Topic: Analysing the infectious disease burden and the use of vaccines to improve healthy years in aging populations

All information regarding future IMI Call topics is indicative and subject to change. Final information about future IMI Calls will be communicated after approval by the IMI Governing Board.

Topic details

Action type	Research and Innovation Actions (RIA)
Submission & evaluation process	2 Stages

Specific challenges to be addressed

While the initial shape of the demographic age-structure of the population in 1870 was like a pyramid with a small group of elderly people (above 50 years old) on top (Arora S, 2005), today we observe a big change in that shape moving now into a mushroom-like design (EUROSTAT, 2017; Flinch C, 2010). Different factors can explain the dynamic process of the changes such as the life-expectancy at birth that today has now reached above 75 years in Europe with a marked difference -5 to 10 years- between genders in favour of women (EUROSTAT, 2017). Besides that other more recent phenomena could also explain the transformation. First is the baby-boom born after the Second World War who has now reached the age of retirement. In addition, from the nineteen seventies a decrease in birth rates per year is observed: the demographic age-structure up to the age of 60 years has now become a trunk that evolves in being slim or leaner over time. Moreover the life-expectancy of a subject reaching 60 years old today is also increasing with time. In summary, multiple dynamic age-processes are tailoring the age-structure of the population in Europe leading to the situation that the older population augments in size every year also because they live longer (Gloersen E, 2016).

The societal health and health care consequences of that process are two-fold (Sobczak D, 2014). One is a higher exposure to chronic diseases such as cardio-vascular disease and cancer requesting an increased demand for health care at an advanced age which is more costly because those people need more time to recover as they are becoming fragile by aging. Second is that older people are more vulnerable to infectious diseases because their immune system becomes weaker with age (Lambert N, 2012). The consequences of the latter are that one may see an increasing burden of infections among elderly with a high risk of transmission treated with antibiotics causing resistance. In addition, infectious diseases are often the trigger for a starting manifestation and/or for the worsening of chronic disease conditions those elderly were suffering from (Westendorp R, 2006).

We therefore have to tackle two important health problems related to infectious diseases in the elderly: an increasing volume problem of people getting old and an inhomogeneous demand for health care within that group. Older people will need more costly treatment because of their increased frailty condition or limited capacity in living independently leading to longer periods of needed support for care.

If those infections could be avoided, we should be able to delay, reduce, or avoid the exposure to the institutionalised health care system with the many consequences of poor, lengthy and costly stay related to slow recovery in the more aged persons. It impacts therefore the ambition of supporting healthy aging, a condition that helps optimize the opportunities of good health so that aged individuals maintain their activities of social life and enjoy an independent high quality of life (Lagiewka K, 2012).

A potential solution to the latter growing problem is trying to develop a well-conceived vaccination program for the elderly against their infection problems as we did for children years ago to control infections within that age-group. If we apply the same strategy for the elderly we should help reduce the infection problem and its consequences of being exposed to anti-microbial resistance (AMR).

The big issue however is that this whole situation has not been so well studied with enough detail in an integrated way to be able to (i) understand the burden of the problem (incidence of infections and immune responsiveness), (ii) make good projections on the implementation of such a vaccine strategy in health care and its cost for that age-group and society, and (iii) communicate to/train stakeholders working in this field. Rather bits and parts have been assessed but without having a clear overall picture on how this whole process of aging, infection exposure (Ozawa S, 2016), immune response to vaccination (Gruver A, 2007), is developing and potentially evolving. Therefore, before we can get to a well-conceived program of systematic vaccination of the elderly, we need to study the whole infection problem among the elderly in greater detail.

We are therefore exposed to the following challenges in getting the full picture well presented.

