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MEDICINE



**Adolescent decision-making and Human Papillomavirus
vaccination in France**

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**Thesis submitted in accordance with the requirements for the
degree of Doctor of Philosophy of the University of London**

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Declaration

I, Emilie Karafillakis, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

I have read and understood the School's definition of plagiarism and cheating given in the Research Degrees Handbook. I have acknowledged all results and quotations from the published or unpublished work of other people.

I declare that no copy editing and/or proofreading services were availed by me in the preparation of this thesis. I have exercised reasonable care to ensure that the work is original and does not to the best of my knowledge break any UK law or infringe any third party's copyright or other intellectual property right.

Emilie KARAFILLAKIS

21/03/2022



Abstract

Vaccination programmes around the world have faced challenges due to low or decreasing public confidence in vaccination. Human Papillomavirus (HPV) vaccination, administered to adolescents, is particularly mistrusted, reflected in low uptake rates in countries such as France. While a range of psychosocial factors have been found to influence vaccine confidence among adults, less evidence exists for adolescents.

A qualitative research was conducted as part of this PhD to identify and characterise psychosocial factors influencing adolescent girls' decision-making for HPV vaccination in France. Between October 2018 and March 2019, 24 semi-structured interviews were conducted with 15-16-year-old adolescent girls and 21 with their mothers in Paris.

Additionally, 12 girls took part in two focus groups. A codebook approach to thematic analysis based on deductive and inductive coding was used to analyse the transcripts.

Adolescents were found to make decisions based on vaccine risks and benefits' perceptions and to be influenced by information, group dynamics, trust, and contextual factors. While these factors are similar to the ones influencing mothers, differences in the type of influence were identified. Adolescents, for example, reported more positive and beneficial views and emotions towards HPV vaccination or expressed more trust in vaccines and health authorities than mothers. Maturity was also found to influence adolescents' involvement in decisions and their decision-making process. Interestingly, the conflicting and sometimes anxiety-inducing vaccination environment led to adolescents showing more signs of rational rather than impulsive or emotional decision-making than mothers.

These findings are summarised in an innovative model of adolescent vaccination decision-making, which can be helpful for the development of strategies aimed at increasing

confidence in adolescent vaccines, especially in the recent context of the COVID-19 pandemic in which adolescents have been more engaged and empowered to take control over their own health.

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List of abbreviations

AIDS – Acquired immunodeficiency syndrome

CRPS – Complex Regional Pain Syndrome

ECDC – European Centre for Disease Prevention and Control

EEA – European Economic Area

EU – European Union

GP – General practitioner

HIV – Human immunodeficiency virus

HCW – Healthcare worker

HPV – Human Papillomavirus

LSHTM – London School of Hygiene & Tropical Medicine

MSM – Men who has sex with men

PoTS – Postural Tachycardia Syndrome

STI – Sexually transmitted infection

UK – United Kingdom

VCP – Vaccine Confidence Project

WHO – World Health Organization

Chapter 1: Introduction

Public resistance to vaccination can be traced back to the introduction of the first vaccine against smallpox in the 18th century, when populations expressed worries about vaccine safety and effectiveness, religious and philosophical concerns, resistance to compulsory vaccination, and a lack of understanding of the principles of vaccination (1). Nowadays, a decline of confidence in vaccination can be seen in many pockets of populations around the world, threatening the success of vaccination programmes and leading to outbreaks of vaccine-preventable diseases such as measles or poliomyelitis (2, 3).

The World Health Organization (WHO) has coined the term “vaccine hesitancy” in an effort to bring this issue higher on the research agenda and to develop a better understanding of this heterogeneous group of individuals who delay or refuse some or all vaccines, or who accept vaccines but remain concerned about them (4). Vaccine hesitancy has been described in relation to three concepts: complacency (i.e. perceived need or value for the vaccine), convenience (i.e. access to the vaccine) and confidence (i.e. trust in the vaccine or provider). However, the use of the term vaccine hesitancy comes with negative connotations and can have a victim blaming and polarising effect. In fact, individuals rarely identify as ‘vaccine hesitant’ or, as often reported in the media, as ‘anti-vaxxers’. This PhD research therefore mostly focuses on vaccine decision-making and the concept of vaccine confidence, acknowledging the existing spectrum of confidence levels.

Various frameworks and theories of vaccination decision-making have been developed in recent years, describing the factors influencing individuals’ confidence in vaccination and their decisions to accept or refuse vaccines for themselves or for their children (5-7).

However, while evidence assessing the psychosocial factors influencing vaccine confidence has flourished among parents and adults, including healthcare professionals and pregnant

women, less evidence exists about adolescents. Some studies have looked at the reasons behind adolescents' refusal or concerns about certain vaccines, but frameworks of vaccination decision-making are rarely adapted to adolescents. Yet, adolescents are not only the recipient of certain vaccines (e.g. COVID-19, Human Papillomavirus (HPV), or Meningococcal) and increasingly involved in decision-making, but they are also the adults and parents of tomorrow. As vaccine confidence is population specific, varying by socio-economic status, age or gender, it is therefore essential to understand how the factors influencing vaccination decision-making apply in the context of this distinct period of life.

1.1 Factors influencing vaccination decision-making in adolescence

1.1.1 Adolescence: a transitional period

Adolescence refers to the transitional period between childhood and adulthood, when an individual reaches biological and psychological maturity. Adolescence entails physical, neurodevelopmental, psychological and social changes (8). It is a period “marked by developmental changes and transitions across multiple areas, including greater independence from parents, increased closeness with peers and multiple school transitions” (9). Those transitions and changes can have important implications for health and behaviour, with studies for example showing an increase in depression during early and middle adolescence (10, 11). Some studies have also found that adolescent females were more at risk than males to suffer from depression (10, 12), which could be due to females reporting greater peer closeness and self-disclosure (13).

Adolescence also corresponds to a time when peer selection and socialisation appear, as adolescents become more intimate and start sharing more personal thoughts, feelings and empathy with their friends (9). This can help adolescents develop a sense of personal identity

and receive validation of their beliefs and attitudes by their peers (9, 14). Schools can also have an important influence on adolescents' behaviours due to stressful events such as exams, graduation, or social gatherings (15, 16). Different school transitions or even drop-outs have also been shown to influence selection and socialisation processes among adolescents, with the loss of old friendships associated with reduced self-esteem and increased rates of depression and loneliness (17).

1.1.2 Factors influencing vaccination decision-making

In the same way that vaccine confidence cannot be explained by a single factor but is instead the consequence of a multitude of psychological, social and contextual factors; the study of decision-making pulls together a range of intellectual disciplines, including psychology, sociology, political sciences, anthropology and public health. While all these disciplines need to be considered in order to develop a comprehensive understanding of factors influencing decision-making related to vaccination, this research focuses on psychosocial factors: adolescence is associated with powerful psychosocial development which have only rarely been characterised and studied in the context of vaccination.

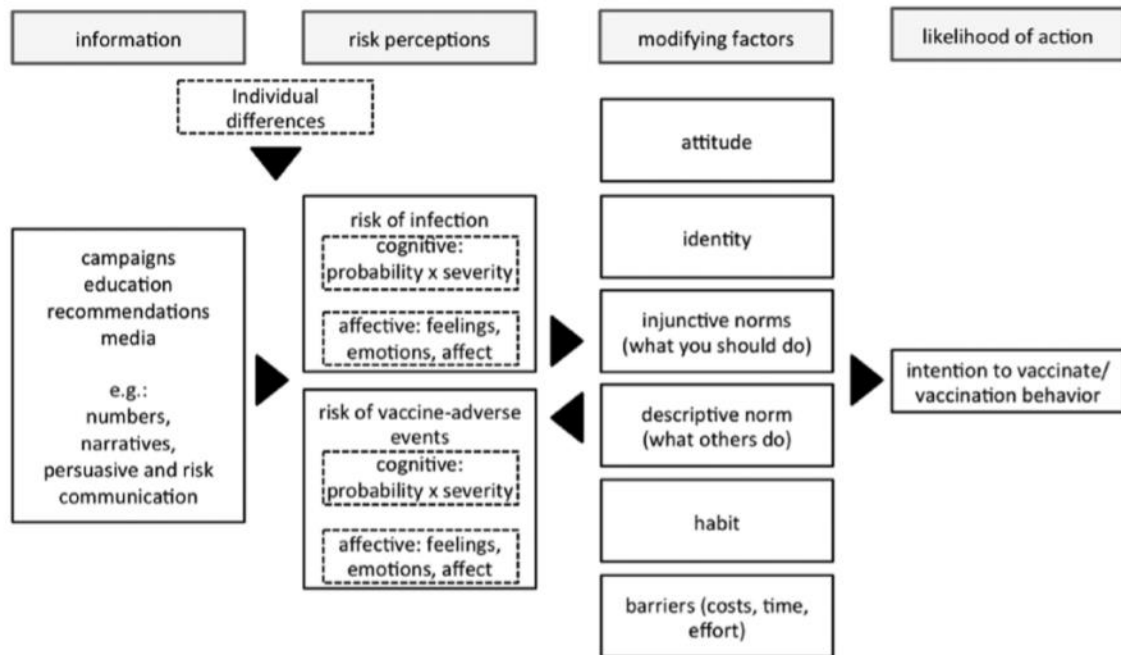
Models, frameworks and theories are useful to understand why individuals engage in certain behaviours such as vaccination and how they can be empowered to modify their behaviour when necessary (18). Various models have been applied to help explain vaccination behaviours, including health promotion models such as the Health Belief Model that explains individuals engage in certain behaviours based on perceived threats (i.e. susceptibility and seriousness of consequences of a problem), outcome expectations (i.e. benefits of engaging in the behaviour and possible barriers) and cues to action (i.e. triggers that can activate a behaviour such as health education campaigns) (19) or the Theory of Planned Behaviour

which argues that behaviours are a direct consequence of one's intentions which are formed by attitudes, subjective norms and perceived behavioural control (18, 20, 21).

Yet, as models constitute simplified representations of reality, they cannot by themselves explain all the complexities of individual, social or organisational behaviours (18).

Vaccination behaviours are particularly affected by a wide diversity of vaccines, populations and settings and newer models have therefore been adapted to specifically focus on behaviours related to vaccination. This includes the “*Determinants of vaccine decision-making model*”, developed by Betsch, Böhm and Chapman (Figure 1) (6). This model was selected as the theoretical background for this thesis because it was developed based on a thorough review of existing behavioural models and concentrates on psychosocial factors, one of the focus of this study. The model incorporates both individual-level factors influencing vaccination behaviours as well as social or contextual ones such as information, or norms. Finally, it differs from other vaccination-specific models such as the WHO ‘Determinants of vaccine hesitancy’ framework (listing vaccination-specific, individual/social group and contextual influences of vaccine hesitancy) (7) or the 5C model (describing vaccine hesitancy as a consequence of confidence, convenience, complacency, calculation and collective response) (22) as it focuses on behaviour and decision-making around vaccination rather than vaccine confidence or hesitancy. While the model does not directly include some essential elements such as the role of trust or contextual factors, it is one of the most comprehensive models of vaccination decision-making.

