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Development of vaccines and vaccinal strategies against COVID-19: the information contributing to shared decision-making

INTRODUCTION

In December 2019, an epidemic caused by an emerging virus known as SARS-CoV-2 (Severe acute respiratory syndrome coronavirus 2, due to its similarities with SARS-CoV, which appeared in 2003) broke out in the city of Wuhan, China. On 11 March 2020 the World Health Organization (WHO) characterized the phenomenon as a pandemic[1]. By 4 December 2020 the number of COVID-19 cases (coronavirus disease 2019) throughout the world was estimated at 65 million, while the number of deaths ascribed to COVID-19 had exceeded 1.5 million[2]. In France, by 9 December 2020 the number of confirmed cases was 2,324,216, and the number of deaths ascribed to COVID-19 was 56,648[3].

In the face of this pandemic, different nations have drawn up non-pharmaceutical strategies to limit transmission of the virus[4]. In the modeling developed by Li, the closing of schools and workplaces, the prohibition of public events and of gatherings of more than ten persons, the imposition of home confinement and restrictions on mobility seemed associated with reduced transmission of SARS-CoV-2[4]. That said, these different strategies have major social costs; in France, the first lockdown (17 March to 11 May 2020) led to a decrease in economic activity of 25%[5].

Multiple active principles have been the subject of highly numerous randomized clinical trials in different parts of the world, the common objective being to reduce the transmission and/or severity of COVID-19[6]. As the majority of the world population is not immunized against this emerging infection, vaccination against COVID-19 is shaping up as the long-term solution.

For one century, vaccination in general has been considered as the procedure saving a maximum number of lives, and little by little, it has come to represent the optimal solution against infectious diseases[7]. With this in mind, the WHO considers vaccinal hesitation as one of the ten most menacing threats to health. Vaccinal hesitation has been defined as "*the reluctance or refusal to vaccinate despite the availability of vaccines [...] Several factors come into play, including misinformation, complacency, inconvenience and lack of trust* [8]. Feelings regarding vaccine safety vary according to country. In 2016, France seemed to be the most vaccine-hesitant nation, with 41% of vaccine skeptics as opposed to 13% worldwide[9]. In March 2020, 10 days after the outset of the initial lockdown, nearly 25% of the 5108 French persons interrogated, a representative sample of the overall population, stated that if a COVID-19 vaccine were to exist, they would probably or certainly refuse to have it administered to them[10].

The initial results of phase I and phase II trials were published in August and November 2020[11,12]. In December, the United States Food and Drug Administration (FDA) rendered public its reports including effectiveness and safety data on the Pfizer-BioNTech® and Moderna® vaccines, and *The Lancet* published intermediate data derived from the randomized clinical trial for the ChAdOx1 nCoV-19 vaccine[13,14]. At the request of the French ministries of health and social solidarity and of higher education, research and innovation, and in coordination with different hospitals and the *Collège national des généralistes enseignants* (CNGE), the French national institute of health and medical research (INSERM) has

been commissioned to put into place an infrastructure for the organization of clinical trials on COVID-19 vaccines: COVIREIVA-C[15].

The structure has as objectives *(i)* to set up a nationwide platform for volunteer recruitment, *(ii)* to establish coordination between investigation centers in the pursuit of industrial and academic trials, *(iii)* to conduct work on vaccine acceptability *(iv)* and to assess vaccine tolerance in close conjunction with pharmacovigilance activities. On 30 November 2020, the French health authority (HAS) proposed a five-phase vaccination strategy prioritizing the most fragile individuals in France[16], and the first vaccinations against COVID-19 are slated to take place in January 2021.

The French prime minister has emphasized the central role of general practitioners (GP) with regard to this vaccination. According to a BVA poll, during the first lockdown 93% of his fellow countrymen maintained confidence in their GPs; for 74%, he or she represents their entranceway to the health care system[17]. General practitioners and, more broadly speaking, the caregivers tasked with administering anti-COVID-19 vaccination, will be called upon to answer the questions put forward by healthcare users. In Australia, a letter to GPs aimed at "building vaccine confidence" and "optimizing uptake"[18] has been published.

