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Comprendre les déterminants de l'hésitation à l'égard du vaccin contre les papillomavirus humains en France

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Fadia Dib. Comprendre les déterminants de l'hésitation à l'égard du vaccin contre les papillomavirus humains en France. Vaccinologie. Sorbonne Université, 2022. Français. NNT : 2022SORUS317 . tel-03966959

HAL Id: tel-03966959

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**THESE DE DOCTORAT DE
SORBONNE UNIVERSITE**

Spécialité
Epidémiologie

ECOLE DOCTORALE PIERRE LOUIS DE SANTE PUBLIQUE A PARIS : EPIDEMIOLOGIE ET
SCIENCES DE L'INFORMATION BIOMEDICALE

Présentée par

Mme Fadia DIB

Pour obtenir le grade de

DOCTEUR de SORBONNE UNIVERSITE

**Comprendre les déterminants de l'hésitation à l'égard
du vaccin contre les papillomavirus humains en France**

Soutenue le 16/09/2022 devant le jury composé de :

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Cette thèse a été réalisée au sein de l'Équipe de Recherche en Épidémiologie Sociale (ERES) de l'Institut Pierre Louis d'Épidémiologie et de Santé Publique (IPLESP, Inserm-Sorbonne Université) et au CIC 1417 Cochin-Pasteur de Vaccinologie.

Cette thèse est dédiée à mes parents.

Remerciements

Merci à la vie, pour cette opportunité inouïe, ce merveilleux cadeau. C'est une magnifique chance que de pouvoir réaliser un travail qui me tenait tant à cœur, et par-delà apporter ma contribution à la science et je l'espère, à l'aide à la décision, sur un sujet qui demeure un enjeu de santé publique dans notre pays.

Merci à mes directeurs de thèse, je suis sincèrement honorée d'avoir bénéficié de votre encadrement. Vous m'avez tous deux accueillie à bras ouverts alors que vous ne me connaissiez pas, soutenue et aidée à améliorer mon projet, me permettant d'obtenir les financements de cette recherche dans des délais restreints. Merci pour cette collaboration riche d'enseignements scientifiques et humains, merci pour votre encadrement bienveillant et la qualité de nos discussions. Merci pour l'aide que j'ai pu obtenir à travers les équipes. Sans votre rencontre, cette enquête téléphonique, cette thèse n'auraient tout simplement pas été possibles. Merci Odile d'être celle que tu es, ta réussite à haut niveau dans le domaine de la vaccinologie est une inspiration pour les femmes médecins, un modèle o combien précieux. Merci Pierre d'avoir été présent jusqu'au point final de cette thèse, malgré l'interruption de tes activités. Ta gentillesse n'a d'égal que ton dévouement pour l'épidémiologie sociale.

Merci à l'Institut National du Cancer pour la subvention doctorale et à MSD Vaccins pour le financement de l'enquête téléphonique. Merci au Dr Laurent Abramowitz, au Pr Florence Tubach et au Pr Jean -Damien Ricard d'avoir soutenu ma démarche.

Merci à GSK pour le partage des données de Vaccinoscopie® analysé dans l'article II.

Merci à Ipsos d'avoir réalisé l'enquête téléphonique dans des délais record.

Merci à toi Philippe d'être le mentor que tu es. Je n'oublierai jamais mon stage d'internat à tes côtés à la *London School* il y a maintenant dix ans de cela, sur la prévention du cancer du col utérin. Depuis, l'idée de poursuivre une thèse sur le sujet m'a poursuivie. Merci d'avoir écrit cette histoire avec moi, en m'inspirant, me faisant aimer la recherche, m'aidant à rédiger mon projet de recherche jusqu'à sa valorisation.

Merci à mes parents, vous m'avez transmis la détermination et la soif de la connaissance. Votre patience sans faille et votre amour inconditionnel me bercent depuis ma première respiration et me font grandir encore et toujours. Merci de m'avoir encouragée à aller vers mes rêves et aspirations. Merci de m'avoir supportée dans mes moments de doutes et échecs. Je suis extraordinairement chanceuse de vous avoir.

Merci à mes frères et sœurs, la benjamine en moi a toujours été inspirée par vos belles réussites. Merci de me permettre d'être aussi fière de vous. J'espère être à la hauteur.

Merci à toi, le messenger, tu te reconnaîtras. Ta lumière a embelli mes sombres jours, m'a appris à travailler et avancer jour après jour vers mes visions et mes rêves dans la gratitude.

Merci à Laurent Butor, Stéphanie Sahuc Depeigne et tout l'équipe « PP4 » à la Direction Générale de la Santé. Le bonheur de travailler à vos côtés, la satisfaction de découvrir grâce à vous un univers auquel j'ai été peu familiarisée jusqu'ici m'ont accompagnée dans la sérénité nécessaire à la finalisation de cette thèse.

Merci aux jolies fées qui ont croisé mon chemin, qui ont donné encore plus de sens à ce travail. C'est pour elles et toutes les femmes que ce travail a été pensé.

Enfin, merci aux défis et obstacles rencontrés sur mon chemin, mais également à ceux qui n'ont pas cru en moi, en ce projet. Cela m'a poussé à redoubler d'efforts.

« J'aimais la pratique clinique, mais en santé publique, vous pouvez avoir un impact sur plus d'une personne à la fois. La société entière est votre patient »

Dr Tom Frieden

Abstract

This thesis consists of three scientific articles related to the factors influencing HPV vaccine coverage. More specifically, it analyses the factors linked to this vaccination among mothers of girls aged 11 to 14 years in metropolitan France, from the perspective of vaccine hesitancy.

The first article reports on the development of an instrument aimed at questioning the factors involved in HPV vaccination uptake using the World Health Organization conceptual model of determinants of vaccine hesitancy. We relied on a review of the scientific literature of validated questionnaires and on a multidisciplinary panel of fifteen experts solicited using the Delphi methodology. This two-round web-based consultation led to the inclusion of 57 questions in the instrument.

The second article presents the results of a telephone survey among a representative sample of 1102 mothers of girls aged 11 to 14 years in metropolitan France, selected by the quota method, following the pilot testing of the instrument of the first article among a representative sample of thirty mothers. The interviews included additional questions and were conducted using the computer-assisted telephone interviewing method. The strongest factor negatively associated with HPV vaccination uptake was the age of the adolescent girl: mother's belief that her daughter was too young to be vaccinated (OR=0.16; CI95% 0.09-0.29), and the younger age of the adolescent girl (OR=0.17; CI95%, 0.10-0.28 for girls aged 11 years compared to those aged 14 years). Two factors were positively associated with HPV vaccination uptake: agreeing with the statement that doctors believe that vaccinating girls against HPV is a good idea and having asked questions to the attending doctor about HPV vaccines (OR=4.99; CI95%, 2.09-11.89, and OR=3.44; CI95%, 2.40-4.92, respectively).

The third paper presents a secondary analysis of the Vaccinoscopie® survey data assessing the role of Internet use as a source of information on vaccination among vaccine-hesitant mothers on their daughters' HPV vaccination uptake. We performed a pooled analysis of data from 2015 to 2018 in mothers of 14- and 15-year-old girls, first through a multivariate logistic regression model, then through structural equation modeling. Logistic regression adjusted for physician recommendation of HPV vaccination, attitudes towards vaccines in general, perceived usefulness of the HPV vaccine, mother's education level, region of residence, and survey year, showed that mothers' use of the internet was significantly associated with a lower HPV vaccination uptake in their daughters (OR= 0.66; CI95%, 0.47-0.91). The structural equation modeling confirmed the negative effect of Internet use, revealing the underlying mechanistic links leading to lower HPV vaccine uptake.

The results of this thesis have implications for public policy on HPV vaccination. They raise questions about the opportunity of lowering the eligibility threshold for HPV vaccination in the general

population from 11 to 9 years. Furthermore, they emphasize the need to strengthen the training and involvement of general practitioners in recommending HPV vaccination.

Future studies based upon random samples are needed to confirm the generalisability of the results and the precision of the confidence intervals obtained in this thesis. In the future, it will be interesting to interview fathers and investigate factors associated with HPV vaccination of boys in the general population who were recently included in the recommendations.

Keywords: HPV vaccination; vaccine hesitancy; factors; Delphi method, Internet.

Résumé

Cette thèse consiste en trois articles scientifiques s'intéressant aux facteurs influençant la couverture vaccinale par le vaccin anti-HPV. Plus spécifiquement, elle analyse les facteurs liés à cette vaccination chez les mères de filles âgées de 11 à 14 ans en France métropolitaine, sous l'angle de l'hésitation vaccinale.

Le premier article restitue l'élaboration d'un instrument visant à interroger les facteurs influençant la couverture vaccinale par le vaccin anti-HPV, selon le modèle conceptuel des déterminants de l'hésitation vaccinale de l'OMS. Nous nous sommes appuyés sur une revue de la littérature scientifique de questionnaires validés, et sur un panel multidisciplinaire d'une quinzaine d'experts sollicités selon la méthodologie de Delphi. Cette consultation réalisée sur Internet en deux tours a permis d'identifier 57 questions.

Le deuxième article présente les résultats d'une enquête téléphonique menée sur un échantillon de représentatif de 1102 mères de filles âgées de 11 à 14 ans sélectionné par la méthode des quotas, faisant suite à une phase pilote testant l'instrument du premier article sur un échantillon représentatif d'une trentaine de mères. Les entretiens comprenaient des questions additionnelles, et avaient été conduits selon la méthode d'entretien téléphonique assisté par ordinateur. Le facteur le plus fortement négativement associé à la vaccination anti-HPV était l'âge de l'adolescente : la croyance de la mère selon laquelle sa fille était trop jeune pour être vaccinée (OR=0,16 ; IC95% 0,09-0,29), et l'âge plus jeune de l'adolescente (OR=0,17 ; IC95%, 0,10-0,28 pour les filles âgées de 11 ans par rapport à celles âgées de 14 ans). Deux facteurs étaient positivement associés à la couverture vaccinale : être en accord avec l'affirmation selon laquelle les médecins croient que vacciner les filles contre les HPV est une bonne idée, et avoir posé des questions au médecin traitant sur les vaccins HPV (OR=4,99 ; IC95%, 2,09-11,89 ; et OR=3,44 ; IC95 %, 2,40-4,92, respectivement).

Le troisième article présente une analyse secondaire des données de l'enquête Vaccinoscopie® visant à évaluer le rôle du recours à Internet comme source d'information sur la vaccination chez les mères hésitantes vis-à-vis d'une vaccination, sur la vaccination anti-HPV de leurs filles. Nous avons réalisé une analyse poolée des données de 2015 à 2018 portant sur les mères de filles âgées de 14 et 15 ans, d'abord à travers un modèle de régression logistique multivarié, puis par des modèles d'équations structurelles. La régression logistique ajustée sur la recommandation de la vaccination anti-HPV par le médecin, les attitudes à l'égard des vaccins en général, la perception de l'utilité du vaccin anti-HPV, le niveau d'éducation de la mère, la région de résidence et l'année de l'enquête montrait que l'utilisation

d'Internet par les mères était significativement associée à une moindre vaccination anti-HPV chez leurs filles (OR= 0,66 ; IC95%, 0,47-0,91). Les modèles d'équations structurelles ont confirmé l'effet négatif de l'utilisation d'Internet, en révélant les liens mécanistiques sous-jacents à la moindre couverture vaccinale du vaccin anti-HPV.

Les résultats de cette thèse ont des implications en matière de politiques publiques de vaccination anti-HPV. Ils interrogent notamment sur l'opportunité d'abaisser le seuil d'éligibilité de la vaccination anti-HPV en population générale de 11 à 9 ans et soulignent, entre autres, la nécessité de renforcer la formation et l'implication des médecins généralistes quant à la recommandation de vacciner contre les HPV.

De futures études réalisées par échantillonnage aléatoire sont nécessaires pour confirmer la généralisabilité des résultats et les précisions autour des intervalles de confiance. A l'avenir, il sera opportun d'interroger les pères et d'étudier les facteurs associés à la vaccination anti-HPV des garçons en population générale, suite à la récente extension de la vaccination chez les garçons.

Mots-clés : vaccination anti-HPV ; hésitation vaccinale ; facteurs ; méthode Delphi ; Internet.

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Liste des publications et communications en congrès en lien avec la thèse

PUBLICATIONS

Dib E, Mayaud P, Launay O, Chauvin P. Design and content validation of a survey questionnaire assessing the determinants of human papillomavirus (HPV) vaccine hesitancy in France: A reactive Delphi study. *Vaccine*. 2020;38(39):6127-40. DOI: 10.1016/j.vaccine.2020.07.027

Dib E, Mayaud P, Longfier L, Chauvin P, Launay O. Effect of Internet use for searching information on vaccination on the uptake of human papillomavirus vaccine in France: A path-analysis approach. *Prev Med*. 2021;149:106615. DOI: 10.1016/j.ypmed.2021.106615

Dib E, Mayaud P, Renaudie C, Launay O, Chauvin P. Determinants of human papillomavirus (HPV) vaccine uptake among girls in France: a population-based telephone survey. *Hum Vaccin Immunother*. 2022; Online ahead of print. DOI: 10.1080/21645515.2022.2083894

COMMUNICATIONS ORALES ET AFFICHEES

World Congress on Public Health (WCPH 2020), conférence virtuelle (12-16 Octobre 2020)

Dib E, Longfier L, Mayaud P, Chauvin P, Launay O, Le Groupe d'étude Vaccinoscopie®. Association between online vaccine-related information-seeking in mothers and HPV vaccine uptake in their daughters. (communication orale)

European Research Organisation on Genital Infection and Neoplasia (EUROGIN 2019), Monaco (3-7 Décembre 2019)

Dib E, Mayaud P, Launay O, Chauvin P et le groupe d'étude FSQD-HPVH. Design and content validation of a survey questionnaire assessing the determinants of HPV vaccine hesitancy in France: a Delphi study Eurogin, Décembre 2019 (communication orale)

International Papillomavirus Conference (IPVC 2020), conférence virtuelle (20-24 Juillet 2020)

Dib E, Mayaud P, Launay O, Chauvin P et le FSQD-HPVH Study Group. Development of a tool to assess the determinants of HPV vaccine hesitancy in France: results of a Delphi study (communication affichée).

European Congress of Clinical Microbiology & Infectious Diseases (ECCMID 2020)

Dib F, Longfrier L, Mayaud P, Chauvin P, Launay O; Le Groupe d'étude Vaccinoscopie®. Factors associated with non-vaccination against Human Papillomavirus (HPV) among girls aged 14-15 years in France: a pooled cross-sectional analysis. (abstract 5203)

AUTRES PUBLICATIONS EN LIEN AVEC LA THEMATIQUE DE LA THESE

Dib F, Le Sage FV, Cohen R, Launay O. Recommendation of HPV vaccination to boys in France - An unhappy coincidence with the WHO call to pause the implementation of this vaccination in boys. *Vaccine*. 2020;38(23): 3919-21. DOI: 10.1016/j.vaccine.2020.04.017

Dib F, Mayaud P, Chauvin P, Launay O. Online mis/disinformation and vaccine hesitancy in the era of COVID-19 : Why we need an eHealth literacy revolution. *Hum Vaccin Immunother*. 2022;18(1): 1-3. DOI: 10.1080/21645515.2021.1874218

Dib F, Launay O. Vaccination contre les infections à papillomavirus : données de pharmacovigilance. *Rev Prat*. 2020;70(1):96-8.

Dib F, Menvielle G, Chauvin P. Tous égaux face aux papillomavirus. L'infection et la vaccination HPV au prisme des inégalités sociales de santé. *Questions de santé publique*. 2019;(38):1-8.

Contribution à *INSERM Le Magazine*. Opinions : « Papillomavirus : faut-il généraliser la vaccination ? », mars 2020, n°46, p. 47.

Liste des abréviations

AAP	<i>American Academy of Pediatrics</i>
ACIP	<i>Adivisory Committee on Immunization Practices</i>
ACS	<i>American Cancer Society</i>
ADN	Acide désoxyribonucléique
CATI	<i>Computer-assisted telephone interview</i>
CIN _{2/3}	<i>Cervical intraepithelial neoplasia grade 2/ 3</i>
CIRC	<i>Centre international de recherche sur le cancer</i>
FCV	<i>Frottis cervicovaginal</i>
GVCI	<i>Global Vaccine Confidence Index</i>
HAS	Haute Autorité de santé
HPV	<i>Human Papillomavirus</i>
HV	Hésitation vaccinale
Inserm	Institut national de la santé et de la recherche médicale
OMS	Organisation mondiale de la santé
PAPM	<i>Precaution Adoption Process Model</i>
PPV	Particules pseudo-virales
SAGE	Strategic Advisory Group of Experts
SEP	Sclérose en plaques
SNDS	Système national des données de santé

CHAPITRE 1 – INTRODUCTION

Contexte général et rationnel scientifique de la thèse

Selon les estimations de modélisation, plus de 80 % des femmes et des hommes contractent une infection par les papillomavirus humains (HPV) avant l'âge de 45 ans (Chesson et al. 2014). Ainsi, l'infection par HPV est une des infections sexuellement transmissibles (IST) les plus répandues au monde. Les HPV sont des virus à acide désoxyribonucléique (ADN) double brin appartenant à la famille des Papillomaviridae. Ils se propagent par contact avec la peau génitale, les muqueuses ou les fluides corporels infectés, et peuvent être transmis lors de rapports sexuels, y compris les relations orales. Les préservatifs ont un impact modeste. Bien que la plupart des infections soient asymptomatiques et disparaissent dans un délai de deux ans, l'infection génitale par HPV peut entraîner des pathologies. Il existe plus de 150 génotypes HPV, classés selon leur risque oncogène (de Villiers 2013). Les génotypes à faible risque oncogène sont responsables de verrues anogénitales et cutanées, tandis que les génotypes à haut risque oncogène (HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68) peuvent engendrer des cancers de l'oropharynx (oral, amygdale et gorge) et des cancers anogénitaux (col utérin, anus, vulve, vagin et pénis (Brianti, De Flammineis, et Mercuri 2017)).

Le cancer du col de l'utérus est le plus fréquent des cancers liés à l'HPV, et le quatrième cancer le plus fréquent chez les femmes dans le monde, avec une incidence estimée à 604 000 nouveaux cas et 342 000 décès en 2020 (Sung et al. 2021). En France, le cancer du col utérin est classé au 12ème rang des cancers chez la femme, représentant le quatrième cancer féminin le plus fréquent chez les femmes âgées 15 à 44 ans (3300 nouveaux cas et 1400 décès en 2020 (Centre International de Recherche sur le Cancer 2021)). Au total on estime à 6326 le nombre de cancers liés à l'HPV en France chaque année, dont plus de 90% attribuables aux génotypes couverts par le vaccin anti-HPV nonavalent (Hartwig et al. 2017).

Les vaccins actuellement approuvés (bivalents, tétravalents et nonavalents) sont efficaces pour prévenir l'infection par HPV et réduire l'incidence des maladies liées à l'HPV. Le dernier vaccin nonavalent, Gardasil9, mis sur le marché en France en 2017, cible sept des génotypes à haut risque détectés dans approximativement 90 % des cancers liés au HPV (16, 18, 31, 33, 45, 52 et 58) et deux génotypes à bas risque (6, 11) (Saraiya et al. 2015; Chatterjee 2014).

La vaccination anti-HPV a été introduite dans le calendrier vaccinal français en 2007 pour la prévention des dysplasies de haut grade du col de l'utérus (CIN2/3 pour *Cervical Intraepithelial Neoplasia* de grade 2/3), des cancers du col de l'utérus, des dysplasies de haut grade de la vulve et des verrues génitales externes (condylomes acuminés). En 2022, la vaccination anti-HPV est recommandée chez les adolescents âgés de 11 à 14 ans révolus (deux doses espacées de 6 à 13 mois), avec rattrapage pour ceux âgés de 15 à 19 révolus (3 doses administrées selon un schéma 0, 2 et 6 mois). Elle est également recommandée chez les hommes ayant des relations sexuelles avec des hommes jusqu'à l'âge de 26 ans (schéma à 3 doses), en prévention des lésions précancéreuses anales, des cancers anaux et des condylomes, et chez les garçons et les filles immunodéprimées aux mêmes âges que dans la population générale, avec un rattrapage jusqu'à l'âge de 19 ans révolus. Chez les enfants des deux sexes, candidats à une transplantation d'organe solide, la vaccination peut être initiée dès l'âge de 9 ans (Ministère des Solidarités et de la Santé 2021).

En France, 65 % du coût du vaccin (115,20 € la dose) est pris en charge par l'Assurance maladie et les 35% restants sont à la charge de l'individu (ou pris en charge par une assurance complémentaire). La vaccination anti-HPV est recommandée en France, mais reste opportuniste puisqu'il n'existe pas de programme de vaccination au collège, ou autrement organisé. Les parents doivent prendre rendez-vous avec un médecin pour obtenir une ordonnance, se procurer le vaccin dans une pharmacie, puis prendre un autre rendez-vous pour son administration. La recommandation concernant les jeunes garçons en population générale est récente en France (Haute Autorité de Santé (HAS) 2019) comparativement à d'autres pays européens (Dib et al. 2020); elle date de 2019

et est postérieure à la conception de ce travail de thèse. C'est la raison pour laquelle ce travail porte exclusivement sur la vaccination chez les adolescentes.

Après avoir atteint un niveau proche de 30 % pour la première dose en 2009-2010, la couverture vaccinale du vaccin anti-HPV a fortement diminué les années suivantes (environ 19 % en 2014). La France est le seul pays européen à enregistrer une telle baisse de couverture vaccinale HPV (Déphine Héquet et Rouzier 2017). Toutefois, la forte diminution observée entre 2011 et 2014 a été suivie par une augmentation après 2015 pour atteindre 35% pour une dose à 15 ans (et 33% pour le schéma complet à 16 ans) en 2020 (Santé Publique France (SpF) 2022) (Fonteneau, Barret, et Levy Bruhl 2019). Malgré cette augmentation, la couverture vaccinale du vaccin anti-HPV en France reste bien au-dessous de l'objectif de couverture de 60 % fixé par le plan cancer 2014-2019 (Institut National du Cancer (INCa) 2015) (Haut Conseil de Santé Publique (HCSP) 2009) et du taux de couverture atteint dans d'autres pays européens (par exemple : 90-94 % au Portugal, 91% en Belgique, et 89 % à Malte) (Bonanni et al. 2020).

Le vaccin anti-HPV a fait l'objet de controverses quant à son association supposée avec des maladies auto-immunes. Pourtant, lors de la pharmacovigilance intensive du vaccin anti-HPV, aucun effet indésirable grave n'a été attribué au vaccin, qui présente donc un excellent profil de sécurité (Grimaldi-Bensouda et al. 2017; Phillips et al. 2018). Malgré cela, la communauté médicale française a débattu des bénéfices et des risques du vaccin anti-HPV ; en mai 2014, une pétition adressée au ministère de la Santé a demandé une enquête parlementaire sur ce vaccin (*Pétition pour la mise en place d'une mission parlementaire concernant le gardasil*, 2014). Des informations erronées ont également circulé sur Internet, selon lesquelles cette vaccination serait responsable d'une augmentation du taux de cancers invasifs du col utérin. Notons qu'une telle déclaration ne repose sur aucune plausibilité biologique. En effet, les vaccins anti-HPV sont composés de particules pseudo-virales (PPV), plus précisément de la L1, la principale protéine structurale du virion. Les PPV ne contiennent pas le génome de l'ADN viral et sont donc non infectieuses et non oncogènes.

Problématique de recherche

Dans une étude réalisée dans plus de 140 pays, la France a été identifiée comme le pays ayant la plus faible confiance en la sécurité des vaccins, avec un tiers de répondants qui considéraient que les vaccins étaient peu sûrs (Wellcome Trust 2019) (Figure 1).

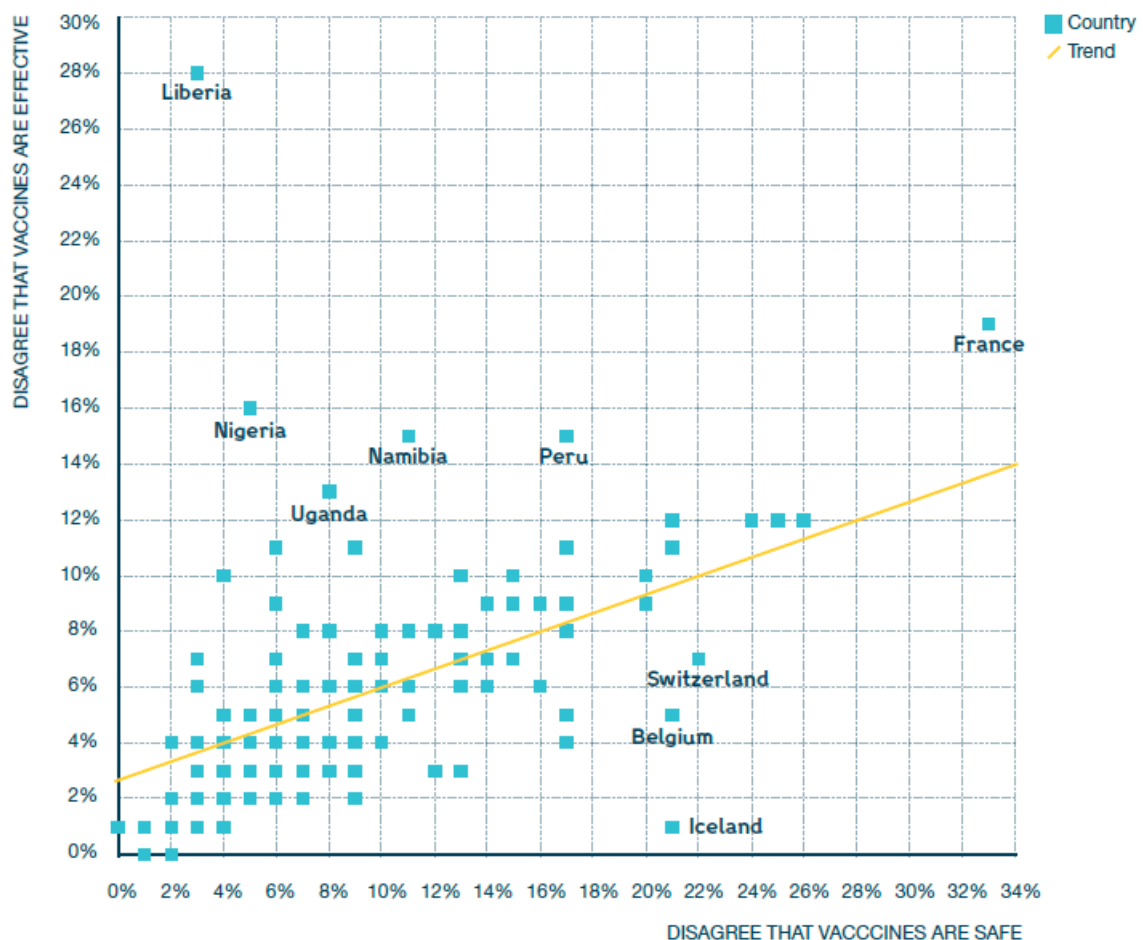


Figure 1. Proportion de personnes n'étant pas d'accord avec l'affirmation selon laquelle les vaccins sont sûrs et l'affirmation selon laquelle les vaccins sont efficaces (source : Wellcome Global Monitor 2018).

Dans ce contexte, la vaccination anti-HPV est l'une des plus controversées. La faible couverture vaccinale du vaccin anti-HPV en France est due, au moins en partie, au phénomène d'hésitation vaccinale (HV). Cependant, rares sont les études qui se sont intéressées au modèle conceptuel de l'HV pour étudier les facteurs associés à cette vaccination en France. Une meilleure compréhension des facteurs influençant la couverture vaccinale du vaccin anti-HPV sous l'angle de l'HV permettra

de développer des interventions reposant sur des données probantes afin de d'améliorer cette couverture vaccinale.

Objectifs de la recherche et organisation de la thèse

L'objectif général de cette thèse était de comprendre les déterminants de la couverture vaccinale du vaccin anti-HPV sous l'angle de l'HV, chez les mères de filles éligibles à cette vaccination. Cette recherche a adapté les outils proposés par l'Organisation mondiale de la santé (OMS) pour identifier les déterminants de la couverture vaccinale du vaccin anti-HPV en France. La recherche a consisté en deux études interconnectées sur données primaires et une analyse secondaire de données :

- L'Étude 1 : était une enquête de Delphi en ligne pour développer un instrument sur les déterminants de la vaccination anti-HPV sous l'angle de l'HV (à partir des outils de l'OMS) (Chapitre 3).
- L'Étude 2 : était une enquête téléphonique transversale, auprès d'un échantillon de 1102 mères de filles âgées de 11 à 14 ans fondée sur l'instrument développé par l'Étude 1 (Chapitre 4).
- L'Étude 3 : consistait en l'analyse secondaire des données de l'enquête Vaccinoscopie® (Denis et al. 2014) afin d'évaluer l'influence du recours à Internet comme source d'information sur la vaccination chez les mères de filles âgées de 14 et 15 ans, hésitantes vis-à-vis de cette vaccination, sur le statut de la vaccination anti-HPV de leurs filles (Chapitre 5).

La population d'étude de l'enquête téléphonique incluait exclusivement les mères de filles âgées de 11-14 ans. Il a en effet été démontré que les mères sont très impliquées dans la décision de leurs enfants en matière de santé, en particulier en ce qui concerne la vaccination anti-HPV. À part les cas rares de familles monoparentales masculines, les mères ont dans l'immense majorité des cas le pouvoir décisionnel principal en ce qui concerne cette vaccination (Allen et al. 2012; Dempsey et al.