Figure 1: Determinants of vaccine decision-making (6)



The model describes vaccination behaviours or intentions in relation to how individual perceive the risks of infection with a vaccine-preventable disease in comparison to the risks associated with the vaccine itself. These cognitive and affective risk perceptions can be influenced by information (including how information is processed, depending on individual differences) as well as a range of modifying factors that can also influence vaccine intentions and behaviours directly.

The sections below present the core factors influencing vaccine decision-making, discussed in the context and through the lens of theories about adolescent decision-making: risk perceptions (including modifying factors), information (including individual differences), as well as two additional modifying factors, namely trust and peer influences. While these are not distinctly included in the model, they constitute additional important modifying factors that can influence the impact of risk perceptions and information on vaccine behaviours.

Risk perception

In health, risk has been defined as “the probability that a specific action or exposure will give rise to a negative health outcome” (23). Various experts have stated that the recent development and complexification of technologies have led to a strong need for the establishment of the field of ‘risk assessment’ focusing on the scientific understanding and measurement of risks (24, 25). At the same time, however, individuals have been left to face the difficult task of comprehending and assessing the risks posed by new technologies, such as vaccines, for themselves. They have therefore relied on their intuition to form their own perception of risks (25). While actual risks are measured by experts, perceived risks refer to subjective and experienced versions of risks by laypersons and therefore sometimes represent a distorted version of risks, shaped by psychosocial and cultural factors (25, 26).

The study of risk perception has been essential to the understanding of vaccine confidence and acceptance. In fact, risk perception is the core component of most decision-making models that explain that decisions or intentions to receive a vaccine are influenced by an individual’s perception of the risks of vaccinating (e.g. possible side effects) vs the risks of not vaccinating (e.g. suffering from vaccine-preventable diseases). If the risk of vaccination is perceived to be greater than the risk of the disease it prevents, then an individual will be less likely to vaccinate (and vice versa) (6, 27).

Adolescents’ perception of risks is fundamentally different from adults, primarily because they tend to overestimate risks (28, 29). This could be explained by factors such as peer influences and emotional reactions to risks. However, while they have a heightened perception of risks, adolescents are also known to be higher risk takers than adults. This has been referred to as the paradox of adolescent risk perception and can be explained by two main factors. First, adolescents place more weight on perceived benefits than perceived risks when

making a decision, even when they overestimate these risks (28). This explains why adolescents might still engage in risky behaviours if they perceive certain benefits associated with the behaviour, even if these benefits are not related to health such as social benefits. As adolescents process risk information superficially and focus more on the present rather than the future, short-term benefits (peer acceptance) have more impact than long-term benefits or goals (cancer prevention) (28, 30). The second factor that could explain why adolescents engage in risky behaviours is the perception that they are less vulnerable to certain risks than their peers (28, 31). However, this optimistic bias could be absent in the context of perceived risks of vaccination. The recent occurrence of mass psychogenic illnesses following HPV vaccination (15) could indicate that as adolescents hear more rumours and/or are exposed to more peers who believe they have been physically affected by HPV vaccination, they could be led to believe that they are actually more vulnerable. Mass psychogenic illnesses refer to the rapid spread of a range of symptoms such as fainting without a biological or organic cause but a psychological one such as anxiety. With the rise of social media, these symptoms can now spread without the need for physical closeness, which could lead to higher vulnerability of adolescents to the spread of rumours.

Additionally, individuals have been shown to comprehend risks in two ways: an experiential and/or an analytical way (32, 33). The analytical system is slow, effortful and uses “algorithms and normative rules, such as probability calculus, formal logic, and risk assessment” while the experiential system is “intuitive, fast, mostly automatic, and not very accessible to conscious awareness” (34). Slovic referred to those two systems as an assessment of risks as *feelings* or as *analysis* (34). Although both systems operate in parallel, it is faster, easier and more efficient to rely on the experiential system to navigate a complex, uncertain, and sometimes dangerous world. When making decisions about vaccination, individuals are influenced both by emotional and by cognitive representations of risks (32).

Adolescents also use those two systems to comprehend risks (34) but studies have shown that they cannot control impulses or emotions as well as adults because their cognitive system is not fully developed yet (35). This means that they rely much more on their socio-emotional systems. For example, they can be highly influenced by *anticipated* emotions such as regret they expect as a result of certain decisions but also by imitation, habits (past vaccination status), social conventions, and heuristics (28, 36).

However, some evidence also contradicts the influence of impulses on adolescent decision-making. The fuzzy trace theory model claims that adolescents rely less on intuition than adults and that decision-making relies both on gist and verbatim representations of information (37). Events, information, or description of risks are encoded into an individual's memory in two separate but parallel forms. Verbatim representation is an objective, precise and quantitative representation of information (in the form of text, graphs, numbers, pictures, or statistics). Gist representation is the subjective, vague, qualitative interpretation of information: it is the bottom-line meaning an individual gives to information based on emotions, education, culture, and experience (37). The model makes the assumption that adolescents rely more on verbatim representations as they do not have enough experience to rely on gist-based intuition, which develops with age and maturity (37).

The role of information

In recent years, various movements in public health have called for “patient empowerment” and the inclusion of the general population in shared-decision making in relation to their own health, together with their doctors or other healthcare professionals (38). These movements have brought to light the central role and impact of information (i.e. facts or details about a specific topic) on health decision-making. Health information comes in different shapes and forms, with medical professionals using medical or scientific information to support their

proposed diagnosis, treatments or preventive measures and individuals engaging in health information-seeking behaviours to obtain information to help them make a health decision (39). Additionally, in today's communication environment, individuals are also constantly exposed to information, including information about health or vaccination, whether they engage in information-seeking behaviours or not.

The study of vaccination behaviours and decision-making is therefore closely linked to the study of information. Information individuals receive or seek around vaccination, and most particularly around the risks and benefits of vaccination, can greatly influence beliefs and behaviours, with different sources of information, content, quality and quantity of information affecting individuals differently. For example, studies have shown that individuals respond differently to information coming from different sources (e.g. mass media, social media, healthcare professionals, friends and peers), depending in part on their perceived trustworthiness of this source of information (40, 41). Information presented in the media or coming from friends and family might also be presented in a more narrative format, which can be more influential than statistical or scientific information provided through more 'trustworthy' sources of information (27, 42). For this reason, it is not always because individuals receive positive, high-quality information about vaccination (for instance in the form of official information coming from health authorities or health professionals) that they will be more confident in vaccination. This complexity also explains why individuals might be more influenced by rumours or misinformation relating personal stories that are more memorable and often more emotional than recommendations to vaccinate. Finally, while individuals often complain about a lack of information about vaccines (43), too much information can also have a negative impact on vaccine confidence. While information used to be disseminated by a handful of organisations, people are now facing an increasingly fragmented information environment in which they can constantly access information coming

from a multitude of sources (44). The development of social media and other interactive communication channels also means that everyone can now become producers, distributors and editors of information, which has facilitated the spread of information both supporting and criticising vaccination (44). The important rise of misinformation around vaccination means that people are now being asked to make decisions about vaccination while exposed to conflicting or contradictory information, which has been shown to increase uncertainty and reluctance to act on recommendations (45). In fact, conflicting information environments are difficult to navigate and lead to a lack of clear guidance or cues that individuals can use to predict possible outcomes and make decisions with high confidence (45).

It is important to highlight that individuals perceive vaccines in a certain way based on information they receive (for instance from mass campaigns or healthcare professionals) but most importantly, based on a subjective representation of this information (6). This means that individuals do not always make rational decisions, based on knowledge and objective information they have about a vaccine. Any information adults or adolescents receive about risks or benefits of vaccination is processed and given personal meaning based on individual characteristics such as heuristics, emotions, and ability to process statistics or health literacy (which can translate to trust if an individual does not possess these abilities) (6). Heuristics constitute a good example of how individuals take mental shortcuts to make decisions, which can lead to cognitive biases in the representation of risks. Tversky and Kahneman have described three main heuristics that are used to facilitate decision-making and process information, particularly in a context of uncertainty: representativeness (e.g. making judgement of who is at risk of vaccine-preventable diseases on the basis of similarity), availability (e.g. assessing likelihood or frequency of an event such as vaccine side effects, based on how easily that event can be brought to mind), and anchoring (i.e. estimating a

number such as the prevalence of a vaccine-preventable disease or of vaccine side effects based on a readily available value, even if incorrect) (46).

However, perceived lack of information and associated uncertainty can also influence decision-making about vaccination. Uncertainty refers to a situation when an individual does not have confidence in one's own level of knowledge (internal uncertainty) or in the general or others' state of knowledge (external uncertainty) to make a decision (47, 48). Although uncertainty could reflect an actual lack of knowledge, when information is lacking, incomplete, unclear, or too abundant (47, 49-52); it is more often related to an independent *perceived* lack of knowledge which means individuals could still feel uncertain even if they were to possess all the sufficient and available information to make a decision (53). External and internal uncertainty are interrelated, as the perception that an institution (i.e. health authorities or scientific experts) does not possess sufficient information about vaccination could also result in an individual's personal uncertainty around the vaccine.

Uncertainty is not always negative: if individuals are uncertain about the benefits of vaccination (prevention of diseases), this could have positive consequences such as hope, optimism, and an intention to receive a vaccine. On the other hand, uncertainty about potential side effects of vaccination, corresponding to risk perception, could create fear and anxiety and dissuade individuals from getting vaccinated (53-55). Evidence on the effects of this uncertainty on adolescents' decision-making remains sparse.

Trust

Trust has been defined as the belief that "someone is good and honest and will not harm you, or that something is safe and reliable" (56) as well as a "psychological state comprising the intention to accept vulnerability based upon positive expectations of the intentions or behaviour of another" (57). Trust is different from confidence, in that confidence is often

expressed in systems (e.g. vaccination programmes) while trust is more often related to interpersonal relations (e.g. individuals, groups or institutions) which means it often depends on others' behaviours and their competences (both moral and affective) (58). The model of Trust, Confidence, and Cooperation take a slightly different approach and further differentiates between trust and 'confidence', described in relation to perceived performance or competency as well as 'social trust' described in relation to perceived morality or shared values (59). This distinction is particularly important in the study of risk and vaccination, highlighting the central role of trust in vaccination decision-making. In fact, trust can for example play a key role in one's appraisal of information or their perception of the risks and benefits of vaccination.