The primary objective of this article is to address and answer questions on vaccine development, vaccination strategy and vaccine acceptability. The second objective is to facilitate shared decision-making involving the caregiver and the health care user[19].

VACCINE DEVELOPMENT DURING A PANDEMIC

From the outset of the COVID-19 pandemic, a race against the clock clicked into gear, the objective being to develop safe and effective vaccines, most often via public-private partnerships[20]. By 2 December 2020, 214 vaccines had been identified by the WHO and were being developed, and 51 of them had entered into a phase of clinical development, that is to say phase I (Figure 1)[21]. Usually, as depicted in Figure 1a, the development of a vaccine takes 10 to 15 years[18] and consists in *(a)* the preclinical phase (cellular and animal models), *(b)* Phase I (safety tests involving dozens of volunteers), *(c)* Phase II (safety and immunogenicity involving hundreds of volunteers), *(d)* Phase III (effectiveness and safety involving thousands of volunteers), and *(e)* commercialization after having been granted market authorization by national medicines regulatory authorities (*Agence nationale de sécurité du médicament et des produits de santé*/ national agency of drug and health product safety - ANSM in France) and post-commercialization monitoring of possible side effects (phase IV). As concerns Covid-19, scarcely 12 months have elapsed between the first reported cases of COVID-19 and the first emergency authorizations of vaccine use (Pfizer/BioNtech vaccine in the United Kingdom and the United States)[22].

HOW IS IT POSSIBLE TO ACCELERATE SO MANY THINGS, PRACTICALLY ALL AT ONCE?

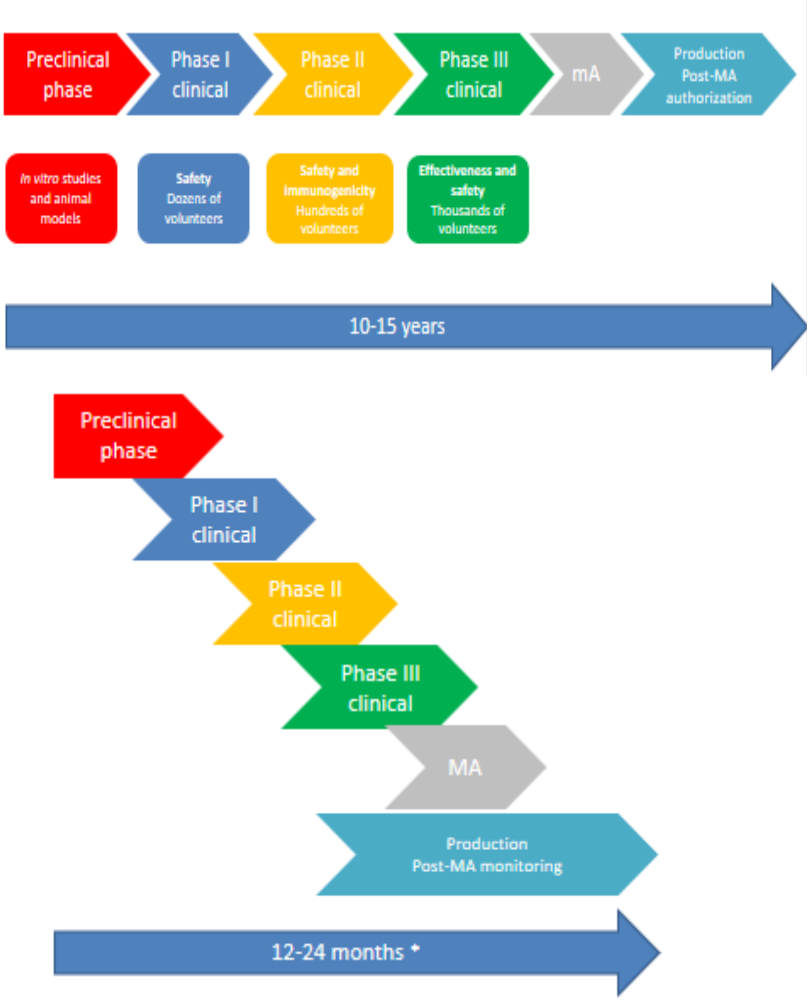
First of all, the 2003 SARS epidemic determined the role of the Spike protein and made it the target of vaccination[23]. What is more, in the midst of an epidemic the vaccine development phases tend to overlap (Figure 1b). That said, safety and effectiveness assessment during clinical trials remains in compliance with the usual rules governing clinical vaccine research. Authorization processes have been accelerated and vaccine production anticipated[18].

