark. The next task will be to transfer the protocols to other regions with local adjustments (Hungary, Italy, the Netherlands, Norway, and Serbia). This should allow us to build and consolidate a database on the BoD in ageing adults in Europe. With the database, it will be possible to identify potential risk factors and the development of an epidemiologic immuno-senescence score among ageing adults to help identify individuals who manifest regular infections. The data findings of WP1 will feed the research activities of WP3 and WP4, as seen in Fig. 1.

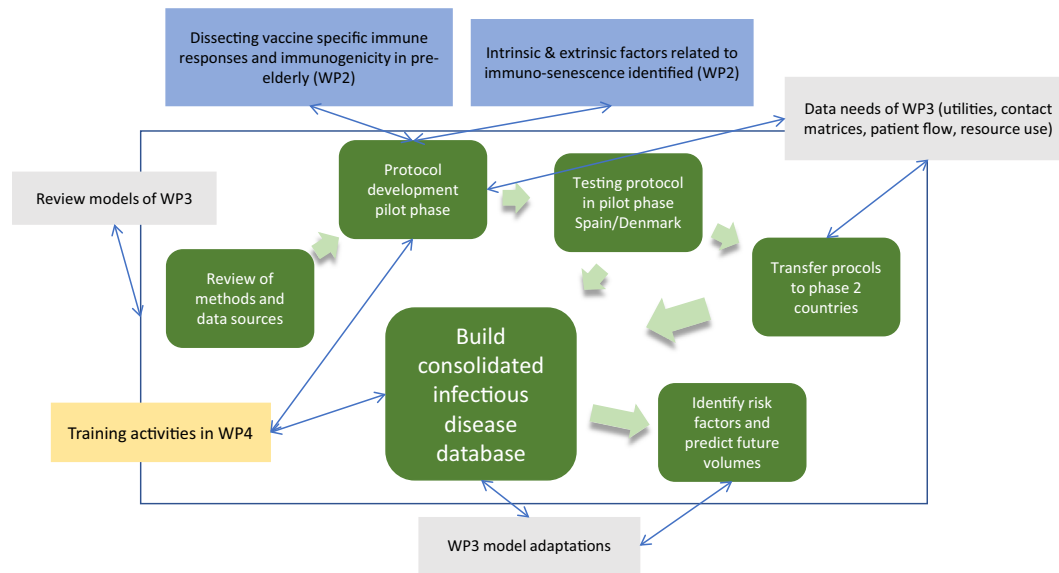


Fig. 1. WP1 (green boxes) and working with the other WPs of VITAL. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

4.2. WP2: understanding and improving immunity to infections and vaccination in the ageing population

To make a success of the future vaccination strategies, immune profiles predicting effective immune responses in the ageing adults should be identified. This requires the understanding of the factors responsible for immuno-senescence. WP2 aims to give a better insight into age-induced changes in the immune response, to evaluate the impact of external factors, such as co-morbidities, diet, exercise, or life-style. It also aims to assess vaccine immunogenicity in the ageing adults, and to formulate evidence-based rationale strategies for correcting immuno-senescence by vaccination, which might be by vaccinating pre-ageing adults [36–40].

A prospective study using influenza vaccine and pneumococcal vaccine will be carried out to determine the immune profiles underlying immuno-senescence in three age-groups: the aging adults (≥ 65 years), pre-aging adults (50–65 years) and adults (25–49 years). We aim to characterize the immune response in the aging-adults and pre-aging adults by identifying the intrinsic age-induced immunological changes on the main vaccine outcomes, such as the induced antibody levels. This includes determining the role of inflammaging [29], and identifying external factors that influence immune responsiveness using samples from unique cross-sectional and longitudinal studies, such as Stimul-Age and Doetinchem, both conducted at the Rijks Instituut voor Volksgezondheid en Milieu, The Netherlands [41]. We will perform advanced immune profiling to predict vaccine-induced response and pinpoint the exact features that correlate with reduced responsiveness to vaccine. The prospective clinical vaccination study will focus on innate and adaptive immunity, both systemic and mucosal. This is expected to enable the identification of immune signatures and (bio)markers associated with immuno-senescence that later could be used to identify at-risk groups. This work will form the basis for selecting vaccination-responsive target populations and identifying possible interventions and improvements to protect the ageing adults by vaccination (Fig. 2). Furthermore, the outputs of the research studies will be applied in disease models that will assess the impact and the economics of specific strategies that may be integrated into vaccination programs (link with WP3).