1. Getting access and demonstrating how to evaluate and report good epidemiologic data for obtaining a clear picture on the infectious disease burden in the aged people (50 years +) over time (trend analysis, frequency, Quality of Life (QoL), and cost) split by specific age- and gender groups, vaccine-preventable or upcoming vaccine preventable diseases, and exposure to the health care system (at home care, day care, medical care, institutional care (hospital, recovery))
2. Better understanding the immune response in elderly (65 years +) by deciphering the changes taking place due to age and to other factors, the role of different facets of the immune responses, the role of new immune-modulation techniques to explore the potential to develop better vaccines for the elderly
3. Having disease and economic models available that can accurately predict on the one hand how the current situation may further evolve without any specific intervention, and how we may project a change in disease frequency, cost and QoL of the elderly, if we try to implement an extended vaccination program to reduce the infection burden with the overall societal consequences
4. Being able to communicate an integrated view of the problem (epidemiology, cost, and QoL burden, vaccine and immunology working, economic consequences of implementing a vaccination program among elderly) through training and education of health care professionals (HCP).

Need and opportunity for public-private collaborative research

Public and private sectors are today involved at varying degrees in a variety of assessments on aging such as research on immune-senescence (Gruver A, 2007; Lambert N, 2012; Ovsyannikova I,2012; Boraschi D, 2013), identifying external factors that could influence the process, epidemiology and the cost of vaccine preventable infectious diseases in elderly (Ozawa S, 2016). Industry has a long-lasting experience with approaches of vaccinating the elderly adults as demonstrated with the development of specific vaccines for that target group. For example, progress has been reported in the past few years by various industries in the development of vaccines for influenza, pneumococcal infections, and herpes zoster for elderly (DiazGranados et al, NEJM 2014; Bonten et al, NEJM 2015; Lal et al NEJM 2015; Cunningham et al, NEJM 2016). However, success in these approaches is often based on empirical knowledge and observations rather than on understanding well the underlying mechanics of the vaccine working. On the other side, various public groups such as academic teams, governmental and public health bodies, small- and medium-sized entities (SMEs) have an established track record of expertise and achievements in specific aspects of ageing (epidemiology, immunology, health economics, training). This suggests that a more integrated approach between public and private sectors may pave the way to a deeper understanding of the problem and to the definition of novel solutions.

Only through joined efforts of public and private sponsors can a holistic approach be successful adding value as compared with the many projects in the area of aging which mostly have focussed on a single aspect (most of the time on immune-senescence).

For example:

- Vaccine industries and academic groups may currently perform their own epidemiologic studies with the collection of cost information and QoL data that are conducted independently from each other, using different types of analysis, QoL instruments, and reporting with different definitions because different age-groups have been selected or different time horizon perspectives have been considered. There is a need for more cooperation between the different groups, for sharing of information, pooled analyses of larger anonymised datasets, uniformed analysis and reporting. This should lead to more robust findings that will increase the credibility of the research.
- Developing new programs to study the immune response amongst aged persons is often a very costly undertaking, which makes it challenging for individual organisations or stakeholder sectors to conduct such studies. Collaboration between sectors will result in optimal use of financial resources and avoid duplication of efforts.

- Vaccine industries and academic groups can develop their own disease and economic models to explore the cost-benefit of new interventions. While those models are today often developed in different environments with little incentive to share the full details of their construction, for third party evaluators they remain black boxes with a low possibility of achieving a high level of transparency. There is a need for working together on model development between industry and academia, and possibly governmental institutions, so that maximum transparency and agreement is reached on how the models are constructed, tested and validated. This should create a deeper trusted relationship, including with decision makers, about the model output and sensitivity analyses.
- Once the problem is understood and once potential solutions are found, it will be key that the results become an integral part of communication and teaching programs involving all stakeholders working with the elderly. Such communication and reporting about the project requires intense collaboration between public and private organisations, to develop joined messages for healthcare professionals and decision-makers.

Scope

The scope of the project is to obtain a clear picture on the infectious disease burden in an aging population (50 years +), to quantify the problem such as number and type of hospitalisations and medical visits when the group is exposed to the health care system, to understand this evolution over the coming years, to obtain a better insight in the immune response in the age-group of 65 years +, to develop cost-benefit predictions based on an extended vaccination program, to better control the burden in that age-group through simulations with advanced disease models, and finally to develop strategies to educate all stakeholders working with the elderly.

Four major pillars will represent the objectives under the overall scope of the project:

Burden of infectious diseases in aging adults (50+)

It is expected that the activities of the project will lead to the development of an appropriate protocol design for collecting epidemiologic and economic data about infectious diseases in an aged population (50 years +) across health care systems in place. A starting point could be a pilot project in a specific region that has the facilities to develop and test in depth the designed approach for collecting and analysing the data. Based on that experience and depending on budget and time allocation the program could then be progressively expanded to different regions in Europe with the goal of obtaining a consolidated data-base system.