The relation between trust and risk has been studied extensively. As risks have become increasingly difficult to assess and measure, individuals lacking a high scientific knowledge sometimes take a leap of faith in experts to assess the severity and likelihood of risks for them (24, 46, 60, 61). This has sometimes been referred to as 'reluctant trust' as individuals feel the need to place their trust in others, sometimes reluctantly (62, 63). The delegation of risk assessment to trustworthy individuals (family, friends, healthcare providers) or institutions (healthcare authorities, governments, schools) can influence adolescents' subjective cognitive and emotional comprehension of risks (64). Most of the time, trust towards proximal actors is stronger than trust in more distal actors: Giddens has explained that true relationships of trust can only be formed in the case of face-to-face interactions (65). It is easier to place trust in someone one can see, talk to and have known for a long time, such as a general practitioner (GP) or a friend, than in a foreign, more abstract institution. For some vaccines such as HPV, both the benefits (preventing cancer) and perceived risks (feared long-term side effects) are long-term and therefore invisible at the time of vaccination.

Therefore, adolescents can rely on parents, teachers, doctors, scientists and experts to assess them and communicate what is known and unknown.

However, trust can rapidly be eroded by changes of circumstances, particularly when individuals believe doctors or institutions have mismanaged specific events or have failed to communicate risks (66-68). Mistrust could lead to individuals doubting the credibility of scientific information and placing their trust in other sources of information which could influence risk perception (51).

Peer influences and group dynamics

Many decision-making models acknowledge that risk perception is mediated by social influences from friends, families, or peers. Social influences relate to how individuals may change their behaviours, or even their beliefs or values, based on their social environment. While social influence can happen on purpose, when individuals or organisations intentionally try to change someone's mind (for example when public health authorities or anti-vaccination groups try to change people's beliefs about vaccination in one way or another), it can also happen inadvertently, with individuals not realising that they are being influenced (69). In relation to vaccination decision-making, social influence can take varied forms. For instance, it can refer to exposure to information from peers or family members: discussions about vaccination (or other beliefs) with loved ones can influence one's own perception or simply provide more information (or misinformation) to individuals (70). Another mechanism is the impact of "social norms": individuals are known to modify their behaviours to fit in with others, either by copying others' behaviours (descriptive norms) or by acting how they believe others would like one to behave (injunctive norms) (71, 72). Slovic has also shown that individuals part of certain social groups will either emphasise or downplay risks in order to maintain and control the group (71). Additionally, the study of

group dynamics shows that we tend to associate with people who share the same beliefs as us, sometimes thereby reinforcing our own views and attitudes and creating clusters of individuals with particularly strong views for or against vaccination (73). Our new communication environment and how we connect with others, for example through social media, has further changed group dynamics and it is possible that social influences now also take place within groups that have never physically met (74).

Adolescents are more susceptible to social influences than adults because they are less family-centred, spend more time with friends, and are more influenced by what their peers think about them (75). Adolescents' unique sense of belonging to very close-knit groups with shared values and emotional reactions could explain why they are more prone to have heightened risk perceptions: peers and social networks often provide a stable relationship through uncertain times by offering validation of beliefs as well as psychological support (53). Group amplification of rumours and anxiety, together with hypersensitivity to peer rejection and approval could explain why adolescents make decisions differently when they are in the presence of peers, often taking more risks (75, 76).

1.1.3 Adolescents' participation in vaccination decisions

Understanding the factors influencing adolescents' decision-making in vaccination first requires adolescents to participate in vaccination decisions. It is therefore equally important to understand how and why adolescents are part of vaccination decision-making processes.

Respect for autonomy is one of the core principles of healthcare ethics, with Beauchamp and Childress defining autonomy as "acting freely in accordance with a self-chosen plan, analogous to the way an independent government manages its territories and establishes its policies" (77). This means that any healthcare intervention, whether curative or preventative, should respect individuals' autonomy and take into account their preferences, for example by

asking for their informed consent (18). While the principle of autonomy is not always respected, for example in the case of mandatory vaccination imposed to protect the health of the greater community, it still plays an important role in vaccination policies. However, definitions of health autonomy have focused on the right of ‘competent adults’ to make informed healthcare decisions (78), implying that adolescents or children do not have the same rights as adults in terms of respect for autonomy until they have reached maturity. In fact, healthcare and vaccination remain under parental responsibility in most countries until children reach the age of legal maturity (e.g. 18 years old) (79, 80). Yet, legal maturity does not always correspond to the age at which adolescents become competent to make medical decisions. This is recognised in certain countries such as the United Kingdom (UK), where adolescents can decide to get vaccinated without their parents’ consent based on the ‘Gillick competency tool’ that allows health professionals to assess their competency to provide consent and therefore their health autonomy (81, 82).

While no international standard defines the age at which adolescents are competent to make medical decisions, studies have shown that it can be as early as 11 years old, depending on the individual, context, and type of medical decision (83-85). Adolescents’ competency to make medical decisions is influenced by a range of factors, including their maturity level (86). The concept of maturity has been defined in a variety of ways across various disciplines. While maturity simply refers to the state of being fully developed or reaching ‘adulthood’, the use of the term shows the complexity of what it represents. First of all, maturity should be studied as a continuum rather than a binary concept: children progress through life and experience physical, neurological, psychological and social changes at different speeds (8, 86). Adolescents may also reach different types of maturity, such as emotional, social or intellectual maturity, at different times, which could impact their competency to make medical decisions (83, 87).

Cauffman and Steinberg have proposed a definition of maturity in relation to judgement in decision-making (86), which is particularly relevant when looking at vaccination. According to their work, one's maturity of judgement in decision-making is related to three psychosocial factors: 1- responsibility (i.e. development of personal identity and ability to make independent decisions), 2- temperance (i.e. control of emotions and impulses), and 3- perspective (i.e. acknowledgement of the environment and context in which decisions are made) (86). This means that even if adolescents have not reached legal maturity, they may be able to take part in decision-making, for example by participating in discussions with their parents or doctors, which could influence final vaccination decisions. More evidence is required to further understand how these factors affect adolescent participation in vaccination decision-making in a real-world context.

1.2 The role of adolescent decision-making in HPV vaccination

In order to study the role of adolescents in vaccination decision-making and factors influencing their confidence in vaccination, this PhD research focuses on HPV vaccination in France.

1.2.1 HPV infection and vaccination

HPV infection is one of the most common sexually transmitted infections (STI) (88). HPV prevalence among women in Europe is 8.1%, ranging from 29.1% in Eastern Europe to 5.7% in Southern Europe (89). HPV prevalence is also high among men who have sex with men (MSM) and Human immunodeficiency virus (HIV) seropositive men (90).

While most HPV infections will be cleared out naturally by the immune system, it can sometimes be associated to the development of genital warts as well as cervical, anal, oropharyngeal, penile, vaginal, and vulvar cancers (91). More than 40 types of HPV exist,

classified as low or high risk depending on their potential to cause cancer. Following breast cancer, cervical cancer is the second most important cancer for women aged 15-44 years in Europe in terms of incidence (8-29.9/100,000 females) and mortality (88, 92). Evidence has shown that 85% of new cases of cervical cancer in Europe are caused by eight “high-risk” types of HPV (16, 18, 31, 33, 35, 45, 56, and 58) and that HPV 16 and 18 alone contribute to an estimated 73% of these new cases (93, 94).

Cervical cancer prevention in Europe consists of routine cytological screening programmes and vaccination programmes (88). Three different vaccines are available in Europe: Cervarix, a bivalent vaccine targeting HPV types 16 and 18, Gardasil, a quadrivalent vaccine targeting HPV types 6, 11, 16, and 18 and Gardasil 9, a 9-valent vaccine targeting HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58 (95, 96). Vaccines are given over a six months period in two or three doses before onset of sexual activity (97). Following cost-effectiveness modelling studies, many countries initially decided to include vaccination for adolescent girls only (98). However, in an effort to address the risks posed by HPV to men as well as some of the moral issues of programmes focusing solely on girls, gender neutral programmes have now been introduced in 10 out of 27 EU Member States, with another eight countries planning to introduce the vaccine to boys (99).

While HPV vaccination has been introduced in most European countries (100) with different financing systems and delivery infrastructures (97), countries have had varying degrees of success, with coverage rates ranging from 17% in Luxembourg to 84% in Portugal (2012) (97). Many immunisation programmes, such as the one in France, are facing important public questioning of HPV vaccination (101).

The routine HPV vaccination programme started in France in 2007, targeting 14-year-old girls with a catch-up campaign for girls up to 23. Since 2012, the programme targets 11 to 14

year old girls with a catch-up campaign for those aged 15 to 19 (102). This age group corresponds to major life changes and school transitions, as children move from primary school (ages 6-11) to middle school, or *Collège* (ages 11-15) and then high school, or *Lycée* (ages 15-18). In 2014, the official recommendation changed from three to two doses and boys were added to the vaccination programme in 2020 (102). Both Cervarix and Gardasil vaccines are available for purchase at pharmacies and can be injected by GPs, paediatricians and gynaecologists. The social security system only reimburses 65% of the cost of the vaccine, which can make it difficult for some to purchase the vaccine as one dose costs around 110-130€. In 2012, HPV vaccination coverage for the complete course was between 25-29.3% (103), dropping to 14% in 2015 (104) and increasing again to 32.7% in 2020 (105).

1.2.2 Determinants of HPV vaccine hesitancy in Europe and France

In 2016, Europe was identified as the region in the world with the lowest levels of public confidence in the safety and importance of vaccines, with France one of the most affected countries of the region (106). Some of the factors influencing European populations' confidence in vaccination include beliefs that vaccines might be unsafe and have important side effects, perceptions vaccines are not needed as the diseases they prevent are not severe, and beliefs vaccines are not effective (43). While public questioning of vaccination has been identified in relation to various vaccines such as measles or influenza, concerns are particularly high with regards to HPV vaccination (107).

In order to understand the factors that influence confidence in HPV vaccination in Europe, a systematic literature review was conducted as part of this PhD research (see chapter 2). The review offers an overview of the factors influencing different population groups in Europe, which will provide an opportunity to contextualise factors influencing adolescent girls in France. While the review is not linked to any overarching objective of this thesis (see section

1.3 for the list of aim and objectives), findings from the review were used to further refine the qualitative methods for this research (see chapter 3, section 3.1.2 for more details).

1.3 Aim and objectives

The aim of this PhD research was to **identify and characterise psychosocial factors influencing adolescent girls' decision-making with regards to HPV vaccination in France**. The decision to focus on HPV relates to the less than optimal uptake rates across many European countries, particularly in France, which constitutes a good example of a country with low confidence in vaccination. Furthermore, adolescent girls were selected for this research, as they were the sole recipients of the HPV vaccine in France at the time of the study. As parental consent is required for HPV vaccination in France and mothers are often the final decision-makers when it comes to HPV vaccination, mothers were also included in this study to contextualise adolescent girls' responses.

The specific research objectives of the PhD research, which are explored in the different chapters of the thesis, were to:

1. Characterise HPV vaccination risk and benefit perceptions and their influence on decision-making among adolescent girls and their mothers (chapter 4)
2. Explore the influence of information and trust on HPV vaccination decision-making among adolescent girls and their mothers (chapter 5)
3. Investigate decision-making processes between mothers and adolescent girls around HPV vaccination (chapter 6)
4. Develop a model synthesising the psychosocial factors influencing adolescent vaccine decision-making (chapter 7)

Chapter 2: HPV vaccination in a context of public mistrust and uncertainty: a systematic literature review of determinants of HPV vaccine hesitancy in Europe

RESEARCH PAPER COVER SHEET

SECTION A – Student Details

Student ID Number	315566	Title	Ms
First Name(s)	Emilie		
Surname/Family Name	Karafillakis		
Thesis Title	Adolescent decision-making and Human Papillomavirus vaccination in France		
Primary Supervisor	Heidi J Larson		

If the Research Paper has previously been published please complete Section B, if not please move to Section C.