Concerning production, it can be accelerated in accordance with the vaccine platform procedure, as is the case with RNA messenger (RNAm) platforms. That is why the two vaccines that were the first to have completed Phase III and to have communicated their effectiveness results are RNAm vaccines (Pfizer/BioNTech® and Moderna®). Developed for more than 20 years in the framework of anticancer and anti-infective vaccine approaches, the platforms do not necessitate a step-by-step procedure utilizing cell lines and embryonated eggs, which means that and vaccine production can be exceedingly (sidebar 1)[24]. Different clinical trials utilizing other vaccine platforms are concomitantly ongoing. Two platforms that currently stand out are *(i)* non-replicating viral vector (for example, phase III Adenovirus vector: AstraZeneca®/University of Oxford or Janssen; *(ii)* whole inactivated or subunit vaccine type (for example, phase II Sanofi/GSK).

Most vaccines necessitate two injections[21]. RNAm vaccines require conservation at- 80°C (Pfizer/BioNTech) and at - 20°C (Moderna), and the latter can be conserved for 30 days at 2 to 8°C, and for 12 hours at room temperature.

Information on the effectiveness of the Pfizer/BioNTech®, Moderna® and AztraZeneca®/Oxford vaccines was initially communicated in the press. Data on phases II/III of the Pfizer/BioNTech® vaccine were subsequently disseminated by the FDA and published in the New England Journal of Medicine[13,25], while AstraZeneca®/Oxford recently published its aggregated data on phase I/II, II/III and III trials (United Kingdom, Brazil, and South Africa)[14]. As regards the Moderna® vaccine, the FDA has made available data from the phase III trial and immunogenicity data on elderly patients (a small population)[12,26-28]. At this time, the reported effectiveness of the Pfizer/BioNTech® vaccine is 95% for the entire population (93.7 % in persons over 55 years of age)[13]. As for the AstraZeneca®/Oxford vaccine, overall effectiveness neighbors 70%, and is greater in volunteers having received first a ½ dose followed by a full dose than in those having received two full doses; that said, the difference has yet to be wholly elucidated[14]. As concerns Moderna®, the data transmitted to the FDA show 94.5% effectiveness (CI95 = 86.5 – 97.8). In addition to immunity engendering neutralizing antibodies, cellular immunity is apparently triggered by these 3 vaccines[20].

Concerning safety, the reported adverse effects of these vaccines are essentially benign side effects and seem more or less pronounced according to age. With the Pfizer/BioNTech® vaccine, local "reactogenicity" has appeared after the 2nd injection among over 60% of volunteers, and general signs (fever, myalgias, asthenia) have been found in 5



Figures 1 – The phases of vaccine development (usual process *versus* epidemic context) [figures based on the article by Danchin *et al.*[18]]

to 10%[13]. As regards the AstraZeneca/Oxford® vaccine, frequent "reactogenicity" (> 60 %) has likewise been reported (pain at the injection site, feverish sensation, muscle pain)[14]. Available safety data are being communicated and monitored, after as well as prior to commercialization[13,14].

Any caregiver or citizen can make a declaration of an adverse event following vaccination on https://signalement.social-sante.gouv.fr/psig_ihm_utilisateurs/index.html#/accueil.

Analysis of the different reports is carried out by a French network composed of 31 regional pharmacovigilance centers, each of which is commissioned to provide expert appraisal of a precise type of adverse event. Ongoing monitoring enables open and transparent communication on the safety of COVID-19 vaccines.