The protocol in the pilot region could begin with the collection and analysis of retrospective data moving to a more advanced and well-established prospective epidemiologic study program.

Objectives of this epidemiologic/economic investigation would be to:

- obtain more accurate knowledge on the epidemiology and the economics of infectious diseases in aging adults split into 2 categories: existing vaccine-preventable (VP) diseases and upcoming potential vaccine-preventable (PVP) diseases. VP included vaccines against influenza, pneumococcal, zoster, pertussis, meningococcal, and rotavirus. PVP included vaccines against for example RSV, Clostridium difficile, staphylococcus, E coli, enterococcus, urinary tract infections, and specific anti-microbial resistant germs.
- be able to report precisely on specific mortality, morbidity, hospitalization, medical visits, access to health care, cost and productivity loss, overall QoL, and specific QoL;
- investigate and explore potential links to diseases/co-morbidities and risks in which infectious diseases could be the trigger for developing more complex disease conditions (cardio-vascular, respiratory, stroke, metabolic problems, etc.);
- generate a consolidated database on infectious disease burden in aging adults (epidemiology & cost) across Europe to be consulted by decision makers on selecting new vaccines to be implemented;
- be able to estimate the increase of the infectious disease volume in the aged population and the level of heterogeneity of the problem (different demand of health support by age and gender);
- obtain the necessary building blocks for creating a natural infectious disease pattern of the elderly.

Changes in immune response with age (65+ years compared to adults 18-50 years of age) and internal factors influencing the process

The objectives would be to:

- give priority in selecting those novel approaches that pave the way to enlarge our knowledge about processes that lead to the decline of immune responsiveness causing higher susceptibility to infectious diseases and poorer response to vaccination.
- expand the field of investigating immune decline with age (termed, immune-senescence) and to identify the several compartments of the immune system that senesce with age.
- expand the vaccination field of analysis beyond influenza to create an optimal vaccination program with durable protection for non-influenza vaccines in elderly as well, namely Tdap/Td, Herpes Zoster and Pneumococcal. This is particularly important for those vaccines for which the elderly are immunologically naïve and which should provide a strong priming, which is expected to be difficult to achieve in subjects with a paucity of naïve T and B cells. Therefore equal emphasis should be put in place on the assessment of immune-senescence in response to influenza and to non-influenza vaccines.
- develop and perform a prospectively designed clinical research study to assess the immune response of the elderly (65+ years) compared with adults (18-50 years) following vaccination. An appropriate informed consent would allow the collection of serum and whole blood to assess systems biology profiles and biomarker signatures. A frailty assessment at enrolment could be established. A state-of-the-art dissection of the immune response could be conducted focussed on immune compartments not well studied or not studied to date; – for example, T-cell follicular help (TfH), individual cell profiling(e.g. RNA sequencing), mucosal markers and B-cell immune compartments. Particular attention should also be given to innate immunity in the peripheral blood and, whenever possible at the site of priming of the immune system (e.g. skin, muscle, mucosal level). The role of dendritic cells, macrophages, NK cells is becoming more important in the events triggered by novel adjuvants, novel delivery systems, etc. Their role in the elderly is still poorly understood.
- be able to apply the technique of machine learning to unravel the complex inter-relations between immunological biomarkers and vaccination in the elderly, to better understand complex patterns associated with aging and vaccination. New profiles of immune aging should direct areas of research for the application of immunomodulation and/or new vaccine technologies, able to overcome or mitigate immune devolution.
- test the hypothesis on extrinsic factors that could influence the immune response: nutrition, physical exercise, medical treatments, other technologies applied in medical care. It is well known that nutrition significantly influences immune responsiveness in the old subjects. Caloric restriction has a positive effect, while obesity has a negative effect on immune responses. In addition, some drugs have been recently unexpectedly shown to have either positive or negative effect on vaccination in old people. Prospective studies should be developed to investigate the relationship and its strength.
- based on the responses obtained from the research questions studied in the project, help create the right vaccine development program against certain infectious healthcare problems in elderly.
- be able to apply new data analysis methods to derive immune profiles associated with aging.