SECTION B – Paper already published

Where was the work published?	Human Vaccines & Immunotherapeutics, Taylor & Francis		
When was the work published?	20/02/2019		
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion	n/a		
Have you retained the copyright for the work?*	No	Was the work subject to academic peer review?	Yes

*If yes, please attach evidence of retention. If no, or if the work is being included in its published format, please attach evidence of permission from the copyright holder (publisher or other author) to include this work.



SECTION C – Prepared for publication, but not yet published

Where is the work intended to be published?	_____
Please list the paper's authors in the intended authorship order:	_____
Stage of publication	Choose an item:

SECTION D – Multi-authored work

<p>For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)</p>	<p>I am the first author on this paper, published with 10 other authors. I led the design of the study and methodology for the systematic review, conducted the search in various databases, screened articles by title and abstract and by full text, extracted data, analysed and interpreted data and wrote the manuscript.</p> <p>HL supported with the development of the study design and methodology. CS was the second reviewer for the selection/screening of articles. CJ conducted the critical appraisal of studies, which I revised.</p> <p>Other authors supported with various elements of the article, such as data extraction or interpretation and analysis of the findings.</p>
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SECTION E

Student Signature	
Date	11/03/2022
Supervisor Signature	
Date	18/03/2022

This chapter is the accepted manuscript of an article published by Taylor & Francis in Human Vaccines & Immunotherapeutics on 20 February 2019, available online: Karafillakis E, Simas C, Jarrett C, Verger P, Peretti-Watel P, Dib F, et al. HPV vaccination in a context of public mistrust and uncertainty: a systematic literature review of determinants of HPV vaccine hesitancy in Europe. Human Vaccines & Immunotherapeutics. 2019;15 (7-8): 1615-1627. <https://doi.org/10.1080/21645515.2018.1564436>

2.1 Introduction

HPV vaccination was introduced into national immunisation programmes in all European Union (EU) countries, apart from Poland, between 2006 and 2018 (108).

The HPV vaccine is mainly given to adolescent girls (9-18 years old) to prevent cervical cancer and/or genital warts, but sometimes also given to boys (e.g. Austria) or MSM (e.g. the UK) to prevent other HPV-induced cancers (108). Coverage rates have been suboptimal in some EU countries, particularly in Eastern Europe but also in Ireland, France, and Denmark (100). Romania had initiated a programme in 2008, but discontinued their HPV vaccination in 2014, due to very low acceptance (108). These variations could partly be explained by contextual and implementation factors because the vaccine is currently delivered through schools or public or private health systems, depending on the country and immunisation programme. However, HPV vaccination coverage rates are also affected by healthcare worker (HCW) recommendations and public demand which are both known to be influenced by confidence in the vaccine (43).

In recent years, HPV vaccination has suffered from growing public distrust and criticism in Europe (109). Vaccine hesitancy has been defined by the WHO SAGE working group as a behaviour influenced by issues of confidence, complacency, and convenience. Vaccine hesitancy does not always imply vaccine refusal, as hesitant individuals can accept certain vaccines but still have doubts about them (4). European vaccine hesitancy can partly be attributed to a lack of confidence in vaccine safety, perceptions that vaccines do not work,

distrust of information, perceived low risks of vaccine-preventable diseases, as well as a lack of trust in HCWs, authorities, and pharmaceutical companies (106, 109).

Many studies have been conducted in Europe and around the world to explore public confidence in HPV vaccination. Some reviews have tried to summarise these studies (110-113), but they have generally focused on a particular population group or outcome. The aim of this study was to systematically review all available literature on determinants¹ of HPV vaccine hesitancy for any population group in Europe. The specific objectives of the review were to understand determinants of HPV vaccine hesitancy in the EU, compare determinants of HPV vaccine hesitancy in different European Member States, and examine the importance of safety concerns around HPV vaccination.

2.2 Methods

2.2.1 Search strategy and inclusion/exclusion criteria

A search strategy was developed in OVID Medline and adapted for use across Embase, PsycINFO, Social Policy and Practice, and Global Health in November 2016. Keywords were drawn from the SAGE review on vaccine hesitancy (4) and reviewed by a panel of European experts, selected by the European Centre for Disease Prevention and Control (ECDC) as reviewers for this project. A grey literature search was simultaneously conducted across Open Grey, Web of Science, PsycEXTRA, and organisation websites (ECDC, WHO, the UK Department for International Development, and the Communication Initiative Network).

The selection criteria, developed from the research question by two researchers (EK, HL) and reviewed by the European experts, were broad enough to ensure access to as many studies as

¹ In this paper, the expression “determinant” refers to “*influences of vaccine acceptance*”, as understood by the WHO Sage working group on vaccine hesitancy, and does not always imply causation

possible on determinants of HPV vaccine hesitancy in Europe. The search also focused on reasons for refusal or concern, public trust and confidence, perceptions, attitudes, and beliefs about HPV vaccination as the expression “vaccine hesitancy” was not commonly used before the WHO SAGE Working Group on Vaccine Hesitancy brought more attention to and usage of the term, as well as characterising and defining it (7). Articles were excluded when they did not include results about hesitancy, confidence, or trust in HPV vaccination, for instance, articles focusing solely on reasons for accepting HPV vaccination, knowledge or awareness, or uptake or intentions to vaccinate (without reasons). While certain socio-economic determinants (i.e. age, income, education level) may be associated with HPV vaccination uptake or intentions, they were excluded from this study in order to retain focus on the less-studied, non-socio-economic determinants such as mistrust and uncertainty. Articles about all types of HPV vaccine were included.

No restrictions were made on study participants, settings, or publication year. Articles from any EU or European Economic Area (EEA) countries and language were included, although only English language search terms were used. Articles comparing different vaccines or countries from inside and outside Europe were included only if data for HPV vaccination and/or EU countries were included. Quantitative (observational cross-sectional studies) and qualitative studies were included, but articles without original data (i.e. commentaries or editorials) or those which had the following foci were excluded: safety or efficacy research, serologic or immunogenicity studies, pre-clinical trials, cost-benefit or cost-effectiveness analysis. Intervention studies without data about determinants of vaccine hesitancy were also excluded as this review focused only on determinants of vaccine hesitancy.

2.2.2 Selection, management, and analysis of articles

Articles were stored in Endnote X7 (Thomson Reuters) and after duplicates were removed, were screened independently by two (EK, CS) reviewers (title and abstract followed by full text appraisal). Reviewers met to discuss differences in selection by reviewing reasons for exclusion or inclusion until consensus was met. The number of articles included at various stages were summarised using the PRISMA chart. Data from articles in English, Spanish, French, or Italian was directly collected by EK and CS on a Microsoft Excel spreadsheet while articles in other European languages were first translated by experts at ECDC.

Methodologies for mixed-methods systematic literature reviews – which combine the synthesis and analysis of qualitative and quantitative research – are relatively new and developing rapidly (114). There is currently insufficient methodological evidence on how to conduct mixed-methods reviews to identify and develop an understanding of health-related beliefs and/or behaviours. The methods for this study were therefore developed by combining and adapting methodologies from different types of mixed-methods reviews and are described in more details in the paragraph below (114-121).

Data extraction and analysis were performed by one researcher (EK) and reviewed by two researchers (CJ, HL). Two separate descriptive summaries and analyses of the studies were undertaken: one qualitative and one quantitative. No integration of qualitative and quantitative studies was performed. Data from mixed methods studies were included in both analyses. Qualitative studies were analysed thematically: a set of relevant themes was developed inductively, into which each concern was categorised and analysed. No meta-analysis could be performed for the quantitative studies, due to the heterogeneity of the studies. Instead, a descriptive analysis was performed by reporting average proportions of participants with specific concerns about HPV vaccination. Due to some studies not presenting the raw data, each proportion was calculated by averaging proportions extracted

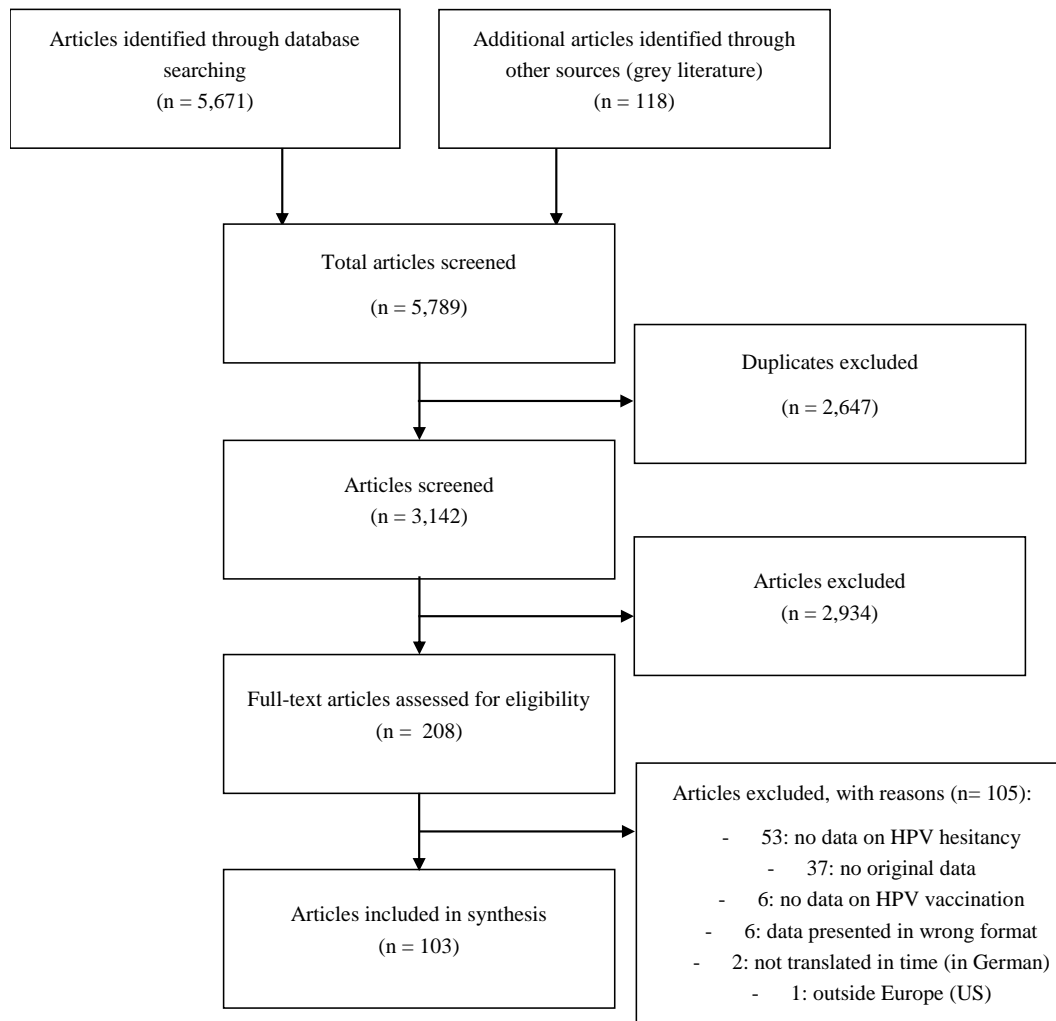
from the studies. The quantitative studies identified through the systematic review were found to assess determinants of vaccine hesitancy by looking at i) concerns among participants who had refused (or would refuse) the HPV vaccine; ii) concerns among participants who had accepted (or would accept) the HPV vaccine; or iii) concerns among participants in general (those do not correspond to the sum of the two first groups but to studies that did not specify whether participants had refused or accepted the HPV vaccine). These three categories, summarised respectively as i) “*hesitant*” participants, ii) vaccine “*favourable*” participants and iii) “*general*” participants were created by the reviewer (EK) to sort data extracted from all studies, and to limit bias when reporting proportions based on different denominators. It is important to note that concerns or doubts were reported in all three groups, and hesitant individuals can be found in hesitant, favourable and general participants (see definition of hesitancy in the introduction).