2009; Kahn et al. 2009) comme en ce qui concerne l'ensemble de la prévention gynécologique de leurs filles. Seule une meilleure compréhension des déterminants de l'hésitation à l'égard du vaccin anti-HPV dans cette population permettra de développer des interventions sur-mesure reposant sur des données probantes pour augmenter la couverture vaccinale du vaccin anti-HPV chez les filles de moins de 15 ans, et par là même, minimiser le recours au rattrapage vaccinal qui est d'ailleurs plus difficile à promouvoir.

CHAPITRE 2 – REVUE DE LITTÉRATURE

Place de la vaccination anti-HPV dans la prévention primaire du cancer du col utérin

La stratégie mondiale de l'OMS pour accélérer l'élimination du cancer du col de l'utérus, lancée en novembre 2020, définit trois étapes : la vaccination, le dépistage et le traitement. La mise en œuvre réussie de ces trois mesures pourrait réduire de plus de 40 % les nouveaux cas de ce cancer et de 5 millions les décès qui y sont liés d'ici 2050 (Organisation Mondiale de la Santé (OMS) 2020a). On estime que la couverture vaccinale actuellement atteinte, principalement dans les pays à revenu élevé, permettra d'éviter environ un million de cas de cancer du col utérin au cours du demi-siècle prochain ; toutefois, si aucune mesure supplémentaire n'est prise, 44,4 millions de cas devront encore survenir au cours de cette période (Simms et al. 2019).

En juin 2020, 107 pays au total avaient mis en place des programmes nationaux de vaccination anti-HPV dont 33 recommandaient le vaccin chez les filles et les garçons (Bruni et al. 2021). L'Australie est le premier pays à avoir déployé un vaste programme national de vaccination anti-HPV dans les collèges, en 2007 (Brotherton et al. 2011). Initialement, il ciblait les filles âgées de 12 à 13 ans, tandis qu'un programme d'actions communautaire ciblait les femmes jusqu'à l'âge de 26 ans. En 2013, le programme de vaccination scolaire a été étendu aux garçons âgés de 12 à 13 ans avec un rattrapage pour les garçons âgés de 14 à 15 ans. En janvier 2018, le programme est passé à l'utilisation du vaccin nonavalent. Une réduction significative des infections par HPV et de pathologies liées à l'HPV a été observée seulement 3 ans après l'introduction de programme de vaccination anti-HPV en Australie. Six ans après le lancement du programme australien de vaccination, une diminution significative des génotypes ciblés par le vaccin chez les femmes vaccinées, et une prévalence plus faible des génotypes ciblés par le vaccin chez les femmes non vaccinées avaient déjà été observés suggérant une immunité de groupe (Tabrizi et al. 2014). En plus de la diminution des taux de prévalence d'infection par HPV, une diminution des taux d'incidence des CIN2/3, de verrues génitales et de la papillomatose respiratoire récurrente juvénile ont été observés après l'introduction du programme

de vaccination en Australie (Patel et al. 2018). Si la vaccination et le dépistage sont maintenus à un taux élevé, le cancer du col utérin pourra être considéré comme un problème de santé publique éliminé en Australie dans les 20 prochaines années (Hall et al. 2019).

Efficacité de la vaccination anti-HPV

L'efficacité de la vaccination anti-HPV fait consensus dans la littérature scientifique. Une méta-analyse publiée en 2019 portant sur les données de 60 millions d'individus et jusqu'à 8 ans de suivi post-vaccination montre l'impact substantiel des programmes de vaccination anti-HPV sur l'infection HPV, les CIN2/3 chez les filles et les femmes, ainsi que sur les diagnostics de verrues anogénitales chez les filles, les femmes, les garçons et les hommes (Drolet et al. 2019). La méta-analyse de la Cochrane publiée en 2018 a démontré une réduction significative du risque de lésions pré-cancéreuses chez les jeunes femmes qui avaient reçu la vaccination HPV et n'a retrouvé aucune augmentation des effets indésirables par rapport aux contrôles (Arbyn et al. 2018). Cette méta-analyse portait sur 26 essais contrôlés randomisés sur l'efficacité et la sécurité des vaccins bi et quadrivalents, impliquant plus de 70 000 femmes et jeunes filles. Quant aux données sur les taux réels de cancers, elles demeurent rares puisque les premières personnes vaccinées n'atteignent que maintenant un âge où l'on s'attendrait à ce que le cancer du col utérin se manifeste. Toutefois, une étude de cohorte en population générale menée en Suède ayant suivi 1 672 983 filles et femmes âgées de 10 à 30 ans de 2006 à 2017 a démontré que la vaccination quadrivalente était associée à une réduction significative de cancers invasifs du col utérin (Lei et al. 2020). Plus récemment, une étude observationnelle publiée dans le Lancet a démontré une réduction significative des taux de cancers et des CIN3 chez les jeunes femmes après l'introduction du programme de vaccination anti-HPV en Angleterre, en particulier chez les personnes chez qui le vaccin avait été proposé à l'âge de 12-13 ans. Les auteurs de cette étude concluaient que le programme de vaccination anti-HPV a réussi à éliminer presque totalement les cas de cancers du col utérin chez les femmes nées depuis le 1er septembre 1995 (Falcaro et al. 2021).

L'hésitation vaccinale

L'HV a été classé en 2019 parmi les dix principales menaces pour la santé mondiale (Organisation Mondiale de la Santé (OMS) 2019). Elle est définie par l'OMS comme « le retard dans l'acceptation ou le refus des vaccins malgré la disponibilité de services de vaccination. C'est un phénomène complexe, spécifique au contexte et variant selon le moment, le lieu et les vaccins. Il inclut certains facteurs comme la sous-estimation du danger, la commodité et la confiance » (MacDonald 2015). La communauté scientifique s'intéresse de plus en plus à l'HV, avec un doublement des publications scientifiques sur ce sujet au cours de la période 2007-2012 (Larson et al. 2014). En outre, le vaccin anti-HPV se situait au deuxième rang des vaccins étudiés- après le vaccin contre la grippe - dans une analyse bibliométrique de la littérature scientifique mondiale sur l'HV portant sur des articles publiés entre 1990 et 2019 (Sweileh 2020).

Trois catégories de déterminants d'hésitation vaccinale selon le modèle de l'OMS

L'HV et ses impacts négatifs sur les taux d'utilisation des vaccins ont été de plus en plus reconnus par le Groupe stratégique consultatif d'experts (SAGE) sur la vaccination de l'OMS, conduisant à la mise en place en 2012 du groupe de travail du SAGE sur l'HV et la publication d'un recueil d'instruments pour mesurer l'HV et ses déterminants en 2015 (Larson et al. 2015; MacDonald 2015). Les facteurs influençant l'HV sont par essence multiples. Le modèle développé par le groupe SAGE visait à orienter le type de questions explorant les facteurs liés à l'HV. Il a été élaboré à partir d'une revue systématique de la littérature (Larson et al. 2014) et d'entretiens avec les directeurs de programmes de vaccination, proposant une classification des déterminants en trois grands groupes :

- i) Influences contextuelles: elles découlent de facteurs historiques, socio-culturels, environnementaux, liés au système de santé/ institutionnels, économiques ou politiques.

- ii) Influences individuelles et de groupe: elles découlent de la perception personnelle du vaccin ou d'influences liées à l'environnement social et à l'entourage.
- iii) Aspects spécifiques des vaccins/de la vaccination: par exemple le calendrier vaccinal, les coûts ou encore l'attitude des professionnels de santé face au vaccin en question.

Questionnaires portant sur la vaccination anti-HPV

La littérature fait état d'un nombre considérable d'études sur le sujet de l'hésitation à l'égard du vaccin anti-HPV (Sweileh 2020). Les questionnaires administrés dans les études européennes pour interroger les parents d'enfants éligibles à la vaccination anti-HPV étaient spécifiquement développés pour chaque étude, tels ceux utilisés dans les travaux réalisés aux Pays Bas (Gefenaite et al. 2012; Lenselink et al. 2008) et en Suède (Dahlström et al. 2010; Grandahl et al. 2017). Le même constat vaut pour les études publiées outre-Atlantique (Brown, Gabra, et Pellman 2017; Fuchs, Rahman, et Berenson 2016) bien que certaines d'entre elles aient utilisé des instruments validés tels que l'échelle *Carolina HPV Immunization Attitudes and Beliefs Scale* (CHIAS) (Allison et al. 2020; McRee et al. 2010), l'échelle *HPV Attitudes and Beliefs Scale* (HABS) (Perez et al. 2016), ou encore la *Parental HPV Survey* (Thomas, Caldera, et Maurer 2019). Ces instruments, validés ou non, n'incluaient qu'une partie des facteurs listés dans la matrice des déterminants de l'OMS.

Déterminants de l'hésitation à l'égard du vaccin anti-HPV

La prévalence de l'HV est estimée à 48 % (IC95 %; 45,1-51,4) chez les parents français d'adolescentes de 11 à 15 ans ; elle est particulièrement élevée chez ceux qui ont un niveau d'éducation élevé (Rey et al. 2018). Le profil des personnes défavorables aux vaccins anti-HPV et hépatite B est similaire : les personnes à hauts revenus, âgées de 45 à 54 ans et les femmes (Rey et al. 2018). Rappelons la controverse des années 1990 sur le lien supposé entre la vaccination anti-hépatite B et le développement de la sclérose en plaques (SEP) (Nau 2008), lorsque des cas de SEP ont été signalés comme des effets indésirables du vaccin contre l'hépatite B et qu'un programme de vaccination contre l'hépatite B en milieu scolaire a été interrompu en conséquence (Monteyne et André 2000).

En ce qui concerne le vaccin anti-HPV, une étude réalisée en région Rhône Alpes en 2008 chez 210 mères de filles âgées de 14 à 18 ans indiquait que le principal frein à l'acceptation du vaccin était le caractère récent de son introduction et la crainte d'éventuels effets secondaires. Les facteurs associés à l'acceptation du vaccin anti-HPV étaient le fait d'avoir déjà vacciné un enfant contre le pneumocoque (OR=3,28 ; IC95%, 1,32-8,11) et de connaître la population cible de la vaccination anti-HPV (OR=2,12 ; IC95%, 1,15-3,90) (Lutringer-Magnin et al. 2011).

Une revue systématique sur les déterminants de l'hésitation à l'égard du vaccin anti-HPV en Europe (Karafillakis et al. 2019) montre que les préoccupations les plus répandues incluent des informations insuffisantes et inadéquates sur la vaccination anti-HPV et les effets secondaires potentiels du vaccin. Les résultats obtenus dans le cadre d'une autre revue systématique d'études européennes (López et al. 2020) indiquent également que les doutes sur le profil de sécurité du vaccin figurent parmi les freins les plus fréquemment associés à l'hésitation à l'égard de la vaccination anti-HPV. D'autres freins ont été identifiés, tels que la conviction que le vaccin aura un impact sur le comportement sexuel de l'enfant, la faible perception de la susceptibilité à l'infection HPV et les doutes sur l'efficacité du vaccin anti-HPV (López et al. 2020).

Déterminants de la couverture vaccinale du vaccin anti-HPV

Une méta-analyse d'études internationales a montré que la recommandation du médecin avait la plus grande influence sur la vaccination anti-HPV, suivie – pour les freins à la vaccination - par les inquiétudes concernant la sécurité du vaccin, les croyances négatives des parents en matière de vaccins, le montant restant à charge pour les parents concernant la vaccination anti-HPV ainsi que l'absence de consultation de prévention de routine pour les enfants dans les 12 derniers mois (Newman et al. 2018). En outre, une méta-analyse d'études nord-américaines a montré que les minorités ethniques étaient plus susceptibles de recevoir une dose de vaccin anti-HPV mais moins susceptibles de recevoir le schéma complet de vaccination (Spencer, Calo, et Brewer 2019). Les considérations religieuses sont parfois un frein, comme cela a été observé au Canada (Touyz et

Touyz 2013). D'autres freins ont été rapportés dans la littérature internationale : milieu défavorisé, absence de couverture santé, ou encore résidence dans une zone peu urbanisée (Fernández de Casadevante, Gil Cuesta, et Cantarero-Arévalo 2015; Kessels et al. 2012). La réalisation d'un frottis cervico-vaginal (FCV) chez la mère, des antécédents maternels ou familiaux de FCV anormaux, le niveau de connaissances sur le cancer du col utérin/HPV, le niveau de connaissances sur la vaccination anti-HPV ont quant à eux été rapportés dans la littérature comme étant positivement associés à la vaccination anti-HPV (Newman 2018).

En France, une étude rétrospective publiée en 2017, réalisée à partir des données du système national des données de santé (SNDS) a évalué les facteurs influençant la couverture vaccinale du vaccin anti-HPV dans la région d'Ile de France (Héquet et Rouzier 2017). Cette étude retrouvait peu de facteurs socio-économiques influençant la couverture vaccinale dans l'analyse univariée, et aucun des facteurs étudiés n'était indépendamment associé aux taux de vaccination dans l'analyse multivariée. Cependant, les taux de vaccination étaient inversement corrélés à la proportion des immigrés et des étrangers dans la population générale des 8 départements franciliens de la région - avec des couvertures vaccinales plus faibles dans les départements comptant le plus d'immigrés ou d'étrangers, tant dans l'analyse univariée que dans l'analyse multivariée pour les étrangers. Plus récemment, Santé Publique France a mené une étude à partir des données du SNDS sur l'intégralité du territoire français.

Les résultats de cette étude suggèrent des inégalités sociales et territoriales associées à la vaccination anti-HPV, avec une couverture vaccinale inversement associée au niveau de désavantage social de la commune de résidence. Toutefois, cette association était variable selon le département (Blondel et al. 2019).

**PREMIERE PARTIE : DEVELOPPEMENT DE L'INSTRUMENT DE RECUEIL DES
DETERMINANTS DE LA VACCINATION ANTI-HPV**

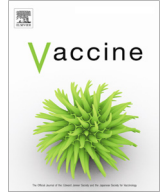
CHAPITRE 3 – ARTICLE I DÉVELOPPEMENT DU QUESTIONNAIRE VISANT À ÉVALUER LES DÉTERMINANTS DE LA COUVERTURE VACCINALE DU VACCIN ANTI-HPV EN FRANCE SOUS L'ANGLE DE L'HÉSITATION VACCINALE

Ce premier travail a été motivé par l'absence, en France, d'instrument visant à évaluer les facteurs associés à la vaccination anti-HPV sous l'angle de l'HV. Au vu de la complexité du phénomène de l'HV et de la multiplicité des facteurs y étant possiblement associés, une méthodologie de type Delphi mobilisant un panel francophone d'experts multidisciplinaire apparaissait nécessaire, afin d'obtenir un consensus sur le type de questions à inclure dans l'instrument.

Nous avons réuni un panel de 15 experts francophones avec des spécialités réunissant la médecine générale, la gynécologie médicale et obstétrique, la maïeutique, les maladies infectieuses et tropicales, la virologie, la santé publique, l'épidémiologie, la sociologie de la santé, la psychologie de la santé, la psychologie sociale, et l'anthropologie (Annexe 1).

Nous avons consulté leurs opinions par voie électronique à travers deux tours de recueil. Le premier tour consistait en l'évaluation d'un questionnaire structuré comprenant trois parties - (i) Influences contextuelles, (ii) Influences individuelles et de groupe, et (iii) Questions spécifiques au vaccin/à la vaccination - conformément au modèle de déterminants de l'HV du groupe SAGE de l'OMS. Les éléments inclus dans ce questionnaire étaient basés sur une revue de la littérature. Seuls les items pour lesquels un accord n'avait pas été atteint au premier tour et les items nouvellement proposés ont été soumis au second tour.

Sur les 83 éléments évalués lors du premier tour, 35 ont fait l'objet de consensus. Au second tour, 66 items ont été soumis au même panel, et un consensus a été atteint pour 22 items. La version finale du questionnaire ainsi obtenu comprenait 57 items (Annexe 2).



Design and content validation of a survey questionnaire assessing the determinants of human papillomavirus (HPV) vaccine hesitancy in France: A reactive Delphi study



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ARTICLE INFO

Article history:

Received 16 December 2019

Received in revised form 9 July 2020

Accepted 13 July 2020

Available online 25 July 2020

Keywords:

Human papillomavirus (HPV)

Vaccine

Vaccine hesitancy

Determinants

Questionnaire

Delphi study

ABSTRACT

Introduction: This study aimed to develop and undertake a preliminary validation of a French Survey Questionnaire for the Determinants of HPV Vaccine Hesitancy (FSQD-HPVH).

Methods: We undertook an electronic-based Delphi consultation among a panel of Francophone experts in two rounds. Round 1 consisted of the assessment of a structured questionnaire comprising of three parts ((i) Contextual influences, (ii) Individual and group influences, and (iii) Vaccine/vaccination-specific issues), in line with the WHO Strategic Advisory Group of Experts (SAGE) Vaccine Hesitancy (VH) Model of Determinants. Items included in this questionnaire were based on a literature review. Definitions of the factors included in the SAGE model were provided in the questionnaire. The panel of experts was asked to score each item using a 3-point Likert scale, in which 1 meant "Essential", 2 "Useful but not essential", and 3 "Not necessary". The panel was also invited to comment on the clarity/comprehension of the questions and suggest reformulations/additional items. Lawshe's Content Validity Ratio (CVR) was computed to assess the level of consensus for each statement. Only items upon which agreement was not reached in Round 1 (CVR < 0.6) and newly proposed items were submitted for evaluation in Round 2, using the same procedure.

Results: Fifteen experts completed the two rounds. Of 83 items evaluated in Round 1, 35 (42%) had a CVR \geq 0.6 and were accepted without modification. In Round 2, 66 items were submitted to the same panel and consensus was reached for 22 (33%) items using the threshold of 0.6. The final FSQD-HPVH version includes 57 items.

Conclusion: This study developed a survey instrument for the evaluation of HPV VH in France with good content validity. It will be used to assess the determinants of HPV VH, the first step towards an evidence-based approach to improving HPV vaccination rates in France.

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1. Introduction

In a global study conducted by the Wellcome Trust in over 140 countries, France was identified as the country with the lowest

confidence in vaccine safety with "one in three people disagree that vaccines are safe" [1]. In this context, vaccination to prevent human papillomavirus (HPV) infection, the most common sexually transmitted infection (STI) worldwide and the etiological agent of a range of conditions including anogenital and oropharyngeal cancers, is one of the most challenging in France.

In 2019, HPV vaccination in France is recommended for all girls aged 11–14 years and for those aged 15–19 years as a catch-up strategy. It is also recommended for girls and boys with immune deficiency conditions at ages 11–19, and for men who have sex with men (MSM) up to the age of 26 [2]. The Ministry of Health is considering widening the target groups to include boys as the same ages of girls. Recently, the French National Authority for

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² The two last authors contributed equally to the work.

Health (HAS) (an independent public scientific advisory body) issued a favourable opinion on the widespread vaccination of boys [3].

HPV vaccination in France relies on individual initiative, requires parental authorization for those under 18 years, and is prescribed and administered by medical doctors. It can also be administered by nurses with a medical prescription. It is costly and only partially (65%) reimbursed by the National Health Insurance Fund, but those covered by a voluntary private health insurance (more than 95% of the French population [4]) or by the Subsidized Supplementary Health Insurance (“Complémentaire santé solidaire”/ CSS, granted for individuals whose income is below a given ceiling) are fully reimbursed.

Twelve years after its introduction, HPV vaccine uptake in France remains low, despite the extensive safety data accumulated for this vaccine both nationally and internationally [5–8]. In 2018, the estimated coverage rate for full (two-dose) HPV vaccination was estimated at 23.7% in girls aged 16 years [9], well below the objective of a 60% coverage for a two-dose vaccination set by the National Cancer Control Plan (NCCP) 2014–2019 [10], and the coverage reached in other European countries, which ranged from less than 40% in Germany [11] to more than 85% in the United Kingdom [12].

Addressing the challenge of improving HPV vaccine coverage has been on the French government's and public health agencies' agenda since 2009. The second NCCP (2009–2013) aimed to improve the uptake of HPV vaccination in 14-year-old girls through the dissemination of appropriate information to the public

on the HPV vaccination while emphasizing that cervical cancer screening using a cervical smear is still essential from the age of 25 onwards [13]. The current (third) NCCP 2014–2019 has aimed to improve the uptake by increasing access to the vaccines in free vaccination centers and by training healthcare professionals [10].

The reasons for the low HPV vaccination coverage in France remain unclear [14–17]. There are conflicting data on the role of socioeconomic status in vaccine uptake. In a large study using the French National Health Insurance Database, the authors concluded that no clear factor was identified as a vaccination determinant; they suggested that complex associations between socioeconomic and cultural factors could explain the low HPV vaccination coverage [15]. A European survey estimated that only 56% of French parents intended to have their eligible daughters vaccinated (versus 67% in the United Kingdom) [18]. Furthermore, Verger and colleagues have found in a national panel of 1 712 general practitioners (GPs) that 28% did not recommend HPV vaccines to young girls [19], raising the issue of the negative influence of GPs in vaccination decision-making.

The phenomenon known as “vaccine hesitancy” may partly explain low HPV vaccine coverage in France. This term refers to a complex, multifaceted phenomenon which occurs within a spectrum, from full and partial, to no vaccination. It is defined by the World Health Organization (WHO) Strategic Advisory Group of Experts (SAGE) vaccine hesitancy working group as “the delay in acceptance or refusal of vaccines despite availability of vaccination services (...) It is influenced by factors such as complacency, convenience and confidence”[20]. The prevalence of vaccine hesitancy

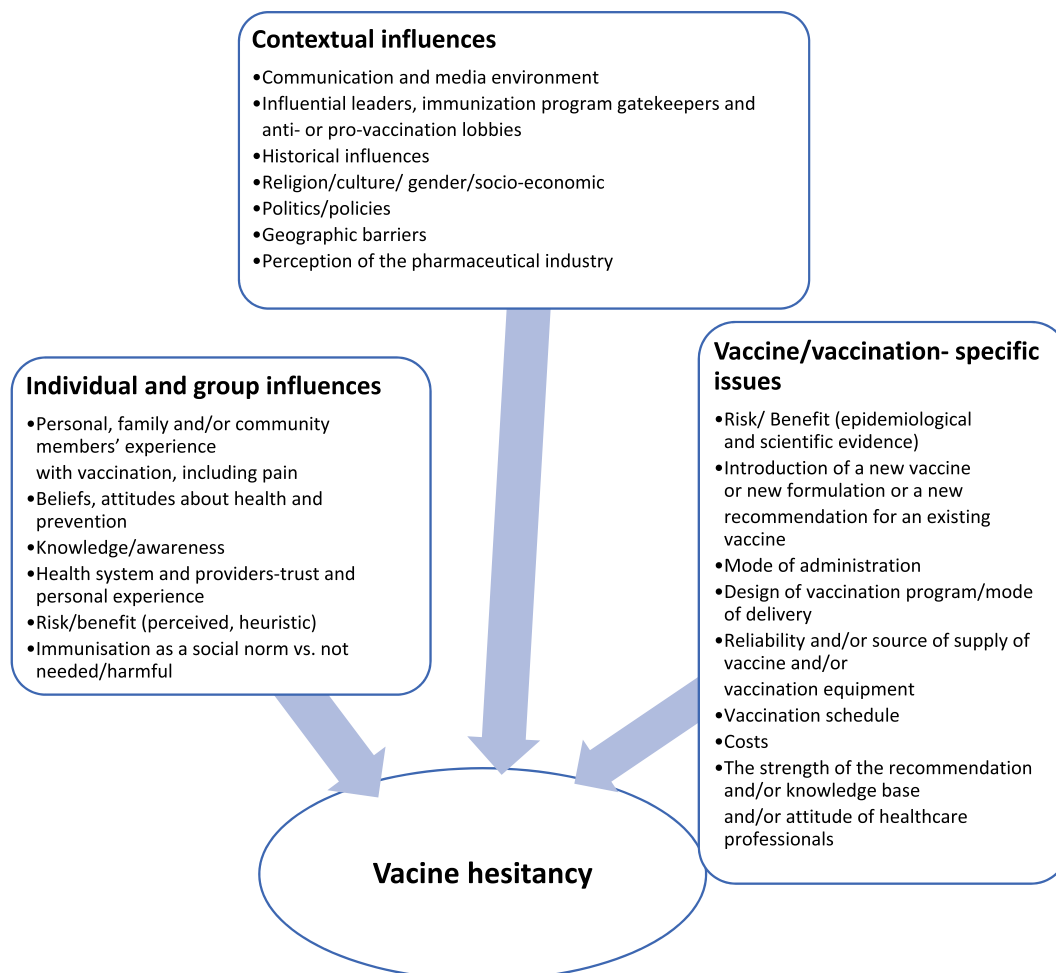


Fig. 1. Conceptual framework of vaccine hesitancy and its determinants (Strategic Advisory Group of Experts model).

is estimated to be 48% (95% confidence interval [CI] 45.1–51.4) among French parents of adolescent girls aged 11–15 years; it is particularly high among those with a higher education level [21].

Hesitancy and its adverse impacts on vaccine uptake rates have been increasingly recognized by the WHO Strategic Advisory Group of Experts (SAGE) on Immunization, leading to the publication in 2015 of a compendium of tools to measure vaccine hesitancy [22]. These tools include a matrix of vaccine hesitancy determinants organized in three main categories of survey questions: (i) contextual influences (e.g., cultural reasons, communication and social media), (ii) individual and group influences (e.g., immunization as a social norm versus not needed/harmful, distrust in the vaccine and lack of perceived benefit of the vaccine), and (iii) vaccine/vaccination-specific issues (e.g., vaccination schedule, costs, and strength of the recommendation and/or attitude of healthcare professionals). This tool is a useful comprehensive approach to help diagnose major determinants of vaccine hesitancy (Fig. 1). However, it was not designed as a survey-ready format for straightforward use in investigational activities, as acknowledged by the Working Group [22]. Besides, the questions displayed in this matrix address vaccines in general, not the HPV vaccine in particular. This matrix was developed following a systematic review of existing research, the findings from an immunization managers' survey of vaccine hesitancy and expert consultation [23].

The problem at the heart of the failed efforts to increase HPV vaccination coverage may lie in the inability in identifying and addressing the actual root causes of vaccine hesitancy and refusal. It is, therefore, crucial to gain a greater understanding of the determinants of HPV vaccine hesitancy in the French context so that targeted interventions can be developed accordingly. There is currently no specific tool to assess the determinants of HPV vaccine hesitancy in France. This study aimed to develop and validate a specific French Survey Questionnaire for the Determinants of HPV Vaccine Hesitancy (FSQD-HPVH) to be later administered to mothers of girls of eligible to HPV vaccination, using the SAGE Working Group Determinants of Vaccine Hesitancy Matrix. Preliminary validation was undertaken through assessment of the items for content validity, i.e., the extent to which they are reflective of the factors considered in the SAGE working group model [24].

2. Materials and Methods

2.1. Study design

A two-round modified electronic Delphi methodology was implemented using an instrument developed in the online Research Electronic Data Capture (REDCap) survey system hosted at the Pierre Louis Institute of Epidemiology and Public Health (IPLESP), Paris Sorbonne University. REDCap is a secure, web-based software platform designed to support data capture for research studies [25]. We used a Delphi approach since it is a universally recognized scientific technique for tapping individual judgments among experts from varying practices to build consensus [26,27]. The Delphi methodology, developed by the Rand Corporation, is a structured approach to group interaction using self-completed questionnaires. Through an iterative process of consultation rounds, the members of the group (the “experts”) can reconsider their responses to the questionnaire after receiving feedback about how their responses compare to those from the rest of the group. The numbers of iterations of experts review and consensus criteria were established before starting the study [28,29]. Each panel member responded to the questionnaire individually and independently, unbiased by the identity and opinions of other panellists.

2.2. Delphi panel selection

The study scientific committee (comprised of FD, PC, and OL) identified potential participants providing a range of expertise and professional representation to ensure a broad knowledge base on the issue of HPV vaccine hesitancy. Experts were selected if they satisfied the following criteria: (1) had been engaged in clinical or research work related to the field of vaccination or HPV for at least 3 years and, (2) were based in France or spoke French. There are no hard rules for the number of Delphi panel participants, however, a panel of 10 to 18 experts is generally recommended [30]. Thus, we decided to invite at least twice the recommended number of panellists, allowing for a minimum 50% participation rate. In May 2019, we e-mailed invitation letters, including the information on the aim of the study and a description of the Delphi study procedures to each potential panel member. Willing participants completed a brief form regarding their demographic and professional data.

2.3. Survey instrument

Following an extensive literature review, the scientific committee drafted a list of items, covering the three main thematic categories ((i) contextual, (ii) individual and group and (iii) vaccine/vaccination specific influences) and sub-categories of the Working Group Determinants of Vaccine Hesitancy Matrix.