4.3. WP3: vaccine impact assessment and economic value of vaccination in ageing adults

WP3 aims to develop economic analyses of extended preventative programs using models that allow appropriate sensitivity and scenario analyses [42,43]. Current management status of infectious diseases in ageing adults will be assessed with disease models linked to utilities, resource use, and costs. The models will simulate the impact of vaccine prevention using constrained optimisation methods and exploration of fiscal consequences. They will incorporate records of immuno-senescence and frailty to understand their effect in the frame of the proposed intervention strategies for healthy ageing.

Different tasks are split into three baskets: collecting background information; model development and testing; and model implementation (see Fig. 3). The first basket will review the literature on models (type, focus, gaps, input and output measures). It will identify the construction of summary measures for heterogeneity (frailty, benefit-risk ratios, immuno-senescence). It will develop maps on current patient flow within and outside the healthcare system, looking for trace marker points and hot spots of increased infection rates. An inventory of the different intervention options to reduce and control the infectious disease spread will be made. The second basket will develop three model types (static, compartmental-dynamic and/or agent-based) that allow the assessment of extensive sensitivity analysis. Because different options of prevention and treatment will be assessed, the models will elaborate on combinations of intervention types under budget limitation using constrained optimization and linked to fiscal evaluations [44]. Finally, the third basket will evaluate and test the feasibility of the model into different European countries. This basket will also evaluate new prevention strategies as they may come up. The evaluation models will be made available so that the methods can be standardised and comparisons be made across diseases, regions, and countries in Europe. Contact matrices will be assessed by developing a standard format to be tested in a few locations. The results will enhance the dynamic transmission/agent-based models. WP1 and WP3 will support on a regular basis the infrastructure that VITAL is building to evaluate vaccination programs that impact the BoD with improved immunity.