Vaccine impact assessment and economic value of vaccination in aging adults

The objectives would be to:

- be able to evaluate the effectiveness and impact of vaccination through modelling exercises with simulations and scenario-analysis (best, worst case) using well-developed epidemiologic and economic models including optimization and a vaccine portfolio management approach.
- develop a natural disease model with data obtained from the epidemiologic studies that should also help in answering the questions: when do we need to vaccinate to obtain optimal results of prevention?
- be able to elaborate on what could be the consequences expressed financially (private, public), in health gain (life years and quality life years), and in health care development (more beds, more home care, improvement in quality of care)?
- estimate what could be the new threat of living longer under healthier conditions for our social security system with increased spending in pensions? Do we need to work longer to make the program sustainable?
- be able to demonstrate whether vaccination may help reducing the anti-microbiological drug resistance over time?

How to best communicate to stakeholders through education and training of HCPs

The objective would be to:

- Build a framework of innovative educational and training initiatives on infectious diseases based on adequate prevention strategies including vaccination in aging adults for all HCPs.

Expected key deliverables

The expected key deliverables of the project should be:

- A database on infectious disease burden in aging adults (repository of knowledge)
- Standard methods and definitions on how to analyse and report the disease burden for that age-group
- An estimation of the full burden of infectious diseases for VP and PVP. The burden should include frequencies, costs, Quality of Life (QoL), with trend results stratified by age-groups, risk level, relative importance of hospitalization/surgery, gender, social classes, access to medicine, underlying chronic diseases or sequelae.
- The identification and validation of intrinsic parameters impacting the decline of immune responsiveness with age characterized to advance the prevention of infectious disease in the elderly through vaccination.
- Computational models to conduct simulations of immune function in elderly (with /without disease)
- The characterisation and validation of the role of external environmental factors (nutrition, physical exercise, pharmacological treatments, etc.) on the immune responsiveness in the elderly.
- Models with scenario-testing that simulate the impact of different vaccination programs based on their health benefit and economic consequences
- A recommendation for optimal vaccination strategies of the older adults based on model simulations and the data collection
- The development of a vaccine confidence roadmap targeting HCPs: understanding of the levers/barriers to vaccination and drafting of possible actions.

Expected impact

The project will have an impact at many different levels:

- Societal gain for healthy aging: based on the data-collection and model simulation, a recommendation will come out on how to create an optimal vaccination strategy for the older adults. If that strategy will be implemented, an evidence-based vaccination programme for the aging adult will enhance the health condition of the elderly, make important cost offsets in health care, result in benefits in leisure time of the target group and the care-givers, reduction in production loss of care-givers, and improve the quality of care. In addition, an enhanced overall knowledge of what matters among the elderly will be an important societal gain.
- Health science development: Agreed-upon standards of analysis and reporting in the field of epidemiology and economic evaluation in people over 50 years old will have a positive impact on the results of vaccination.
- Basic research in immunology and vaccinology: it is expected that the results of the project will significantly contribute to a deeper understanding of the immune-response in aging adults. This new knowledge would not be a stand-alone acquisition, but it would instead reside within the frame of a more comprehensive body of knowledge encompassing epidemiology, environmental factors, etc. The results should help to develop better vaccines or better vaccination-schedules/ programs for the target group
- Economic analysis: elderly are a challenging group to assess in health economic evaluations when it comes to measuring precisely health and health gain. In elderly the cohort of evaluation isn't fixed but reduces over time because of the deaths moving into the absorbing state. Many competing causes of death and interactions between the various co-morbidities do not allow a readily valuation of the expected health benefit. It is expected that this project will allow us to more accurately estimate health gains achieved through new interventions like vaccination and cost calculations using more appropriate techniques of modelling
- Communication strategies: our society is evolving very rapidly in a modern area of communication that is well established in the young generation with the social media. Having a good communication strategy in place will enhance the promotion of prevention strategies such as new vaccination programs to reduce the infection burden in elderly.

- Through the participation of industrial partners, in particular small and medium-sized entities (SME's), an additional impact in relation to strengthening the competitiveness and industrial leadership of Europe can be expected.