All of the matrix sub-categories were covered in our instrument, except “Geographic barrier” (which may be best assessed by objective measures such as indicators of health care supply in the area of residence), “Mode of administration” (which is unlikely to be a sizable concern in teenagers as opposed to babies and very young children), “Risk/benefit of scientific and epidemiologic evidence” and “Influential leaders, gatekeepers and anti-vaccination lobbies” (whose related items could fit another matrix category; for example, an item about past issues regarding another vaccine could also fit the “Historical influences” category – a limit of the matrix which has been described previously [31]). The survey instrument was developed in French. In addition, 19 items were taken from the HPV Attitudes and Beliefs Scale [32] (HABS) and 19 from the HPV General Knowledge and HPV Vaccination Knowledge Scales [33], all of which have been validated in the French-Canadian setting. When drawing from this instrument, we paid particular attention to the need for transcultural adaptation, and so we slightly reworded/reformulated 12 of the French-Canadian items. One item on religion was taken from the Vaccine Confidence Project™ [34]. Five items were taken from the Holistic Complementary and Alternative Medicine Questionnaire (HCAMQ) [35]. As there is no version of the HCAMQ validated in French, translation was performed. An initial translation (English into French) was performed by two French native-speaking authors (FD and PC). Back-translation (French to English) was then independently performed by a third author (PM, non-English native speaker but a fluent-speaking researcher who has been working in the UK for almost three decades). The list of websites information was drawn from the Vaccine Confidence Project™ data [36]. Items that did not reach consensus and have not either attracted specific suggestion for reformulation were recirculated without modification in the wording.

2.4. Round 1

In June 2019, we launched the first round of our modified reactive Delphi consultation by sending the structured questionnaire to the expert panellists. Different from the traditional first stage of Delphi procedure which requests participants to deliver new thoughts on their own, we asked the experts panel to react to

the items that we had pre-generated, hence the “reactive” feature of our Delphi study [37]. The items included the set of response options if the questions required modalities of responses other than a numeric rating scale, i.e., yes/no or true/false/I do not know. Experts were queried as to whether or not each of the items proposed by the scientific committee was essential to assess a specific factor on a 3-point Likert scale, in which 1 point meant “Essential”; 2 “Useful but not essential”, and 3 “Not necessary”. Besides, experts were also invited to comment on items clarity/comprehension and suggest items potentially missing. As per the experts’ comments, the scientific committee reworded original items that did not reach consensus and generated new ones.

2.5. Round 2

Two months later, in August 2019, we e-mailed individualized questionnaires to those experts who had returned Round 1 responses. Only items upon which consensus was not reached in Round 1 were retained for re-assessment in Round 2 [38], thereby allowing experts to focus on the questionable items and consider changing their score (especially for those that have been reformulated) [39] while reducing participant dropouts due to a burdensome questionnaire. For each statement, participants were shown their initial individual evaluation (which could be confirmed or modified) and feedback from the Round 1: frequency distribution of the ratings (thereby showing the general extent of agreement in the experts’ opinions) and a summary of anonymous comments made by the panel on Round 1. Participants were asked to re-rate the items using the same method as in Round 1. The possibility to amend previous scores, taking into consideration the overall picture is a fundamental part to reach consensus. Participants were also asked the rate the newly generated items, in line with the suggestions of Round 1. Participants were asked to return Round 2 responses within four weeks, with the help of e-mail reminders. The survey instrument was finalised by excluding the questions that did not reach consensus in Round 2.

2.6. Data analysis

Lawshe’s Content-Validity Ratio (CVR) was computed after each round to assess the consensus level for each statement. The CVR measures agreement among raters regarding how a particular item is essential to a particular construct. It is a function of the number of participants and their ratings and ranges from –1 to 1. When fewer than half of the participants rate the item as “essential,” the CVR is negative, when half rate the item as “essential” and half do not, the CVR is 0 and when all rate “essential,” the CVR is 1. The formula for computing the CVR is $CVR = (n - N/2)/(N/2)$, where n = the number of participants rating the item as “essential” and N = the total number of participants. Items with CVR values equal to or greater to a certain threshold (determined according to the number of respondents) were considered excellent in agreement evaluation [40]. Traditionally, Lawshe’s method requires experts to provide their ratings just once, and items are immediately discarded if they fail to meet the minimum critical value. In this study, we decided to subject the items that did not reach the minimum critical value to further evaluation (whether as initially formulated or reformulated as per the experts’ comments). This conservative approach ensured no question would be missed out, given the complexity and multifaceted nature of HPV vaccine hesitancy.

Demographic data of the experts’ panel, the percentages of responses to each statement, and the CVR were analysed using SAS (version 9.4, SAS Institute Inc., Cary North Carolina).

2.7. Ethics statement

In France, ethics approval is not required for research that does not involve patients. The written invitations to the experts requesting them to participate in the study incorporated items conveying confidentiality procedures, and the prerogative to erase their data and thus revoke participation at any time. Data privacy and confidentiality of all participants were ensured, although total anonymity could not be achieved due to the need to directly e-mail participants. However, participant identities were known only to the main author, and participants were unaware of the identities of the other panel members.

3. Results

3.1. Panel composition and response rates

Of the 40 potential panel members invited to participate in the study, 18 (45%) responded and sent their demographic data. Of them, 15 (6 health care professionals and 9 non-clinicians academics/researchers) sent back Rounds 1 and 2 questionnaires. Panel members were all based in France, except two, based in Canada and the UK (Table 1). For 15 participants, the minimum critical value of the content validity ratio (CVR) was calculated to be 0.6 (Round 1) at $\alpha = 5\%$.

3.2. Round 1

In Round 1, 83 items were evaluated by the expert panel, and participants gave comments on 66 items (79%). A total of 35 (42%) items reached or exceeded the CVR minimum critical value and were set aside for inclusion in the final questionnaire. The analysis of the CVR of the individual items is shown in Table 2. Items rated “essential” by all the experts pertained to “Knowledge/awareness”, “Communication and media environment”, “Immunisation as a social norm versus not needed/harmful” and “The strength of the recommendation and/or knowledge base and/or attitude of healthcare professionals” factors.

Table 1
Demographic and professional characteristics of the expert panel (n = 15).

	N	%
Gender		
Female	10	(67)
Male	5	(33)
Discipline		
Medical gynaecology	1	(6)
Obstetrics and gynaecology	2	(13)
Midwifery	1	(6)
General medicine	1	(6)
Infectious and tropical diseases	1	(6)
Virology/immunology	1	(6)
Public Health	2	(13)
Epidemiology	1	(6)
Anthropology	1	(6)
Sociology	2	(13)
Health and social psychology	1	(6)
Health psychology	1	(6)
Clinical practice		
Yes	6	(40)
No	9	(60)
Practice site		
Academic	11	(74)
Private practice	3	(20)
Public health agency	1	(6)
Years of experience		
≤10	2	(13)
]10–20]	6	(40)
greater than20	7	(47)

Table 2
Measures of agreement and content validity ratio from Rounds 1 and 2.

Factor	Initial item	Round 1 (n = 15)			Reformulated item	Additional item	Round 2 (n = 15)		
		N	% agreement for "essential"	Content Validity Ratio			n	% agreement for "essential"	Content Validity Ratio
Contextual factors Communication and media environment	I think that there is sufficient communication on vaccination, in general	15	60	0.20	I think there is enough official information campaigns about vaccination in general	-	15	67	0.33
	I think that there is sufficient communication on HPV vaccination in particular	15	73	0.47	I think there is enough official information campaigns about HPV vaccination in particular	-	14 ^a	71	0.43
	How did you hear about the HPV vaccine? Recommendation of the attending physician/ Recommendation of a paediatrician/ Recommendation of a gynaecologist/ Television/Social media/ Written press/Family /Friends/School / Other	14 ^a	100	1*	-	-	-	-	-
	A lot of information and testimonials have been reported, which one (s) have worried you the most? The HPV vaccine can give multiple sclerosis / The HPV vaccine is responsible for the increase in the number of cancers of cervical cancer/ The HPV contains mercury, which is harmful to health/ The HPV vaccine contains aluminium, which is harmful to health/Other/ None	15	71	0.43	<i>Identical item with the addition of the response mode "I have not heard about it » for each proposal</i>	-	14 ^a	71	0.43
Historical influences	Since the H1N1 influenza scandal, I have less confidence in the healthcare system	15	73	0.47	Since the controversy over vaccination against H1N1 flu, I have less confidence in French vaccination recommendations	-	15	87	0.73*
	Since the controversy over the hepatitis B vaccine, I have less confidence in the healthcare system	15	80	0.60*	-	-	-	-	
	The scandal of the Mediator** makes me doubt the integrity of the healthcare system	15	67	0.33	The Mediator's case makes me doubt the integrity of the health system	-	15	67	0.33
Religion/culture/gender/socio-economic	With regard to religion, do you have a regular religious practice/an occasional religious practice/no practice, but the feeling of belonging to a religion/neither practice nor feeling of belonging?	15	60	0.20	-	-	15	53	0.07
	(If practice religious/sense of belonging) Is the HPV vaccine compatible with your religious beliefs? ¶	15	67	0.33	-	-	15	67	0.33
	I think that vaccinating girls against HPV encourages them to have sex	15	93	0.87*	-	-	-	-	-
	The fact that the HPV vaccine protects against a sexually transmitted infection makes me hesitate to vaccinate my daughter	15	53	0.07	I hesitate to get my daughter vaccinated against the papillomavirus because it is a sexually transmitted infection	-	15	67	0.33

Table 2 (continued)

Factor	Initial item	Round 1 (n = 15)			Reformulated item	Additional item	Round 2 (n = 15)			
		N	% agreement for "essential"	Content Validity Ratio			n	% agreement for "essential"	Content Validity Ratio	
Politics/policies	It is hard to talk to my daughter about her sexual health †	15	60	0.20	-	-	15	87	0.73*	
	I am not comfortable discussing my daughter's sexual health with a doctor/health care provider †	15	73	0.47	I feel uncomfortable discussing my daughter's sexual health with a doctor or another health professional	-	15	93	0.87*	
	Sex is not a subject I talk about with my daughter †	15	53	0.07	Sexuality is a subject I approach with difficulty with my daughter	-	15	73	0.57	
	I am not comfortable talking to my daughter about the HPV vaccine †	15	53	0.07	I am uncomfortable talking to my daughter about the HPV vaccine	-	15	73	0.57	
	I do not know how to approach the topic of HPV vaccine with my daughter †	15	73	0.47	I have difficulty in addressing the subject of HPV vaccine with my daughter	-	15	93	0.87*	
	I am favourable to the 11 vaccines mandatory for children born since January 1st, 2018	14 ^a	86	0.71*	-	-	-	-	-	
	-	-	-	-	-	Everyone should be able to choose whether or not to do vaccinate his/her children	15	93	0.87*	
	-	-	-	-	-	Everyone should be able to decide which vaccines are necessary for his/her children	15	67	0.33	
	Perception of the pharmaceutical industry	The pharmaceutical industry is concerned above all by its financial interests	15	60	0.20	The pharmaceutical industry is more concerned about its financial interests than by public health	-	15	67	0.33
		The pharmaceutical industry follows strict manufacturing procedures	15	80	0.60*	-	-	-	-	-
The HPV vaccine is being pushed to make money for pharmaceutical companies †		15	73	0.47	The recommendation of the papillomavirus mainly serves the financial interests of the pharmaceutical industry	-	15	73	0.57	
-		-	-	-	-	The pharmaceutical industry follows rigorous procedures to control the safety of vaccines	15	67	0.33	
-		-	-	-	-	-	-	-	-	
Individual and group factors Personal, family and/or community members' experience	I happened to refuse a vaccine for my daughter (or choose not to get her vaccinated)	15	93	0.87*	-	-	-	-	-	
	I happened to refuse a vaccine for myself (or choose not to get vaccinated)	15	87	0.73*	-	-	-	-	-	
	I know a person who fell seriously ill after getting vaccinated	15	87	0.73*	-	-	-	-	-	
	I know someone who became seriously ill because s/he was not vaccinated	15	87	0.73*	-	-	-	-	-	
	Personally, I have already had abnormal pap smears for which treatment was needed (conization/surgery)	15	93	0.87*	-	-	-	-	-	
	-	-	-	-	-	-	-	-	-	

Table 2 (continued)

Factor	Initial item	Round 1 (n = 15)			Reformulated item	Additional item	Round 2 (n = 15)		
		N	% agreement for "essential"	Content Validity Ratio			n	% agreement for "essential"	Content Validity Ratio
Beliefs, attitudes about health and prevention	Complementary medicine should be subject to more scientific testing before it can be accepted by conventional doctors §	15	47	-0.06	Alternative medicines (i.e. non-conventional medicines, for example phytotherapy, homeopathy, naturopathy...) should be subjected to more scientific studies before they can be accepted by conventional physicians.	-	15	27	-0.46
	Complementary medicine can be dangerous in that it may prevent people getting proper treatment §	15	33	-0.33	Alternative medicines (i.e. non-conventional medicines, for example phytotherapy, homeopathy, naturopathy...) may be dangerous as they can prevent people from obtaining/accessing appropriate treatment	-	14 ^a	28	-0.43
	Complementary medicine should only be used as a last resort when conventional medicine has nothing to offer §	15	67	0.33	Alternative medicines should only be used as a last resort when conventional medicine has nothing to offer	-	14 ^a	43	-0.14
	It is worthwhile trying complementary medicine before going to the doctor §	15	40	-0.20	It is interesting to try alternative medicines (i.e. non-conventional medicines, for example phytotherapy, homeopathy, naturopathy...) before going to the doctor	-	14 ^a	36	-0.29
	Complementary medicine builds up the body's own defenses, so leading to a permanent cure §	15	80	0.60*	-	-	-	-	-
	-	-	-	-	-	Alternative medicines (i.e.non-conventional medicines, for example phytotherapy, homeopathy, naturopathy...) can replace some vaccines	15	73	0.57
	-	-	-	-	-	I prefer that my daughter develops naturally defences against papillomavirus rather than by vaccination	15	80	0.60*
Knowledge/awareness	Have you ever searched for information on the HPV vaccine in the past?	14 ^a	100	1*	-	-	-	-	
	(If already researched information) Cite the 3 most consulted sources of information: Attending physician/ Other health professional/Internet/ Family/ Books/Print media/Other	15	87	0.73*	-	-	-	-	
	(If used the internet) How did you use the internet? I went to forums/I visited blogs/I looked at social media/ I consulted news websites/Other	15	87	0.73*	-	-	-	-	
	(If consulted information sites) Which website? Santé Publique France/ Vaccination info service/	15	73	0.47	(If consulted information sites) Which website? Santé Publique France /Vaccination info service/	-	15	80	0.60*
	-	-	-	-	-	-	-	-	-

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Table 2 (continued)

Factor	Initial item	Round 1 (n = 15)			Reformulated item	Additional item	Round 2 (n = 15)		
		N	% agreement for "essential"	Content Validity Ratio			n	% agreement for "essential"	Content Validity Ratio
	Doctissimo, Allodocteur/Pourquoi docteur/Infovac/ France Info/Le Monde/Le Figaro/Alter Info/ Alternative Health/Initiative citoyenne/Other				Doctissimo, Allodocteur/Pourquoi docteur/Infovac/France Info / Le Monde/Le Figaro/Alter Info/ Alternative Health/Initiative citoyenne/ Mesvaccins.net/INCa/ other				
	(If has already searched for information) After having had all this information, were you able to take a decision regarding the HPV vaccination?	15	87	0.73*	-	-	-	-	-
	HPV can cause HIV/AIDS ††	15	53	0.07	-	-	15	47	-0.06
	The HPV vaccine requires only one dose ††	15	53	0.07	-	-	15	40	-0.20
	The HPV vaccines offer protection against all sexually transmitted infections ††	15	67	0.33	-	-	15	87	0.73*
	The HPV vaccines are most effective if given to people who've never had sex ††	15	73	0.47	-	-	15	87	0.73*
	Someone who has had the HPV vaccine cannot develop cervical cancer ††	15	67	0.33	A person who has been vaccinated against HPV can still develop cervical cancer	-	15	80	0.60*
	The HPV vaccines offer protection against most cervical cancers ††	15	67	0.33	-	-	15	73	0.57
	The HPV vaccines offer protection against genital warts ††	15	87	0.73*					
	Girls who have had the HPV vaccine do not need a Pap test when they are older ††	15	71	0.33	Girls who have been vaccinated against HPV need Pap test when they are older	-	15	87	0.73*
	The HPV vaccine protects (you) from every type of HPV ††	15	53	0.07	-	-	14 ^a	64	0.43
	You can cure HPV by getting the HPV vaccine ††	15	73	0.47	-	-	15	80	0.60*
	HPV is very rare ††	15	80	0.60*	-	-	-	-	-
	HPV always has visible signs or symptoms ††	15	60	0.20	There are always signs or symptoms visible in case of papillomavirus infection	-	15	67	0.33
	Men cannot get HPV ††	15	87	0.73*	-	-	-	-	-
	A person could have HPV for many years without knowing it ††	15	86	0.60*	-	-	-	-	-
	Having sex at an early age increases the risk of getting HPV ††	15	67	0.33	-	-	14 ^a	78	0.57*
	HPV can be transmitted through oral sex ††	15	80	0.60*	-	-	-	-	-
	HPV can cause cancer of the penis ††	15	67	0.33	-	-	15	73	0.57
	HPV infections always lead to health problems ††	14 ^a	43	- 0.14	-	-	15	53	0.07
	HPV can cause oral cancer ††	13 ^b	70	0.36	-	-	15	80	0.60*
	-	-	-	-	-	HPV can cause anal cancer ††	15	60	0.28

Table 2 (continued)

Factor	Initial item	Round 1 (n = 15)			Reformulated item	Additional item	Round 2 (n = 15)		
		N	% agreement for "essential"	Content Validity Ratio			n	% agreement for "essential"	Content Validity Ratio
Health system and providers-trust and personal experience	Please indicate to what extent you trust the following sources to tell the truth about vaccinations: pharmaceutical industry/government/your attending physician/physicians in general/pharmacists/other health professionals/scientific researchers / mainstream media/alternative media (media that convey information alternatives to the commercial mass media and state media, e.g. Agoravox, Atlantic, and Alterinfo)	15	93	0.87*	-	-	-	-	-
	I know someone in my circle who has already been victim of a medical error	15	53	0.07	-	-	15	33	-0.28
	I consider that I have already been victim of a medical error	15	53	0.07	-	-	15	33	-0.28
	Giving my daughter the HPV vaccine would be like performing an experiment on her †	15	27	-0.46	-	-	15	20	-0.57
	The HPV vaccine may lead to long-term health problems †	15	80	0.60*	-	-	14 ^a	50	0
	There has not been enough research done on the HPV vaccine †	15	93	0.87*	-	-	-	-	-
	The HPV vaccine is unsafe †	15	80	0.60*	-	-	-	-	-
	The HPV vaccine has many benefits †	15	53	0.07	-	-	14 ^a	50	0
	The HPV vaccine will protect my daughter's sexual health †	15	74	0.46	Vaccinating my daughter against HPV will help protect her against i sexually transmitted infections	-	15	80	0.60*
	The HPV vaccine is effective in preventing HPV †	15	80	0.60*	-	-	-	-	-
Risk/benefit (perceived, heuristic)	The HPV vaccine is effective in preventing genital warts †	15	80	0.60*	-	-	-	-	-
	The HPV vaccine is effective in preventing HPV-related cancers †	15	71	0.42	-	-	14 ^a	93	0.86*
	-	-	-	-	-	Without the HPV vaccine, my daughter would be at risk of getting HPV later in life †	15	53	0.07
	-	-	-	-	-	Without the HPV vaccine, my daughter would be at risk of getting genital warts later in life †	15	53	0.07
	-	-	-	-	-	Without the HPV vaccine, my daughter would be at risk of getting an HPV related cancer later in life †	15	67	0.33
	-	-	-	-	-	The use of a condom prevents the transmission of HPV infection	15	87	0.73*
	-	-	-	-	-	The pap smear is sufficient to prevent cervical cancer	14 ^a	86	0.85*

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Table 2 (continued)

Factor	Initial item	Round 1 (n = 15)			Reformulated item	Additional item	Round 2 (n = 15)			
		N	% agreement for "essential"	Content Validity Ratio			n	% agreement for "essential"	Content Validity Ratio	
	-	-	-	-	-	HPV can be passed on during sexual intercourse ††	15	67	0.33	
	-	-	-	-	-	Having many sexual partners increases the risk of getting HPV ††	15	67	0.33	
Immunisation as a social norm vs. not needed/harmful	My friends are getting their daughter vaccinated with the HPV vaccine †	14 ^a	93	0.87*	-	-	-	-	-	
	Most 'girls around my daughter 's age are getting vaccinated for HPV †	14 ^a	100	1*	-	-	-	-	-	
	It is expected of me that I should vaccinate my daughter against HPV †	14 ^a	57	0.14	-	-	14 ^a	43	-0.14	
	-	-	-	-	-	-	Most of my friends think vaccinating my daughter against HPV is a good idea †	14 ^a	43	-0.14
	-	-	-	-	-	-	Doctors/health care providers believe vaccinating girls against HPV is a good idea †	15	93	0.87*
	-	-	-	-	-	-	My family thinks it is a good idea to vaccinate my -daughter against HPV †	15	60	0.28
Vaccine/vaccination specific factors										
Introduction of a new vaccine or new formulation or a new recommendation for an existing vaccine	The HPV vaccine is too new †	15	74	0.46	The HPV vaccine is too recent so we can know if it's safe and reliable	-	15	80	0.60*	
	Design of vaccination program/Mode of delivery	15	80	0.60*	-	-	-	-	-	
	It is complicated to vaccinate my daughter against HPV because it requires 3 steps: see the doctor for the vaccine prescription, go buy the vaccine at the pharmacy, and return to the doctor for the vaccine injection	15	67	0.33	-	-	14 ^a	71	0.43	
	It would be easier to vaccinate my daughter if the pharmacist could perform the injection	15	80	0.60*	-	-	-	-	-	
	It would be easier to vaccinate my daughter if the doctor had vaccines at his office for vaccinating my daughter the same day	15	80	0.60*	-	-	-	-	-	
	-	-	-	-	-	-	15	73	0.57	
	-	-	-	-	-	It would be easier to get my daughter vaccinated against HPV if this vaccination was carried out at school (instruction: ask the question in the past if the vaccine has been administered)	15	73	0.57	
Reliability and/or source of supply of vaccine and/or vaccination equipment	I am concerned about the quality of the vaccines because they can be manufactured elsewhere than in Europe	15	60	0.20	-	-	15	47	-0.06	
	I trust the pharmacists to keep vaccines cold as required	15	47	-0.06	-	-	15	40	-0.20	
	I do not find it normal that some vaccines are out of stock	15	67	0.33	-	-	15	60	0.28	

Table 2 (continued)

Factor	Initial item	Round 1 (n = 15)			Reformulated item	Additional item	Round 2 (n = 15)		
		N	% agreement for "essential"	Content Validity Ratio			n	% agreement for "essential"	Content Validity Ratio
Vaccination schedule	If the HPV vaccine was important, it would have been made mandatory	14 ^a	86	0.71*	–	–	–	–	–
	The HPV vaccine has not been made mandatory because it is risky	14 ^a	73	0.47	–	–	15	80	0.60*
	I think my daughter is too young to be vaccinated against HPV	15	87	0.73*	–	–	–	–	–
Costs	I think that the HPV vaccine is too expensive for my budget	15	73	0.47	I think the HPV vaccine is too expensive for me	–	15	73	0.47
The strength of the recommendation and/or knowledge base and/or attitude of healthcare professionals	Has a doctor or another health professional ever recommended that you vaccinate your daughter against HPV?	15	100	1*	–	–	–	–	–
	Have you asked any questions to your attending doctor about HPV vaccines?	15	93	0.87*	–	–	–	–	–
	(If has already asked questions) Were you satisfied with his/her answers?	15	87	0.73*	–	–	–	–	–
	–	–	–	–	–	(If has already asked questions of her doctor concerning vaccination against HPV) Was your attending physician hesitant regarding this vaccine?	15	100	1*

^aCVR for 14 respondents = 0.57.

^bCVR for 13 respondents = 0.54.

^cWe replaced the term "other" used in the original instrument by "most".

† Items from the HPV Attitudes and Beliefs Scale (19 items submitted in Round 1 and 6 items submitted in Round 2).

†† Items from the HPV General Knowledge and the HPV Vaccination Knowledge Scales (19 items submitted in Round 1 and 3 items submitted in Round 2).

§ Items from the Holistic Complementary and Alternative Medicine Questionnaire (5 items submitted in Round 1)

¶ Items from the Vaccine Confidence Project (1 item submitted in Round 1).

* Response over the predefined threshold according to Lawshe's formula.

**Mediator was an antidiabetic drug given as a slimming agent, leading to national scandal in France.

Bold values indicate content validity ratio above the threshold.

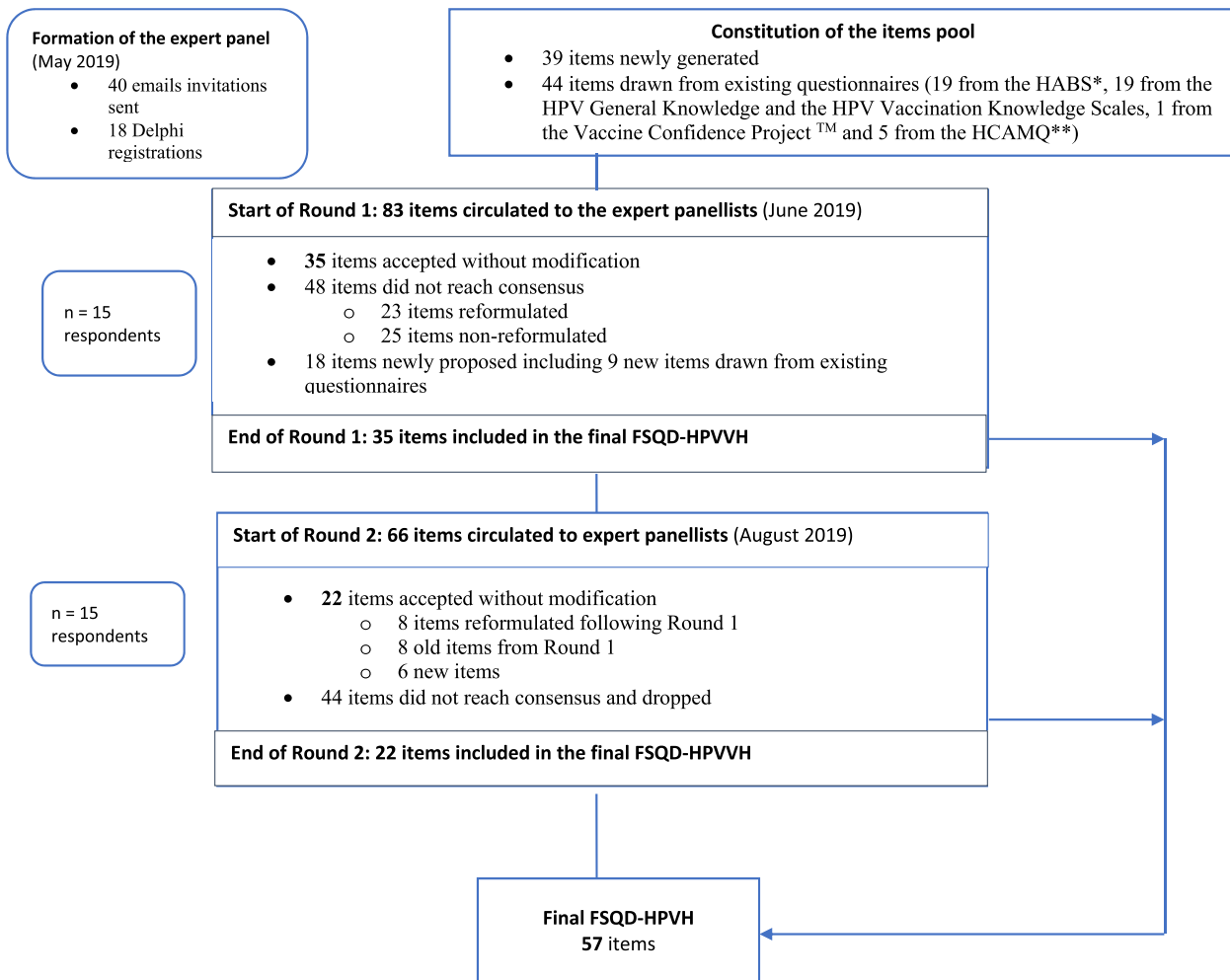


Fig. 2. Flow chart of the modified Delphi method for two survey rounds. *HABS: HPV Attitudes and Beliefs Scale (HABS). ** HCAMQ: Holistic Complementary and Alternative Medicine Questionnaire.

3.3. Round 2

In Round 2, 66 items were submitted to the expert panel. Of those, 48 were items that did not reach consensus at Round 1 and were recirculated either as initially worded ($n = 25$, 52%) or after rewording ($n = 23$, 48%), and 18 were new items. Among the new items, 9 were drawn from existing instruments (one item about “Knowledge/awareness” drawn from the HPV General Knowledge and HPV Vaccination Knowledge Scales [33], 3 items about “Immunisation as a social norm vs. not needed harmful” drawn from the HABS (32), and 5 items about “Risk/benefit (perceived/heuristic)” drawn from the HABS ($n = 3$) and from the HPV General Knowledge and HPV Vaccination Knowledge Scales ($n = 2$) [33]); the remaining were developed by the scientific committee (Table 2, Fig. 2). In total, consensus was reached on 22 items (33%). The analysis of the CVR of the individual items is shown in Table 2.

The final version of the survey instrument will include 57 items (Fig. 2 and Supplemental File 1): 10 items in the category “Contextual influences”, 37 items in the category “Individual and group influences”, and 10 items in the category “Vaccine/vaccination-specific issues”.

4. Discussion

In this study, we developed a survey instrument specifically intended to evaluate HPV vaccine hesitancy among mothers of

age-vaccination daughters in France. Within two rounds of a reactive Delphi methodology that took 12 weeks from preparation to conclusion, we generated a pool of items and consulted a panel of 15 experts who helped develop and validate a list of questions that reflect the many factors identified in the SAGE Working Group Determinants of Vaccine Hesitancy Matrix and that should now be applied to a survey of HPV vaccination vaccine hesitancy among mothers in France.