Critical appraisal of studies was performed by one researcher (CJ) and checked by another (EK). The “Effective public health practice project quality assessment tool” (122) was used to appraise quantitative studies and the “Critical appraisal skills programme qualitative checklist” (123) was used for qualitative studies. Mixed methods studies were appraised using both of these tools. Studies were included regardless of the outcome of their appraisal.

2.3 Results

The systematic literature review yielded 3,143 unique peer-reviewed and grey literature articles, of which 2,934 were excluded after title and abstract review based on the inclusion and exclusion criteria. From the 209 full text articles screened, 103 were included in the final analysis (see Figure 2).

Figure 2: PRISMA flow diagram



Twenty out of the 31 qualitative studies were found to be of “good” quality (vs. 6/31 “reasonable” and 5/31 “insufficient”); and 1/65 studies with quantitative data were assessed as “strong” (vs. 25/65 “moderate” and 39/65 “weak”) (see supplementary material 1, Appendix B). From the mixed methods studies, 0/7 were assessed as “strong” for their quantitative sections (vs. 2/7 “moderate” and 5/7 “weak”), while 2/7 were as assessed as “good” for their qualitative sections (vs. 3/7 “reasonable” and 2/7 “insufficient”).

Most studies were conducted with parents (34/103, 10 of which were with mothers only) and HCWs (22/103); and reported results from the UK (28/103), Italy (12/103), France (10/103),

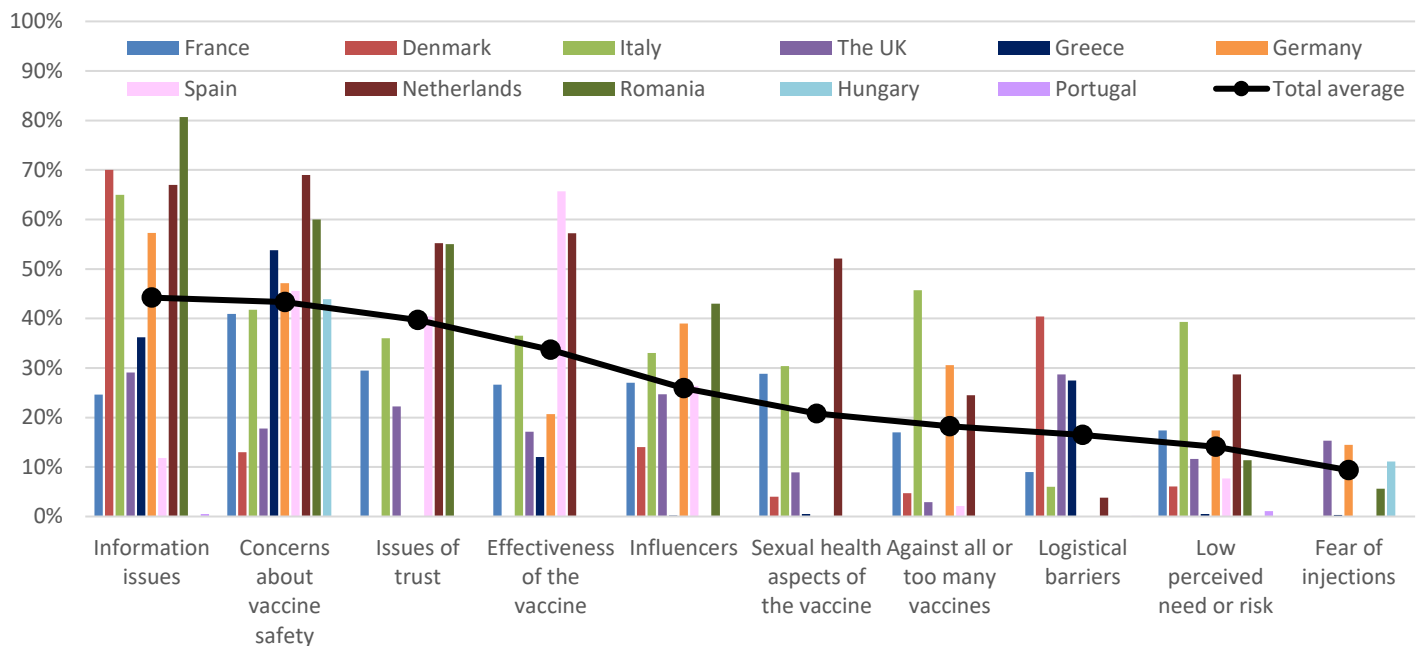
and Sweden (10/103). Readers should exert caution when looking at the data, as studies included in the review were conducted both before or after the introduction of the vaccine (from 2005–2016), which could have influenced some public opinions and therefore might not be representative of current public perceptions in countries. The years in which study data were collected are added in the results section wherever country-specific data is presented (if data collection year was not available, the publication year is instead presented). More information about study characteristics, including whether the study was conducted before or after the vaccine was introduced, are available in supplementary material 2 (Appendix B).

2.3.1 Determinants of HPV vaccine hesitancy in Europe

Ten thematic categories of determinants of HPV vaccine hesitancy in Europe were identified across the literature: i) information issues, ii) concerns about vaccine safety, iii) issues of trust, iv) effectiveness of the vaccine, v) influencers, vi) issues related to sexual behaviour, vii) against all or too many vaccines, viii) access barriers, ix) perceived need for the vaccine and risk of disease, and x) fear of injections. These are discussed in more detail in the following sub-sections. The themes most frequently identified in qualitative studies (Figure 3) were: concerns about potential side effects of HPV vaccination (37 studies with qualitative data), beliefs that information about the vaccine is insufficient and inadequate (31), and issues related to the sexual health aspects of the vaccine (22). The categories of concerns raised by the highest average proportions of hesitant participants across all quantitative studies in the review (Figure 3) were: perceived insufficient and/or inadequate information and knowledge about the vaccine (average of 44.2% of participants across all studies), fear of perceived side effects (43.3%), mistrust of health authorities, any type of doctor and new vaccines (39.7%), and doubts about the effectiveness of the vaccine (33.7%). Fear of needles and injections (9.4%) and low perceived need for the vaccine or low risk of HPV/cervical

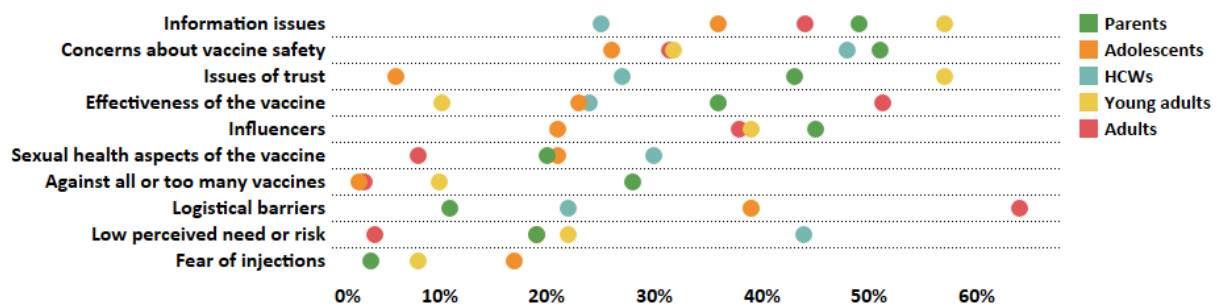
cancer (14.1%) were the categories least often reported by hesitant participants across all studies.

Figure 3: Average proportions of hesitant participants who reported certain categories of determinants of HPV vaccine hesitancy, by country



Differences between countries (Figure 3) and population groups (Figure 4) were identified, although care should be taken when looking at these differences throughout the paper as they could be due to differences in study design, variable definitions, and participant selection. For instance, overall results for a specific theme such as perceived lack of information could reflect the views of a particular population if more studies were conducted with this group. While perceived insufficient and inadequate information about HPV vaccination was found to be the most important theme in studies with hesitant participants in Romania, Denmark, Italy, Germany, and the UK, fear about potential vaccine side effects predominated the studies in the Netherlands, Greece, Hungary, and France. In Spanish studies, the most commonly reported theme was doubt about the effectiveness of the vaccine.

Figure 4: Average proportions of hesitant participants who reported certain categories of determinants of HPV vaccine hesitancy, by population groups



Concerns about potential side effects of HPV vaccination were commonly reported by hesitant parents and HCWs in studies but came second for studies with hesitant adolescents. Adolescents included in studies mostly reported dissatisfaction with the quality and quantity of information available about HPV vaccination. This was the second most important issue for hesitant parents included in studies. For studies with hesitant HCWs, the second most commonly reported theme was a low perceived need for the vaccine or a low perceived risk of HPV and/or cervical cancer.

2.3.2 Information issues

Quantitative results

Insufficient knowledge or information, and beliefs that the information available is unclear, biased and/or inadequate were identified in almost all articles reviewed. An average of 44% of hesitant participants from quantitative studies reported that there was insufficient information available about HPV vaccination, and/or that their own knowledge was insufficient (124-143), particularly in studies in Romania (2015, 81%) (132), the Netherlands (2009-2011, 67%) (128, 130), and Denmark (2010, 70%) (137). This was also reported by 53% of general study participants (144-153) and 11% of favourable study participants (127).

Additionally, 92% of hesitant parents in a study from 2009 from the Netherlands believed information about the vaccine was biased and unclear (128), while 32% of general parents in a study from 2012 in Italy (147) and 18% of general parents in a study from 2009 in the Netherlands (146) believed information was unreliable. General parents in studies in the UK (2005) and Italy (2007) most frequently reported a need for more information about HPV vaccination efficacy (74%) (152, 153), followed by vaccine safety (48%) (152), and duration of protection (10%) (152).