Potential synergies with existing consortia

The project is expected to directly contribute to the goals and activities of the European Innovation partnership on Active and on Healthy Ageing.

Applicant consortia will propose a strategy to emphasis/maximize potential synergies with other initiatives in the field of health interventions on aging adults such as epidemiology, economics, immunology, physiology, among other initiatives. For example, links to existing lists of initiatives within Horizon 2020, Millennium goals, Healthy Aging programs via EuroHealthNet, should be explored, such as the H2020 I-MOVE+ project.

In addition, special consideration should be given to exploring synergies with existing IMI projects and utilising learnings generated there to build upon in this project. The following non-exhaustive list of IMI projects might be of relevance in this respect:

- projects under the New Drugs for Bad Bugs (ND4BB) programme, http://www.imi.europa.eu/content/nd4bb
- RESCEU (Respiratory syncytial virus consortium in Europe), www.resc-eu.org
- the Better Data for Better Outcomes (BD4BO) programme,
- SPRINTT (Sarcopenia and physical frailty in older people: multi-component treatment strategies), www.mysprintt.eu
- other IMI projects dealing with vaccine data analysis, such as ADVANCE **(**Accelerated development of vaccine benefit-risk collaboration in Europe), www.advance-vaccines.eu, and the project selected for funding under the topic Joint influenza vaccine effectiveness studies (IMI2C9).
- any other project or initiative of relevance, in order to avoid duplication of efforts.

Industry Consortium

The EFPIA in-kind contribution will take the form of:

- Personnel costs by providing expertise in Health economics and Outcomes, Immunology, Epidemiology, Statistics, regulatory affairs, patients engagement, project leadership, .
- Prospective study protocols.,
- Disease and economic models already developed for elderly,
- Roadmaps for good communication practices.

Indicative duration of the project

The indicative duration of the project is 60-months.

Future Project Expansion

Potential applicants must be aware that the Innovative Medicines Initiative 2 (IMI2) Joint Undertaking may, if exceptionally needed, publish at a later stage another Call for proposals restricted to the consortium already selected under this topic, in order to enhance the results and achievements by extending the duration and funding. The consortium will be entitled to open to other beneficiaries as it sees fit.

Applicant Consortium

The successful applicant consortium will be selected on the basis of the submitted short proposals.

The applicant consortium is expected to address all the research objectives and make key contributions to the defined deliverables in synergy with the industry consortium.

The consortium should combine partners with established and well-recognized experience in the field of aging, encompassing aspects related to vaccination, public health, immunology, epidemiology, infectious diseases, physiology, medicine, nutrition, economics, advanced disease modelling, training and education capacities and experiences, etc.

The applicant consortium is expected to consist of small- and medium-sized enterprises as project management offices (SMEs), academic centers (both clinical and experimental), centers from national and/or supranational public health bodies. Furthermore, the consortium should include partners with experience in assessing vaccination programmes and the decision-making processes leading to the implementation of new vaccination programmes, as well as regulatory experience.

The applicant consortium is expected to address all the research objectives and make key contributions to the defined deliverables in synergy with the industry consortium.

The applicant consortium is expected to include the necessary project management skills suitable for the expected funded project.

Suggested architecture of the full proposal

The applicant consortium should submit a short proposal which includes their suggestions for creating a full proposal architecture, taking into consideration the industry contributions and expertise provided below.

The final architecture of the full proposal will be defined by the participants in compliance with the IMI2 rules and with a view to the achievement of the project objectives. In the spirit of the partnership, and to reflect how IMI2 Call topics are built on identified scientific priorities agreed together with EFPIA beneficiaries/large industrial beneficiaries, it is envisaged that IMI2 proposals and projects may allocate a leading role within the consortium to an EFPIA beneficiary/large industrial beneficiary. Within an applicant consortium discussing the full proposal to be submitted at stage 2, it is expected that one of the EFPIA beneficiaries/large industrial beneficiaries may elect to become the coordinator or the project leader. Therefore to facilitate the formation of the final consortium, all beneficiaries are encouraged to discuss the weighting of responsibilities and priorities therein. Until the roles are formally appointed through a Consortium Agreement the proposed project leader shall facilitate an efficient negotiation of project content and required agreements.

