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Recommendation of HPV vaccination to boys in Francean unhappy coincidence with the WHO call to pause the implementation of this vaccination in boys

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► To cite this version:

Fadia Dib, François Vie Le Sage, Robert Cohen, Odile Launay. Recommendation of HPV vaccination to boys in Francean unhappy coincidence with the WHO call to pause the implementation of this vaccination in boys. *Vaccine*, 2020, 38 (23), pp.3919-3921. 10.1016/j.vaccine.2020.04.017 . hal-03126962

HAL Id: hal-03126962

<https://hal.sorbonne-universite.fr/hal-03126962v1>

Submitted on 1 Feb 2021

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1 **TITLE PAGE**

2 **Recommendation of HPV vaccination to boys in France -**
3 **an unhappy coincidence with the WHO call to pause the**
4 **implementation of this vaccination in boys**

5

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26 **Short title:** Extension of HPV vaccination to boys in France

27 **Keywords:** HPV vaccine, boys, recommendations, World Health Organization, vaccine
28 hesitancy, misinformation

29 Word count text=1465 words

30 References=12

31 **MANUSCRIPT**

32

33 While France was one of the first three countries in the world to introduce Human
34 Papillomavirus (HPV) vaccination for girls in 2006 (1), it has been lagging behind when it
35 comes to the introduction of HPV vaccine for boys from the general population. Indeed,
36 several countries have expanded HPV vaccination to boys (2). A number of arguments
37 could justify gender-neutral HPV vaccination, and in 2016, a push from patients'
38 associations in particular led to the French recommendation of HPV vaccination in men
39 who have sex with men, as they have an increased risk of exposure to and infection with
40 HPV.

41

42 On December 16th 2019, the French National Authority for Health (HAS) finally issued a
43 recommendation for all boys aged 11 to 14 years to receive HPV vaccine, with possible
44 catch-up until the age of 19 years (3) . It has been a long road to reach this milestone. A
45 citizen consultation on vaccination held in 2016 in France pushed among other things for
46 adoption of universal HPV vaccination of boys and girls. At the beginning of 2019, the
47 French Minister of Health declared that she was personally in favour of extending HPV
48 vaccination to boys and that she had referred the matter to the HAS the previous year. In
49 March 2019, a press release was put out by a collective of Academies, Colleges, Societies
50 and Medical Unions, leading medical personalities and patients' associations calling for
51 action to synergistically expand HPV vaccination to boys and strengthen cervical cancer
52 screening (4). In October 2019, the HAS issued a favourable opinion on the widespread
53 vaccination of boys and called for accompanying measures such as strengthening the

54 recommendation of HPV vaccination by healthcare professionals and facilitating access to
55 HPV vaccination through full reimbursement by the national health insurance system. This
56 opinion was accompanied by an online public consultation of a draft recommendation for
57 the vaccination of boys at the ages mentioned above. Multiple considerations were taken
58 into account in the HAS recommendation, including the burden of HPV-related diseases in
59 men, the favourable opinion of the general practitioners who felt that vaccinating boys
60 would help increase the uptake of vaccination in girls -which remains low in France (23.7%
61 for two-dose HPV vaccination among 16-year-olds, in 2018)- and ethical considerations
62 (according to the principle of equity in preventing diseases in both sexes). While this
63 recommendation represents a major step forward to promote gender-neutral HPV
64 vaccination in France, future challenges are foreseen. Now is the time to prepare to meet
65 these challenges, if the implementation of this recommendation is to be successful.

66
67 First, we need to be ready to correct misinformation (5) and strive to do this in a timely
68 manner. Anti-vaccination movements started even before the HAS recommendation was
69 issued. The benefit of vaccinating boys was put into question shortly (6) after the World
70 Health Organization (WHO) Strategic Advisory Group (SAGE) on immunization stated that
71 “All countries should temporarily pause implementation of boy, older age group (>15
72 years) and multi-age cohort (MAC) HPV vaccination strategies until vaccine supply allows
73 equitable access to HPV vaccine by all countries. This will significantly relieve supply
74 constraints in the short term and enable allocation of doses to high-burden countries that
75 are currently planning to introduce or sustain HPV vaccination” (7). The WHO call, which
76 was made on the grounds of equity and solidarity in the face of global HPV vaccine

77 shortages, soon became an instrument to feed the anti-vax movement with claims that “If
78 this vaccination is really useful for boys, as some have repeatedly said, how can we explain
79 this WHO appeal which could appear to discriminate against boys?”. This unfortunate use of
80 the WHO call must be addressed at the national and global levels and future
81 instrumentalization must be prevented. Equally disturbing are the claims stated in an
82 online petition that “We must protect our little girls but also soon our little boys from these
83 mass vaccination campaigns with Gardasil [...] If even the government closes its eyes and
84 blindly supports Gardasil, what can we do?”. Historically, based on cost-effectiveness
85 considerations, selective vaccination programs for girls have first been implemented. This
86 selectivity possibly conveyed the message that HPV vaccine was not effective or
87 unimportant in boys. From an ethical point of view, it leaves us torn regarding the sex to
88 prioritize over the other.