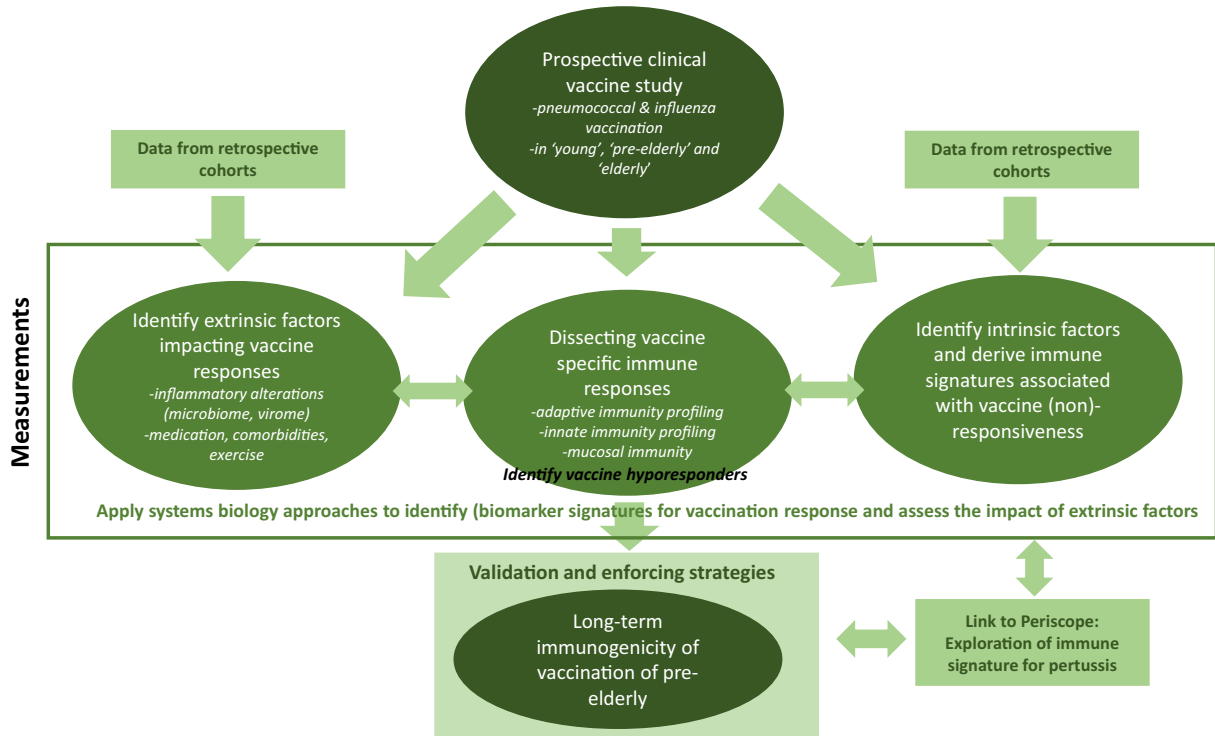


Fig. 2. Identifying the different tasks of WP2.

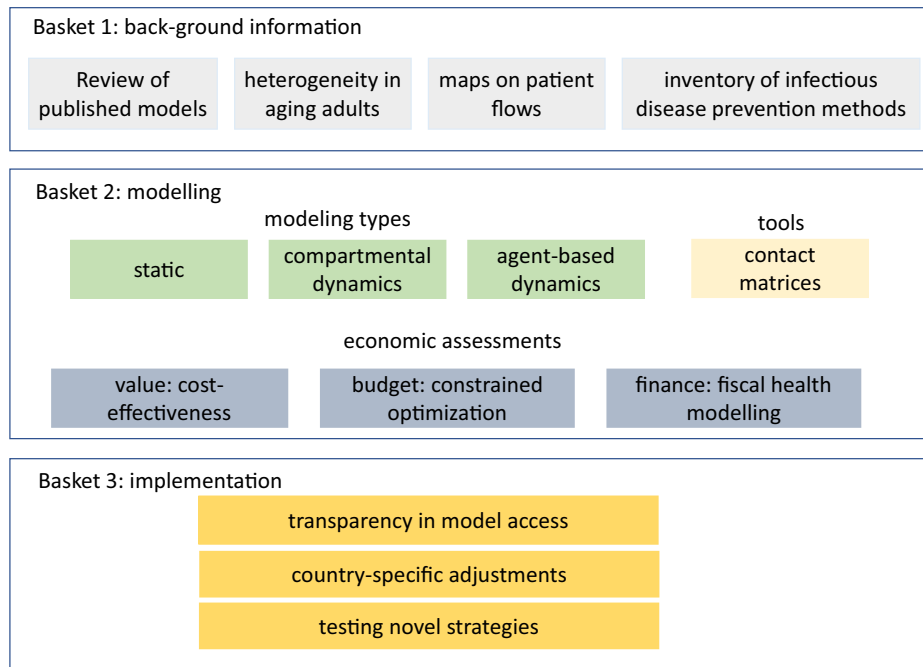


Fig. 3. Specifying the different baskets with specific tasks of WP3.

4.4. WP4: roadmap on training and education of HCPs

WP4 will develop strategies for educating and training HCPs and will engage those providing care to ageing people into a multidisciplinary approach by training experts, researchers, vaccinologists, clinicians and public health experts. The ageing adult perspective will be assessed and incorporated into innovative learning principles, such as adult learning and inter-professional education.