The architecture of the proposal is based on four major pillars. It is expected to support the development of a comprehensive program about the relationship between vaccine and healthy aging. The architecture outlined below for the full proposal is a suggestion. Different innovative project designs are welcome, if properly justified, as long as the objectives of the project are fully supported.

It is expected that the objectives of the project can be achieved by the following five work packages.

Work Package 1: To determine the burden of infectious diseases in aging adults (50+)

The objectives of this work package will be as follows:

- Through retro- and prospective epidemiologic study design and review of existing data-bases, starting with a pilot project in a particular region in order to obtain a robust protocol of evaluation that can be expanded progressively over time.
- Acquiring a deeper knowledge on the epidemiology of infectious diseases split into 2 categories (existing vaccine-preventable (VP) diseases (e.g influenza, pneumococcal, zoster, pertussis, meningococcal, rotavirus), upcoming potential vaccine-preventable (PVP) diseases (e.g. RSV, C diff, staphylococcus, E coli, enterococcus, urinary tract infections, specific anti-microbial resistance germs) in aging adults.
- Acquiring a deeper knowledge on the economics of the infectious diseases (cost of illness) split into the 2 categories (VP, PVP).

- Investigate potential links to diseases/co-morbidities and risks within that age-group in which infectious diseases could be the trigger for developing more complex disease conditions (cardio-vascular, respiratory, stroke, metabolic problems, etc.).
- The work package 1 should report about the volume increase of the infectious disease in the aged population because of the demographic age-change and about the level of heterogeneity in the target group related to possible immune response rates.

Work Package 2: To better understand the immune response of aging adults (65+) and how it is modulated or affected by internal and external factors after vaccination

The objectives of this work package will be as follows:

- Prospectively designed clinical research studies to assess the immune response of the elderly (65+ years) compared to adults (18-50 years) following vaccination. An appropriate informed consent would allow the collection of serum and whole blood to assess systems biology profiles and biomarker signatures. Establishment of a frailty assessment related to the infection condition at enrolment.
- Learning about mechanisms leading to immune waning or reduced immune responsiveness at the level of both innate and adaptive (both T- and B-cell) immunity, and the ability to respond to vaccination with age.
- State-of-the-art dissection of immune responses at the site of the priming of the immune response (e.g. related to skin condition, muscle condition, mucosal conditions), role of B and T-cell immunity, immune modulators (PD-1) among others, in order to better understand why the immune-response reduces with age. This large field of exploration needs an urgent, well-focussed and designed research program for obtaining reliable and workable results that can improve next generation of vaccines and vaccination-schedules and programs for the elderly. The field is starting to know and to observe important processes of immune-senescence occurring with age, but we need to focus on immune compartments pertinent to optimal vaccine elicited responses and other immune processes not yet adequately addressed such as T-cell follicular help (TfH), B-cell immunity, innate immunity (e.g. dendritic cells, macrophages, monocytes, NK cells, etc. in the blood and, whenever possible, at other priming and/or effector sites of the immune response), mucosal markers, antibody effector functions, immune profiling at the individual cell level (e.g. single cell RNA sequencing), among others.
- The waning of the immune responsiveness is not merely due to the “physiological” decline by age, but also by extrinsic factor, which can accelerate or retard the decline. Understanding how these factors such as physical activity, nutrition, other medical treatments, existing comorbidities may affect the immune responsiveness in aging adults becomes important to better appreciate the heterogeneity of the phenomenon of immune-senescence.
- Application of new data analysis methods to derive immune profiles associated with aging. Machine learning should be applied to identify complex profiles of inter-related factors.

Work Package 3: To assess with disease models the current management status of infectious diseases in older adults and to simulate the impact of (potentially) vaccine preventable infections

The objectives of this work package will be as follows:

- The models should set new standards of analysing and reporting health economic results for such population (cost-effectiveness analysis, budget impact, optimisation modelling). It is expected to advance the impact options in a transparent way when analysing and reporting health economic results.
- Based on information collected in Work Package 1, developing advanced modelling programs (agent based modelling simulating different conditions in which elderly people may normally operate (home care, day care, hospital care) to demonstrate the impact of vaccination according to various level of immune-senescence and to define best strategies to maximise the overall public health impact of vaccination for aging adults, taking into account potential enablers. The models developed through this program, should be made available across all the participants to the project.