This study builds on the limited literature to date about how to measure the determinants of HPV vaccine hesitancy. Before starting this exercise, we had found only tools focusing on partial aspects of the factors contributing to vaccine hesitancy, e.g., the Carolina HPV immunization attitudes and beliefs scale (CHIAS) [41] and HABS [32], but none looking at determinants comprehensively. The domains covered by the FSQD-HPVH that the above-mentioned tools do not include are essentially those that fall under “Contextual factors”, for example, “Historical influences”, “Politics/policies” and “Communication and media environment”. The other domains not covered by existing questionnaires include the “Strengths of the recommendations and/or knowledge base and/or attitudes of healthcare professionals” and “Design of vaccination program/mode of delivery”. This study is novel in considering using the SAGE Working Group Determinants of Vaccine Hesitancy Matrix. This matrix has been used to classify the data of the Annual WHO/UNICEF JRF (which are collected globally across WHO Member States to monitor vaccine hesitancy) [42], but not as a data col-

lection tool. We hope the current study will stimulate further use of this matrix to investigate vaccine hesitancy related to other vaccines or settings.

We constructed a questionnaire with the most content-valid items. It appeared that only 42% of the items were deemed representative of the construct (factor) they intended to measure at Round 1. This finding emphasizes the relevance of including the perspectives of a multidisciplinary panel of experts. However, some of the items could be selected after rewording ($n = 8/23$, 35%). Each factor is represented by at least one item, except “Reliability and/or source of supply of vaccine and/or vaccination equipment” and “Costs”, which ended up without any item.

The main strengths of our study include the composition of a multidisciplinary and multi-stakeholder panel of experts and the rigorous multistage quantitative analysis of their responses. As vaccine hesitancy is a complex, multifaceted phenomenon, the problem needs to be examined in a multidisciplinary manner. An excellent retention rate (100%) was achieved in Round 2, avoiding the risk of response bias. However, some limitations need to be acknowledged. First, the length of the final questionnaire might be challenging from a practical point of view. In a subsequent study, we aim to propose a shortened version based on factor analysis of the data collected through this questionnaire. Second, the sample size of the panel of experts was small, although it falls within the range recommended in the literature, and the calculation of the consensus criterion was weighted by the number of respondents. Third, we only performed the a priori-planned two rounds of Delphi survey. There is a delicate trade-off between the number of rounds and the risk of attrition, and it turned out that no modification in terms of rewording was required following Round 2, since the experts did not suggest any reformulations for the items that did not meet consensus. In addition, three factors (“Communication and media environment”, “Perception of the pharmaceutical industry”, “Health system and providers-trust and personal experience”) ended up with only one item. Although single-item measures for each facet of multifaceted constructs have been suggested in the literature [43], these are often considered to compromise on reliability. Finally, the questionnaire was designed to target only the mothers as they often have the main decision-making power with regard to the HPV vaccination [44–46]. Adaptation of the item “Personally, I have already had abnormal pap smears for which treatment was needed (conization/surgery)” would be required if the questionnaire is to be administered to fathers. Finally, the FSQD-HPVH was designed to be administered to the French population, with reference to the French health system and culture. However, our approach could provide a reference for other settings. The FSQD-HPVH has not yet been pilot-tested, but it is intended to aid in the evaluation of HPV vaccine hesitancy in France through administration to a large sample of mothers, which will, in turn, allow further validation.

5. Conclusion

In conclusion, 57 items of FSQD-HPVH with good content validity were developed in this study in preparation of a thorough evaluation of HPV vaccine hesitancy in France. Unlike other existing tools, the FSQD-HPVH is the first to comprehensively consider all factors that may influence HPV vaccine hesitancy, the first step towards an evidence-based approach to curbing the low HPV vaccination rates in France.

6. Author's contributions

FD has participated in the design of the study, the generation of Delphi items, the data analysis, the redaction of the manuscript,

and the revision process. PC and OL have participated in the design of the study, the generation of Delphi items, and the revision process. PM has participated in the redaction of the manuscript and the revision process. All authors have approved the final manuscript. All members of the FSQD-HPVH study group have participated in the Delphi procedure.

Funding

Financial support for the study was provided by a PhD fellowship from the French National Institute of Cancer awarded to FD. This fellowship has been used to support the development of the study design, data collection, data analysis, and manuscript preparation.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: [Fadia Dib declares that MSD vaccines have covered registration fees, transport and accommodation costs for attendance to a conference. Philippe Mayaud, Odile Launay and Pierre Chauvin declare no conflict of interest.]

Appendix A. Supplementary material

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.vaccine.2020.07.027>.

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DEUXIEME PARTIE : ENQUÊTE TÉLÉPHONIQUE EN POPULATION

CHAPITRE 4 – ARTICLE II ENQUÊTE TÉLÉPHONIQUE ÉVALUANT LES FACTEURS ASSOCIÉS À LA COUVERTURE VACCINALE DU VACCIN ANTI-HPV EN FRANCE

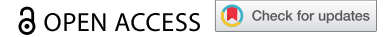
L'instrument développé en première partie de thèse a constitué le fondement du travail décrit dans cette deuxième partie. L'instrument a, en effet, été administré au cours d'une enquête téléphonique conduite spécialement dans le cadre de cette thèse auprès d'un échantillon de 1102 mères de filles de 11 à 14 ans résidant en France métropolitaine, sélectionné par la méthode des quotas, après une phase pilote test sur un échantillon de 30 mères. Les entretiens téléphoniques comprenaient des questions relatives au stade de décision concernant la vaccination anti-HPV selon le modèle du processus d'adoption du comportement de précaution (PAPM, pour *Precaution Adoption Process Model*) (Shapiro et al. 2018) et de la mesure de confiance envers les vaccins (GVCI, pour *Global Vaccine Confidence Index*) (Larson et al. 2016), et ont été conduits par l'institut de sondage Ipsos selon la méthode CATI (*Computer-Assisted Telephone Interview*, en français entretien téléphonique assisté par ordinateur).

Dans l'ensemble, 38,6 % des mères avaient indiqué que leur fille avait reçu au moins une dose du vaccin anti-HPV. L'analyse multivariée a révélé que le fait d'être d'accord avec l'affirmation selon laquelle les médecins/ professionnels de santé croient que vacciner les filles contre les HPV est une bonne idée et le fait que la mère ait posé des questions au médecin traitant sur les vaccins HPV étaient significativement associés à une probabilité plus élevée que leur fille soit vaccinée (OR=4,99 ; IC95%, 2,09-11,89 ; et OR=3,44 ; IC95 %, 2,40-4,92, respectivement). La croyance de la mère selon laquelle leur fille était trop jeune pour être vaccinée (OR=0,16 ; IC95% 0,09-0,29]) et l'âge plus jeune de leur fille (OR=0,17 ; IC95%, 0,10-0,28 pour les filles âgées de 11 ans par rapport à celles âgées de 14 ans) se sont avérés inversement associés à la couverture vaccinale, ainsi que la croyance des

* Enquête ayant bénéficié du soutien de l'Inca (subvention doctorale) et de MSD (*Merck Investigator Studies Program*) dans le cadre d'une convention de recherche avec l'Inserm obtenue par la doctorante.

mères selon laquelle le vaccin anti-HPV n'est pas sûr (OR=0,42 ; IC95%, 0,26-0,67), leur affirmation selon laquelle les HPV sont très rares (OR=0,49 ; IC95%, 0,31-0,77) et un précédent refus de la mère de recevoir une vaccination la concernant personnellement (OR=0,57 ; IC95%, 0,40-0,80).

RESEARCH PAPER



Determinants of human papillomavirus (HPV) vaccine uptake among girls in France: A population-based telephone survey

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ABSTRACT

Introduction: The uptake of human papillomavirus (HPV) vaccination in France remains low. The aim of this study was to identify factors associated with the uptake of the HPV vaccine in girls aged 11–14 years in France.

Methods: We conducted a telephone survey among a quota sample of 1102 mothers of 11–14-year-old daughters residing in mainland France, using the French Survey Questionnaire for the Determinants of HPV Vaccine Hesitancy (FSQD-HPVH). The dependent variable was the uptake of at least one dose of the HPV vaccine in the daughter. The independent variables included the FSQD-HPVH item variables, the Global Vaccine Confidence Index item variables, the daughter's age, and the mother's socioeconomic status.

Results: Overall, 38.6% of the mothers indicated that their daughter received at least one dose of the HPV vaccine. The multivariate analysis revealed that agreeing with the statement that doctors/health care providers believe vaccinating girls against HPV was a good idea, and having asked questions to the attending doctor about HPV vaccines were associated with a higher HPV vaccine uptake (OR = 4.99, 95% CI [2.09–11.89]; and OR = 3.44, 95% CI [2.40–4.92]). Mother's belief that her daughter was too young to be vaccinated against HPV (OR = 0.16, 95% CI [0.09–0.29]) and lower daughter's age (OR = 0.17, 95% CI [0.10–0.28]) for girls aged 11 compared to those aged 14) were found strongly inversely associated with HPV vaccination, followed by agreeing with the statement that the HPV vaccine was unsafe (OR = 0.42, 95% CI [0.26–0.67]), identifying as true the statement that HPV was very rare (OR = 0.49, 95% CI [0.31–0.77]), and the mother's refusal of own vaccination (OR = 0.57, 95% CI [0.40–0.80]).

Conclusion: We have identified important determinants associated with HPV vaccine uptake in France. Interventions designed to improve HPV vaccine uptake should be tailored to address these determinants.

ARTICLE HISTORY

Received 22 February 2022
Revised 16 May 2022
Accepted 25 May 2022

KEYWORDS

HPV vaccine; vaccine hesitancy; determinants; mothers; daughters

Introduction

Cervical cancer is the fourth most common cancer among women worldwide. With an estimated 2 835 new cases of cervical cancer diagnosed and 1 084 related deaths in France,¹ it is also the fourth most common female cancer in women aged 15 to 44 years in France.²

Cervical cancer remains a deadly disease, but it is preventable through screening and vaccination against the papillomavirus (HPV) infection, its etiologic agent. The World Health Organization (WHO) and the World Health Assembly have called for its elimination by 2030.³

In France, vaccination against HPV has been recommended since 2007 for girls and 2019 for boys. In 2022, it is recommended for adolescent girls and boys aged 11 to 14 years (with catch-up vaccination until 19 years old),⁴ with the recommendation for boys implemented since January.⁵ Although France was one of the first three countries to introduce HPV vaccination for girls, the uptake of HPV vaccine in French girls remains low. Coverage of the full course of HPV vaccine coverage in France in 2020 was around 33% in girls aged 16 years,⁶ well below the 2014–2019 French national cancer control plan goal of 60%,^{7,8} In

2017, the French National Authority of Health (*Haute Autorité de Santé*, HAS) recognized primary cervical cancer prevention through vaccination and screening as a public health priority.⁹ In 2019, the French Prime Minister issued a decree relating to the implementation of two regional experiments aiming at improving HPV vaccination coverage. The selected regions were French Guiana and the Grand-Est region. The interventions included health care professionals training and school based vaccination-campaigns.¹⁰

HPV vaccination in France remains opportunistic, since there is no national school-vaccination program, or otherwise organized. Thus, parents must make an appointment with their doctor to obtain vaccine prescription, obtain the vaccine from a pharmacy, and then make another appointment for its administration. The national social security system covers 65% of the cost of the vaccine (115.20 € per dose) and the remaining 35% has to be paid by the individual (or covered through complementary insurance cover).

Multiple barriers to HPV vaccination have been reported in the literature, including disadvantaged background, lack of health coverage, residence in a less urbanized area,^{11,12} and

mother's ethnicity.¹³ The literature has also reported levels of knowledge about cervical cancer/HPV, maternal history of abnormal cytology, and opinions about vaccination, in general, as determinants of HPV vaccination.¹⁴ In France, several studies have examined the role of common epidemiologic factors such as socioeconomic status and healthcare supply,^{15,16} or cervical cancer screening attitudes in the mothers¹⁷ as determinants of HPV vaccination coverage. However, no study has investigated this issue through the prism of factors related to vaccine hesitancy, defined by the WHO Strategic Advisory Group of Experts (SAGE) working group as "the delay in acceptance or refusal of vaccines despite availability of vaccination services." This approach classifies the determinants of vaccine hesitancy into three main domains: (i) contextual influences (e.g., communication and social media); (ii) individual and group influences (e.g., lack of perceived benefit of the vaccine); and (iii) vaccine/vaccination-specific issues (e.g., the strength of the recommendation of healthcare professionals).¹⁸ This approach was used in a recently published systematic literature review of factors affecting vaccination coverage in Latin America.¹⁹ Being mindful that "vaccine hesitancy is complex and context-specific, varying across geographies and vaccine types",²⁰ we have developed the French Survey Questionnaire for the Determinants of HPV Vaccine Hesitancy (FSQD-HPVH) to be used in the French context.² The purpose of the present study was to pilot-test this questionnaire in a representative group of French mothers and use it to identify factors associated with the uptake of HPV vaccine in girls aged 11–14 years in France.

Material and methods

Study design and population

We conducted a cross-sectional telephone survey among a sample of mothers of 11-14-year-old daughters residing in mainland France. The study population was enrolled using quota sampling, a non-probability sampling method, to ensure a nationally representative sample of mothers of girls aged 11 to 14 years. Because the proportion of households with teenage girls of this age is very low, random sampling would have been challenging to implement in this setting. The quota sample was representative according to the following characteristics: region of residence, socio-professional category (SPC) of the reference person in the household, and the number of children in the household by comparison with the latest national census.²¹ IPSOS, a global market, and social research company, conducted the sampling and the field interviews using computer-assisted telephone interviewing (CATI) systems. The interviewers underwent training and were required to follow standard recruitment and data collection procedures. After a week of pilot-testing among a sample of 30 mothers using the same eligibility and quota criteria as for the primary survey, the data-collection period started in April 2021 and lasted three weeks.

After obtaining oral informed consent on a study on HPV vaccination conducted on behalf of the French national institute of health and medical research (Inserm, *Institut National*

de la Santé et de la Recherche Médicale), the interviewer introduced the survey with the following explanatory paragraph: "Vaccination against Human Papillomaviruses (HPV) prevents infection by these widespread and sexually transmitted viruses, responsible for cervical cancer. Despite more than ten years of experience with efficacy and safety, HPV vaccination coverage remains exceptionally low in France (<30%) compared to other European countries. Like many mothers of teenage girls, you will have to make a decision about your daughter's HPV vaccination. By interviewing mothers, researchers will be able to understand better their attitudes toward this vaccination, which will then allow health professionals to better assist them in deciding to vaccinate their daughters". Agreements were made with the interviewer on participant recruitment appointment if the mother was not immediately available. Participants received no incentive whatsoever for completing the survey.

Study variables

The dependent variable was the uptake of at least one dose of the HPV vaccine in the 11-14-year-old daughter (the oldest in the case of two daughters of the same age range). This binary variable was derived from the response to the single answer question about the Precaution Adoption Process Model (PAPM) stage for HPV vaccination:^{22,23} "Which of the following best describes your thoughts about the human papillomavirus (HPV) vaccine for your daughter": unaware that the HPV vaccine could be given to their daughter (stage 1)/aware that the HPV vaccine could be given to their daughter, but never thought about vaccinating their daughter against HPV (stage 2)/undecided about vaccinating their daughter against HPV (stage 3)/have decided they DO NOT want to vaccinate their daughter against HPV (stage 4)/decided they DO want to vaccinate their daughter against HPV (stage 5)/daughter has already received the HPV vaccine (stage 6). This later stage is our dependent variable.

The independent variables included the FSQD-HPVH item variables,² the Global Vaccine Confidence Index (GVCI) item variables,²⁴ daughter's age, the three quotas variables (region of residence, SPC of the reference person in the household, and the number of children in the household), and mother's socioeconomic status: age, level of education, nationality, whether they had at least one immigrated parent, health insurance status (private supplementary insurance, public insurance for the underprivileged).

Mother's awareness about the HPV vaccine before the survey was assessed by the answer to the question "Have you heard about the HPV vaccine before taking this survey?"

Sample size calculation

A sample size of 1100 mothers was deemed necessary to detect as statistically significant an odds ratio of uptake of at least one dose of HPV vaccine of 1.8. This sample size provided 80% power to perform a multivariate analysis with 33 independent variables to assess the determinants of HPV vaccine uptake according to the rule of thumb of 10 events per independent variable.²⁵ The sample size calculation assumptions were: alpha

risk of 5%; the prevalence of exposure to factors influencing HPV vaccine uptake of 10%; and uptake rate of at least one dose of HPV vaccine in the non-exposed mothers of 30%.

Statistical analysis

The data set provided by IPSOS included data weighted according to the French general population census of the French National Institute for Statistics and Economic Studies. We used descriptive statistics to summarize the responses to each question. We reported continuous variables as mean \pm standard deviation (SD) and categorical variables as absolute count and relative frequency (%). Weighted data were reported for sociodemographic descriptive statistics, along with raw data, to indicate the quality of sampling. Since we observed no difference between weighted and raw data (Table 1), the rest of the analyses were performed using raw data. We used the χ^2 test to compare the FSQD-HPVH variables between the mothers who reported that their daughters received at least one dose of the HPV vaccine and the group of mothers who reported that their daughters did not receive any dose of the HPV vaccine. To identify the variables that were independently

associated with HPV vaccination uptake, we conducted multivariate logistic regression models using weights to account for the quota sampling method. The multivariate model was built using a backward process, with a significance level of 0.05 for a variable to stay in the model. Initial candidate variables were the variables from the FSQD-HPVH (except the responses to the conditional questions that were not asked to the whole sample; for example, the type of internet website for mothers responding Internet to the question related to the source of information), the four items of the GVCI, as well as the sociodemographic variables with $P < 0.20$ in the χ^2 test for differences group. We checked multicollinearity before including variables in the multivariate logistic model. We reported adjusted odds ratios (ORs) with their respective 95% confidence intervals (95% CI).

Inferential statistical measures (95% CI and P -values), commonly used to make inferences about the larger population from which the sample is drawn, are meant only for indicative purposes in the present study, as it is difficult to guarantee that the study sample was representative for characteristics other than those for which quotas units have been determined.

All statistical analyses were performed using SAS (version 9.4, SAS Institute Inc., Cary, North Carolina). All statistical tests involved were two-sided, and a P -value of < 0.05 was considered statistically significant.

Table 1. Characteristics of the 1102 mothers included in the study.

		Unweighted data		Weighted data	
		n or mean	(% or SD)	n or mean	(% or SD)
Age (years)		43.4	(3.6)	43.3	(3.6)
Lives with a partner					
	Yes	818	(74.2)	814	(73.9)
	No	284	(25.8)	288	(26.1)
Level of education (2 missing values)					
	< High school diploma	137	(12.4)	142	(13.0)
	High school diploma-Two year post high school diploma	513	(46.6)	521	(47.4)
	> Two year post high school diploma	449	(40.7)	435	(39.6)
Nationality (1 missing value)					
	French by birth	1024	(92.9)	1023	(92.8)
	French by acquisition	53	(4.8)	53	(4.8)
	Foreign	24	(2.2)	25	(2.2)
Immigrated parent (1 missing value)					
	Yes	157	(14.2)	158	(14.3)
	No	944	(85.7)	943	(85.6)
Supplemental health insurance (1 missing value)					
	Yes	1049	(95.2)	1046	(94.9)
	No	52	(4.7)	55	(5.0)
Subsidized Supplementary Health Insurance (1 missing value)					
	Yes	66	(6.0)	70	(6.3)
	No	1035	(93.9)	1031	(93.6)
Recipient of minimal social benefit					
	Yes	47	(4.3)	50	(4.6)
	No	1055	(95.7)	1052	(95.4)

Results

Pilot phase

Changes were made to the wording of one question: “I am favorable to the 11 vaccines mandatory for children born since 1 January 2018,” reformulated to “I am favorable to the mandatory vaccination for children under two years of age.” One item was removed because it was redundant. No problem of questions understanding was detected.

Sociodemographic characteristics of the study participants

As shown in Table 2, adequate numbers were achieved for all quotas.

The mean age of the survey respondents was 43.3 years (SD, 3.6). The majority of mothers had attained an educational level between high school diploma and two-year post-high school diploma (47%), lived with a partner (74%), had private health insurance (95%), and were of French nationality by birth (93%); and 84% had more than one child (Table 2). Ninety seven percent of the mothers reported having heard about the HPV vaccine before taking the survey (Table 1).

Global vaccine confidence index

The majority of respondents agreed with the statement that “Vaccines are important for children to have” (94.6%), “Overall, I think vaccines are safe” (79.9%), “Overall I think vaccines are effective” (92.6%), “Vaccines are compatible with my religious beliefs” (71.5%) (Figure 1).

Table 2. Representativeness of demographic quotas.

Quota category	Quota	Percentage of respondents in each quota (%)	Percentage representative of the French general population (%)
Geographic region of residence	Parisian Region	19.0	19.2
	North West	23.4	23.5
	North East	22.4	22.6
	South West	10.7	10.4
	South East	24.5	24.3
Socio-professional category (SPC) of the reference person in the household	Upper	51.5	48.4
	Medium and low	45.5	47.7
	Unemployed	3.1	3.9
Number of children in the household	One	15.7	16.1
	More than one	84.3	83.9

Precaution Adoption Process Model stage and HPV vaccination rate

A minority of mothers were in PAPM stages 1 (4.3%) and 2 (6.1%) (unaware that the HPV vaccine could be given to their daughter, and aware that the HPV vaccine could be given to their daughter but never thought about vaccinating them, respectively). While 16.1% were undecided (stage 3), 7.1% decided not to (stage 4) and 27.8% decided to (stage 5) vaccinate their daughter. Thus, HPV vaccination uptake (reported daughter’s receipt of at least one dose of HPV vaccine) was 38.6% (PAPM stage 6) (Figure 2).

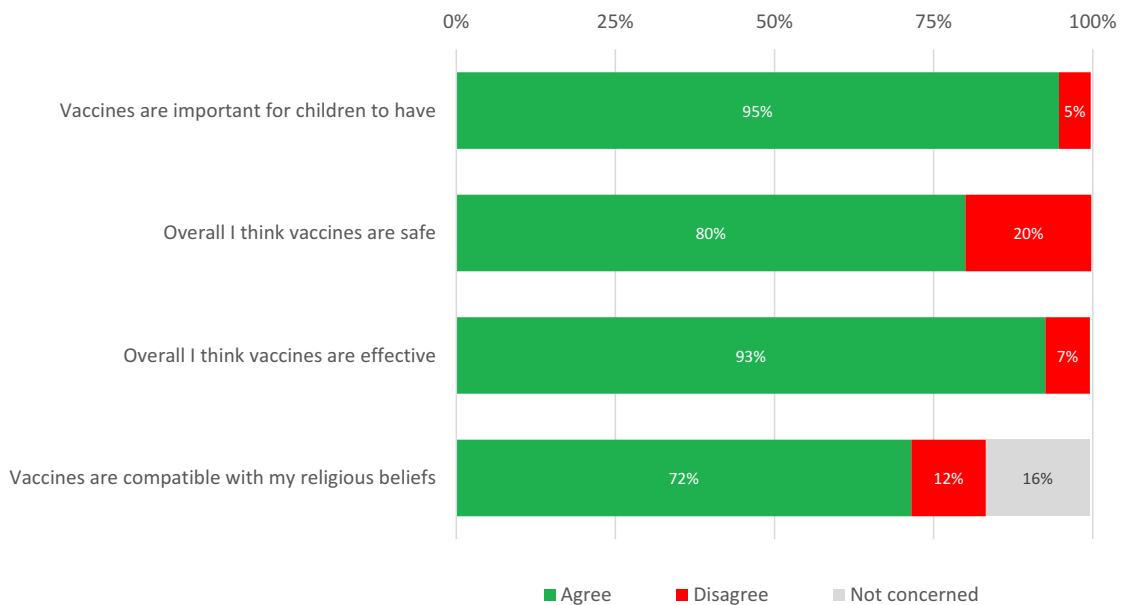


Figure 1. Global vaccine confidence index items.

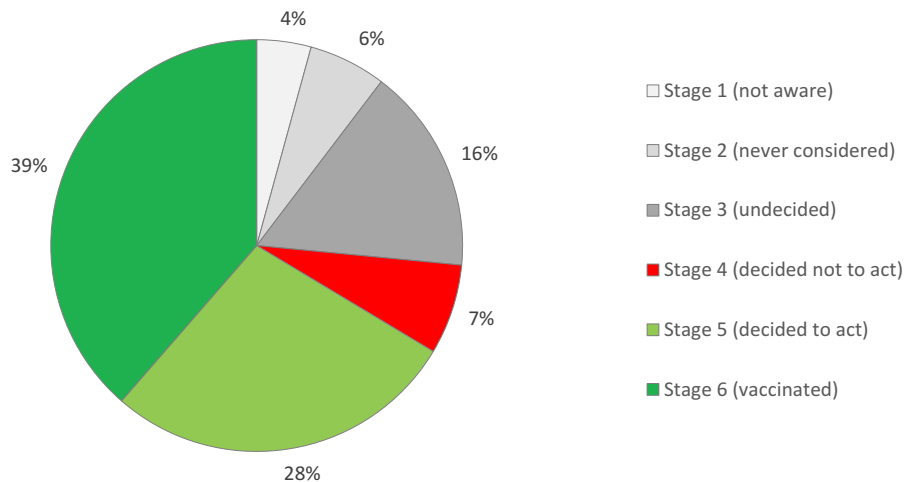


Figure 2. Precaution Adoption Process Model stage for HPV vaccination.

Descriptive and group comparison analyses of FSQD-HPVH variables

The responses to the FSQD-HPVH are presented in Table 3.

Contextual factors

Communication and media environment

The most frequent sources through which mothers had heard about HPV vaccination were the recommendation of their attending physician (44.6%), the Television (24.1%), and the recommendation of a gynecologist (21.1%). Mothers with vaccinated daughters heard more frequently about HPV through a recommendation from their attending physician and gynecologist than mothers of unvaccinated daughters ($p < 0.0001$ and $p = 0.0066$, respectively). Mothers of vaccinated daughters heard less frequently about HPV through Television than mothers of unvaccinated daughters ($p = 0.0109$).

Historical influences

Nearly a third of the respondents agreed with the statement that “Since the controversy over vaccination against H1N1 flu, I have less confidence in French vaccination recommendations” and that “Since the controversy over the hepatitis B vaccine, I have less confidence in the healthcare system” (31.6% and 31.8%, respectively). The percentage of agreement with those statements was lower among mothers of vaccinated daughters ($p < 0.0001$ for both).

Religion/culture/gender/socioeconomic factors

The majority of respondents disagreed that vaccinating girls against HPV encourages them to have sex (94.6%), that is hard to talk to them about their sexual health (82.4%), that they have difficulty in addressing the subject of HPV vaccine with them (92.4%) and that they feel uncomfortable discussing their daughter’s sexual health with a doctor or another health professional (95.9%). Significant differences were observed between the mothers of vaccinated daughters and mothers of unvaccinated daughters in the statement “I think that vaccinating girls against HPV encourages them to have sex” and “I have difficulty in addressing the subject of HPV vaccine with my daughter” with a percentage of agreement higher in the group of mothers of unvaccinated daughters ($p = 0.0180$ and $p < 0.0001$, respectively).

Politics/policies

Nearly a fifth (21.1%) of respondents disagreed with the statement that they favored compulsory vaccination for children under the age of two, and less than half (42.8%) agreed that everyone should be able to choose whether or not to vaccinate their children. Significant differences were observed between the mothers of vaccinated and unvaccinated daughters for those two statements: agreement with the statement of compulsory vaccination was higher among mothers of vaccinated daughters ($p < 0.0001$), while the agreement with the second statement was lower among mothers of vaccinated daughters ($p = 0.0004$).

Perception of the pharmaceutical industry

The majority (83.4%) of respondents agreed that the pharmaceutical industry follows strict manufacturing procedures, with a significantly higher proportion of mothers of vaccinated daughters agreeing ($p = 0.0002$).

Individual and group factors

Personal, family, and or community members’ experiences

Nearly a third of respondents (34.4%) indicated having refused a vaccine for themselves (or chose not to get vaccinated), and fewer (27.3%) refused a vaccine for their daughter (or chose not to get her vaccinated). Nearly a fifth (18.5%) of respondents stated that they knew a person who fell seriously ill after getting vaccinated, that they knew someone who became seriously ill because s/he was not vaccinated (20.8%), and that they already had abnormal pap smears for which treatment was needed (18.1%). The HPV vaccine uptake was lower in the group of mothers who previously refused a vaccine for themselves ($p < 0.0001$) and their daughters ($p = 0.0176$) and who knew a person who fell seriously ill after getting vaccinated ($p = 0.0029$).

Beliefs and attitudes about health and prevention

Nearly half (43.7%) of the respondents agreed that complementary medicine builds up the body’s defenses leading to a permanent cure, and nearly a quarter (24.8%) preferred that their daughter developed natural defenses against HPV rather than through vaccination. The percentage of agreement with those statements was significantly higher in the mothers of unvaccinated daughters ($p = 0.0004$ and $p < 0.0001$, respectively).