Qualitative results

In qualitative studies, a need for clearer, more transparent, and unbiased information about HPV vaccination (154-171) was identified by some participants, together with the need for more verbal, interactive communication (154, 157, 159, 167, 171). Additionally, some participants recommended providing information in schools, for instance by organising peer discussion groups with vaccinated girls (155, 157-159, 163, 164, 169, 171); while others preferred social media or communication methods that allow more discretion (154-156, 164, 171).

2.3.3 Concerns about vaccine safety

Quantitative results

Concerns about the safety of HPV vaccination and potential long- or short-term side effects were reported by an average of 43% of hesitant study participants (125-131, 133, 134, 136-140, 142, 144, 148, 151, 172-183). Fear of side effects was reported by an average of 52% of general study participants (153, 184-199) and 17% of favourable study participants (127, 139, 173). Concerns about side effects were particularly prevalent among hesitant participants

from studies in the Netherlands (2009-2011, 69%) (128, 130), Romania (2010, 60%) (181), and Greece (2005-2014, 54%) (133, 136, 142, 144, 180).

Qualitative results

Almost all qualitative articles described concerns about potential side effects of HPV vaccination (154-159, 161, 162, 164, 166, 168, 171, 200-209), often described as fears of long-term side effects not yet identified through trials (156, 157, 161, 162, 164, 166, 168, 171, 183, 200-206, 208). In qualitative studies, the most commonly reported perceived side effect by parents was infertility (154, 159, 161, 162, 167, 202, 204, 208). Other perceived side effects included: autoimmune complications (158, 159, 166, 201, 206, 210), resistance of the virus to vaccines and/or treatment (201, 204, 207), cancer (154), menstrual complications (167), HPV infection (161), and death (167).

In France, mothers and HCWs in studies conducted between 2007-2010 discussed rumours about Hepatitis B vaccination allegedly causing multiple sclerosis and some expressed worries HPV vaccination could have similar side effects (124, 183, 209, 211). In Sweden, study participants in 2012 worried about the safety of HPV vaccination due to reports of narcolepsy following H1N1 vaccination (158).

2.3.4 Issues of trust

Quantitative results

Mistrust of health authorities was reported by an average of 47% of general participants from studies in Sweden (2007) (212), Hungary (2009) (174), and the UK (2006) (193) as well as 55% of hesitant participants from studies in France (2015) (176) and the Netherlands (2009) (128). Additionally, 12% of GPs in general in a study conducted between 2007-2010 in France reported mistrust because of “excessive marketing” around HPV vaccination (124).

Mistrust of doctors was raised by 41% of hesitant parents in a 2009 study from the Netherlands (128), and 45% of general parents and young adults in studies from Hungary (2009) (174) and the UK (2006) (193).

Mistrust of new vaccines and concerns about the relative newness of the HPV vaccine was reported by an average of 36% of hesitant study participants (124, 129, 147, 176, 177, 209, 213, 214). In French studies, concerns about the newness of the vaccine, reported by general GPs, decreased with time but remained important: from 42% in 2007 (124, 209) to 37% in 2010 (124) and 30% in 2015 (176). Mistrust of new vaccines was reported only by 9% of general study participants in 2010 in Germany (197) and 1% of favourable study participants in Italy in 2013 (213).

Qualitative results

Beliefs that governments were not transparent (159, 161), influenced by vaccine manufacturers (154, 200) or were withholding information about side effects (167, 200) were reported in some qualitative studies. Some participants shared concerns about transparency (154, 161), commercial influences from pharmaceutical companies (154, 200, 206, 215), and perceptions that doctors were dismissive and deliberately withheld information about side effects (154, 167, 200, 206). Mistrust of pharmaceutical companies due to their underlying profit-making motives and doubts about the trustworthiness of vaccine trials and safety claims were also reported in studies in Bulgaria (2009-2014) (200, 206), Romania (2010-2012) (154), Sweden (2010, 2012) (157, 158), Ireland (2012) (165), the Netherlands (2008) (162), Spain (2014) (200) and the UK (2014) (200).

Finally, conspiracy theories about the vaccine allegedly contributing to reducing world population or being an experiment on young girls were reported in studies in Bulgaria (2010-

2013) (206), Romania (2010-2012) (154), Sweden (2014) (159), the Netherlands (2015) (167), and the UK (2007-2016) (161, 202, 207).

2.3.5 Effectiveness of the vaccine

Quantitative results

Across all studies, an average of 34% of hesitant participants were found to doubt the effectiveness of the vaccine (125, 126, 128, 134, 136, 139, 175-177, 179, 216), as well as 39% of general participants (145, 148, 184, 186-188, 198), and 3% of favourable participants (128, 139). Perceived low vaccine effectiveness was particularly prevalent among hesitant participants in studies in Spain (2013, 66%) (214), the Netherlands (2009, 57%) (128), and Italy (2006-2014, 37%) (175, 177, 216). Additionally, 41% of hesitant study participants (176, 214) and 31% of general study participants (186, 188, 199) doubted the length of protection of the vaccine.

Qualitative results

In addition to worries about the duration of effectiveness of the vaccine (124, 154, 157-159, 162, 166, 169, 201, 206, 207, 210, 211, 217), participants in qualitative studies also reported concerns that the vaccine did not protect against all types of HPV (124, 160, 203, 207, 211, 217, 218).

2.3.6 Influencers

Quantitative results

While an average of 30% of hesitant parents reported not having received any recommendation to vaccinate from HCWs in studies in Spain (2010-2011) (138), Italy (2012-2015) (131, 147, 177), Denmark (2010) (137) and France (2015) (131), an average of 26% of

hesitant parents in studies from Spain (2010-2011) (138) and Italy (2012-2014) (129, 177) were advised not to vaccinate by their HCW. Additionally, 19% of general adolescents in a study from Germany in 2010 reported having been advised not to get the HPV vaccine by their physician (197).

Furthermore, an average of 47% of hesitant parents from studies in Romania (2010) (181) and Italy (2012) (129, 147) mentioned they had received contradictory advice and opinions from different healthcare professionals or specialists. A study published in 2015 in Italy, where both boys and girls have been vaccinated since 2017, showed 38% of general men who attended sexual health clinics reported receiving contradictory advice (189).

Some adolescents also reported being influenced by their parents, with 25% of hesitant adolescent girls from studies in the UK (2008-2013)(125, 170), 39% of general adolescent girls from a study in Germany (2010) (197) and 1% of general adolescent girls from a study in Sweden (2008) (149) mentioning they could not get vaccinated because their parents had refused the vaccine (127, 172). Additionally, 11% of hesitant adolescent girls from a 2015 study from Romania reported that their parents thought the vaccine was unsafe (132).

An average of 75% of hesitant parents from a 2010 study from Romania (181) and 39% of hesitant young women from a 2013 study from Germany (139) reported being influenced by others who had refused HPV vaccination or who had recommended against it. Additionally, 49% of general adolescent girls from a 2007 study from the UK reported being influenced by rumours (125).

Qualitative results

Healthcare professionals, including school nurses and GPs, were commonly referred to in qualitative studies as having the most influence on HPV vaccination decisions (154, 159, 170,

182, 201, 206, 219). Additionally, the influence of family members, friends, and parents of other children who did not vaccinate or who recommended against the vaccine were reported across some studies (154, 159, 169, 202).

2.3.7 Issues related to sexual behaviour

Quantitative results

The belief that HPV vaccination might encourage promiscuity or earlier sexual debut in young girls was observed in an average of 11% of hesitant study participants (124, 125, 128, 134, 152, 173). This belief was also reported among 30% of general study participants (153, 177, 187, 191, 192, 212, 220) and 6% of favourable study participants (124, 173).

An average of 20% of hesitant study participants (124, 128, 129, 152, 176, 177, 209) 20% of general study participants (145, 192, 195, 199, 212) and 23% of favourable study participants (124) also believed that the vaccine would lead to unsafe sexual behaviour and a decrease in the use of condoms and cervical cancer screening. This fear was reported by 19% of hesitant HCWs in studies in France (2007-2015) (124, 176, 209) and 23% of hesitant parents in studies in Italy (2007-2014) (129, 152, 177).

Concerns about girls being too young were reported by an average of 13% of hesitant study participants (125, 128, 129, 131, 132, 134, 137, 147, 177) and 30% of general study participants (150, 212). It was most commonly reported by hesitant parents in a study in the Netherlands (2009, 52%) (128) and hesitant school nurses in a study in Sweden (2013, 48%) (212). The concern that it is too difficult to discuss HPV vaccination with adolescent girls was also discussed in studies by an average of 21% of hesitant parents and paediatricians (137, 175), and 11% of general parents and HCWs (124, 153, 184, 209, 211). An average of 27% of GPs in a 2014 study in France (184) and 32% of general adolescents in a 2008 study

in Sweden (149) also believed it was difficult to talk about the vaccine with parents, while 21% of general adolescents in a study in the UK (2007-2008) reported embarrassment around getting a vaccine against an STI (187).

Cultural and religious barriers to vaccination were indicated by an average of 16% of hesitant participants (128, 131, 133, 134), particularly in a study in the Netherlands (2009, 70%) (128).

Qualitative results

Qualitative studies reported beliefs that HPV vaccination might encourage promiscuity or earlier sexual debut in young girls (163, 167-169, 202, 203, 208, 210, 221) and that the vaccine could lead to unsafe sexual behaviour and a decrease in the use of condoms and cervical cancer screening (157, 159, 165, 166, 168, 169, 182, 208, 210, 211, 221).

Additionally, some participants mentioned that the vaccine is being given to girls when they are too young because they have not started to menstruate, are not yet sexually active or married (156, 159, 160, 163, 202, 210), or because they are too “naïve and immature” to give their consent (200, 205). Some also reported that it is not easy to talk about HPV vaccination with girls that are so young (155, 156, 161, 163, 165, 181, 200, 201, 207, 210, 216).

Finally, cultural and religious influences on vaccine acceptance reported in studies included perceived low risk of infection because of certain lifestyles (being virgins when marrying, having only one partner) (156, 159, 162, 163, 167, 201, 202, 207, 210, 211), and having a strong sense of fatality and/or belief that God will protect girls (215).

2.3.8 Against all or too many vaccines

Quantitative results

An average of 18% of hesitant study participants (127, 128, 134, 138, 139, 179, 182) were against all vaccines in general. Additionally, 33% of general study participants (192, 193) and 28% of hesitant study participants (128, 131, 137, 152, 177, 182) believed children already receive too many vaccines, with 47% of hesitant parents in a 2015 study in Germany (131) and 46% of hesitant parents in studies in Italy (2007-2015) (131, 152, 177) raising this concern.

Qualitative results

A few qualitative studies reported that some participants were against all vaccines (156, 159, 161, 171, 201, 206).