89
90 Second, notwithstanding the reassuring safety data accumulated over the years and across
91 countries, safety issues of HPV vaccination have been raised repeatedly in France and other
92 parts of the world, fuelling anti-vax movements. People’s concerns regarding HPV vaccine
93 safety issues must be heard and addressed. Confidence towards HPV vaccination must be
94 restored. After all, let us not forget that in France “one in three people disagree that
95 vaccines are safe” (8).

96
97 Third, we need to take into account the particular context of HPV vaccination of adolescent
98 girls in France. The reasons for the low uptake of HPV vaccine in French girls remain
99 unclear, are probably multifactorial and the subject of current research. However, vaccine

100 hesitancy, which is recognized by the WHO as one of the 10 threats to global health (9), is
101 certainly one of the contributing factors. In France, growing vaccine hesitancy combined
102 with low uptake of certain vaccines have led the Ministry of Health to recommend extension
103 of mandatory vaccination for children as of January 1, 2018 from three to eleven
104 vaccinations (10). There is no apparent reason to expect that HPV vaccine hesitancy would
105 be limited to the case of girls. Lessons can be learned from the detailed examination of the
106 failed attempts to increase HPV vaccine uptake in girls in France. It is now widely
107 recognized that school-based vaccination programs have been successful in achieving high
108 HPV vaccine uptake (11) and should be (re)considered when expanding HPV vaccination to
109 boys. However, it appears a daunting task in France where a school-based vaccination
110 program against hepatitis B was discontinued as a result of the controversy over the alleged
111 causal link between hepatitis B vaccination and the development of multiple sclerosis, in
112 the 1990s (12). A lack of dedicated human resources within French school health services
113 may be an additional barrier for the successful deployment of a school-based HPV
114 vaccination program in France. Alternatively, in some countries such as Spain and Portugal,
115 high levels of HPV vaccination coverage are reached without school programs. Otherwise,
116 interventions on text messaging (reminder/recall) to parents have been tested and shown
117 promising results. Such an approach represents a scalable and sustainable strategy that
118 warrants wider consideration in France.

119

120 Finally, there needs to be a well-developed mass communication strategy in place to
121 support the introduction of HPV vaccine in boys. Such campaigns would represent a golden
122 opportunity to address low HPV vaccine uptake in girls, perhaps by repositioning it as an

123 effective tool to prevent the infection by the most common sexually transmitted infection
124 which unfortunately can cause genital and extra-genital cancers in both sexes. Education
125 and communication campaigns should explain the sexual transmission nature of HPV and
126 promote the equal responsibility that boys and girls should share in the prevention of these
127 diseases, including through vaccination. They should convey the message that due to the
128 mode of HPV transmission, boys owe it to the girls they sexually interact with to be
129 vaccinated, particularly in areas where the rate of unvaccinated girls is high.

130

131 The long-awaited recommendation statement for universal HPV vaccination has been
132 received with enthusiasm by a large part of the French medical community. However, we
133 need to acknowledge the challenges ahead of us in implementing this recommendation so
134 as to overcome them. In particular, the issue of HPV vaccine shortages leading to the WHO
135 recommendation to prioritize girls versus boys, which fuelled anti-vaccination movements,
136 should not hinder progress towards achieving universal HPV vaccination in France. The
137 temporary WHO recommendation to pause vaccination programs in boys in all countries
138 could be legitimately justified by equity and solidarity considerations, but careful
139 application on a case-by-case basis according to the specific context of the countries seems
140 also warranted. As often is the case, one size does not fit all. In France, strictly following
141 these recommendations risks conveying false messages that HPV vaccine is not beneficial
142 for boys and by extension for girls, further impacting their low vaccination uptake.
143 International stakeholders should constructively engage in dialogue with vaccine
144 manufacturers in order to address and minimise the impact of this HPV vaccine supply
145 shortage on both girl and boy vaccination. In the future, a possible solution to both global

146 shortages and perhaps low coverage would be to reduce the number of doses required. The
147 results of studies looking at the effectiveness of single-dose schemes are eagerly awaited. If
148 efficacious, the single-dose vaccination might represent a more affordable and sustainable
149 strategy for better and equitable coverage to prevent diseases in both women and men in
150 all settings.

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186

187 **Author's contributions**

188 FD and OL have participated in the redaction of the manuscript and the revision process. FV
189 and RC have participated in the revision process. All authors have approved the final
190 manuscript.

191 **Acknowledgment**

192 A sincere thank you to Pr Philippe Mayaud for his diligent editing and reviewing of this
193 manuscript for English language.

194

195 **Funding**

196 The authors received no specific funding for this work.

197 **Conflict of interest**

198 FD declares that MSD has covered registration fees, transport and accommodation costs for
199 attendance to a conference and a research grant (Merck Investigator Studies Program HPV
200 Grant 2018). FV and RC have participated to scientific board for GSK and MSD and were

201 investigators for GSK and MSD studies. OL served as principal investigator for vaccine
202 clinical trials (MSD, GSK bio, Sanofi Pasteur, Janssen, Pfizer) and participated to advisory
203 boards (Sanofi Pasteur, MSD, GSK bio, Janssen, Pfizer).