PRIORITIZING STRATEGY FOR POPULATIONS

The launching of a vaccination campaign in the midst of an epidemic, at a time when the clinical development of vaccines is ongoing, imposes a number of possibly unprecedented organizational constraints, which are partially associated with dose availability (initial critical period, followed by supply ramp-up and deployment of vaccination systems), the conditioning of single dose or multi-dose vials, and the ensuring of conservation (refrigeration chain).

Public policy makers are tasked with defining a prioritization strategy for populations to be vaccinated[16]. In public health as well as clinical practice, it is initially of paramount importance to identify the **populations at risk of hospitalization or death in the overall context of SARS-CoV-2 infection.** Age is the factor most closely associated with this risk; while less pronounced, other factors are cumulative (sidebar 2).

Following which, the overriding priority is to identify **populations at risk of exposure to the disease**. The categories are stratified: on the one hand, health professionals (medical practitioners and auxiliaries, pharmacists, stretcher-bearers, firefighters, etc.) and human services professionals; on the other hand, persons in community residence or housing projects for dependent elderly individuals (EHPAD), prisoners, persons with disabilities inhabiting a group home, persons dwelling in temporary or insecure accommodations.

Taking into account these different objectives and constraints, as well as models from other countries, the HAS (French health authority) has proposed a 5-phase schedule (Table 1) with two categories of targets: system users, and their caregivers[16,18].

During **phase 1**, which is deemed critical, vaccination priority is given to: residents in establishments accommodating the elderly, long-term residents in medicalized facilities; and professional caregivers at heightened risk of severe form/death (over 65 years old and/or with comorbidities). This phase is placed under the responsibility of the coordinating doctors.

La **phase 2** is stratified into 3 stages: all persons more than 75 years old, prioritizing those with comorbidities; persons from 65 to 74 years old presenting with comorbidities; caregivers over 50 years old presenting with comorbidities. Stratification entails the attentive participation of general practitioners in the detection and identification of comorbidities.

Starting with **phase 3**, vaccination policy is addressed to

RNA vaccines consist in messenger RNA coding for the Spike protein of SARS-CoV-2. These synthetic RNAs are encapsulated in lipid nanoparticles protecting them from enzymatic degradation (fragile material) and enabling them to enter into our cells. These RNA messengers are not infectious, and cannot be incorporated into the human genome (DNA); men and women do not possess reverse transcriptase. The RNA messengers consequently remain in the cell cytoplasm and code for the spike protein, which will serve as an antigen stimulating cellular and humoral immunity. Their half-life in cells lasts for several days. Prior to the COVID-19 pandemic, RNA vaccines against the Zika and Ebola viruses, Chikungunya and the Cytomegalovirus were in a phase of clinical evaluation.

Sidebar 1. RNAm vaccines (based on Pardi *et al.*[24])

- obesity (BMI > 30), particularly in young children,
- COPD and respiratory insufficiency,
- complicated arterial hypertension,
- cardiac insufficiency,
- diabetes (type 1 and type 2),
- chronic renal insufficiency,
- cancers and malignant hematological pathologies, active or fewer than 3 years previous,
- solid organ transplantation or hematopoietic stem cells,
- Down's syndrome.

Sidebar 2. Comorbidities entailing confirmed risk of hospitalization and death (according to HAS[16])

the rest of the at-risk population (over 50 years old and/or with comorbidities). The different caregivers are called upon to undergo vaccination, as are non-caregiving professionals in the essential sectors of the economy (security, education, food supply, banking, transportation). Determination of who belongs to the last two categories remains open to debate; during this phase, occupational physicians are likely to have a major role to assume.

As for **phase 4,** which targets marginalized, precarious and homeless populations, it entails the mobilization not only of general medicine, but also of associational and institutional networks in contact with a problematically accessible public that does not necessarily receive regular medical care. During this phase, the professionals assisting these persons are likewise targeted. Occupational physicians shall be called upon to orient