Knowledge/awareness

Nearly half (48.7%) of respondents had already searched for information on the HPV vaccine; the most frequent source of information had been the Internet (75.0%), followed by their attending physicians (58.7%) and other health professionals (33.0%). The vast majority of mothers who searched for information on the Internet consulted news websites (89.6%), of whom nearly three-quarters (70.9%) reported consulting *Doctissimo* (a website dealing with health and well-being-related topics). Just over half (51.5%) of mothers who searched the Internet for information on HPV vaccine reported consulting the *Santé Publique France* website (the official French national public health agency website), and fewer than a third (29.6%) reported consulting *Vaccination Info Service*, a service linked to *Santé Publique France*. After having consulted the information, the majority of the mothers declared this helped them decide on HPV vaccination of their daughters (80.8%). Significant differences were observed between the mothers of vaccinated and unvaccinated daughters, with a higher rate of information search among mothers of vaccinated daughters ($p < 0.0001$). Significant differences were observed between the mothers of vaccinated and unvaccinated daughters, with a higher rate of mothers of vaccinated daughters being able to take a decision regarding the HPV vaccination after having searched for information ($p < 0.0001$).

Table 3. Distribution of FSQD-HPVH survey variables by HPV vaccination status (unweighted data). Percentages may not total 100% due to rounding.

		Total (n=1102)		Vaccinated daughters (n=425)		Unvaccinated daughters (n=677)		P value			
		n	(%)	n	(%)	n	(%)				
CONTEXTUAL INFLUENCES COMMUNICATION AND MEDIA ENVIRONMENT	How did you hear about the HPV vaccine? ^{a, b}	Recommendation of the attending physician	491	(44.6)	251	(59.1)	240	(35.5)	<0.0001		
		Recommendation of a pediatrician	95	(8.6)	41	(9.6)	54	(8.0)	0.4705		
		Recommendation of a gynecologist	232	(21.1)	110	(25.9)	122	(18.0)	0.0066		
		Television	266	(24.1)	88	(20.7)	178	(26.3)	0.0109		
		Social media	55	(5.0)	15	(3.5)	40	(5.9)	0.0531		
		Written press	150	(13.6)	53	(12.5)	97	(14.3)	0.2384		
		Family	196	(17.8)	74	(17.4)	122	(18.0)	0.5379		
		Friends	202	(18.3)	76	(17.9)	126	(18.6)	0.5029		
		School	39	(3.5)	16	(3.8)	23	(3.4)	0.8632		
		Other	175	(15.9)	58	(13.6)	117	(17.3)	0.0525		
HISTORICAL INFLUENCES	Since the controversy over vaccination against H1N1 flu, I have less confidence in French vaccination recommendations	Agree	348	(31.6)	88	(20.7)	260	(38.4)	<0.0001		
		Neither agree nor disagree	16	(1.5)	3	(0.7)	13	(1.9)			
		Disagree	724	(65.7)	329	(77.4)	395	(58.3)			
		Don't know	8	(0.7)	3	(0.7)	5	(0.7)			
		Unanswered question	6	(0.5)	2	(0.5)	4	(0.6)			
		Since the controversy over the hepatitis B vaccine, I have less confidence in the healthcare system	Agree	350	(31.8)	85	(20.0)	265		(39.1)	<0.0001
			Neither agree nor disagree	13	(1.2)	3	(0.7)	10		(1.5)	
			Disagree	726	(65.9)	334	(78.6)	392		(57.9)	
			Don't know	4	(0.4)	1	(0.2)	3		(0.4)	
			Unanswered question	9	(0.8)	2	(0.5)	7		(1.0)	
RELIGION/ CULTURE/ GENDER/ SOCIO ECONOMIC	I think that vaccinating girls against HPV encourages them to have sex		Agree	48	(4.4)	10	(2.4)	38	(5.6)	0.0180	
		Neither agree nor disagree	8	(0.7)	2	(0.5)	6	(0.9)			
		Disagree	1042	(94.6)	413	(97.2)	629	(92.9)			
		Don't know	3	(0.3)	0	(0.0)	3	(0.4)			
		Unanswered question	1	(0.1)	0	(0.0)	1	(0.1)			
		It is hard to talk to my daughter about her sexual health	Agree	167	(15.2)	59	(13.9)	108	(16.0)		0.7946
Neither agree nor disagree	20		(1.8)	7	(1.6)	13	(1.9)				
Disagree	908		(82.4)	356	(83.8)	552	(81.5)				
Don't know	7		(0.6)	3	(0.7)	4	(0.6)				
I feel uncomfortable discussing my daughter's sexual health with a doctor or another health professional	Agree		39	(3.5)	9	(2.1)	30	(4.4)	0.0766		
	Neither agree nor disagree		5	(0.5)	2	(0.5)	3	(0.4)			
	Disagree	1057	(95.9)	413	(97.2)	644	(95.1)				
	Don't know	1	(0.1)	1	(0.2)	0	(0.0)				
I have difficulty in addressing the subject of HPV vaccine with my daughter	Agree	56	(5.1)	9	(2.1)	47	(6.9)	<0.0001			
	Neither agree nor disagree	18	(1.6)	1	(0.2)	17	(2.5)				
	Disagree	1018	(92.4)	415	(97.6)	603	(89.1)				
	Don't know	10	(0.9)	0	(0.0)	10	(1.5)				

(Continued)

Table 3. (Continued).

		Total (n=1102)		Vaccinated daughters (n=425)		Unvaccinated daughters (n=677)		P value	
		n	(%)	n	(%)	n	(%)		
POLITICS/POLICIES	I am favorable to the mandatory vaccination for children under two years of age	Agree	860	(78.0)	362	(85.2)	498	(73.6)	<0.0001 <0.0001
		Neither agree nor disagree	6	(0.5)	3	(0.7)	3	(0.4)	
	Everyone should be able to choose whether or not to do vaccinate his/her children	Disagree	232	(21.1)	60	(14.1)	172	(25.4)	0.0004
		Does not know	4	(0.4)	0	(0.0)	4	(0.6)	
		Agree	472	(42.8)	152	(35.8)	320	(47.3)	
		Neither agree nor disagree	11	(1.0)	3	(0.7)	8	(1.2)	
PERCEPTION OF THE PHARMACEUTICAL INDUSTRY	The pharmaceutical industry follows strict manufacturing procedures	Disagree	618	(56.1)	270	(63.5)	348	(51.4)	0.0002
		Don't know	1	(0.1)	0	(0.0)	1	(0.1)	
	Agree	919	(83.4)	381	(89.6)	538	(79.5)		
	Neither agree nor disagree	20	(1.8)	4	(0.9)	16	(2.4)		
INDIVIDUAL AND GROUP INFLUENCES PERSONAL, FAMILY AND OR COMMUNITY MEMBERS' EXPERIENCE	I happened to refuse a vaccine for my daughter (or choose not to get her vaccinated)	Disagree	144	(13.1)	34	(8.0)	110	(16.2)	0.0176
		Don't know	19	(1.7)	6	(1.4)	13	(1.9)	
	I happened to refuse a vaccine for myself (or choose not to get vaccinated)	Yes	301	(27.3)	99	(23.3)	202	(29.8)	<0.0001
		No	801	(72.7)	326	(76.7)	475	(70.2)	
	I know a person who fell seriously ill after getting vaccinated	Yes	379	(34.4)	116	(27.3)	263	(38.8)	0.0029
		No	723	(65.6)	309	(72.7)	414	(61.2)	
	I know someone who became seriously ill because s/he was not vaccinated	Yes	204	(18.5)	60	(14.1)	144	(21.3)	0.2098
		No	898	(81.5)	365	(85.9)	533	(78.7)	
		Don't know	3	(0.3)	1	(0.2)	2	(0.3)	
	Personally, I have already had abnormal pap smears for which treatment was needed (conization/surgery)	Yes	229	(20.8)	99	(23.3)	130	(19.2)	0.3605
		No	870	(78.9)	325	(76.5)	545	(80.5)	
		Unanswered question	1	(0.1)	0	(0.0)	1	(0.1)	
BELIEFS, ATTITUDES ABOUT HEALTH AND PREVENTION	Complementary medicine builds up the body's own defenses, so leading to a permanent cure	Yes	199	(18.1)	84	(19.8)	115	(17.0)	0.0004
		No	902	(81.9)	341	(80.2)	561	(82.9)	
		Agree	482	(43.7)	154	(36.2)	328	(48.4)	
		Neither agree nor disagree	38	(3.4)	16	(3.8)	22	(3.2)	
	I prefer that my daughter develops naturally defenses against papillomavirus rather than by vaccination	Disagree	563	(51.1)	250	(58.8)	313	(46.2)	<0.0001
		Don't know	19	(1.7)	5	(1.2)	14	(2.1)	
		Agree	273	(24.8)	42	(9.9)	231	(34.1)	<0.0001
		Neither agree nor disagree	20	(1.8)	7	(1.6)	13	(1.9)	
		Disagree	793	(72.0)	374	(88.0)	419	(61.9)	
		Don't know	16	(1.5)	2	(0.5)	14	(2.1)	

(Continued)

Table 3. (Continued).

		Total (n=1102)		Vaccinated daughters (n=425)		Unvaccinated daughters (n=677)		P value		
		n	(%)	n	(%)	n	(%)			
KNOWLEDGE/AWARENESS	Have you ever searched for information on the HPV vaccine in the past?								<0.0001	
		Yes	537	(48.7)	246	(57.9)	291	(43.0)		
		No	565	(51.3)	179	(42.1)	386	(57.0)		
		(If already researched information) Cite the 3 most consulted sources of information								
			Attending physician	315	(58.7)	161	(65.5)	154	(52.9)	.0033
			Other health professional	177	(33.0)	71	(28.9)	106	(36.4)	0.0632
			Internet	403	(75.0)	187	(76.0)	216	(74.2)	0.6331
			Family	88	(16.4)	42	(17.1)	46	(15.8)	0.6930
			Books	21	(3.9)	7	(2.9)	14	(4.8)	0.2417
			Print media	94	(17.5)	41	(16.7)	53	(18.2)	0.6385
			Other	57	(10.6)	26	(10.6)	31	(10.7)	0.9749
		(If used the internet) How did you use the internet? ^a								
			I went to forums	83	(7.5)	30	(16.1)	53	(24.5)	0.0355
			I visited blogs	34	(8.4)	9	(4.8)	25	(11.6)	0.0149
			I looked at social media	21	(5.2)	6	(3.2)	15	(6.9)	0.0924
			I consulted news websites	361	(89.6)	169	(90.4)	192	(88.9)	0.6265
			Other	23	(5.7)	9	(4.8)	14	(6.5)	0.4714
			Does not know	1	(0.3)	1	(0.5)	0	(0.0)	0.4640
		(If consulted information sites) Which website?								
			<i>Santé Publique France Vaccination Info Service</i>	186	(51.5)	88	(52.1)	98	(51.0)	0.8452
			<i>Doctissimo</i>	256	(70.9)	117	(69.2)	139	(72.4)	0.5088
			<i>Allodocteur</i>	72	(19.9)	23	(13.6)	49	(25.5)	0.0047
			<i>Pourquoi Docteur</i>	5	(1.4)	3	(1.8)	2	(1.0)	0.6682
			<i>Infovac</i>	37	(10.3)	17	(10.0)	20	(10.4)	0.9110
			<i>France Info</i>	55	(15.2)	25	(14.8)	30	(15.6)	0.8262
			<i>Le Monde</i>	53	(14.7)	24	(14.2)	29	(15.1)	0.8089
			<i>Le Figaro</i>	21	(5.8)	12	(7.1)	9	(4.7)	0.3284
			<i>Alter Info</i>	1	(0.3)	1	(0.6)	0	(0.0)	0.4681
			<i>Alternative Santé Initiative</i>	50	(13.9)	18	(10.7)	32	(16.7)	0.0987
			<i>Citoyenne</i>	12	(3.3)	5	(3.0)	7	(3.7)	0.7163
			Other national press	69	(19.1)	31	(18.3)	38	(19.8)	.7269
			Other regional press	27	(7.5)	11	(6.5)	16	(8.3)	0.5108
			Other	44	(12.2)	23	(13.6)	21	(10.9)	0.4387
		Does not know	11	(3.1)	4	(2.4)	7	(3.7)	0.4805	
	(If has already searched for information) After having had all this information, were you able to take a decision regarding the HPV vaccination?								<0.0001	
		Yes	434	(80.8)	232	(94.3)	202	(69.4)		
		No	102	(19.0)	14	(5.7)	88	(30.2)		
		Does not know	1	(0.2)	0	(0.0)	1	(0.4)		

(Continued)

Table 3. (Continued).

		Total (n=1102)		Vaccinated daughters (n=425)		Unvaccinated daughters (n=677)		P value
		n	(%)	n	(%)	n	(%)	
HPV is very rare	True	211	(19.1)	47	(11.1)	164	(24.2)	<0.0001
	False	870	(78.9)	375	(88.2)	495	(73.1)	
	Does not know	21	(1.9)	3	(0.7)	18	(2.7)	
A person could have HPV for many years without knowing it	True	1024	(92.9)	402	(94.6)	622	(91.9)	.2073
	False	69	(6.3)	21	(4.9)	48	(7.1)	
	Does not know	9	(0.8)	2	(0.5)	7	(1.0)	
Having sex at an early age increases the risk of getting HPV	True	516	(46.8)	195	(45.9)	321	(47.4)	0.7527
	False	565	(51.3)	223	(52.5)	342	(50.5)	
	Does not know	21	(1.9)	7	(1.6)	14	(2.1)	
Men cannot get HPV	True	231	(21.0)	81	(19.1)	150	(22.2)	0.0909
	False	851	(77.2)	340	(80.0)	511	(75.5)	
	Does not know	20	(1.8)	4	(0.9)	16	(2.4)	
The HPV vaccines offer protection against all sexually transmitted infections	True	36	(3.3)	13	(3.0)	23	(3.4)	0.7946
	False	1058	(96.0)	410	(96.5)	648	(95.7)	
	Does not know	8	(0.7)	2	(0.5)	6	(0.9)	
The HPV vaccines are most effective if given to people who've never had sex	True	846	(76.8)	355	(83.5)	491	(72.5)	<0.0001
	False	235	(21.3)	67	(15.8)	168	(24.8)	
	Does not know	21	(1.9)	3	(0.7)	18	(2.7)	
A person who has been vaccinated against HPV can still develop cervical cancer	True	900	(81.7)	346	(81.4)	554	(81.8)	0.7852
	False	186	(16.9)	74	(17.4)	112	(16.6)	
	Does not know	16	(1.5)	5	(1.2)	11	(1.6)	
Girls who have been vaccinated against HPV need Pap test when they are older	True	829	(75.2)	328	(77.2)	501	(74.0)	0.4247
	False	259	(23.5)	93	(21.9)	166	(24.5)	
	Does not know	14	(1.3)	4	(0.9)	10	(1.5)	
You can cure HPV by getting the HPV vaccine	True	217	(19.7)	74	(17.4)	143	(21.1)	.2629
	False	875	(79.4)	348	(81.9)	527	(77.8)	
	Does not know	10	(0.9)	3	(0.7)	7	(1.0)	
HPV can be transmitted through oral sex	True	429	(38.9)	166	(39.1)	263	(38.8)	0.3940
	False	631	(57.3)	247	(58.1)	384	(56.7)	
	Does not know	42	(3.8)	12	(2.8)	30	(4.4)	
HPV can cause oral cancer	True	209	(19.0)	91	(21.4)	118	(17.4)	0.1782
	False	847	(76.9)	314	(73.9)	533	(78.8)	
	Does not know	46	(4.1)	20	(4.7)	26	(3.8)	

(Continued)

Table 3. (Continued).

		Total (n=1102)		Vaccinated daughters (n=425)		Unvaccinated daughters (n=677)		P value		
		n	(%)	n	(%)	n	(%)			
HEALTH SYSTEM AND PROVIDERS- TRUST AND PERSONAL EXPERIENCE	Please indicate to what extent you trust the following sources to tell the truth about vaccinations									
	Pharmaceutical industry									
		Trust	562	(51.0)	251	(59.1)	311	(45.9)	<0.0001	
		Neither trust nor distrust	21	(1.9)	12	(2.8)	9	(1.3)		
		Distrust	514	(46.6)	162	(38.1)	352	(52.0)		
		Does not know	4	(0.4)	0	(0.0)	4	(0.6)		
		Unanswered question	1	(0.1)	0	(0.0)	1	(0.1)		
		Government								
			Trust	465	(42.2)	217	(51.1)	248	(36.6)	<0.0001
			Neither trust nor distrust	19	(1.7)	10	(2.4)	9	(1.3)	
			Distrust	616	(55.9)	198	(46.6)	418	(61.7)	
			Does not know	1	(0.1)	0	(0.0)	1	(0.1)	
			Unanswered question	1	(0.1)	0	(0.0)	1	(0.1)	
		Your attending physician								
			Trust	1062	(96.4)	417	(98.1)	645	(95.3)	0.0376
			Neither trust nor distrust	1	(0.1)	1	(0.1)	0	(0.0)	
			Distrust	36	(3.3)	7	(1.6)	29	(4.3)	
		Physicians in general								
			Trust	1004	(91.1)	402	(94.6)	602	(88.9)	0.0040
			Neither trust nor distrust	7	(0.6)	1	(0.2)	6	(0.9)	
		Pharmacists								
			Trust	947	(85.9)	386	(90.8)	561	(82.9)	.0003
			Neither trust nor distrust	13	(1.2)	4	(0.9)	9	(1.3)	
			Distrust	141	(12.8)	34	(8.0)	107	(15.8)	
		Other health professionals								
			Trust	974	(88.4)	384	(90.4)	590	(87.1)	0.1974
		Neither trust nor distrust	10	(0.9)	3	(0.7)	7	(1.0)		
		Distrust	116	(10.5)	37	(8.7)	79	(11.7)		
		Does not know	1	(0.1)	1	(0.2)	0	(0.0)		
		Unanswered question	1	(0.1)	0	(0.0)	1	(0.1)		
	Scientific researchers									
		Trust	994	(90.2)	398	(93.6)	596	(88.0)	<0.0001	
		Neither trust nor distrust	5	(0.5)	1	(0.2)	4	(0.6)		
		Distrust	100	(9.1)	26	(6.1)	74	(10.9)		
	Mainstream media									
		Trust	353	(32.0)	166	(39.1)	187	(27.6)	<0.0001	
		Neither trust nor distrust	20	(1.8)	11	(2.6)	9	(1.3)		
		Distrust	727	(66.0)	248	(58.4)	479	(70.8)		
	Alternative media									
		Trust	240	(21.8)	80	(18.8)	160	(23.6)	0.1872	
		Neither trust nor distrust	28	(2.5)	14	(3.3)	14	(2.1)		
		Distrust	750	(68.1)	298	(70.1)	452	(66.8)		
		Does not know	83	(7.5)	33	(7.8)	50	(7.4)		
		Unanswered question	1	(0.1)	0	(0.0)	1	(0.1)		

(Continued)

Table 3. (Continued).

RISK/BENEFIT (PERCEIVED/ HEURISTIC)		Total (n=1102)		Vaccinated daughters (n=425)		Unvaccinated daughters (n=677)		P value
		n	(%)	n	(%)	n	(%)	
The HPV vaccine may lead to long-term health problems	Agree	354	(32.1)	93	(21.9)	261	(38.6)	<0.0001
	Neither agree nor disagree	29	(2.6)	6	(1.4)	23	(3.4)	
	Disagree	676	(61.3)	314	(73.9)	362	(53.5)	
	Does not know	42	(3.8)	12	(2.8)	30	(4.4)	
	Unanswered question	1	(0.1)	0	(0.0)	1	(0.1)	
There has not been enough research done on the HPV vaccine	Agree	321	(29.1)	74	(17.4)	247	(36.5)	<0.0001
	Neither agree nor disagree	24	(2.2)	5	(1.2)	19	(2.8)	
	Disagree	704	(63.9)	335	(78.8)	369	(54.5)	
	Does not know	53	(4.8)	11	(2.6)	42	(6.2)	
	Unanswered question	1	(0.1)	0	(0.0)	1	(0.1)	
The HPV vaccine is unsafe	Agree	225	(20.4)	46	(10.8)	179	(26.4)	<0.0001
	Neither agree nor disagree	19	(1.7)	3	(0.7)	16	(2.4)	
	Disagree	831	(75.4)	372	(87.5)	459	(67.8)	
	Does not know	26	(2.4)	4	(0.9)	22	(3.2)	
	Unanswered question	1	(0.1)	0	(0.0)	1	(0.1)	
Vaccinating my daughter against HPV will help protect her against sexually transmitted infections	Agree	412	(37.4)	170	(40.0)	242	(35.7)	0.0944
	Neither agree nor disagree	7	(0.6)	1	(0.2)	6	(0.9)	
	Disagree	678	(61.5)	254	(59.8)	424	(62.6)	
	Does not know	5	(0.5)	0	(0.0)	5	(0.7)	
	Unanswered question	1	(0.1)	0	(0.0)	1	(0.1)	
The HPV vaccine is effective in preventing HPV	Agree	1010	(91.7)	411	(96.7)	599	(88.5)	<0.0001
	Neither agree nor disagree	6	(0.5)	0	(0.0)	6	(0.9)	
	Disagree	77	(7.0)	13	(3.1)	64	(9.5)	
	Does not know	9	(0.8)	1	(0.2)	8	(1.2)	
	Unanswered question	1	(0.1)	0	(0.0)	1	(0.1)	
The HPV vaccine is effective in preventing genital warts	Agree	404	(36.7)	162	(38.1)	242	(35.7)	0.3516
	Neither agree nor disagree	23	(2.1)	5	(1.2)	18	(2.7)	
	Disagree	580	(52.6)	223	(52.5)	357	(52.7)	
	Does not know	95	(8.6)	35	(8.2)	60	(8.9)	
	Unanswered question	1	(0.1)	0	(0.0)	1	(0.1)	
The HPV vaccine is effective in preventing HPV-related cancers	Agree	877	(79.6)	357	(84.0)	520	(76.8)	0.0049
	Neither agree nor disagree	12	(1.1)	4	(0.9)	8	(1.2)	
	Disagree	182	(16.5)	60	(14.1)	122	(18.0)	
	Does not know	31	(2.8)	4	(0.9)	27	(4.0)	
	Unanswered question	1	(0.1)	0	(0.0)	1	(0.1)	
The use of a condom prevents the transmission of HPV infection	Agree	795	(72.1)	312	(73.4)	483	(71.3)	0.8166
	Neither agree nor disagree	4	(0.4)	1	(0.2)	3	(0.4)	
	Disagree	287	(26.0)	107	(25.2)	180	(26.6)	
	Does not know	16	(1.5)	5	(1.2)	11	(1.6)	
	Unanswered question	1	(0.1)	0	(0.0)	1	(0.1)	
The pap smear is sufficient to prevent cervical cancer	Agree	581	(52.7)	233	(54.8)	348	(51.4)	0.1784
	Neither agree nor disagree	2	(0.2)	0	(0.0)	2	(0.3)	
	Disagree	510	(46.3)	191	(44.9)	319	(47.1)	
	Does not know	9	(0.8)	1	(0.2)	8	(1.2)	
	Unanswered question	1	(0.1)	0	(0.0)	1	(0.1)	

(Continued)

Table 3. (Continued).

		Total (n=1102)		Vaccinated daughters (n=425)		Unvaccinated daughters (n=677)		P value		
		n	(%)	n	(%)	n	(%)			
IMMUNIZATION AS A SOCIAL NORM VS. NOT NEEDED/HARMFUL	My friends are getting their daughter vaccinated with the HPV vaccine	Agree	481	(43.6)	251	(59.1)	230	(34.0)	<0.0001	
		Neither agree nor disagree	22	(2.0)	5	(1.2)	17	(2.5)		
		Disagree	442	(40.1)	125	(29.4)	317	(46.8)		
		Does not know	73	(6.6)	21	(4.9)	52	(7.7)		
		Unanswered question	84	(7.6)	23	(5.4)	61	(9.0)		
	Most (other) girls around my daughter 's age are getting vaccinated for HPV	Agree	374	(33.9)	189	(44.5)	185	(27.3)	<0.0001	
		Neither agree nor disagree	28	(2.5)	7	(1.6)	21	(3.1)		
		Disagree	543	(49.3)	186	(43.8)	357	(52.7)		
		Does not know	93	(8.4)	24	(5.6)	69	(10.2)		
		Unanswered question	64	(5.8)	19	(4.5)	45	(6.6)		
	Doctors/health care providers believe vaccinating girls against HPV is a good idea	Agree	942	(85.5)	416	(97.9)	526	(77.7)	<0.0001	
		Neither agree nor disagree	14	(1.3)	1	(0.2)	13	(1.9)		
		Disagree	94	(8.5)	7	(1.6)	87	(12.9)		
		Does not know	17	(1.5)	0	(0.0)	17	(2.5)		
		Unanswered question	35	(3.2)	1	(0.2)	13	(1.9)		
VACCINE/VACCINATION SPECIFIC ISSUES INTRODUCTION OF A NEW VACCINE OR NEW FORMULATION OR A NEW RECOMMENDATION FOR AN EXISTING VACCINE	The HPV vaccine is too recent so we can know if it's safe and reliable	Agree	390	(35.4)	105	(24.7)	285	(42.1)	<0.0001	
		Neither agree nor disagree	16	(1.5)	1	(0.2)	15	(2.2)		
		Disagree	679	(61.6)	315	(74.1)	364	(53.8)		
		Does not know	17	(1.5)	4	(0.9)	13	(1.9)		
DESIGN OF VACCINATION PROGRAM MODE OF DELIVERY	It is complicated to vaccinate my daughter against HPV because it requires 3 steps: see the doctor for the vaccine prescription, go buy the vaccine at the pharmacy, and return to the doctor for the vaccine injection	Agree	240	(21.8)	81	(19.1)	159	(23.5)	0.1486	
		Neither agree nor disagree	5	(0.5)	1	(0.2)	4	(0.6)		
		Disagree	855	(77.6)	343	(80.7)	512	(75.6)		
		Does not know	2	(0.2)	0	(0.0)	2	(0.3)		
	It would be easier to vaccinate my daughter if the doctor had vaccines at his office for vaccinating my daughter the same day	Agree	596	(54.1)	206	(48.5)	390	(57.6)	0.0005	
		Neither agree nor disagree	4	(0.4)	4	(0.9)	0	(0.0)		
		Disagree	502	(45.6)	215	(50.6)	287	(42.4)		

(Continued)

Table 3. (Continued).

		Total (n=1102)		Vaccinated daughters (n=425)		Unvaccinated daughters (n=677)		P value	
		n	(%)	n	(%)	n	(%)		
VACCINATION SCHEDULE	If the HPV vaccine was important, it would have been made mandatory	Agree	402	(36.5)	110	(25.9)	292	(43.1)	<0.0001
		Neither agree nor disagree	7	(0.6)	2	(0.5)	5	(0.7)	
		Disagree	687	(62.3)	310	(72.9)	377	(55.7)	
		Does not know	6	(0.5)	3	(0.7)	3	(0.4)	
	The HPV vaccine has not been made mandatory because it is risky	Agree	159	(14.4)	33	(7.8)	126	(18.6)	<0.0001
		Neither agree nor disagree	19	(1.7)	4	(0.9)	15	(2.2)	
		Disagree	904	(82.0)	384	(90.4)	520	(76.8)	
		Does not know	20	(1.8)	4	(0.9)	16	(2.4)	
	I think my daughter is too young to be vaccinated against HPV	Agree	269	(24.4)	17	(4.0)	252	(37.2)	<0.0001
		Neither agree nor disagree	6	(0.5)	0	(0.0)	6	(0.9)	
		Disagree	823	(74.7)	408	(96.0)	415	(61.3)	
		Does not know	4	(0.6)	0	(0.0)	4	(0.6)	
THE STRENGTH OF THE RECOMMENDATION AND/OR KNOWLEDGE BASE AND/OR ATTITUDE OF HEALTHCARE PROFESSIONALS	Has a doctor or another health professional ever recommended that you vaccinate your daughter against HPV?	Yes	750	(68.1)	373	(87.8)	377	(55.7)	<0.0001
		No	352	(31.9)	52	(12.2)	300	(44.3)	
	Have you asked any questions to your attending doctor about HPV vaccines?	Yes	639	(58.0)	338	(79.5)	301	(44.5)	<0.0001
		No	462	(41.9)	87	(20.5)	375	(55.4)	
		Does not know	1	(0.1)	0	(0.0)	1	(0.1)	
	(If has already asked questions) Were you satisfied with his/her answers?	Yes	580	(80.8)	329	(97.3)	251	(83.4)	<0.0001
		No	58	(9.1)	9	(2.7)	49	(16.3)	
		Does not know	1	(0.1)	0	(0.0)	1	(0.3)	
	(If has already asked questions) Was your attending physician hesitant regarding the vaccine?	Yes	40	(6.3)	4	(1.2)	36	(12.0)	<0.0001
		No	596	(93.3)	333	(98.5)	263	(87.4)	
		Does not know	2	(0.3)	1	(0.3)	1	(0.3)	
		Unanswered question	1	(0.1)	0	(0.0)	1	(0.3)	

^aTotals exceed 100% because multiple responses were coded per participant.

^bQuestion answered by the mothers who heard about the HPV vaccine (n = 1068).

Proportion of correct answers

The highest proportions of incorrect answers to general HPV knowledge were for the questions of HPV as a cause of oral cancer (76.9%), whether HPV can be transmitted through oral sex (57.3%), and whether having sex at a young age increases the risk of HPV infection (51.3%). The highest proportions of correct answers were for the questions of whether the HPV vaccine protects against all sexually transmitted infections (96.0%), whether a person can be infected with HPV for many years without knowing (92.9%), and whether a person who has been vaccinated against HPV can still develop cervical cancer (81.7%) (Figure 3). Significant differences were observed between the mothers of vaccinated daughters and mothers of unvaccinated daughters for the statement “HPV is

very rare” and “HPV vaccines are most effective if given to people who never had sex,” with a higher rate of correct answers in mothers of vaccinated daughters ($p < 0.0001$).