2.3.9 Access barriers

Quantitative results

In quantitative studies, cost was raised as an issue by an average of 32% of hesitant participants (133, 140, 176, 177, 182), particularly in studies in Denmark (2009, 62%) (182) and Greece (2008-2014, 54%) (133), and was also raised as a concern for an average of 47% of general study participants in Germany, Greece, Hungary, Ireland, and Sweden (148, 149, 196, 199, 222). The inconvenience of receiving multiple doses was reported by 56% of general participants in studies in Sweden (2007-2013) (198, 212), 25% of hesitant participants in studies in France (2015) (176) and the UK (2007-2008) (173), and 10% of favourable participants in a study in the UK (2007-2008) (173).

Increased workload created by administering the vaccine was raised as a barrier by general school nurses in a study in Sweden (2013, 40%) (212), while general adolescents in studies in Germany (2010, 12%) (197) and Greece (2008-2014, 1%) (133) reported being too busy to get vaccinated.

Other accessibility issues such as not having a consent form, being absent from school when vaccination was being administered, recent migration or not being in the target age group were also reported by an average 10% of hesitant participants in studies in the Netherlands (2009) (128), the UK (2011-2013) (127, 141), Italy (2008-2009) (223), Denmark (2009) (182), and Portugal (2007-2008) (135).

Qualitative results

The high cost of the HPV vaccine was mentioned in five qualitative studies, from 2009-2010 in Sweden (166, 204), 2010-2014 in Bulgaria (200, 206), 2014 in the UK (200), 2014 in Spain (200), and 2012 in Ireland (165). Another access barrier was the inconvenience of going to get multiple injections (169, 217).

The challenge of vaccinating in schools was discussed in studies in Sweden (2010-2014) (157-159) and in the UK (2006-2015) (161, 163, 203, 218), with reasons including a lack of privacy, children needing a calmer environment, missing classes, and parental informed consent. The question of which healthcare professional should administer the vaccine was raised in studies in Sweden (2010) (157, 166) and the UK (2007-2008) (161), with feelings of competition and distrust between gynaecologists and paediatricians identified in a study in Greece (2016) (201).

2.3.10 Perceived need for the vaccine and risk of disease

Quantitative results

A perceived lack of need for the HPV vaccine was reported by an average of 14% of hesitant study participants (127, 133, 134, 138, 140, 172, 177, 223), 5% of general study participants (190, 197), and 2% of favourable study participants (127).

A perceived low risk of contracting HPV infection or developing cervical cancer was reported by an average of 22% of hesitant study participants (125, 126, 128, 135, 137, 151, 178, 179, 181, 182, 216) and 26% of favourable study participants (128). Among hesitant participants, the perceived low risk of HPV was particularly prevalent in studies in Italy (2007-2015, 44%) (151, 178, 216) and the Netherlands (2009, 38%) (128).

Qualitative results

Some participants in qualitative studies expressed a perceived lack of need for the HPV vaccine due to a perceived low risk of contracting HPV and/or cervical cancer (157, 161, 168, 182, 202, 211, 217), a perceived low severity of the disease (165, 168, 183), and/or the availability of alternative prevention methods or abstinence (156, 162, 168, 171, 203, 207, 210, 217).

2.3.11 Fear of injections

Quantitative results

Fear of needles and injection pain was reported by 29% of general study participants (149, 187, 191, 194), 9% of hesitant study participants (126, 127, 132, 133, 139, 141, 148, 174), and 5% of favourable study participants (127).

Qualitative results

Qualitative studies reported rumours among adolescents about vaccination pain (204, 218), the size of the needles and the pain at injection increasing with each dose (164, 218), the mistaken belief of the vaccine being administered in the cervix (208, 218), concerns about needle cleanliness (218), and the fear that the injection could lead to a loss of virginity (170).

2.4 Discussion

This systematic literature review identified 103 unique articles on determinants of HPV vaccine hesitancy in Europe. Across European studies, the most prevalent concerns were about: insufficient and inadequate information about HPV vaccination; potential side effects of the vaccine; issues around trust of health authorities, doctors, and new vaccines; and perceived low vaccine effectiveness. While issues about the sexual health aspects of the vaccine were reported in many qualitative studies, they were less prevalent in quantitative studies, which could be explained by the nature of qualitative studies that ask open-ended questions.

Some differences were observed between studies from different European countries, with studies from Italy reporting the highest average proportion of participants with concerns about vaccination in general, issues related to the sexual health aspects of the vaccine, and perceived low risk of HPV/cervical cancer and consequent doubts about the need for the HPV vaccine. Differences might be explained by different contexts and national immunisation programmes as well previous experiences with vaccination confidence crises but could also be due to differences in study designs and the methodology used for the systematic review.

Many concerns identified in this review were more frequently observed among study participants in general rather than in vaccine-hesitant participants, while some concerns were

also reported by large proportions of favourable participants. This could be an effect of the methodology used to summarise proportions from different studies in this review: the differences could be explained by the fact that proportions from different years, countries, and population groups were averaged and compared. However, it could also point to other issues. More research should therefore be conducted to further explain these differences and explore perceptions about HPV vaccination across the continuum of vaccine hesitancy.

The most frequent concerns reported across studies and among most study participants were a perceived lack of information together with a fear of potential HPV vaccine side effects. This confirms results from previous studies about perceptions of vaccine safety being the most important determinant of vaccine hesitancy for vaccines in general in Europe (106, 109).

While some study participants raised specific concerns about infertility, most reported having general safety fears that they could not explain or specify. This could be a consequence of the vaccine still being perceived as too new and general uncertainty about the vaccine. A number of studies have shown that uncertainty can influence as much as empirical evidence in vaccination decision-making (27, 224).

Uncertainty is still often framed as something that can be overcome by filling information gaps with more facts; however, mistrust of health authorities and some doctors was commonly reported in this review, indicating that communication strategies need to include efforts to build and maintain public trust (225). Communication strategies should engage communities, for instance by building alliances with civil society or disease associations, organising school information and discussion sessions with parents and peers, and online discussion groups overseen and managed by local health professionals. More research is needed to understand information-seeking behaviours as well as how individuals appraise and use information about HPV vaccination, and finally to evaluate which communication and

engagement strategies are most effective with different population groups (e.g. parents, teenagers, ethnic/religious minorities, or HCWs) (109, 226, 227). Evaluations should focus on communication and engagement strategies developed by health authorities, but also on information that the public is exposed to every day, such as social media, online news, or television documentaries.

While influences from family members, friends, other parents or HCWs were commonly reported by parents in certain studies, adolescents in those studies also reported rumours circulating about HPV vaccination. The viral spread of negative rumours, particularly among adolescents through social media, could prove to be an important challenge should a confidence crisis arise. An example is the recent spread of unverified and subsequently disproved concerns in Denmark through YouTube videos and other social media that HPV vaccine might cause Postural Tachycardia Syndrome (PoTS) and Complex Regional Pain Syndrome (CRPS), as well as the occurrence of mass-psychogenic illnesses that have been observed and linked to HPV vaccination in Colombia and Australia (228-230). These examples illustrate the rapidity by which rumours can spread through social media and the importance of influencers and group dynamics in HPV vaccination confidence among adolescents as well as parents. Faster research is therefore needed, such as through media monitoring, to identify possible anxiety reactions, and to inform time-sensitive strategies – including crisis communication plans – on how to respond to them. The confidence crisis that occurred in Denmark provides a good example of how comprehensive strategies using a combination of social and online media interventions, engagement with mothers and adolescents, and risk communication strategies can successfully reinstate public trust in vaccination. Denmark’s success in reversing the decreasing vaccination coverage trend is in the process of being evaluated and will constitute a good case study for other countries facing similar issues.

HCWs, including GPs, paediatricians, and school nurses were identified in many studies as strong influencers for parents and adolescents but they were also found to have concerns about the safety and effectiveness of HPV vaccination, which could prevent them from recommending the vaccine (211, 230). As HCWs are often considered the most trustworthy source of medical information (231), it is important to address their own hesitancy, for instance by improving their training on the introduction of new vaccines. Additionally, as HCWs also reported facing difficulties talking about HPV vaccination in some studies, it is important to provide more support to HCWs and develop skills to manage difficult conversations. Some methods, such as motivational interviewing (232, 233) have been employed outside of Europe and could be adapted and evaluated in European countries.

2.4.1 Limitations

The results from this systematic literature review should be interpreted with some caution. While the screening of articles was conducted by two independent reviewers, data extraction and critical analysis of studies could only be conducted by a single reviewer. The results from the critical appraisal showed that many quantitative studies were methodologically weak, which can mainly be explained by the fact that the tool used to assess quantitative studies was designed for intervention studies while most studies in the field of vaccine hesitancy are observational, and often cross-sectional. This resulted in low scores for studies that did not use methods such as blinding, which are not applicable to observational studies. This limitation means that the results in this paper could not be discussed together with the critical appraisal results. While readers can refer to the results from the critical appraisal in the supplementary materials, they should therefore interpret these with caution. Information about each article's reported conflicts of interests and funding sources was also extracted and is available at readers' request. Additionally, two articles from Germany had to be omitted

due to translations not being finalised in time for this report, which could have affected the findings for the country. The database searches were also only performed in English, which means some articles in other languages might have been omitted.

The heterogeneity of the data and the analysis conducted in the different studies, which did not allow for a meta-analysis, might have introduced some bias in the quantitative analysis. For instance, proportions of participants with specific concerns were compared across countries and population groups, although the denominators (i.e. entire population, vaccine refusers, or vaccine acceptors) were sometimes very different. This was partly managed by separating the analysis for different groups. Averages were used to quantify different concerns, although data from individual studies might have been misrepresented especially as very high ranges of proportions were observed. Finally, articles looking at socio-economic determinants of vaccine hesitancy were excluded as they were outside the scope of this review. Future reviews should be conducted looking specifically at the impact of those determinants on hesitancy.

2.4.2 Conclusion

Trust in HPV vaccination is currently being shaken in many European countries, the impact of which is indicated by low and/or decreasing coverage rates. Strategies developed with the goal of addressing HPV vaccine hesitancy should not only focus on providing more information about the safety and effectiveness of the vaccine, but also aim to rebuild and maintain trust in public health institutions, including HCWs and health authorities, in order to prevent or manage future potential confidence crises.

Chapter 3: Methods

The research presented in this thesis is the work of a doctoral student at the London School of Hygiene & Tropical Medicine, Emilie Karafillakis, who is also a full-time researcher with the Vaccine Confidence Project (VCP). While her involvement with the VCP has been beneficial in providing contextual knowledge and experience to analyse and interpret the findings in this thesis, the student confirms that the design and conduct of the study is entirely her own and was developed independently of the VCP. Some of the findings included in the thesis have been published in peer-reviewed journals together with some co-authors. The literature review (chapter 2) includes Heidi Larson (the student's supervisor) who provided support and guidance on the review, Clarissa Simas who was a second reviewer for the selection and screening of articles, and Caitlin Jarrett who conducted the critical appraisal of articles, then reviewed by the student. Other authors (not members of the VCP) provided support with the analysis and interpretation of the findings. The three articles presenting the research findings of this thesis (Chapter 4, 5 and 6) were co-authored with the student's supervisors (Heidi Larson and Patrick Peretti-Watel) and advisors (Pierre Verger and Tracey Chantler), who provided support and guidance on the design, data collection, analysis and interpretation of findings. The coding framework developed to analyse the qualitative findings of this thesis was also reviewed by Clarissa Simas from the Vaccine Confidence Project to increase the quality of the research. The model developed and described in Chapter 7 was revised by the students' supervisors.