Phases	Key actors	Targets (users) / Targets (professionals)
Phase 1	Coordinating doctors	Long-term residents in medicalized facilities.
		Professionals who care for residents, and themselves present heightened risk of severe form/death (over 65 years old and/or with comorbidities).
Phase 2 (in 3 stages)	GP	S1 : All persons over 75 years old, prioritizing those with comorbidities,
		S2 : … persons from 65 to 74, and presenting with comorbidities,
		S3 : … … caregivers over 50, and presenting with comorbidities.
Phase 3	GP, OP	At-risk populations (50 years and/or comorbidities)
		All caregivers and non-caregiving professionals in essential sectors of the economy (security, education, food supply, banking, transportation)
Phase 4	Associations, MG, OP	Marginalized, precarious populations; homeless persons,
		Professionals assisting precarious populations, workers in enclosed areas (construction, slaughterhouses), persons residing in confined living quarters
Phase 5	MG	The entire adult population not yet vaccinated

Table 1. Chronological phases of the vaccination campaign and target populations (according to HAS[16])

vaccination of workers in enclosed areas (construction, slaughterhouses). General practitioners shall help to identify persons at risk due to confined living quarters. This period may exacerbate existing health care inequalities.

Phase 5 extends the vaccination campaign to the entire adult population that has yet to be vaccinated.

ACCEPTABILITY OF THE COVID-19 VACCINE

The herd immunity threshold corresponds to the proportion of individuals who, on account of acquired immunity, can no longer participate in the transmission chain of a pathogenic agent. It depends directly on the reproduction number of the infectious disease (starting with an "index case", the number of infected persons: R0). Given that in SARS-CoV-2 infections, the number ranges from 2 to 3, the herd immunity threshold would be set between 50 and 67%[29]. For comparison's sake, with a RO between 12 and 18, the herd immunity threshold for measles exceeds 90%. Given present-day uncertainty as to post-infection natural immunity by SARS-CoV-2, it remains difficult to determine a target rate for vaccination coverage. That said and most importantly, in order for herd immunity to be acquired it behooves the population to accept vaccination, and in France, vaccine hesitancy is highly pronounced[9].

As regards intentions among the French to be vaccinated against COVID-19, during the first epidemic wave they were estimated at approximately 75%[10,30], and then, in June 2020, at 60%[31]. Today, as vaccines are beginning to become available, the intentions collected in the latest public opinion polls range from 40 to 60%[17,32,33]. While an overwhelming majority (>85%) of health professionals, particularly physicians and pharmacists, have declared the intention to be vaccinated, among nurses and health assistants only 60 to 65% have concurred[34]. In a context of emerging pathology, the main barriers to vaccination (in order of frequency) are fears concerning vaccine safety, doubts as to vaccine effectiveness, fear of developing COVID-19 due to vaccination, and limited perception of the risks associated with COVID-19[35].

In France, women and youth (under 30 years of age) seem less inclined to be vaccinated than

1. *What is the effectiveness of vaccination in very elderly persons and specific populations (immunosuppressed, pregnant women, etc.)?* These populations are often excluded (or included in an inordinately small proportion) in clinical development studies, which will require relevant supplementation.
2. *How long does vaccinal immunity last?* As of now, it is impossible to answer this question; cohort follow-up studies will be necessary.
3. *What is the interest of vaccination with regard to transmission?* Most vaccine trials have chosen as primary endpoint the occurrence of symptomatic COVID-19. There presently exist few data on systematic search for SARS-CoV-2 among clinical trial volunteers that would facilitate identification of asymptomatic infections. While the Moderna® vaccine seems as of the first dose to reduce the risk of asymptomatic infection, the encouraging results remain to be confirmed.
4. *Can individuals with past COVID-19 history be vaccinated?* In clinical studies, patients having contracted SARS-CoV-2 with positive serology were deemed eligible to be vaccinated. As they most likely represent a small percentage of participants, it is impossible to determine the effectiveness and tolerance of the vaccination. Data on long-term natural immunity have yet to be conclusively established. While Centers for Disease Control and Prevention (CDC) advise vaccination of at-risk persons or health care professionals with COVID-19 history, they suggest to patients having recently developed COVID-19 (within the last 90 days) that they be vaccinated at a later time. Data on natural immunity have shown it to persist at least 90 days after infection. It bears mentioning that the CDCs do not recommend serology or infection screening prior to vaccination[37].
5. *What types of decision-making are suitable for persons incapable of providing informed consent?* For the time being, no special measures have been taken with regard to this population. However, the French minister delegate responsible for personal autonomy has reaffirmed her attachment to free and informed consent concerning COVID-19 vaccination. The legal guardian and the designated support person are likely to be of key importance.
6. *Do COVID-19 vaccines entail long-term adverse effects?* The rapid development of vaccines in a health emergency context provides little if any opportunity for perspective. Monitoring subsequent to market authorization will be imperatively necessary. That said, and as is the case with other vaccines, adverse effects usually occur in the short term.
7. *Who will perform the vaccination?* The general practitioner is the person who seems most apt to vaccinate his or her patients. However, multi-dose packaging and special conditions for storage seem ill-suited for use by GPs and dispensing pharmacists/chemists. As for mass vaccination at dedicated sites, it could prove detrimental to acceptability.
8. *Given the allergy cases reported in the United Kingdom, do any special recommendations exist?* In the United States, it is only as regards persons with a previous and known allergy to one of the vaccine components that the COVID-19 vaccination is contraindicated. In patients with severe allergy history, it is recommended to extend post-vaccinal monitoring from 15 to 30 minutes.