Health system and providers trust. The most trusted source of information about vaccination was their attending physician (96.4%), physicians in general (91.1%), and researchers (90.2%). By contrast, less than half of the respondents trusted the government (42.2%). Significant differences were observed between the mothers of vaccinated daughters and mothers of unvaccinated daughters with a higher trust in the pharmaceutical industry ($p < 0.0001$), the government ($p < 0.0001$), their attending physician ($p = 0.0376$), physicians in general ($p = 0.004$), pharmacists ($p = 0.0003$), researchers, and mainstream media ($p < 0.0001$) among mothers of vaccinated daughters.

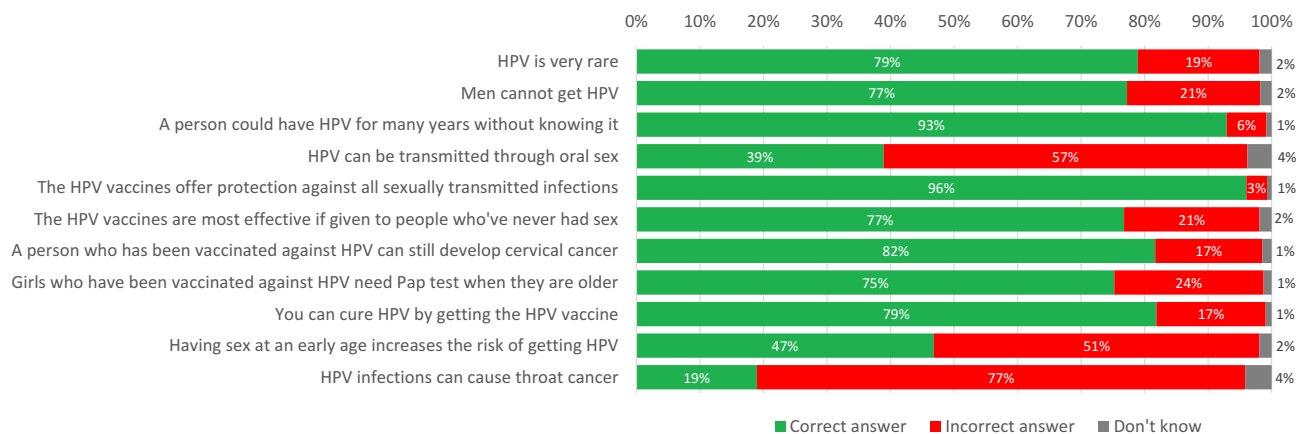


Figure 3. Proportion of correct answers.

Risks and benefits (perceived/heuristic)

Nearly a third (32.1%) of respondents agreed with the statement that the HPV vaccine may lead to long-term health problems and that there has not been enough research done on this vaccine (29.1%). Around a fifth (20.4%) agreed with the statement that the HPV vaccine was unsafe. Significant differences were observed between the mothers of vaccinated and unvaccinated daughters with a higher rate of disagreement with the statements “The HPV vaccine may lead to long-term problems” ($p < 0.0001$), “There has not been enough research done on the HPV vaccine” ($p < 0.0001$), “The HPV vaccine is unsafe” ($p < 0.0001$) among mothers of vaccinated daughters.

The majority of respondents agreed with the statement that the HPV vaccine was effective in preventing HPV (91.7%) and HPV-related cancers (79.6%), while less than 40% of respondents agreed with the statement that the HPV vaccine was effective in preventing genital warts (36.7%). Just over half of respondents (52.7%) agreed with the statement that the Pap smear was sufficient to prevent cervical cancer. Higher rates of agreement with the statements “the HPV vaccine is effective in preventing HPV” ($p < 0.0001$) and “the HPV vaccine is effective in preventing HPV-related cancers” ($p = 0.0049$) were found among mothers of vaccinated daughters.

Immunization as a social norm vs. not needed/harmful

The vast majority of respondents (85.5%) agreed with the statement that doctors/health care providers believe vaccinating girls against HPV is a good idea. Less than half of respondents (43.6%) agreed with the statements that their friends were getting their daughter vaccinated with the HPV vaccine and that most (other) girls around their daughter's age were getting vaccinated for HPV (34.0%). Significant differences were observed between the mothers of vaccinated daughters and mothers of unvaccinated daughters, with a higher rate of agreement in the group of mothers of vaccinated daughters ($p < 0.0001$).

Vaccine/vaccination specific factors

Introduction of a new vaccine or a new formulation or a new recommendation for an existing vaccine

Over a third of respondents (35.4%) agreed with the statement that the HPV vaccine was too recent, so we can know if it is safe and reliable, with a significantly lower rate of agreement among the mothers of unvaccinated daughters ($p < 0.0001$).

Design of vaccination program/mode of delivery

More than half of respondents (54.1%) agreed with the statement that it would be easier to vaccinate their daughter if the doctor had vaccines at their office for same-day vaccination, although only a fifth (21.8%) agreed that it was complicated to vaccinate their daughter against HPV because it required three steps: see the doctor for the vaccine prescription, buy the vaccine at the pharmacy and return to the doctor for the vaccine injection. There was a significantly higher percentage of agreement regarding the same-day vaccination among mothers of unvaccinated daughters ($p = 0.0005$).

Vaccination schedule

Over a third of respondents (36.5%) agreed that if the HPV vaccine were important, it would have been made mandatory, with just under a quarter (24.4%) agreeing with the statement that their daughter was too young to be vaccinated against HPV, and 14.4% agreeing that the HPV vaccine had not been made mandatory because it was risky. Significant differences were observed between the mothers of vaccinated daughters and mothers of unvaccinated daughters, with a lower percentage of agreement with those statements among mothers of vaccinated daughters ($p < 0.0001$).

The strength of the recommendation and/or knowledge base and/or attitude of healthcare professionals

Nearly 70% (68.1%) of respondents have been recommended the HPV vaccine by a doctor or another health professional; 58% have asked questions to their attending physician about HPV vaccination, and the vast majority (90.8%) were satisfied

Table 4. Logistic regression multivariable model showing covariates independently associated with receiving at least one dose of HPV vaccine.

		Adjusted odds ratio	95% confidence interval
Daughter's age	11	0.17	0.10–0.28
	12	0.24	0.16–0.38
	13	0.50	0.33–0.76
	14	Reference	-
I happened to refuse a vaccine for myself (or choose not to get vaccinated)	Yes	0.57	0.40–0.80
	No	Reference	-
HPV is very rare	True	0.49	0.31–0.77
	False	Reference	-
The HPV vaccine is unsafe	Agree	0.42	0.26–0.67
	Disagree	Reference	-
Doctors/health care providers believe vaccinating girls against HPV is a good idea	Agree	4.99	2.09–11.89
	Disagree	Reference	-
I think my daughter is too young to be vaccinated against HPV	Agree	0.16	0.09–0.29
	Disagree	Reference	-
Have you asked any questions to your attending doctor about HPV vaccines?	Yes	3.44	2.40–4.92
	No	Reference	-

with the answers. About 6.3% of the physicians who answered the mothers' questions were hesitant about HPV vaccination. Significant differences were observed between the mothers of vaccinated daughters and mothers of unvaccinated daughters for all those statements, with a higher rate of healthcare professional recommendation and questions asked about HPV vaccines among mothers of vaccinated daughters ($p < 0.0001$).

Factors associated with HPV vaccination uptake

Table 4 shows the results of the multivariate analysis of maternal answers associated with HPV vaccination uptake in their daughters. The multivariate analysis revealed that agreeing with the statement that doctors/health care providers believe vaccinating girls against HPV was a good idea, and having asked questions to the attending doctor about HPV vaccines were associated with a higher HPV vaccine uptake among their daughters (OR = 4.99, 95% CI [2.09–11.89]; and OR = 3.44, 95% CI [2.40–4.92]). The mother's belief that her daughter was too young to be vaccinated against HPV (OR = 0.16, 95% CI [0.09–0.29]) and a lower daughter's age (OR = 0.17, 95% CI [0.10–0.28] for girls aged 11 compared to those aged 14) were found to be strongly inversely associated with HPV vaccination, followed by agreeing with the statement that the HPV vaccine was unsafe (OR = 0.42, 95% CI [0.26–0.67]), identifying as true the statement that HPV was very rare (OR = 0.49, 95% CI [0.31–0.77]), and the mother's refusal of own vaccination (OR = 0.57, 95% CI [0.40–0.80]) (Table 4).

Discussion

Low HPV vaccination uptake in teenage girls is a public health concern in France. We conducted a nationwide telephone survey to document the determinants of this uptake. To our

knowledge, this is the first telephone survey to report the determinants of HPV vaccination uptake in France. It is also the first based on the WHO model exploring vaccine hesitancy¹⁸ adapted to the French context.² In this study, 38.6% of eligible teenage girls were reported to have been vaccinated against HPV. This is consistent with the latest national one-dose HPV vaccination coverage estimate of 40.7% (reported for the year 2020) for girls aged 15 years,⁶ considering that the oldest girls in our study were 14 years old.

Agreeing with the statement that doctors/health care providers believe vaccinating girls against HPV was a good idea, and having asked questions to the attending doctor about HPV vaccination were the most influential factors for the decision of getting the daughters vaccinated against HPV. On the other hand, believing that their daughter was too young to be vaccinated against HPV and their daughter's actual age were the most influential factors concerning the decision of not getting the daughters vaccinated. These data confirm other studies demonstrating the influencing role of health care professionals in mothers' decision-making,^{14,26} as well as the influence of the child's age.^{27,28} Similar to previous studies, we found that mothers harboring HPV vaccine safety concerns were less likely to get their daughters vaccinated,²⁹ in particular among mothers who previously refused a vaccine for themselves.³⁰

Although most knowledge items were answered correctly by at least 75% of the mothers, the level of knowledge regarding the oral transmission of HPV infection and association with oral cancers were low. Of note, less than half of respondents correctly answered the question about the risk of HPV infection associated with a younger sexual debut.

Strengths and limitations

Our study had several strengths, including the representativeness of the study sample using the quota recruitment strategy, the phone survey methodology allowing reaching a large population quite rapidly, and the use of a survey instrument on HPV vaccine hesitancy adapted to the French context.² Some limitations should be considered. First, the survey findings might not be generalizable. Second, no record verification was performed in this study to ascertain the daughters' HPV vaccination status or administration of earlier childhood vaccines. However, the parental interview is a common method of measuring vaccination status in adolescents, and recall bias is likely limited as the survey was conducted close to the age recommended for HPV vaccination. Furthermore, only one other vaccine is currently recommended for the French adolescent general population (diphtheria-tetanus-acellular pertussis-inactivated polio), except catch-up vaccinations. Third, our sample was constituted only of mothers. While it would have been interesting to also include fathers' opinions, in the vast majority of cases, mothers have the primary decision-making power about HPV vaccination, as is usually the case regarding their daughters' overall reproductive health matters.^{31–33} Fourth, an inherent weakness of self-reporting is social desirability, which tends to give answers that are thought to be more socially acceptable.

Practical implications

Our study findings have practical implications for designing interventions to increase HPV vaccine uptake in France. They point to the essential role of health care providers in influencing HPV vaccination. Health care providers, family doctors, in particular, have a strong normative function and are trusted by the population, and mothers should be encouraged to seek advice from them. This could be achieved by introducing a consultation offered to mothers of girls turning 11, where they would be offered the opportunity for counseling by their attending physician about the importance of vaccinating their daughter at that age against a virus that is very common, with a vaccine that has been proven to be safe. Mothers who have already refused a vaccine for themselves could be particularly targeted. Such dedicated HPV prevention-focused-visit could also be used to raise awareness about the oral transmission of HPV and the risk of oral cancer. Moreover, our survey reveals that less than 70% of the mothers have been recommended the HPV vaccine by a physician or another health professional, so there is room for improvement. This emphasizes the importance of training to improve health professional recommendation of HPV vaccination as well as accurate and consistent messaging about the efficacy of HPV vaccines. In addition, our findings can also inform communication campaigns to address public awareness and knowledge about HPV, its link with cancers, and its prevention.

Conclusion

We have identified important determinants associated with HPV vaccine uptake in France. Interventions designed to improve HPV vaccine uptake should be tailored to address these determinants; in particular, the role of health care providers should be reemphasized, and wrong beliefs about the daughter's age concerning the need for HPV vaccination should be corrected by relevant communication strategies.

Acknowledgments

We thank the respondents who participated in the phone survey.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Author's contributions

FD, PC and OL had designed the study. FD had performed the data analysis, the redaction of the manuscript, and the revision process of this paper. IPSOS have participated in the revision process and the redaction of the manuscript. All authors have approved the final manuscript. All authors have approved the final manuscript. MSD had no role in the design of the study or the writing of the manuscript.

Ethical approval statement

This study was approved by the French Institute of Health Data (INDS: Institut National des Données de Santé) as an observational study (category MR-4 of Jardé law), and its database was authorized by the French National Committee for Data Protection (CNIL) (n° 920031), dated 11/12/

2020). The Ethics Committee of Inserm also approved this study. Participants received General Data Protection Regulation (GDPR) mentions and were informed about their right to anonymization, confidentiality, and withdrawal from the study with no adverse consequences.

Funding

This work was supported by a PhD fellowship from the French National Institute of Cancer awarded to FD and a grant from Merck Investigator Studies Program. The other authors received no specific funding for this work.

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TROISIEME PARTIE : ANALYSE SECONDAIRE DES DONNEES DE L'ENQUÊTE

VACCINOSCOPIE

CHAPITRE 5 – ARTICLE III ASSOCIATION ENTRE LE RECOURS A INTERNET COMME SOURCE D’INFORMATION SUR LA VACCINATION ANTI-HPV ET LA COUVERTURE VACCINALE HPV EN FRANCE

Dans un contexte de préoccupation croissante concernant l’influence de la mésinformation (information trompeuse diffusée sans un but malveillant) et de la désinformation (tentatives délibérées de manipuler en communiquant des informations trompeuses) sur l’HV, nous avons exploré l’association entre le recours à Internet chez les mères d’adolescentes comme source d’information sur une vaccination pour laquelle elles hésitaient, et le statut de vaccination anti-HPV de leurs filles. L’étude de ce type de liens dans l’enquête *ad hoc* (Article II) était difficile du fait de l’effectif de mères hésitantes trop insuffisant pour permettre des analyses multivariées. Nous avons donc procédé à une analyse secondaire de données, en utilisant les données de Vaccinoscopie[®], une enquête réalisée annuellement depuis 2008 portant sur les opinions et les attitudes des mères françaises d’enfants de différentes tranches d’âge, vis-à-vis de la vaccination de leurs enfants.

À partir des données poolées de Vaccinoscopie[®] de 2015 à 2018 (4 échantillons indépendants) concernant les mères de filles âgées de 14 et 15 ans, nous avons réalisé une régression logistique multivariée et des modèles d’équations structurelles. La régression logistique ajustée sur la recommandation de la vaccination anti-HPV par le médecin, les attitudes à l’égard des vaccins en général, la perception de l’utilité du vaccin anti-HPV, le niveau d’éducation de la mère, la région de résidence et l’année de l’enquête montrait que le recours à Internet était significativement associé à une moindre vaccination anti-HPV (OR= 0,66 ; IC95%, 0,47-0,91). Le modèle d’équations structurelles a confirmé l’effet négatif de l’utilisation d’Internet, en révélant les liens mécanistiques sous-jacents à la moindre couverture vaccinale du vaccin anti-HPV.



Effect of Internet use for searching information on vaccination on the uptake of human papillomavirus vaccine in France: A path-analysis approach

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ARTICLE INFO

Keywords:

HPV vaccine
Vaccine hesitancy
Internet
Sources of information

ABSTRACT

Internet is a popular source of information regarding vaccination. This study aimed to determine whether there is a negative association between Internet use among French vaccine-hesitant mothers and HPV vaccine uptake by their daughters, and to gain insight into the pathways that would link Internet use to the lack of HPV vaccine uptake. We conducted a pooled cross-sectional analysis across the 2015, 2016, 2017 and 2018 Vaccinoscopie® Survey. Multivariate logistic regression and path models were used in the analysis. The study sample included a total of 2038 respondent mothers. Of those, 89 (4.4%) declared having never been in the situation of searching for information regarding a vaccination they had hesitated about, leaving 1949 mothers for the present analysis. Approximately 24% (466/1949) of the mothers declared using the Internet as a source of vaccine information. In multivariate logistic regression adjusted for physician recommendation of HPV vaccination, attitudes towards vaccines in general, perception of HPV vaccine usefulness, maternal level of education, region of residence, and the survey year, the use of Internet by the mothers was significantly associated with a lower HPV vaccination among their daughters (adjusted odds ratio (aOR), 0.66; 95% confidence interval (CI), 0.47–0.91). Path analysis further confirmed the negative effect of Internet use ($\beta = -0.10$, standard error (SE) = 0.02, $P < 0.0001$), highlighting how the Internet plays a detrimental role in HPV vaccine uptake through a lower perceived level of HPV vaccine usefulness, a lower perceived level of information on childhood vaccination, and unfavorable attitudes towards vaccination in general.

1. Introduction

Since its introduction in the French immunization program in 2007, the initiation rate of HPV vaccination in girls aged 15 years only reached 29.4% at its highest point, in 2018 (*Données de couverture vaccinale papillomavirus humains (HPV) par groupe d'âge, 2020*). The same year, the coverage rate for a two-dose regimen among 16-year-olds girls was estimated at 23.7% (*Fonteneau et al., 2019*). This figure represents less than half of the target set for a two-dose regimen (*Plan Cancer 2014–2019 - Ref : PLANKPNRT14 | Institut National Du Cancer, 2018*). The HPV vaccine appears among those viewed less favorably in 2016 in France (*GAUTIER et al., 2016*), against the general background of a noticeable rise in vaccine hesitancy (*Larson et al., 2016*), which may be

viewed as pretty astonishing in Pasteur's country.

Internet has become a popular source of information regarding health-related topics, and HPV vaccine makes no exception. Indeed, this vaccination is a popular topic among "googling" searches for vaccine-preventable infectious diseases (*Bragazzi et al., 2017*). The Eurobarometer Survey on the European citizens' digital health literacy conducted in 2014 showed that around one out of two respondents in France have used the Internet to search for health-related information within the last year, 40% of whom indicated looking on behalf of their children. The French National Health Barometer Survey conducted the same year showed that as many as 69% of the French population used the Internet to search for health-related topics (*SPF. Quelle utilisation d'Internet dans la recherche d'informations santé ?, 2020*).

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<https://doi.org/10.1016/j.ypmed.2021.106615>

Received 16 December 2020; Received in revised form 18 March 2021; Accepted 9 May 2021

Available online 11 May 2021

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Whilst the Internet represents a remarkable tool for health information dissemination, it also provides a medium where misinformation (misinformed advice) and disinformation (deliberate falsehoods) (Grimes et al., 2020) are easily introduced, accessed and spread. This has become more problematic as we live in an era of “post-truth” (defined by Oxford dictionary as “circumstances in which objective facts are less influential in shaping public opinion than appeals to emotion and personal belief” (Dib et al., 2021)). In the use of social media (such as Facebook) and messaging platforms (such as WhatsApp) allows instant global dissemination of false information (Larson, 2018). This comes with its own share of challenges in the health information field. For example, one study analyzing the reach of online disinformation in Europe (9) showed that the most popular false news website in France, a website claiming to “vulgarize information on health and wellness”, had received approximately as many interactions on social media (shares, comments, reactions) as five prominent and reliable French news websites combined (Fletcher et al., 2018). The spread of misinformation on the benefits and risks of vaccines has certainly been fueling vaccine hesitancy (McKee and Middleton, 2019) (Carrieri et al., 2019) (Basch et al., 2017) (Hoffman et al., 2019), although it remains to be seen to what extent this translates into the decision to vaccinate. The World Health Organization has listed the “uncontrolled dissemination of misinformation” - including in the field of vaccination - among its urgent health challenges for the next decade (Urgent health challenges for the next decade, 2020).

HPV vaccination in France provides an interesting case study of challenges facing vaccination in an era of online mis/disinformation, as the introduction of the HPV vaccine in the French vaccine immunization program has coincided more or less with the rise of social media utilization. Furthermore, HPV vaccination in France is delivered opportunistically through healthcare providers, with no dedicated school-based vaccination program. Therefore, parents who have not heard about the HPV vaccine from their healthcare providers may have questions to be answered about this vaccination.

In this context, we aimed to determine whether there was a negative association between Internet use among French vaccine-hesitant mothers and HPV vaccine uptake by their daughters, and to gain insight into the pathways that would link Internet use to a lack of HPV vaccine uptake. Such an understanding is required to fully appreciate the impact of the Internet on the uptake of HPV vaccination in France, and provide relevant data for policymakers and practitioners to take necessary action.

2. Methods

2.1. Data source

This study was carried out using the data acquired from the 2015, 2016, 2017 and 2018 Vaccinoscopie® Survey modules targeting mothers of girls aged 14 and 15 years. The methodology of this survey commissioned by GlaxoSmithKline (GSK) and conducted by IDM Families, an independent market research and polling company, has been published in detail elsewhere (Stahl et al., 2013) (Denis et al., 2014). Briefly, Vaccinoscopie® is a pluriannual web-based survey among French representative quota samples of mothers, with respect to the socio-professional category (SPC) of the reference person in the household, the number of children, and the geographic region of residence, per child's years of age. It has been designed to monitor the dynamics of childhood vaccine coverage, and perception and attitudes towards vaccination in France. A new sample of study participants is interrogated from one year to another.

2.2. Study variables

The dependent variable was HPV vaccine initiation (i.e., the receipt of at least one dose of HPV vaccine) in the 14–15 year-old daughter. The

exposure of interest was “Internet use by the mother” (yes/no), given the mother's answers to the question “When you hesitate about a vaccine, what source(s) of information do you turn to to decide whether or not to have your child vaccinated?”. This question had a multiple-choice response format. For the purpose of this analysis, we derived a dummy variable for each source of information.

Guided by reviews of the literature on the factors associated with HPV vaccine uptake (Kessels et al., 2012) (Rodriguez et al., 2020) (Newman et al., 2018), we took into account the following relevant factors in the association between the exposure of interest and the dependent variable: 1) mother's demographics and socioeconomic status: age, level of education, household income and geographical region of residence; 2) maternal attitudes towards vaccination in general (response to the single answer question “How do you feel about vaccines?”: in favor of vaccinating against all serious diseases if there are vaccines/ opposed to all vaccines/ no opinion), and perception of HPV vaccine usefulness (response to the single answer question “For each of these diseases (cervical cancer), supposing there was a vaccine, would vaccinating your child seem: indispensable/ useful/ not very useful/ useless/ do not know”); 3) physician recommendation of HPV vaccination (response to the single answer question “Has your doctor advised you to have your child vaccinated against HPV”: yes/ no/ do not remember); 4) perceived level of information regarding childhood vaccination (response to the single answer question: “Do you think you are well informed about child vaccinations?”: not at all well-informed/ rather not well-informed/ rather well-informed/ fully informed and); and 5) daughter's usual medical follow-up setting (response to the single answer question: “Your child is followed by : a general practice/ a pediatrician practice/ a free preventive clinic for mother and infants”).

2.3. Statistical analysis

We conducted a pooled cross-sectional analysis across the four aforementioned years of the Vaccinoscopie® Survey. We combined these data sets in order to achieve a large enough sample size to perform multivariate analysis. The data sets included data weighted according to the French general population census of the French National Institute for Statistics and Economic Studies. Although the data were generated each year from a quota sample and not from a random probability one, we decided to conduct inferential statistical analysis commonly used to make inferences about the larger population from which the sample was drawn. Since it is difficult to guarantee that the study sample is representative for characteristics other than those for which quotas units have been set, inferential statistical measures (95% confidence intervals (95% CI) and *P*-values) are meant only for indicative purposes in the present study.

2.3.1. Logistic regression analysis

We conducted a descriptive analysis of study variables followed by a bivariate analysis, where HPV vaccine initiation was regressed on the covariates, which were assessed for multicollinearity beforehand. We then estimated a multivariate logistic regression model using a backward selection process, with a threshold of $P = 0.20$ for a variable to stay in the model. The full model included the year of the Vaccinoscopie® Survey, in addition to the aforementioned exposure variable and covariates. For ease of interpretation, we used the grouping of response modalities required by the path analysis described below. The goodness-of-fit of the final model was tested using the information matrix test.

Crude and adjusted odds ratios were calculated with their 95%CI.

2.3.2. Path analysis

We formulated a general hypothetical model for how Internet use, attitudes towards childhood vaccination, perceived usefulness of HPV vaccine, and the other above mentioned factors might be interrelated to HPV vaccine uptake. The hypothesized interrelationships between the

variables are depicted in a conceptual model in Fig. 1. To test our proposed hypothetical model, we applied path analysis, a form of statistical modeling consisting of a set of linear equations that simultaneously assess the relationships between the measured variables. We conducted these analyses using the PROC CALIS procedure in SAS with the weighted least squares (WLS) estimation method, which handles categorical variables (Browne, 1984). Nominal variables with more than two categories of response modalities (geographic area of residence, perceived usefulness of HPV vaccine, attitudes towards childhood vaccination, and perceived level of information) were dichotomized by grouping responses modalities, as the PROC CALIS procedure handles continuous, binary and ordinal variables, but not nominal variables.

We first tested the hypothesized conceptual model, which included all possible associations between variables (Fig. 1). Afterward, we reviewed the path coefficients to see if any of the paths in the initial model should be deleted, and we dropped non-significant associations from the original hypothetical model. The resulting model, called the “final model”, was then re-estimated (Fig. 2). We used standardized regression coefficients (β) to assess the strength of association between the variables (effect). Total, direct, and indirect effects of each variable on HPV vaccine uptake were estimated (a direct effect represents a path coefficient, an indirect effect represents the product of sequential path coefficients, and a total effect represents the sum of direct and indirect effects).

We used Cohen’s recommendations to interpret the relative size effect of the standardized coefficients (a β value varying around 0.1 is considered as low, a value varying around 0.3 as moderate, and a value greater than 0.5 as large) (Cohen, 1992). To evaluate the goodness-of-fit between the final model and the data, we used the comparative fit index (CFI), the standardized root mean square residual (SRMR), and the root-mean-square error of approximation (RMSEA) including 90%-confidence interval (90%CI). Values for CFI >0.94 suggest a good fit between data and path models, whereas SRMR and RMSEA values less than 0.090 suggest acceptable fit, and values less than 0.055 suggest good model fit (Hatcher PhDL, O’Rourke RDPsychN, n.d.).

All statistical analyses were performed using SAS (version 9.4, SAS Institute Inc., Cary North Carolina), and *p*-values below 0.05 were considered statistically significant.

2.4. Ethics statement

The Vaccinoscopie® Survey is a healthcare market research undertaken by professional market researchers (IDM families) on behalf of a pharmaceutical company (GSK). It has been conducted in accordance with the legal and ethical guidelines issued jointly by the European Society for Opinion and Market Research (ESOMAR) and the International Chamber of Commerce (ICC), as well as the French law on computer data and freedom. It does not require ethical committee review. It warrants the total confidentiality of collected data, which, in any case, cannot be used to any other end than the ones defined for the survey. Furthermore, each participant may stop answering the questionnaire at any time and refuse that some pieces of data to be processed. Study participants consented to IDM terms of use and privacy policy, which indicated that their data would be used anonymously. The Vaccinoscopie® data file was approved by the French National Committee for Data Protection (n°1,551,077, dated 08/12/2011).

3. Results

3.1. Study sample

The global Vaccinoscopie® Survey data set (2015 to 2018) included in total 2038 different respondent mothers. Of those, 89 (4.4%) declared having never been in the situation of searching for information regarding a vaccination they had hesitated about, leaving 1949 records for the present study. The mean (+/– SD) age of the survey respondents was 43.5 (±4.9) years. Approximately half of the participants had a level at high school diploma (baccalaureate) or two-year post high school diploma (49.6%) and had a monthly household income of over 2700 Euros (48.0%). The full characteristics of the study participants, together with their responses to the survey questionnaire, can be found in Table 1.