WP4's tasks are shown in Fig. 4. Firstly, we will explore the older adult perspective through focus group studies in France, Hungary, Italy, and the Netherlands. The studies are designed to gain insight into the factors that influence the decision making and preferences of ageing adults for the format and source of information they use about vaccination. In parallel, a systematic literature review will be performed to identify what determines effective education and training for HCPs. The outcome will support the adoption of healthy preventive behavior and enable to

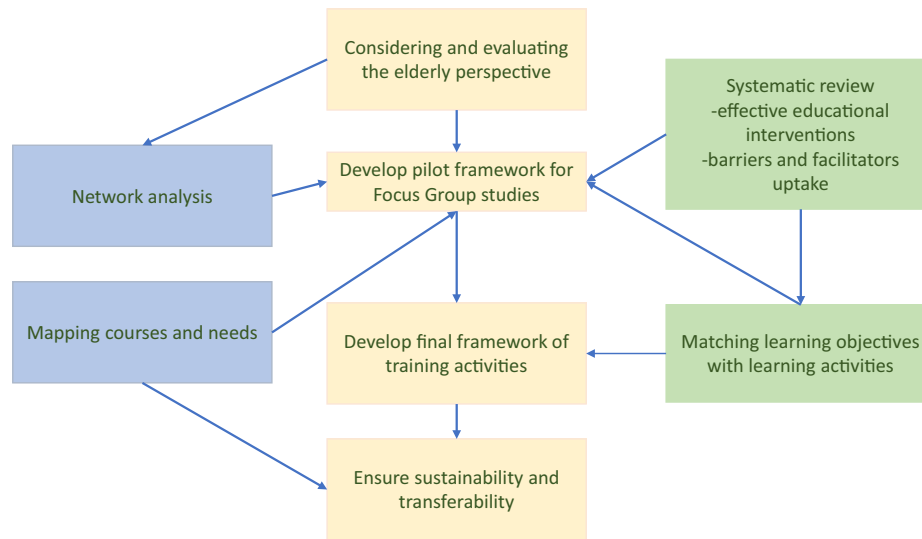


Fig. 4. Tasks of WP4.

match learning objectives with effective learning activities. WP4 will visualize and analyze healthcare networks for ageing adults by establishing a group of specialists: training experts, researchers, vaccinologists and public health experts. This group will review and test educational materials. We will map existing courses and evaluate training and educational needs. The resulting training methods and materials will form a pilot educational framework, including e-learning modules, simulations, and webinars which will be tested and finalized based on current adult learning theory and principles of inter-professional education. The educational activities will be incorporated into Continuous Medical Education (CME), Massive Open Online Courses (MOOC), virtual labs, virtual schools and other relevant courses. A MOOC dedicated to vaccines for ageing adults will be posted on the Claroline platform, a collaborative eLearning and system released under General Public License (GPL) open-source license which afford end-users the freedom to run, study, share and modify the software. The annual VaxInLive meeting (formally VaxInEu) will be a valuable opportunity to promote and disseminate the training activities which will be graded according to the European Credit Transfer and Accumulation System (ECTS). The information and new findings gathered in all the other WPs of VITAL will enable an optimal fit between the educational intervention and the latest epidemiological, immunological, and economic knowledge.

5. Expected impact of the VITAL program

VITAL will enhance our knowledge about vaccine-preventable infectious diseases affecting ageing adults and the determinants of immuno-senescence that can be favourably impacted by vaccination. VITAL will make recommendations to decision makers that will enhance healthy ageing and reduce healthcare costs. The following benefits are expected:

With five years of study and in the absence of having a coordinated action program in Europe against infections and vaccination in ageing adults, VITAL is a critical starting project. VITAL's multi-disciplinary and holistic approach will contribute to develop new policies for the prevention of infection in ageing adults and healthy ageing across borders in Europe. A reduction in infection rate and its consequences on morbidity, disability, hospital admissions, healthcare costs and mortality rates of ageing adults and an improvement of the quality of life of the target group and their direct surrounding care-givers (non-professional and professional)

through adequate communication is the goal. VITAL should enable the development of models for reporting accurate estimations of the benefits to society with respect to lowered costs (spending and taxation), health, medical access, healthcare equity improvement, and better societal functioning of ageing adults. These models will serve to develop an optimal public health policy and to monitor its effects over time as the VITAL-database records the impact of new strategies. In addition, new knowledge on immune signatures could lead to novel strategies for developing improved vaccines.

Through the information obtained from specific subgroups and models inferring the consequences of vaccination of specific target groups, VITAL will provide a balanced view on cost and health impact. Clear and favourable cost-effectiveness results for vaccination will enhance the impact of such interventions, increasing their affordability, and sustainability. VITAL will develop a series of standard protocols that allow European countries to easily investigate the disease burden, criteria of immune status of different age groups, and the economic assessment of the impact of vaccination on ageing adults in the short term (vaccine-preventable) and mid-long term (potential vaccine-preventable disease). VITAL will pioneer new ways to address and quantify the high immunological heterogeneity of ageing adults. It will collect critical information from various countries with different healthcare infra-structures, cultures, and management programs for infectious diseases in ageing adults. The project will develop and maintain open and clear channels of communication with regulatory agencies to share outcome and will contribute to regulatory aspects in the vaccination of ageing adults.

6. Opportunities and challenges of the VITAL program related to the COVID-19 epidemic

The recent COVID-19 outbreak in Europe and across the world created alarming stress situations at different levels in our society. The disease has severely impacted the group we are especially focussing on in VITAL, the ageing adults [45], and has highlighted the potential of the project in providing useful and necessary knowledge to move protection of elderly forward. Although the VITAL project should remain focused on its initial ambition for several tasks planned (see Table 2, red indicators), our research plans are affected as the information we aimed to collect will be altered because of the coronavirus epidemic. Meanwhile, the project also

presents opportunities for new investigations that other projects may not have the chance to undertake. We may consider to follow up COVID patients who recovered and evaluate their vulnerability to new infections in our WP1 epidemiologic studies, to examine whether blood immune signatures of Sars-COV-2-infected persons interfere with vaccination response across the different age-groups (WP2). We may also integrate the costs of controlling the COVID-19 epidemic in our economic model (WP3) and assess again the value of vaccination among ageing adults when performing new focus-group studies in WP4.

7. In summary

VITAL combines advanced epidemiology, immune-ageing research, clinical and high-tech cutting-edge technologies, integrated data analysis and modelling to develop science-based recommendations for vaccine use in ageing adults. The results should inform on the efficient use of available resources and accelerate the innovative use of vaccines to increase the number of healthy years enjoyed by the ageing population.

Our multidisciplinary consortium combines expertise from academia and industry, with partners originating from within and outside the EU, thus supporting the IMI2 objective to enhance engagement across sectors. The integration of VITAL with multiple existing European initiatives will allow the project outputs to be scaled up to increase efficiency. The presence of academic and industry partners at all levels within the proposal (management board, scientific boards, and work package leaders) allows true collaboration, and sharing of ideas, funds, and expertise. Adequate prevention via vaccination is expected to show important benefits for ageing adults living in Europe.

8. Funding, authorship contribution

Funding: the VITAL project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking (JU) under grant agreement No. 806776. The JU receives support from the European Union's Horizon 2020 research and innovation programme, and EFPIA-members.

Authorship contribution: all authors were involved in drafting the content and structure of the manuscript and approved the final version.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Giuseppe Del Giudice and Baudouin Standaert are employees and shareholders of the GSK group of companies, Stephen Lockhart is an employee and shareholder of Pfizer, and Christine Luxemburger is an employee and shareholder of Sanofi.

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