Sidebar 3. Pending questions regarding COVID-19 vaccines

men over 30 years of age[30]. Motivating factors for being vaccinated against COVID-19 have been identified as: strong perception of the potential severity of the infection, and high risk of being infected[30]. The wish to recover a normal life (without restrictive measures) has likewise appeared as a reason for acceptance of vaccination against COVID-19[32].

In a past epidemic situation involving emergence (the 2009 H1N1 flu), the attitudes (vaccine advocacy or hesitancy) of professionals, particularly general practitioners, were of genuine importance in individual decision-making[36]. In today's context of a vaccine developed at "pandemic" speed, it seems legitimate, if only as a basis for discussion with health care users, for caregivers to require reliable, up-to-date information on the safety and effectiveness of a given vaccine. Tools specifically designed for use in -19 vaccination decision-making should be rolled out, a key example being the VAC-SI information system, which will facilitate identification of patients for whom vaccination is recommended, ensure tracing of prevaccinal consultation and subsequent vaccinations, and report adverse effects. At this stage, however, several issues remain pending, and some of them may render the decision-making process conflictual (sidebar 3).

CONCLUSION

Informing patients on the benefit-risk ratio of COVID-19 vaccinations corresponds to both the evidence-based medicine (EBM) model for therapeutic decision and, more generally, to the shared decision-making model[38]. The two models are closely correlated with the 4 core principles of medical ethics, particularly the non-maleficence (*primum non nocere*) ensured by vaccine safety, and the beneficence associated with vaccine effectiveness. Clinically relevant and applicable scientific data are delivered to a patient who consults his or her physician in the form of suitable information enabling the person to make an enlightened choice in accordance with the principle of respect for autonomy. Last but not least, the COVID-19 strategy put into place by the French health authority (HAS) highlights observance of the equity principle.

Summary
The public has many questions about vaccines against COVID-19. Informing general practitioners and other vaccinators provides health care users with clear and reliable information to support a shared decision. These professionals are the defence against vaccine hesitation in the population, but they can be contaminated by doubt if they do not have solid arguments to answer the questions of health care users.

Keywords: SARS-CoV-2; COVID-19; vaccination.

References

1. World Health Organizationorganization. Director-General's opening remarks at the media briefing on COVID-19 - 11 March 2020. Geneva : WHO, 2020. Disponible sur : https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid- 19---11-march-2020 [consulté le 29 novembre 2020].

2. Johns Hopkins University Medecine. COVID-19 Map. Baltimore : JHUM, 2020. Disponible sur : https://coronavirus.jhu.edu/map.html [consulté le 10 décembre 2020].

3. Santé publique France. Coronavirus : chiffres clés et évolution de la COVID-19 en France et dans le Monde. Saint-Denis : Santé publique France, 2020. Disponible sur : https://www.sante-publiquefrance.fr/dossiers/coronavirus-covid-19/ coronavirus-chiffres-cles-et-evolution-de-la-covid- 19-en-france-et-dans-le-monde [consulté le 4 décembre 2020].