3.2. HPV vaccine coverage

The mean uptake of the first dose of HPV vaccine over the study period was 27.7% (23.7% in 2015, 23.5% in 2016, 30.3% in 2017 and 33.1% in 2018). The full 2-dose regimen was completed in 18.7% of

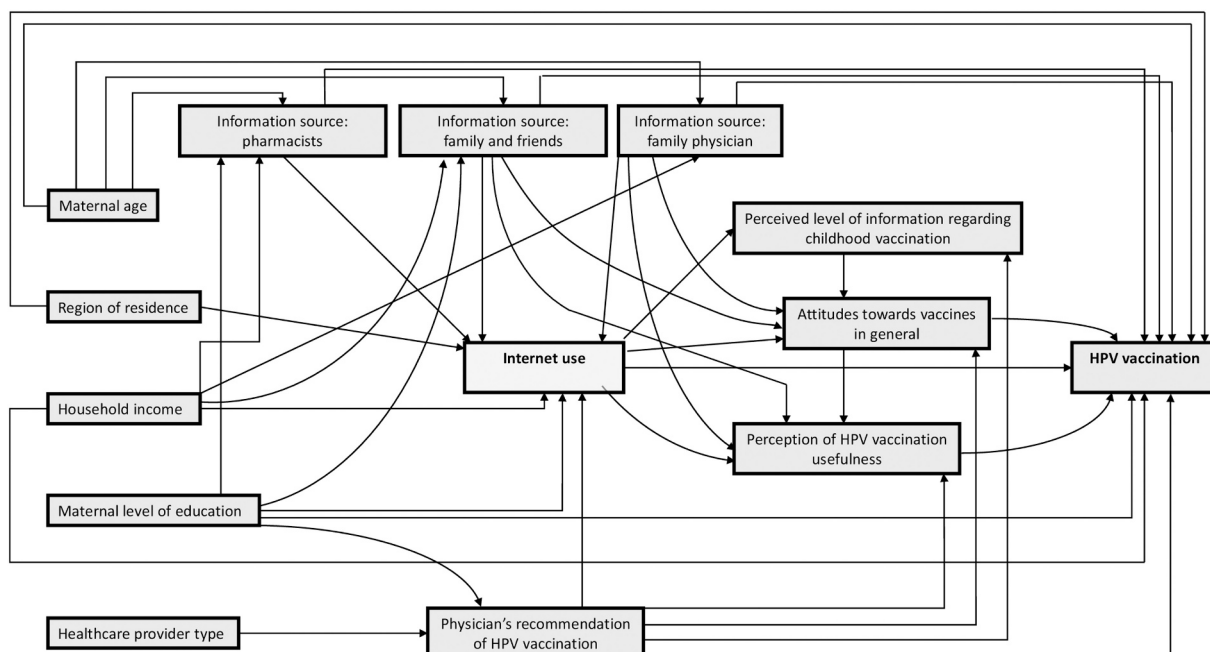


Fig. 1. Conceptual model with the hypothesized interrelationships between the variables.

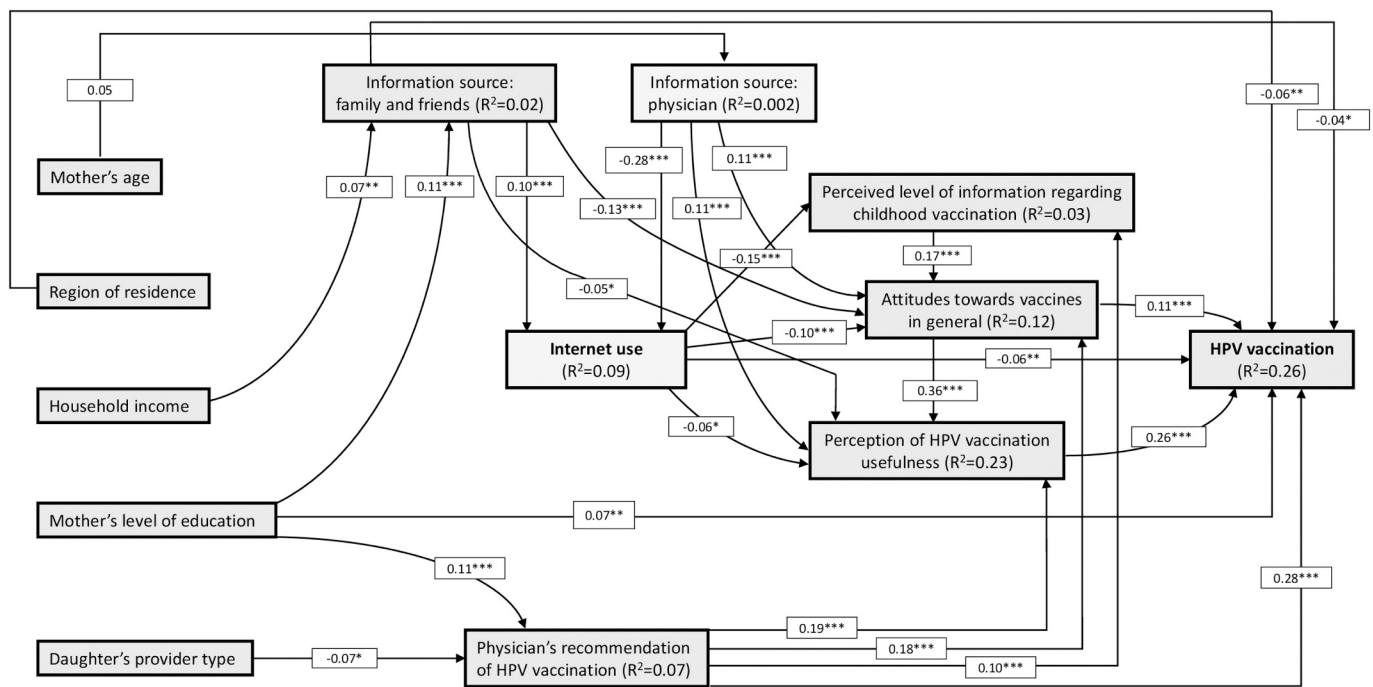


Fig. 2. Final model of associations with standardized path coefficients.

their daughters (14.4% in 2015, 16.1% in 2016, 21.3% in 2017 and 22.6% in 2018).

3.3. Internet and other sources of vaccine information

Approximately 24% of the mothers declared using the Internet as a source of vaccine information. This medium was the third most frequently cited source of information reported by the mothers, after the family physician (91.8%) and the relatives/family/friends (26.1%), and before the pharmacist (14.9%) (Table 1).

3.4. Logistic regression analysis

The uptake of the first dose of HPV vaccine was lower among daughters of the mothers who indicated using the Internet as a source of vaccine information compared to daughters of those who indicated not using it: 18% compared to 31%, respectively (P < 0.0001). In multivariate analysis adjusted for physician recommendation of HPV vaccination, attitudes towards vaccines in general, perception of HPV vaccine usefulness, maternal level of education, geographical region of residence, and the year of the survey, the use of the Internet as a source of vaccine information was significantly associated with a lower HPV vaccination (aOR = 0.66; 95% CI, 0.47–0.91) (Table 2).

3.5. Path analysis

The results of the path analysis modeling are depicted in Fig. 2. The estimated « final model » shows a good overall fit: CFI = 0.97, SRMR = 0.03 and RMSEA = 0.02, 90%CI (0.02–0.03). Overall, 26% of the variance in HPV vaccine uptake was explained by the model. Table 3 shows the direct, indirect, and total effects of Internet use and other sources of information on HPV vaccine uptake (effects of other variables are reported in the Supplementary Table 1). The total effect of Internet use on HPV vaccine uptake was proved to be significant and negative. It is considered as low (β = -0.10, Standard Error (SE) = 0.02, P < 0.0001), and represents in absolute value 27% of the highest total effect on HPV vaccine uptake, which is observed with the physician recommendation of HPV vaccination (β = 0.37, SE = 0.01, P < 0.0001) (Table 3 and

Supplementary Table 1).

A total of 4 paths were significant to explain the relationship between Internet use and HPV vaccine uptake:

- 1) Internet use -> perceived level of information regarding childhood vaccination-> attitudes towards vaccines in general -> perception of HPV vaccination usefulness -> HPV vaccination;
- 2) Internet use -> perceived level of information regarding childhood vaccination -> attitudes towards vaccines in general -> HPV vaccination;
- 3) Internet use -> attitudes towards vaccines in general -> perception of HPV vaccination usefulness -> HPV vaccination;
- 4) Internet use -> attitudes towards vaccines in general -> HPV vaccination (Fig. 2).

Internet use was also found to mediate the negative effect of the « family and friends » source of information on HPV vaccine uptake (β = -0.10, SE = 0.02, P < 0.0001), as Internet use was positively associated with this source of information (β = 0.10, SE = 0.02, P < 0.0001). In reverse, Internet use was negatively associated with the «family physician» source of information (β = -0.28, SE = 0.03, P < 0.0001), which was found to have a total positive effect on HPV vaccine uptake (β = 0.08, SE = 0.01, P < 0.0001).

4. Discussion

The spread of false information online and its influence on vaccination have been frequently addressed in the literature. However, the quantification of the effect of Internet use as a resource for answering questions on vaccination on actual vaccine uptake is much less documented. We found that maternal search for vaccine information in the Internet was associated with a lower HPV vaccination initiation by their daughters. This result is congruent with the findings of the 2016 French National Health Barometer, in which parents of children aged 1 to 15 who relied uniquely on the Internet for information on vaccination were less likely to vaccinate their children against diphtheria, tetanus, and pertussis (Gautier et al., 2017). Path analysis further confirmed the negative effect of Internet use on HPV vaccine uptake (β = -0.10, SE =

Table 1
Distribution of study variables among 1949 vaccine hesitant mothers (Vaccinoscopia® Survey 2015 to 2018).

	Unweighted data		Weighted data	
	Total		Total	
	(N = 1949)		(N = 1835)	
	n or mean	(% or SD)	n or mean	(% or SD)
Demographics				
Maternal age (years) ^a	43.3	(4.9)	43.5	(4.9)
Monthly household income (euros) ^b				
<1700	323	(16.9%)	311	(17.3%)
[1700–2700]	660	(34.5%)	625	(34.7%)
>2700	930	(48.6%)	865	(48.0%)
Educational attainment				
Below high school diploma	395	(20.3%)	379	(20.7%)
High school diploma – Two-year post high school diploma	961	(49.3%)	911	(49.6%)
Beyond two-year post high school diploma	593	(30.4%)	545	(29.7%)
Geographic region of residence				
Greater Paris area	319	(16.4%)	295	(16.1%)
Ile de France	330	(16.9%)	362	(19.7%)
Center-East	275	(14.1%)	238	(13.0%)
East	169	(8.7%)	156.6	(8.5%)
North	141	(7.2%)	126	(6.9%)
West	304	(15.6%)	247	(13.5%)
South-West	206	(10.6%)	182	(9.9%)
Mediterranean	205	(10.5%)	229	(12.5%)
Attitudes towards vaccines in general				
In favor of vaccinating against all serious diseases if there are vaccines	1315	(67.5%)	1234	(67.2%)
In favor of minimizing the number of vaccinations	608	(31.2%)	574	(31.3%)
Opposed to all vaccines	9	(0.5%)	9	(0.5%)
No opinion	17	(0.9%)	18	(0.9%)
Perception of HPV vaccination usefulness				
Indispensable	697	(35.8%)	651	(35.5%)
Useful	622	(31.9%)	589	(32.1%)
Not very useful	244	(12.5%)	230	(12.5%)
Useless	140	(7.2%)	135	(7.4%)
Does not know	246	(12.6%)	229	(12.5%)
Physician` recommendation of HPV vaccination				
Yes	1282	(65.8%)	1199	(65.3%)
No	566	(29.0%)	537	(29.3%)
Does not remember	101	(5.2%)	98	(5.3%)
Perceived level of information regarding childhood vaccination				
Not at all well-informed	32	(1.6%)	30	(1.7%)
Rather not well- informed	280	(14.4%)	267	(14.6%)
Rather well-informed	1347	(69.1%)	1266	(69%)
Fully informed	290	(14.9%)	271	(14.8%)
Information sources				
Internet	466	(23.9)	439	(23.9)
Family physician	1789	(91.8)	1686	(91.8)
Pharmacist	283	(14.5%)	273	(14.9%)
Relatives/family/friends	508	(26.1%)	479	(26.1%)
Other	71	(3.6%)	66	(3.6%)
Daughter`s healthcare provider type				
Free preventive clinic for mothers and infants	7	(0.4%)	8	(0.4%)
General practice	1790	(91.8%)	1687	(91.9%)
Pediatrician practice	152	(7.8%)	140	(7.6%)
HPV vaccination status				
At least one dose	552	(28.3%)	509	(27.7%)
Not vaccinated	1397	(71.7%)	1327	(72.3%)

Abbreviations: HPV, human papillomavirus.

^a 4 missing values.

^b 36 missing values.

0.02, $P < 0.0001$). The analysis further revealed how Internet mediated its effect through a lower perceived level of information on childhood vaccination (which could be explained by the confusion resulting from contradicting pieces of information found on the Internet), unfavorable attitudes towards vaccination in general, and a lower perceived level of HPV vaccine usefulness. This effect runs contrary to the positive effect of obtaining information from a family physician ($\beta = 0.08$, $SE = 0.01$, $P < 0.0001$), through more favorable attitudes towards vaccines and higher perception of HPV vaccine usefulness.

The Internet affords unprecedented opportunities for finding answers to health questions, but also poses some challenges for its users. Parents should take complete responsibility to base their vaccination decision on accurate information, wisely and consciously choosing their sources of information whenever questions arise as to the benefit, efficacy or safety of any given vaccine. Until each and every parent is equipped with the necessary knowledge and skills to interrogate the Internet safely, healthcare providers remain the most suitable and accurate sources of information on the topic of vaccination, and parents should be encouraged to seek information primarily from them. Interventions should be designed to empower parents to better recognize mis/disinformation, and consult only reputable sources of information if they wish to go online. In any case, the need to question the veracity of the information retrieved online should be emphasized, as it is sometimes not easy to distinguish between trustworthy and questionable websites.

4.1. Strengths and limitations

To the best of our knowledge, this is the first study investigating the association between Internet use as a source of information by vaccine-hesitant mothers and the uptake of HPV vaccine by their daughters. A key strength of this study is the use of path analysis to examine specific pathways by which Internet use among vaccine-hesitant mothers is associated with a lack of HPV uptake by their daughters, beyond the traditional logistic regression approach which only allows quantification of the association between two variables, all others things being equal.

The following limitations should be considered when interpreting the results of this study. First, the exposure measure was related to the behavior of seeking online information for vaccines in general, rather than HPV vaccine specifically. Nevertheless, only HPV vaccination is recommended in the target`s age group of the daughters in the surveyed sample, hence most probably the source of questioning among their mothers. Second, the quota sampling approach employed for the recruitment of the mothers in the Vaccinoscopia® Survey allows a study sample that is representative of the general population with respect to specific criteria (SPC, geographic region of residence and number of children), but does not ensure that it is representative of the general population with regard to other criteria. Therefore, caution is warranted when generalizing the results of the responding sample to the broader French population. In particular, confidence intervals and P -values have to be very carefully interpreted: they would apply if the data were obtained from a random probability sample. Furthermore, there is a possibility of selection bias through self-selection of participants, and also because the Internet population might not be fully representative of the general population (excluding the most disadvantaged groups and/or the non-French-speaking immigrants). Third, some factors possibly intervening in the process unfolding between Internet use and HPV vaccine uptake were not questioned in Vaccinoscopia® Survey and could not be introduced in our model. In a Delphi survey based on the World Health Organization Strategy Advisory Group of Experts framework of vaccine hesitancy, we have shown that the factors possibly determining HPV vaccine uptake in France are numerous (Dib et al., 2020). These include, for example, vaccine knowledge, perception of the safety of the vaccine, and trust issues towards the health system. This may explain the direct effect observed of Internet use on HPV vaccine

Table 2
Results of bivariate and multivariate logistic regression analysis exploring the factors associated with HPV vaccination (weighted data).

	Vaccinated daughters (N = 508)		Unvaccinated daughters (N = 1327)		Crude OR	95% CI	Adjusted OR *	95% CI
	n or mean	(% or SD)	n	(% Or SD)				
Vaccinoscopie® Survey year								
2018	159	(33.1)	321	(66.9)	Ref.			
2017	136	(30.3)	314	(69.7)	0.88	0.67–1.16	1.00	0.71–1.41
2016	107	(23.5)	350	(76.5)	0.62	0.46–0.83	0.64	0.45–0.91
2015	106	(23.7)	342	(76.3)	0.63	0.47–0.84	0.66	0.46–0.94
Demographics								
Maternal age (years) ^a	43.6	(4.6)	43.5	(5.0)	1.00	0.98–1.02	–	–
Household income (euros per month) ^b								
<1700	74	(23.7)	238	(76.3)	Ref.			
[1700–2700]	177	(28.3)	448	(71.7)	1.27	0.93–1.74	–	–
>2700	250	(28.9)	615	(71.1)	1.31	0.97–1.77	–	–
Educational attainment								
Below high school diploma	78	(20.5)	301	(79.5)	Ref.			
High school diploma – Two-year post high school diploma	251	(27.6)	660	(72.4)	1.47	1.10–1.96	1.40	0.99–1.98
Beyond two-year post high school diploma	179	(32.9)	366	(67.1)	1.90	1.40–2.58	1.81	1.24–2.64
Geographic region of residence								
Regions other than Ile de France	424	28.8	1049	71.2	Ref.			
Ile de France	84	23.3	278	76.7	0.75	0.57–0.98	0.76	0.55–1.04
Attitudes towards vaccines in general								
In favor of minimizing the number of vaccinations or opposed to all vaccines or no opinion	55	(9.2)	546	(90.8)	Ref.			
In favor of vaccinating against all serious diseases if there are vaccines	453	(36.7)	781	(63.3)	5.70	4.23–7.69	2.34	1.64–3.33
Perception of HPV vaccination usefulness								
No very useful or useless or no opinion	12	(2.1)	582	(97.9)	Ref.			
Useful or indispensable	496	(40.0)	745	(60.0)	31.62	17.76–56.29	19.65	10.36–37.24
Physician’s recommendation of HPV vaccination								
No or does not remember	27	(4.3)	609	(95.7)	Ref.			
Yes	481	(40.1)	718	(59.9)	15.04	10.06–22.46	10.40	6.85–15.80
Perceived level of information regarding childhood vaccination								
Rather not well or not at all well-informed	51	(17.2)	247	(82.8)	Ref.			
Rather well or fully informed	457	(29.8)	1080	(70.2)	2.04	1.48–2.81	–	–
Information sources								
Family physician								
No	15	(10.4)	134	(89.6)	Ref.			
Yes	493	(29.3)	1193	(70.7)	3.55	2.08–6.07	–	–
Pharmacist								
No	429	(27.5)	1133	(72.5)	Ref.			
Yes	79	(29.1)	194	(70.9)	1.09	0.82–1.44	–	–
Relatives/family/friends								
No	407	(30.0)	949	(70.0)	Ref.			
Yes	101	(21.2)	378	(78.8)	0.63	0.49–0.80	0.75	0.55–1.01
Internet								
No	429	(30.8)	967	(69.2)	Ref.			
Yes	79	(18.0)	360	(82.0)	0.49	0.38–0.65	0.66	0.47–0.91
Healthcare provider type								
Pediatrician practice or free preventive clinic for mothers and infants	50	(34.2)	98	(65.8)	Ref.			
General practice	458	(27.1)	1229	(72.9)	0.72	0.50–1.02	–	–

Abbreviations: CI, confidence interval; HPV, human papillomavirus; OR, odds ratio; Ref., reference category for odds ratio, SD, standard deviation.

^a 4 missing values.

^b 36 missing values.

* Adjusted odds ratio determined by backward multivariate logistic regression of HPV vaccination.

Table 3
Total, direct, and indirect effects of Internet and other sources of information on HPV vaccine uptake (weighted data).

Information source	Total effect		Direct effect		Indirect effect	
	Standardized β estimate (standard error)	P value	Standardized β estimate (standard error)	P value	Standardized β estimate (standard error)	P value
Internet	–0.10 (0.02)	<0.0001	–0.06 (0.02)	0.002	–0.04 (0.008)	<0.0001
Family physician	0.08 (0.01)	<0.0001	0	–	0.08 (0.01)	<0.0001
Relatives/family/friends	–0.09 (0.02)	<0.0001	–0.04 (0.02)	0.033	–0.05(0.007)	<0.0001

uptake, which probably indicates a residual effect not captured by the model variables, rather than a genuine direct effect. Fourth, this analysis was based on cross-sectional data. Therefore, causal inferences cannot be drawn, and reverse links between some variables cannot be completely ruled out. For example, the association between Internet use and perceived level of information on childhood vaccination may be due to reciprocal effects. Despite these limitations, this study seems to confirm the detrimental impact of Internet use as a source of vaccine information in vaccine-hesitant mothers. Additional studies are needed using prospective study designs among a random sample of parents.

5. Conclusion

In conclusion, this study found a weak but significant association between vaccine-hesitant mothers' use of the Internet as a source of vaccine information and a lack of HPV vaccine uptake by their daughters, through a lower perceived level of HPV vaccine usefulness, a lower perceived level of information on childhood vaccination, and unfavorable attitudes towards vaccination in general. While further studies are needed to confirm this link, there is no doubt on the need to raise awareness about the importance of seeking information from a healthcare provider, and consulting only reputable sources of information on the Internet.

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jpmed.2021.106615>.

Author's contributions

FD and PC had designed the study. FD had performed the data analysis, the redaction of the manuscript, and the revision process of this paper based on Vaccinoscopie Survey data acquired by OL. PC, OL, PM and LL have participated in the revision process and the redaction of the manuscript. GSK and IDM had no role in the study design nor in the data analysis. All authors have approved the final manuscript which was reviewed by GSK before submission.

Funding

Financial support for the study was provided by a PhD fellowship from the French National Cancer Institute awarded to FD. The other authors received no specific funding for this work.

Declaration of Competing Interest

FD declares that MSD vaccines have covered registration fees, transport and accommodation costs for attendance to a conference in 2018 and received a research grant. PM was an investigator on projects that received funding from GSK and MSD for the evaluation of HPV vaccines in Africa. OL declares punctual interventions and support during conferences with Pfizer, MSD, Sanofi Pasteur, Janssen and GSK. PC declares no conflict of interest.

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CHAPITRE 6 – DISCUSSION

En France, le cancer du col utérin est classé au 12^{ème} rang des cancers chez la femme, représentant le 4^e cancer féminin le plus fréquent chez les femmes âgées 15 à 44 ans. Le taux de couverture vaccinale du vaccin anti-HPV demeure insuffisant (inférieur à 35 % pour un schéma complet à deux doses, en 2020) alors que relever le défi de l'amélioration de la couverture vaccinale HPV figure dans l'agenda du gouvernement français depuis 2009. Le problème au cœur des efforts infructueux en matière d'amélioration de cette couverture vaccinale pourrait résider dans la méconnaissance des déterminants de la vaccination et l'insuffisance de ciblage des actions mises en œuvre. Au commencement de ce travail de thèse en 2018, les données françaises sur le sujet restaient en effet limitées à quelques analyses sur les données du SNDS (avec les limitations inhérentes aux études sur bases de données médico-administratives) (Héquet et Rouzier 2017) ou à une région du territoire français (Lutringer-Magnin et al. 2011)¹. Dès lors, l'objectif principal de ce travail était de mieux comprendre les déterminants de la couverture vaccinale du vaccin anti-HPV sous l'angle de l'hésitation vaccinale, chez les mères de filles éligibles à cette vaccination.

Cette thèse contribue ainsi à la littérature sur les déterminants de la vaccination anti-HPV en France, mais également sur les questionnaires portant sur ces déterminants.

L'Article 1 présente la méthodologie de développement d'un instrument pour recueillir les déterminants de l'hésitation à l'égard du vaccin anti-HPV en France, selon le modèle des déterminants d'HV de l'OMS regroupant les déterminants en trois grandes classes : (i) Influences contextuelles, (ii) Influences individuelles et de groupe, et (iii) Questions spécifiques au vaccin/à la vaccination). Un panel multidisciplinaire de quinze experts a été consulté à travers deux tours selon

¹ Depuis, des analyses du Baromètre santé 2016 ont été publiées en 2019 et celles de l'enquête menée par l'INCa en 2022.

la méthodologie de Delphi afin d'aboutir à un consensus sur les items à inclure dans le questionnaire. La version finale du questionnaire ainsi obtenu comprenait 57 items.

L'Article II présente les résultats d'une enquête téléphonique utilisant l'instrument développé dans l'Article I complété des questions relatives au stade de décision concernant la vaccination anti-HPV (PAPM) (Shapiro et al. 2018) et de la mesure de confiance envers les vaccins (GVC1). L'étude a été réalisée auprès d'un échantillon de 1102 mères de filles de 11 à 14 ans résidant en France métropolitaine, sélectionné par la méthode des quotas. L'analyse multivariée a montré qu'être d'accord avec l'affirmation selon laquelle les médecins/professionnels de santé croient que vacciner les filles contre les HPV est une bonne idée (OR=4,99 ; IC95%, 2,09-11,89), et avoir posé des questions au médecin traitant sur les vaccins anti-HPV (OR=3,44 ; IC95%, 2,40-4,92) étaient positivement associés à la vaccination anti-HPV. Inversement, la croyance selon laquelle sa fille était trop jeune pour être vaccinée contre les HPV (OR=0,16 ; IC95%, 0,09-0,29), l'âge plus jeune de la fille (OR=0,17 ; IC95 % 0,10-0,28 pour les filles âgées de 11 ans par rapport à celles âgées de 14 ans), l'affirmation selon laquelle le vaccin anti-HPV n'est pas sûr (OR=0,42 ; IC95 %, 0,26-0,67) , l'affirmation selon laquelle les HPV sont très rares (OR=0,49 ; IC 95 %, 0,31-0,77) et le refus précédent de la mère de se faire vacciner elle-même (OR=0,57 ; IC95 %, 0,40-0,80) étaient inversement associés à la vaccination anti-HPV.

L'Article III présente, enfin, une analyse poolée des données de Vaccinoscopie® de 2015 à 2018 portant sur les mères de filles âgées de 14 et 15 ans visant à explorer l'association entre le recours à Internet comme source d'information chez les mères hésitantes vis-à-vis d'une vaccination et la vaccination anti-HPV de leurs filles. La régression logistique multivariée montrait que l'utilisation d'Internet par les mères était significativement associée à une moindre vaccination anti-HPV chez leurs filles (OR= 0,66 ; IC95%, 0,47-0,91). Le modèle d'équations structurelles a confirmé l'effet négatif de l'utilisation d'Internet, en révélant les liens mécanistiques sous-jacents à la moindre couverture vaccinale du vaccin anti-HPV.

Implications

Les résultats de cette thèse ont des implications en matière de communication, d'information, de formation et de politiques de prévention.

Communication et information

Il apparaît opportun de développer un plan de communication reprenant notamment les éléments incompris et/ou problématiques mis en évidence dans cette thèse, à destination des parents comme des médecins. Les outils et stratégies de communication, aussi bien sur le fond que sur la forme, devront naturellement s'adapter à la population ciblée.

- Crainte des effets indésirables

Nos résultats montrent que la crainte des effets indésirables influence négativement la vaccination anti-HPV. Cette crainte est fréquemment citée dans la littérature scientifique nationale et internationale (Karafillakis et al. 2019). Ainsi, l'enquête téléphonique menée par Santé Publique France en 2016 auprès de 1 491 parents de filles âgées de 11 à 19 ans rapportait que la perception d'effets secondaires graves du vaccin par les parents était fortement liée à la vaccination anti-HPV (Florian Verrier et al. 2019). De plus, cette crainte figure en tête de liste des freins cités par les parents de filles non vaccinées dans une étude récemment publiée (en 2022), réalisée par l'Inca et la HAS auprès d'un échantillon national représentatif de 1984 parents ayant au moins une fille de 11 à 19 ans et/ou un garçon de 11 à 14 ans dans leur foyer (Derhy et al. 2022). Une revue systématique publiée en 2021 conduite par le Centre international de recherche sur le cancer (CIRC) incluant 14 articles scientifiques et 11 thèses d'exercice de médecine conduites en France indique que la crainte des effets indésirables est rapportée comme un frein majeur pour la recommandation du et/ou la vaccination par le vaccin anti-HPV chez 60 % des médecins généralistes : 30 à 50 % des médecins généralistes rapportant avoir eux-mêmes des inquiétudes concernant les effets indésirables du vaccin anti-HPV (Escriva-Boulley et al. 2021). Étant donné le rôle des médecins dans la recommandation du vaccin anti-HPV (Newman et al. 2018; Yankey et al. 2020; Newcomer et al.

2020), on assiste au développement d'un cercle vicieux autour de cette question de la crainte des effets indésirables. En effet, cette crainte des parents – quand elle est exprimée auprès des médecins ou qu'elle est anticipée (à tort ou à raison) par eux – constitue un frein à la recommandation de la vaccination par les médecins (quand bien même eux-mêmes ne la partagent pas) alors même que l'absence de recommandation de la part du médecin représente un frein évoqué par les parents de filles non vaccinées (Derhy et al. 2022). Au bout du compte, on estime que 40 à 50 % des médecins généralistes ne recommandent pas systématiquement la vaccination anti-HPV à leur patientèle éligible (Florian Verrier et al. 2019; Escriva-Boulley et al. 2021). Il est donc important de briser ce cercle vicieux en communiquant à la fois auprès des médecins généralistes et des parents sur l'objet de cette crainte partagée. Pour cet acte de prévention comme pour d'autres, les médecins devraient au contraire le promouvoir auprès des plus réticents.

- Fréquence de l'infection à HPV, infection orale et lien avec les cancers ORL induits par l'infection à HPV

Nous avons mis en lumière l'influence de la méconnaissance de la fréquence de l'infection par HPV sur la vaccination anti-HPV. Ce constat est retrouvé dans les analyses du Baromètre Santé 2016 et congruent avec les données de la littérature qui montrent que les mères qui avaient reçu des informations dans le cadre d'un cours d'éducation sanitaire étaient plus susceptibles de déclarer que leur enfant avait reçu au moins une dose de vaccin anti-HPV (Berenson et al. 2017). Dans notre étude, les proportions de réponses incorrectes les plus élevées portaient sur le fait que l'infection par HPV peut causer des cancers ORL (77% de réponses fausses), la possible transmission de l'infection par HPV par voie sexuelle orale, et le fait que les rapports sexuels à un âge jeune représentent un facteur de risque d'infection par HPV. Une campagne d'information destinée au grand public insistant particulièrement sur ces aspects apparaît dès lors nécessaire, ce d'autant plus que 50% des parents ne se sentent pas bien informés vis-à-vis de la vaccination anti-HPV, d'après l'enquête menée par l'INCa en 2019 (Derhy et al. 2022). Dans notre enquête téléphonique, près de la moitié des répondantes avaient déjà cherché des informations sur le vaccin anti-HPV. La source d'information la plus

fréquente était Internet (un peu plus de la moitié des mères ayant consulté le site de Santé Publique France, et moins d'un tiers des mères ayant consulté le site Vaccination Info Service), suivie de leur médecin traitant et d'autres professionnels de santé. Or, l'utilisation d'Internet n'est pas la panacée et peut même être néfaste à l'ère post-factuelle dans laquelle nous sommes entrés (Higgins 2016; Dib et al. 2022), cette ère où « l'opinion personnelle, l'idéologie, l'émotion et la croyance l'emportent sur la réalité des faits » (*Oxford Word of the Year 2016 | Oxford Languages, s. d.*).