Work Package 4: To develop a roadmap about training and education of HCPs

The objectives of this work package will be as follows:

- Vaccination of adults and of elder subjects is not fully perceived as a major need with great value assessment for the target population and society, as compared with the vaccination at the paediatric age-group. Appropriate and innovative communication tools on the value of vaccines and on vaccination for all stakeholders (decision makers, prescribers, payers, target population) represent a key need in achieving the scope of healthy aging.
- Building a framework of innovative educational and training initiatives on infectious diseases based on adequate prevention strategies including vaccination in aging adults for all HCPs.
- Developing a network of specialists/experts in the field across Europe to exchange experience and set-up new collaborative projects would be very helpful.
- Demonstrate how to secure training of the HCPs in charge of implementing adult vaccination: include systematic HCPs vaccination training both in curriculum and in Continuous Medical Education (CME) (use of Massive Open Online Courses (MOOC) to be leveraged), taking into account that HCPs should include GPs, specialists, nurses and pharmacists

Work Package 5: project coordination, management, and dissemination activities

The objectives of this work package will be as follows:

- Skilled project management support will be an essential part to ensure project success.
- Managing all aspects of project governance, management and coordination. Facilitation and streamlining of cooperation between the different partners of the project and between work packages.
- Carrying out all aspects of the dissemination of results, and communication strategy.
- Coordinating and communicating with other European initiatives and projects handling complementary activities.

References

1. Arora, S (2005). On epidemiologic and economic transitions: a historical view. In ‘Health and Economic Growth’, Lopèz-Casasnovas G, Rivera B, Currais L (editors). MIT Press.
2. Bonten M, et al. (2015), Vaccine against penumococcal pneumonia in adults. N Engl J Med, 373(1): 93.
3. Boraschi, D., et al. (2013). "The gracefully aging immune system." Sci Transl Med **5**(185): 185ps188.
4. Carone, G (2015). The 2015 Ageing Report, economic and budgetary projectsions for the 28 EU Member States (2013-2060). European Economy series, European Commission: 424.
5. Cunningham A, et al (2016). Efficacy of the Herpes Zoster subunit Vaccine in Adults 70 Years of Age and Older. N ENgl J Med, 375 (11): 1019-32.
6. DiazGranados C, et al (2014). Efficacy of high-dose versus standard-dose influenza vaccine il older adults. N Engl J Med, 371(1): 635-45.
7. EUROSTAT (2017). "Population structure and aging".
8. Flinch, C (2010). Evolution of the human lifespan and diseases of aging: roles of infectoion, inflammation, and nutrition. PNAS, 107 (1).
9. Gloersen, E (2016). The impact of demographic change on European regions: 147.
10. Gruver, A. L., et al. (2007). "Immunosenescence of ageing." J Pathol **211**(2): 144-156.
11. Lagiewka, K. (2012). "European innovation partnership on active and healthy ageing: triggers of setting the headline target of 2 additional healthy life years at birth at EU average by 2020." Arch Public Health **70**(1): 23.
12. Lal H, et al (2015). Efficacy of an adjuvanted herpes zoster subunit vaccine in older adults. N Engl J Med, 372 (22): 2087-96.
13. Lambert, N. D., et al. (2012). "Understanding the immune response to seasonal influenza vaccination in older adults: a systems biology approach." Expert Rev Vaccines **11**(8): 985-994.
14. Sobczak D, (2014). Population ageing in Eruope, facts, implications and policies.
15. Ovsyannikova I, (2012). Impact of cytokine and cytokine receptor gene polymorphisms on cellular immunity after smallpox vaccination. Gene, 510(1): 59-65.
16. Ozawa, S., et al. (2016). "Modeling The Economic Burden Of Adult Vaccine-Preventable Diseases In The United States." Health Aff (Millwood) **35**(11): 2124-2132.
17. Westendorp R, (2006). What is healthy aging in the 21st century? AM J Clin Nutr 83(2):404S-409S.