4. Li Y, Campbell H, Kulkarni D, et al. The temporal association of introducing and lifting non-pharmaceutical interventions with the time-varying reproduction number (R) of SARS-CoV-2: a modelling study across 131 countries. Lancet Infect Dis 2020. Disponible sur : https://doi.org/10.1016/ S1473-3099(20)30785-4.

5. Institut national de la statistique et des études économiques. Un recul de l'activité économique de 25 % pendant le confinement. Paris : Insee, 2020. Disponible sur : https://www.insee.fr/ fr/statistiques/4622442 [consulté le 4 décembre 2020].

6. Wang B, Lai J, Yan X, et al. COVID-19 clinical trials registered worldwide for drug intervention: an overview and characteristic analysis. Drug Des Devel Ther 2020;14:5097-108.

7. Allen A. Vaccine: the controversial story of medicine's greatest lifesaver. 1st ed. New York : W.W. Norton & Company, 2007.

8. World Health Organization. Ten threats to global health in 2019. Geneva : WHO, 2019. Disponible sur : https://www.who.int/news-room/feature-stories/ten-threats-to-global-health-in-2019 [consulté le 10 décembre 2020].

9. Larson HJ, de Figueiredo A, Xiahong Z, et al. The state of vaccine confidence 2016: global insights through a 67-country survey. EBioMedicine 2016;12:295-301.

10. Peretti-Watel P, Seror V, Cortaredona S, et al. future vaccination campaign against COVID-19 at risk of vaccine hesitancy and politicisation. Lancet Infect Dis 2020;20:769-70.

11. Folegatti PM, Ewer KJ, Aley PK, et al. Safety and immunogenicity of the ChAdOx1 nCoV-19 vaccine against SARS-CoV-2: a preliminary report of a phase 1/2, single-blind, randomised controlled trial. Lancet 2020;396:467-78.

12. Jackson LA, Anderson EJ, Rouphael NG, et al. An mRNA Vaccine against SARS-CoV-2 - Preliminary Report. N Engl J Med 2020;383:1920-31.

13. Food and Drug and Administration. Vaccines and related biological products advisory committee meeting december 10, 2020. White Oak: FDA, 2020. Disponible sur : https://www.fda.gov/media/144245/download [Consulté le 10 décembre 2020].

14. DPhil MV, Costa Clemens SA, Madhi S, et al. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. Lancet 2020; 397 (10269):99-111.

15. Institut national de la santé et de la recherche médicale. COVIREIVAC-Devenez volontaire pour tester les vaccins COVID. Paris : Inserm, 2020. Disponible sur : https://www.covireivac.fr/vos-contacts/ le-comite-scientifique-sur-les-vaccins-covid-19/ [consulté le 11 décembre 2020].

16. Haute Autorité de santé. Vaccins Covid-19 : quelle stratégie de priorisation à l'initiation de la campagne ? Saint-Denis : HAS, 2020. Disponible sur : https://www.has-sante.fr/jcms/p_3221237/fr/ vaccins-covid-19-quelle-strategie-de-priorisation-a-l-initiation-de-la-campagne [consulté le 4 décembre 2020].

17. Le groupe BVA. BreakingWeb. La crise du covid-19 : quel impact sur la sante des français ? Paris : BVA, 2020. Disponible sur : https://www. bva-group.com/ sondages/crise-covid-19-impact-sante-francais/ [consulté le 10 décembre 2020].

18. Danchin M, Biezen R, Manski-Nankervis JA, Kaufman J, Leask J. Preparing the public for COVID-19 vaccines: how can general practitioners build vaccine confidence and optimise uptake for themselves and their patients? Aust J Gen Pract 2020;49(10):625-29.

19. Vallot S, Yana J, Moscova L, et al. La décision médicale partagée : quelle efficacité sur les résultats de santé ? exercer 2018;149:25-39.

20. Sharma O, Sultan AA, Ding H, Triggle CR. A review of the progress and challenges of developing a vaccine for COVID-19. Front Immunol 2020;11:585354.