- Age de l'adolescente

Dans notre étude, le jeune âge de l'adolescente était inversement associé à la vaccination anti-HPV. L'influence de l'âge de l'adolescente est décrite dans la littérature internationale (Bodson et al. 2017) comme la littérature française (Escriva-Boulley et al. 2021). Escriva-Boulley et al (Escriva-Boulley et al. 2021) concluaient dans leur revue systématique de littérature relative aux cognitions et comportements des médecins généralistes en France liés à la vaccination anti-HPV que tant les parents que les médecins généralistes avaient tendance à retarder cette vaccination à un âge plus avancé (c'est-à-dire à l'âge de 14 ans), car ils estiment que les filles de 11 ans sont trop jeunes pour être concernées (« parler de ce vaccin c'est parler de la sexualité, donc je dois dire que je suis très ambivalente, pas convaincue de la précocité de l'âge dans le schéma pour qu'elles en comprennent quelque chose » (Esperandieu 2016)), et les parents ne sont pas sûrs de pouvoir parler de sexualité à un si jeune âge et/ou craignent d'encourager une sexualité précoce.

Nous avons d'ailleurs observé une différence entre le groupe des filles vaccinées et non vaccinées dans notre enquête téléphonique, concernant précisément la crainte d'encourager les relations sexuelles précoces et la difficulté d'aborder le sujet de la vaccination anti-HPV par les mères. Cette différence était significative en analyse univariée, mais s'effaçait dans le modèle multivarié ajustant sur l'âge notamment. Ceci pourrait s'expliquer par le fait que la crainte et les difficultés sont accentuées par le jeune âge de l'adolescente. Il conviendra de déconstruire la croyance selon laquelle une jeune fille de 11 ans est trop jeune pour être concernée par la vaccination anti-HPV, en ré insistant sur le rationnel de cette vaccination dès l'âge de 11 ans, tant auprès des médecins, que

des parents. Par ailleurs, Il sera utile sans doute d'équiper les parents d'outils langagiers pour faciliter le dialogue avec leurs filles sur un sujet perçu comme sensible.

Formation

Les médecins, en particulier les médecins généralistes, constituent la pierre angulaire de la vaccination anti-HPV en France. Dans notre enquête, les filles de mères qui étaient d'accord avec le fait que les médecins/les professionnels de santé pensent que vacciner les filles contre les HPV était une bonne idée étaient plus souvent vaccinées que les mères de filles qui n'étaient pas d'accord avec cette affirmation. La recommandation exprimée par le médecin apparaissait comme un facteur statistiquement significatif en analyse univariée ; toutefois, la différence n'était pas maintenue dans l'analyse multivariée. Ceci peut s'expliquer par l'existence d'une corrélation entre « penser que la vaccination est une bonne idée » et la « recommander ». La perception positive par les mères de ce qui constitue la norme au sein du corps médical au sujet de la vaccination anti-HPV est donc déterminante. Partant du constat que près de la moitié des médecins généralistes ne recommandent pas la vaccination anti-HPV, et que la crainte des effets indésirables est un frein à cette recommandation, le renforcement de la formation des médecins sur ces aspects apparaît être un enjeu de taille. La formation médicale initiale est un levier mobilisable au même titre que la formation continue. En effet, une enquête nationale en ligne menée en 2015 dans 27 des 32 facultés de médecine françaises indiquait que près d'un tiers des étudiants en médecine se sentaient insuffisamment préparés aux questions sur la vaccination, notamment pour communiquer avec les patients sur les effets secondaires, et sur les stratégies pour répondre à l'hésitation vaccinale (Kernéis et al. 2017). La formation médicale initiale est un levier mobilisable au même titre que la formation continue.

Politiques de santé publique

- Recommander la vaccination anti-HPV dès l'âge de 9 ans

Au vu des résultats de notre enquête téléphonique sur la barrière de l'âge et sur les données de la littérature concernant les difficultés d'aborder une mesure préventive en lien avec la sexualité auprès de parents et d'adolescentes âgées de 11 ans, abaisser l'âge d'éligibilité de la vaccination permettrait de contourner ce problème en dissociant la vaccination anti-HPV et la sexualité. En France, la vaccination anti-HPV dès l'âge de 9 ans est recommandée uniquement pour les candidats à une transplantation d'organe alors que certains pays européens vaccinent dès l'âge de 9 ans en population générale, tels l'Allemagne et le Luxembourg (Bonanni et al. 2020). Notons, par ailleurs, que l'*American Academy of Pediatrics* (AAP) (Sean T. O'Leary et Ann-Christine Nyquist 2019) et l'*American Cancer Society* (ACS) (Saslow et al. 2020) ont recommandé d'abaisser l'âge de la vaccination anti-HPV à 9 ans en 2018 et 2020, respectivement. La dissociation entre vaccination et sexualité chez les enfants à cet âge est un des arguments avancés par l'AAP (Sean T. O'Leary et Ann-Christine Nyquist 2019) qui est appuyé par les données de la littérature (Biancarelli, Drainoni, et Perkins 2020). Notons par ailleurs que l'âge de 9 ans figurait déjà en 2016 dans les recommandations de l'*Advisory Committee on Immunization Practices* (ACIP) qui élabore le calendrier de vaccination des adolescents approuvé par les *Centers for Disease Control and Prevention*) (Meites 2016)

- Encourager la recommandation de la vaccination par les médecins généralistes

L'attitude des médecins est un facteur important dans l'acceptation ou l'hésitation des parents à l'égard de la vaccination anti-HPV (Aninye et al. 2021). On déplore l'insuffisance de recommandation de cette mesure préventive par les médecins alors même que celle-ci devrait être exploitée comme levier d'action majeur pour améliorer la couverture vaccinale du vaccin anti-HPV en France. C'est d'ailleurs un levier cité par les parents eux-mêmes dans l'enquête menée par l'INCa en 2019. Cela pourrait passer par la mobilisation des moyens de communication de l'Assurance maladie ou par des messages de la Direction générale de la santé (à l'heure où la communication régulière entre

cette dernière et les médecins généralistes par courriel s'est instaurée à la faveur de l'épidémie de Covid 19). Notons que l'introduction en mars 2019 de consultations dédiées aux enfants et aux adolescents, prises en charge à 100 % par l'Assurance maladie (Loi n° 2018-1203 du 22 décembre 2018 de financement de la sécurité sociale pour 2019 (1), 2018) représente une nouvelle opportunité pour recommander la vaccination anti-HPV chez les filles comme chez les garçons (pour les consultations entre 11 et 13 ans) ou de la rattraper (pour les consultations entre 15 et 16 ans). La consultation proposée entre 8 et 9 ans favoriserait par ailleurs l'abaissement à 9 ans du seuil d'éligibilité de la vaccination.

- Organiser un programme d'invitation systématique des bénéficiaires

À l'image des programmes de dépistage organisés des cancers en France, à travers lesquels les bénéficiaires reçoivent un courrier d'invitation à réaliser l'acte de dépistage, il apparaît opportun d'inviter les populations éligibles à la vaccination anti-HPV par le biais d'un courrier postal à solliciter une consultation auprès de leur médecin généraliste, qui pourrait d'ailleurs coïncider avec la consultation pour les 11-13 introduite en mars 2019. Ce type de modèle d'invitation à la vaccination anti-HPV reçue à domicile est par exemple utilisé aux Pays-Bas (van Keulen et al. 2013). L'invitation comporte un dépliant d'information envoyé au domicile des bénéficiaires, un lien renvoyant à un site web contenant des informations sur la vaccination anti-HPV à l'intention des filles et des parents, ainsi qu'un numéro d'assistance téléphonique.

- Promouvoir la littératie en santé numérique

Notre analyse des données de Vaccinoscopie® a montré que le recours à Internet était significativement associé à une moindre vaccination anti-HPV. La qualité de l'information en santé accessible sur Internet est en général préoccupante (Zhang, Sun, et Xie 2015) et la diffusion d'informations erronées sur les bénéfices et les risques des vaccins a certainement alimenté l'hésitation vaccinale (McKee et Middleton 2019) tant et si bien qu'en 2020, l'OMS a inscrit la "diffusion incontrôlée de fausses informations", y compris dans le domaine de la vaccination, parmi ses défis sanitaires urgents pour la prochaine décennie (Organisation Mondiale de la Santé (OMS)

2020b). Promouvoir la littératie en santé numérique, c'est-à-dire un ensemble de compétences en matière de santé liées à l'utilisation de médias électroniques, pourrait être très utile pour contribuer à atténuer les effets néfastes des informations erronées sur la prise de décision en matière de vaccination. L'adoption d'un esprit critique à l'égard de toute allégation relative à la santé trouvée sur Internet devrait être valorisée et encouragée en général, au-delà du seul sujet de la vaccination. Cette approche globale serait moins susceptible de déclencher des réactions de résistance chez les personnes hostiles à la vaccination (Dib et al. 2022). C'est important, car la question de la vaccination est devenue un débat très polarisé (Schmidt et al. 2018).

Limites et perspectives

Cette recherche ouvre un certain nombre de perspectives. Tout d'abord, l'instrument destiné à investiguer les facteurs associés à la vaccination anti-HPV était conçu dans le contexte de la vaccination des filles (avant l'extension de la vaccination aux garçons). Bien qu'à première vue, il puisse être directement utilisé pour interroger les déterminants de la vaccination anti-HPV chez les enfants sans distinction de sexe, la question mérite, en tout cas, d'être posée sur la nécessité d'une (légère) adaptation de l'instrument. Il serait par exemple intéressant d'inclure des questions discriminantes pour évaluer si les croyances, attitudes et connaissances des parents diffèrent selon le sexe de l'enfant (il n'est pas sûr du tout que les risques de l'infection à HPV chez les hommes et les enjeux épidémiologiques de la vaccination des deux sexes soient bien connus)². Aussi, une étude dédiée aux déterminants spécifiques à la vaccination anti-HPV chez les garçons mérite une attention particulière. Au-delà d'une moins bonne connaissance des objectifs de la vaccination des garçons, on peut spéculer à l'inverse que l'influence de l'âge est moins prégnante s'agissant de la vaccination des garçons.

² La HAS estime que cet élargissement de la vaccination anti-HPV aux garçons, au-delà de la protection conférée aux garçons vaccinés, permettrait aussi, sous réserve d'une couverture vaccinale suffisante, de freiner la transmission des HPV au sein de la population générale, de mieux protéger les filles et femmes non vaccinées, et enfin de mieux protéger les garçons et hommes, quelle que soit leur orientation sexuelle.

Par ailleurs, la méthode utilisée pour l'échantillonnage dans l'enquête téléphonique était celle des quotas. Un échantillonnage aléatoire permettrait de confirmer les précisions des intervalles de confiance obtenus, et la généralisabilité des résultats. Cette méthode n'a pas été retenue dans notre enquête téléphonique parce qu'elle est plus coûteuse (taux de perte important sur un échantillon aléatoire de ménages qui doivent compter au moins un enfant de la population cible) mais cet obstacle pourrait être surmonter dans une enquête multi-objectifs (« enquêtes omnibus »).

Même si toutes les enquêtes montrent que les pères sont rarement en charge de la santé et de la prévention des enfants, il pourrait être intéressant d'interroger les pères et de comparer leurs attitudes avec celles des mères : dans les familles recomposées) et, bien sûr, dans les familles monoparentales paternelles (18% des familles monoparentales, soit environ 354000 familles concernées), leur avis peut être déterminant (Institut national de la statistique et des études économiques (INSEE) 2021, 249).

Enfin, l'étude évaluant l'influence d'Internet reposait sur une analyse secondaire de données. Il conviendrait d'affiner les mécanismes sous-jacents à l'effet d'Internet sur la couverture vaccinale via l'analyse de données d'enquête *ad hoc* avec une mesure plus spécifique du facteur d'exposition (recherche d'informations sur la vaccination anti-HPV et non pas sur la vaccination en général), et la prise en compte de facteurs confondants potentiels comme la perception de la sécurité du vaccin anti-HPV et les connaissances sur cette vaccination.

Enfin - et c'est sans doute une perspectives des plus intéressantes - les déterminants mis en lumière par cette thèse pourront opportunément être ciblés par des études d'intervention dont aucune donnée n'a été publiée jusqu'ici en France (Campana V et al. 2019). D'une manière générale, les approches multi- composantes, combinant des stratégies d'action différentes et ciblant à la fois les adolescents, les parents et les professionnels de santé semblent avoir les meilleurs résultats sur la couverture vaccinale (Vollrath, Thul, et Holcombe 2018). Nos résultats appuient la nécessité d'agir tout au moins auprès des parents et des médecins.

CHAPITRE 7 – CONCLUSION

Cette thèse s'est intéressée aux facteurs influençant la vaccination anti-HPV en France à travers une enquête téléphonique réalisée auprès de 1102 mères d'adolescentes de 11-14 ans en France métropolitaine. L'enquête était fondée sur un instrument interrogeant, pour la première fois en France, les facteurs associés à la vaccination anti-HPV sous l'angle de l'hésitation vaccinale en France. Le questionnaire a été développé dans le cadre de cette thèse en sollicitant un panel multidisciplinaire d'une quinzaine d'experts en utilisant une méthodologie de Delphi. Cette thèse a par ailleurs décrit le rôle du recours à Internet comme source d'information sur la vaccination chez des mères hésitantes à l'égard de la vaccination sur la couverture vaccinale du vaccin anti-HPV chez leurs filles, à travers une analyse secondaire de données de l'enquête Vaccinoscopie®. Les travaux explorant les facteurs associés à la vaccination anti-HPV qui avaient été publiés jusqu'ici portaient essentiellement sur les données du SNDS, avec les limitations inhérentes aux analyses sur bases de données médico-administratives.

Les résultats de cette thèse indiquent que le jeune âge de l'adolescente (et en regard la croyance maternelle selon laquelle sa fille est trop jeune pour être vaccinée contre les HPV) était le facteur avec l'effet le plus prépondérant sur la vaccination anti-HPV, bien devant la croyance selon laquelle le vaccin anti-HPV n'est pas sûr et la méconnaissance de la fréquence de l'infection HPV qui avaient été identifiées jusqu'ici. Nous avons, en outre, pour la première fois, mis en évidence la moindre probabilité de la vaccination anti-HPV chez les filles de mères qui avaient déjà refusé une vaccination pour elles-mêmes et confirmé le rôle néfaste du recours à Internet chez les mères hésitantes vis-à-vis d'une vaccination sur le statut de la vaccination anti-HPV de leurs filles, en quantifiant la force de cette association.

Cette thèse indique, de façon intéressante, que les filles de mères d'accord avec le fait que les médecins/les professionnels de santé pensent que vacciner les filles contre les HPV était une bonne idée étaient plus souvent vaccinées que les filles de mères qui n'étaient pas d'accord avec cette

affirmation. Toutefois, notre étude n'a pas permis d'identifier d'influence indépendante de la recommandation effective du vaccin par les médecins/professionnels de santé, ce qui souligne l'importance de l'attitude des médecins/professionnels de santé perçue par les mères, au-delà même de l'expression prescriptrice de la recommandation. Le fait de poser des questions au médecin traitant sur les vaccins anti-HPV était associé à une meilleure couverture vaccinale, ce qui confirme le besoin d'informations par les mères et le rôle crucial des médecins traitants (souvent des médecins généralistes) dans la vaccination anti-HPV en France.

Cette thèse apporte une contribution essentielle à la compréhension des facteurs qui influencent la vaccination anti-HPV en France en confirmant et quantifiant l'influence de l'âge de l'adolescente, un facteur qui avait été suggéré par des études qualitatives réalisées chez les médecins généralistes en France. Elle apporte par ailleurs une contribution originale en proposant un instrument couvrant la complexité et la multiplicité des facteurs possiblement en jeu dans la vaccination anti-HPV en France.

Ces résultats ont des implications en matière de politiques publiques. Plus spécifiquement, ils interrogent sur l'opportunité d'abaisser le seuil d'éligibilité de la vaccination anti-HPV à 9 ans en population générale. De plus, ils mettent en lumière les croyances qui font obstacle à la vaccination anti-HPV (en lien avec l'âge de l'adolescente, la fréquence de l'infection par HPV et la sécurité du vaccin anti-HPV), des obstacles qu'il convient de surmonter. Ils nous invitent également à nous intéresser, en matière d'interventions, à cibler prioritairement la population des mères ayant refusé de se faire elles-mêmes vacciner. Ils confirment enfin le rôle important des médecins, de leurs avis et de leur pratique, et mettent en avant la nécessité de renforcer leur implication dans les mesures visant à améliorer la couverture vaccinale du vaccin anti-HPV en France.

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ANNEXES

Annexe 1. Composition du panel d'experts

	Domaine d'expertise	Affiliation
Pr Themistoklis APOSTOLIDIS	Psychologie sociale	Aix Marseille Université
Mme Céline AUDIGER	Maïeutique	Institut Pierre Louis d'Épidémiologie et de Santé Publique
Mme Anne-Sophie BARRET	Epidémiologie	Santé Publique France
Mr François BECK	Sociologie	Santé Publique France
Mr Aymery CONSTANT	Psychologie de la santé	École des hautes études en santé publique
Dr Mady DENANTES	Médecine générale	Maison de santé Pyrénées-Belleville
Pr Eve DUBE	Anthropologie médicale	Université Laval
Mme Emilie KARAFILLAKIS	Santé Publique	London School of Hygiene and Tropical Medicine
Dr Liliane KEROS	Virologie	Assistance publique -Hôpitaux de Paris
Dr Joseph MONSONEGO	Gynécologie médicale	Institut du col
Mme Isabelle PARIZOT	Sociologie	Centre Maurice Halbwachs
Dr Melinda PETROVIC	Gynécologie obstétricale	Assistance Publique- Hôpitaux de Marseille
Dr Sylvie QUELET	Santé publique	Santé Publique France
Dr Pia de REILHAC	Gynécologie médicale	Fédération nationale des collèges de gynécologie médicale
Dr Nicolas VIGNIER	Infectiologie	Centre Hospitalier de Cayenne

Annexe 2. Questionnaire développé par l'article II

FACTEURS CONTEXTUELS		
Communication et médias	Par quel biais avez-vous entendu parler du vaccin contre les papillomavirus ?	Recommandation du médecin traitant/ Recommandation d'un pédiatre/Recommandation d'un gynécologue/Télévision/Réseau x sociaux/Presse écrite/Famille/Amis/École/Autre (question à choix multiples)
Influences historiques	Depuis la controverse sur la vaccination contre la grippe H1N1, j'ai moins confiance dans les recommandations de vaccination françaises	Pas du tout d'accord - tout à fait d'accord (échelle de Likert à 5 points)
	Depuis la controverse sur le vaccin de l'hépatite B, j'ai moins confiance dans le système de santé	Pas du tout d'accord - tout à fait d'accord (échelle de Likert à 5 points)
Religion/culture/relations hommes-femmes/situation socio-économique	Je pense que vacciner les adolescentes contre les papillomavirus les encouragent à avoir des rapports sexuels	Pas du tout d'accord - tout à fait d'accord (échelle de Likert à 5 points)
	Il est difficile de parler avec ma fille de sa santé sexuelle	Pas du tout d'accord - tout à fait d'accord (échelle de Likert à 5 points)
	Je suis mal à l'aise pour discuter de la santé sexuelle de ma fille avec un médecin ou un autre professionnel de santé	Pas du tout d'accord - tout à fait d'accord (échelle de Likert à 5 points)
	J'ai des difficultés pour aborder le sujet du vaccin contre les papillomavirus avec ma fille	Pas du tout d'accord - tout à fait d'accord (échelle de Likert à 5 points)
Politiques/mandats	Je suis favorable aux 11 vaccins obligatoires pour les enfants nés depuis le 1er Janvier 2018	Pas du tout d'accord - tout à fait d'accord (échelle de Likert à 5 points)
	Chacun devrait pouvoir décider quels vaccins sont nécessaires pour ses enfants	Pas du tout d'accord - tout à fait d'accord (échelle de Likert à 5 points)
Perception de l'industrie pharmaceutique	L'industrie pharmaceutique suit des procédures rigoureuses de fabrication	Pas du tout d'accord - tout à fait d'accord (échelle de Likert à 5 points)

FACTEURS INDIVIDUELS ET DE GROUPE		
Antécédents vaccinaux	Il m'est arrivé de refuser un vaccin pour ma fille (ou choisir de ne pas lui faire)	Oui ; Non
	Il m'est arrivé de refuser un vaccin pour moi-même (ou choisir de ne pas le faire)	Oui ; Non
	Je connais une personne qui est tombée gravement malade après s'être fait vaccinée	Oui ; Non
	Je connais une personne qui est tombée gravement malade parce qu'elle n'était pas vaccinée	Oui ; Non
	Personnellement, j'ai déjà eu des frottis cervico-vaginaux anormaux pour lesquels un traitement était nécessaire (conisation/chirurgie)	Oui ; Non
Croyances, attitudes face à la santé et à la prévention	Les médecines alternatives renforcent les défenses de l'organisme, conduisant ainsi à une complète guérison	Pas du tout d'accord - tout à fait d'accord (échelle de Likert à 5 points)
	Je préfère que ma fille développe naturellement des défenses contre les infections à papillomavirus plutôt que par la vaccination	Pas du tout d'accord - tout à fait d'accord (échelle de Likert à 5 points)
Connaissances/ informations	Avez-vous déjà recherché des informations sur le vaccin contre les papillomavirus dans le passé ?	Oui ; Non
	(Si a déjà recherché des informations) Citez les 3 sources d'information les plus consultées	Médecin traitant/Autre professionnel de santé/Internet/Famille/Livres /Presse écrite/Autre
	(Si a utilisé internet) De quelle façon avez-vous utilisé internet ?	J'ai consulté des forums/J'ai consulté des blogs/J'ai consulté les réseaux sociaux/J'ai consulté des sites d'information/Autre
	(Si a consulté des sites d'information) Quel site ?	Santé Publique France/Vaccination info service/Doctissimo/Allodocteur /Pourquoi Docteur/Infovac/ France Info/Le Monde/Le Figaro/Alter Info/Alternative Santé/Initiative Citoyenne/ Autre

		(question à choix multiples)
	(Si a déjà recherché des informations) Après avoir eu toutes ces informations, avez-vous pu prendre une décision concernant la vaccination contre les papillomavirus ?	Oui, facilement ; Oui, difficilement ; Non, pas vraiment ; Non, pas du tout
	Les infections à papillomavirus sont très rares	Vrai ; Faux ; Je ne sais pas
	Les hommes ne peuvent pas contracter d'infection à papillomavirus	Vrai ; Faux ; Je ne sais pas
	Une personne peut être infectée par un papillomavirus pendant de nombreuses années sans le savoir	Vrai ; Faux ; Je ne sais pas
	Les papillomavirus peuvent être transmis par sexe oral	Vrai ; Faux ; Je ne sais pas
	Le vaccin contre les papillomavirus protège contre toutes les infections transmises sexuellement	Vrai ; Faux ; Je ne sais pas
	Le vaccin contre les papillomavirus protège contre les verrues génitales	Vrai ; Faux ; Je ne sais pas
	Les vaccins contre les papillomavirus sont le plus efficace lorsqu'ils sont administrés à des personnes n'ayant jamais eu de rapports sexuels	Vrai ; Faux ; Je ne sais pas
	Une personne ayant été vaccinée contre les papillomavirus peut néanmoins développer un cancer du col de l'utérus	Vrai ; Faux ; Je ne sais pas
	Les filles ayant été vaccinées contre les papillomavirus ont besoin de faire des frottis cervico-vaginaux lorsqu'elles sont plus âgées	Vrai ; Faux ; Je ne sais pas
	Le vaccin contre les papillomavirus permet de guérir l'infection à papillomavirus	Vrai ; Faux ; Je ne sais pas
	Avoir des relations sexuelles à un jeune âge augmente les risques de contracter une infection à papillomavirus	Vrai ; Faux ; Je ne sais pas
	Les infections à papillomavirus peuvent causer le cancer de la gorge	Vrai ; Faux ; Je ne sais pas
Confiance dans le système et le personnel de santé et expérience personnelle	<p>Veillez indiquer dans quelle mesure vous faites confiance aux sources suivantes pour dire la vérité sur les vaccinations</p> <p>L'industrie pharmaceutique/le gouvernement/votre médecin traitant/les médecins en général/les pharmaciens/les autres professionnels de santé/les chercheurs scientifiques/les médias traditionnels/les médias alternatifs (médias qui véhiculent des informations alternatives aux médias de masse commerciaux ou étatiques, par ex. Agoravox, Atlantico, et Alterinfo)</p>	Pas du tout confiance - tout à fait confiance (Échelle de Likert à 5 points)
Rapports risques/avantages (perçus, heuristiques)	Le vaccin contre les papillomavirus peut être responsable de problèmes de santé à long terme	Pas du tout d'accord - tout à fait d'accord (échelle de Likert à 5 points)
	Il n'y a pas eu assez de recherche faite sur le vaccin contre les papillomavirus	Pas du tout d'accord - tout à fait d'accord (échelle de Likert à 5 points)

	Le vaccin contre les papillomavirus n'est pas sûr	Pas du tout d'accord - tout à fait d'accord (échelle de Likert à 5 points)
	Le vaccin contre les papillomavirus est efficace pour prévenir les infections à papillomavirus	Pas du tout d'accord - tout à fait d'accord (échelle de Likert à 5 points)
	Le vaccin contre les papillomavirus est efficace pour prévenir les verrues génitales	Pas du tout d'accord - tout à fait d'accord (échelle de Likert à 5 points)
	Faire vacciner ma fille contre les papillomavirus contribuera à la protéger contre les infections sexuellement transmissibles	Pas du tout d'accord - tout à fait d'accord (échelle de Likert à 5 points)
	Le vaccin contre les papillomavirus est efficace pour prévenir les cancers associés aux papillomavirus	Pas du tout d'accord - tout à fait d'accord (échelle de Likert à 5 points)
	L'utilisation d'un préservatif empêche la transmission des infections à papillomavirus	Pas du tout d'accord - tout à fait d'accord (échelle de Likert à 5 points)
	Le frottis cervico-vaginal est suffisant pour prévenir le cancer du col utérin	Pas du tout d'accord - tout à fait d'accord (échelle de Likert à 5 points)
La vaccination comme norme sociale par opposition à superflue dangereuse	Mes amis font vacciner leurs filles contre les papillomavirus	Pas du tout d'accord - tout à fait d'accord (échelle de Likert à 5 points)
	La plupart des filles de l'âge de ma fille se font vacciner contre les papillomavirus	Pas du tout d'accord - tout à fait d'accord (échelle de Likert à 5 points)
	Les médecins/les professionnels de santé pensent que c'est une bonne idée de faire vacciner ma fille contre les papillomavirus	Pas du tout d'accord - tout à fait d'accord (échelle de Likert à 5 points)

FACTEURS SPECIFIQUES AU VACCINE/A LA VACCINATION		
Introduction d'un nouveau vaccin ou d'une nouvelle formulation	Le vaccin contre les papillomavirus est trop récent pour qu'on puisse savoir s'il est sûr et fiable	Pas du tout d'accord - tout à fait d'accord (échelle de Likert à 5 points)
Conception du programme de vaccination/mode de délivrance	Il est compliqué de vacciner ma fille contre les papillomavirus parce que ça nécessite 3 étapes : voir le médecin pour qu'il prescrive le vaccin, aller l'acheter en pharmacie, et retourner voir le médecin pour l'injection du vaccin	Pas du tout d'accord - tout à fait d'accord (échelle de Likert à 5 points)
	Il serait plus simple de vacciner ma fille si le médecin avait des vaccins à son cabinet pour vacciner ma fille le jour même	Pas du tout d'accord - tout à fait d'accord (échelle de Likert à 5 points)
Calendrier vaccinal	Si le vaccin contre le papillomavirus était important, il aurait été rendu obligatoire	Pas du tout d'accord - tout à fait d'accord (échelle de Likert à 5 points)
	Je trouve que ma fille est trop jeune pour être vaccinée contre les papillomavirus	Pas du tout d'accord - tout à fait d'accord (échelle de Likert à 5 points)
	Le vaccin contre le papillomavirus n'a pas été rendu obligatoire parce qu'il est risqué	Pas du tout d'accord - tout à fait d'accord (échelle de Likert à 5 points)
Rôle des professionnels de santé	Un médecin ou un autre professionnel de santé vous a-t-il déjà recommandé de faire vacciner votre fille contre les papillomavirus ?	Oui ; Non
	Avez-vous posé des questions à votre médecin traitant concernant les vaccins contre les papillomavirus ?	Oui ; Non
	(Si a déjà posé des questions) Avez-vous été satisfaite de ses réponses ?	Très satisfaite - pas du tout satisfaite (échelle de Likert à 5 points)
	(Si a déjà posé des questions à son médecin traitant concernant la vaccination contre les papillomavirus) Votre médecin traitant était-il réticent vis-à-vis de ce vaccin ?	Oui ; Non