21. World Health organization. Draft landscape of COVID-19 candidate vaccines. Geneva: WHO, 2020. Disponible sur : https://www.who.int/who-documents-detail/draft-landscape-of-covid-19-candidate-vaccines [consulté le 10 décembre 2020].

22. GOV.UK. UK authorises Pfizer/ BioNTech COVID-19 vaccine. Disponible sur : https://www.gov.uk/ government/ news/uk-authorises-pfizer-biontech-covid-19-vaccine [consulté le 10 décembre 2020].

23. Oves M, Ravindran M, Rauf MA, et al. Comparing and contrasting MERS, SARS-CoV, and SARS-CoV-2: prevention, transmission, management, and vaccine development. Pathog Basel Switz 2020 26;9 (12).

24. Pardi N, Hogan MJ, Porter FW, Weissman D. mRNA vaccines - a new era in vaccinology. Nat Rev Drug Discov 2018;17:261-79.

25. Polack FP, Thomas SJ, Kitchin N, et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. N Engl J Med 2020;383(27):2603-15.

26. Food and Drug and Administration. Vaccines and related biological products advisory committee meeting december 17, 2020. White Oak : FDA, 2020. Disponible sur : https://www.fda.gov/ advisory-committees/advisory-committee-calendar/vaccines-and-related-biological-products-advisory-committee-december-17-2020-meeting-announcement [consulté le 17 décembre 2020].

27. Anderson EJ, Rouphael NG, Widge AT, et al. Safety and ilmmunogenicity of SARS-CoV-2 mRNA- 1273 Vaccine in Older Adults. N Engl J Med 2020; 383(25):2427-38.

28. Widge AT, Rouphael NG, Jackson LA, et al. Durability of responses after SARS-CoV-2 mRNA-1273 vaccination. N Engl J Med 2020;NEJMc2032195.

29. Omer SB, Yildirim I, Forman HP. Herd immunity and implications for SARS-CoV-2 control. JAMA 2020;324:2095-6.

30. Detoc M, Bruel S, Frappe P, Tardy B, Botelho-Nevers E, Gagneux-Brunon A. Intention to participate in a COVID-19 vaccine clinical trial and to get vaccinated against COVID-19 in France during the pandemic. Vaccine 2020;38:7002-6.

31. Lazarus JV, Ratzan SC, Palayew A, et al. A global survey of potential acceptance of a COVID-19 vaccine. Nat Med 2020;1-4.

32. ELABE. Covid-19 : seuls 4 Français sur 10 envisagent de se faire vacciner. Levallois-Perret : ELABE, 2020. Disponible sur : https://elabe.fr/ vaccin-covid-19/ [consulté le 10 décembre 2020].

33. IFOP. Les Français et le COVID-19 : confiance dans le gouvernement et intention de se faire vacciner. Paris : IFOP, 2020. Disponible sur : https://www.ifop.com/publication/les-francais-et-le-covid-19-confiance-dans-le-gouvernement-et-intention-de-se-faire-vacciner/ [consulté le 10 décembre 2020].

34. Gagneux-Brunon A, Detoc M, Bruel S, et al. Intention to get vaccinations against COVID-19 in French healthcare workers during the first pandemic wave: a cross sectional survey. J Hosp Infect 2020;S0195-6701(20):30544-2.

35. Malik AA, McFadden SM, Elharake J, Omer SB. Determinants of COVID-19 vaccine acceptance in the US. EClinicalMedicine 2020;26:100495.

36. Ketterer F, Goffin Y, Boyer P, et al. Critères de décision du patient concernant la vaccination contre la grippe AH1N1, en Belgique et en France. Presse Med 2013;42:e63-8.

37. Centers for Disease Control and Prevention. ACIP Presentation slides: December 11 and 12, 2020 Meeting. Atlanta : CDC, 2020. Disponible sur : https://www.cdc.gov/vaccines/acip/meetings/ slides-2020-12-11.html [consulté le 17 décembre 2020].

38. Boussageon R. Le raisonnement thérapeutique dans la démarche EBM. exercer 2020;167: 406-16.