3.1 Overview of methods

While some studies have been conducted to explore the factors affecting adolescents' acceptance of HPV vaccination in France and Europe, these have mostly used quantitative

methodologies such as surveys and questionnaires, highlighting a gap in qualitative studies with more in-depth exploratory data. Qualitative research methodologies offer valuable insight into social phenomena with the aim of understanding the meanings, experiences and views of study participants in natural settings rather than experimental ones (234). They allow researchers to fully explore and understand the meaning behind people's beliefs, attitudes and behaviours (234). A qualitative research approach is ideal to explore and develop a better understanding of the process of HPV vaccination decision-making among adolescents and the psychosocial factors influencing this decision-making process. Therefore, the aim and objectives of this doctoral research were achieved by conducting a qualitative study with adolescent girls and their mothers (included to contextualise adolescents' responses). Due to the existence of quantitative research and the exploratory focus of this thesis, a mixed method approach combining quantitative and qualitative methodologies was not used. In fact, the objective of identifying as many themes and psychosocial factors affecting adolescent vaccination decision-making as possible is more suited to qualitative exploratory approaches and quantitative methodologies could instead be used at a later stage to validate the findings from this research.

3.1.1 Epistemological stance for this research

Epistemology, or the study of the type of knowledge that can be generated through research, is particularly important in qualitative research as researchers' epistemological stance can influence the design, analysis and interpretation of data (235). Some of the main epistemological stances include *positivism*, which assumes that a stable reality exists independently of our perceptions or awareness and sees research as a way to discover facts about the social world and explain reality as precisely and objectively as possible, *interpretivism*, which states that humans interpret the world they live in and research

therefore aims to understand how and why actions unfold while assuming multiple realities and provisional truth, and *constructionism*, which sees research as an interpretation of reality as it assumes that the social world is socially constructed by participants and researchers (236-238).

This thesis follows an interpretivist approach to qualitative research. It views qualitative data collection as a way of accessing authentic accounts of subjective experiences, providing a window into how participants see and experience the world (238). Interpretivism focuses on gaining an in-depth understanding of phenomenon in their unique context, therefore favouring open questions, the creation of an atmosphere conducive to open and sensitive communication by building trust and rapport (being empathetic, respectful or friendly), and active listening and engaging with respondents (236, 239). Interpretivism also means that interviews are co-produced with both interviewers and interviewees constituting active actors in the production of data, thereby acknowledging the subjective influence of researchers on participants' accounts of their experiences and their control over the interviews (240). This means that while some small steps can be taken to limit the influence of interviewers, it cannot be entirely removed and the interpretation of qualitative research should acknowledge that findings are entwined to a researcher's subjectivity.

3.1.2 Incorporating insights from the literature review

A literature review on determinants of HPV vaccine hesitancy in Europe was conducted as part of this thesis to inform the development of the methods for the qualitative research (Chapter 2). This review was conducted in November 2016 with the aim of identifying quantitative and qualitative peer-reviewed as well as grey literature published in any European country and focusing on the factors influencing HPV vaccine hesitancy in various population groups. The reason for including both quantitative and qualitative research was to

obtain information about the most common determinants of vaccine hesitancy in the region (through quantitative data) while also having a more in-depth understanding of these factors (through qualitative data). Additionally, focusing on all European countries and population groups allowed the development of the methods for this research and the contextualisation of the findings from this research, providing an understanding of how adolescents' vaccination decision-making in France fits with other factors affecting vaccine hesitancy in the rest of Europe or for other population groups.

The review found that the most common factors influencing vaccine hesitancy around HPV vaccination in Europe were related to the quantity and quality of information, concerns about vaccine safety and perceived side effects of the vaccine, and mistrust of health authorities, healthcare professionals and new vaccines. Determinants of confidence in HPV vaccination differed by country and population group, highlighting the need for local listening and understanding of the reasons driving public questioning around HPV vaccination. These findings (described in more details in Chapter 2) were used to inform the development of the methods for this research, including the development of the topic guides for the qualitative interviews and focus groups, the initial coding framework used as a baseline before inductive coding was conducted, or the interpretation and contextualisation of the findings from the qualitative research. For instance, the review identified an important gap in research conducted with adolescents, which supported the need for conducting an exploratory qualitative research to obtain a more in-depth understanding of how adolescents make decisions about vaccination. Additionally, while the review was not updated since 2016 due to time and logistical constraints, a notification system was put in place to inform the researcher of any new studies published in the field. These, together with the key findings from the review, were used to discuss, compare and contextualise the findings from the qualitative research (chapters 4-7).

3.1.3 Overview of qualitative methods used in the research

A qualitative study with adolescent girls and their mothers in Paris was conducted to identify and characterise psychosocial factors influencing decision-making with regards to HPV vaccination (*study aim*). Data collection for this study was conducted using two distinct methods with varied objectives: semi-structured interviews and group discussions (objectives 1-3). The justification for using these two methods is provided below. All findings were then interpreted in the context of relevant literature and theoretical concepts and used to design a model synthesising the factors influencing adolescent vaccine decision-making (*objective 4*).

Semi-structured interviews

Semi-structured interviews are conversations led by researchers who have a defined list of topics to be covered, while allowing participants' responses to determine the type of information that is produced about these topics and their importance. They differ from structured interviews (or questionnaires) in which participants do not have any control on the content of the discussions and in-depth or narrative interviews in which researchers provide more power to participants to choose the direction of the conversations (238). Interviews are not suitable for the discovery of what people do or what their reality is, as they instead focus on the discovery of authentic accounts of subjective experiences (i.e. how participants see and experience the world around them) (238). Interview data comes from the interaction between the researcher and the participant and the language participants use to discuss their beliefs, behaviours, or ways of classifying the world. Interviews are also less useful to produce information about interactions or behaviours of individuals in contexts other than interviews.

For these reasons, semi-structured interviews were used in this thesis to obtain accounts of the beliefs, perceptions, and attitudes towards HPV vaccination of adolescent girls and their

mothers, while also looking at the influence of key concepts such as trust or the information environment (*objectives 1-2*). The semi-structured interviews were also used to compare accounts of decision-making processes between mothers and adolescent girls, exploring the role adolescents have in HPV vaccination decision-making (*objective 3*).

Group discussions

Group discussions allow researchers to gather data from more than one participant at a time and have the advantage, compared to individual interviews, of giving access to how people interact with each other. There are various types of group discussions that can be used in qualitative research, including consensus panels, focus groups, natural groups or community interviews (241). Natural groups, in which researchers identify and interview groups that exist independently from the research, were used for this thesis as they offer researchers an insight into shared group cultures and group dynamics (238). Natural groups were therefore conducted with adolescent girls belonging from the same school class to examine in more depth how adolescent girls discuss HPV vaccination among peers (their school class) and how social group dynamics could influence individual perceptions (*objectives 1-3*). In addition to helping understand how social knowledge about HPV vaccination is generated in a natural environment (the school class), this method also allowed access to adolescents' views more easily, as they were in a friendlier environment to share their thoughts and opinions about HPV vaccination. The objective of the natural group discussions was therefore different and complementary to the objective of the semi-structured interviews.

3.2 Setting

The qualitative research was conducted in the city of Paris, in France. France was selected for this qualitative research as a country with low confidence in vaccination and with known

challenges around HPV vaccination acceptance. Selecting a context in which uptake and confidence in HPV vaccination is low was seen as a suitable strategy to explore vaccination decision-making and capture factors influencing vaccination behaviours among those who support and those who question vaccination.

Paris, as the capital of France, is a city with population groups coming from varied religious and cultural backgrounds and with different socio-economic statuses. By choosing to focus the qualitative study in Paris, the aim was to obtain a varied sample of adolescents and mothers to ensure a wide range of opinions and decision-making practices were captured.

While purposive sampling was not used, recruiting participants from such a diverse context was expected to lead to a diverse sample of adolescent girls. Paris is also a city with varying levels of confidence in vaccination, which contributed to the assumption that it would facilitate the recruitment of both vaccinated and unvaccinated adolescent girls. The focus on Paris was therefore chosen to obtain a diverse sample, which is essential for the comprehensive identification of themes (psychosocial factors) around HPV vaccination decision-making among the population of adolescent girls.

Differences in vaccine confidence levels as well as ethnicity, cultural, religious and socio-economic backgrounds appear more distinctly when looking at the different *arrondissements* of the city, or local districts. For this reason, this study aimed to recruit participants from the different *arrondissements* of Paris, in France.

It is important to highlight that the focus on Paris also has implications on the study findings, and that by focusing on the capital city, it is possible that the research failed to identify themes and psychosocial factors affecting decision-making that would have been more prominent in other parts of the country, for instance in rural areas, smaller cities or in areas with more confidence in vaccination.

3.2.1 Information about the French vaccination and healthcare system

France is one of the most populated country of the EU, with around 67 million inhabitants recorded in metropolitan France in 2020. The proportion of young people (<30 years old) has been decreasing in recent years, with 0-14 years old constituting 18% of the population and 15-29 years old constituting around 17% of the population (242). France does not collect data on ethnicity or religious beliefs at a national level.

The French healthcare system provides good access to high-quality care but faces some challenges and structural weaknesses due to low investment in public health, health promotion and the health workforce (243). It is mainly based on a social insurance system (with one of the lowest levels of out-of-pocket expenditure in the EU), with a strong centralised role of the state in the organisation of the health system (244). While preventable mortality is low compared to other European countries, low investment in public health and health promotion means that France is lagging behind some Western European countries such as Italy or Spain (243). This can particularly be seen in areas such as tobacco and alcohol control, as well as in sexual health. Sexually transmitted infections have been increasing in France, particularly in Paris (244). A national strategy for sexual health was only developed in 2017, with a focus on promoting and developing policies such as sexual health education (particularly aimed at young people) as well as prevention and screening of sexually transmitted infections (245).

Vaccination in France falls under the responsibility of the Ministry of Health, with guidance from the Technical Commission on Immunisation of the French National Authority for Health (246). Regional health agencies are then responsible for implementing vaccination programmes as part of maternal and child health policies. Promotion of vaccination is the responsibility of the National Public Health Agency, which develops communication

materials and vaccination campaigns to inform and raise awareness about vaccination among the general population as well as healthcare professionals (246). Childhood vaccines are mostly delivered by self-employed GPs but can also be administered by doctors, nurses and midwives in vaccination centres or mother and child health services (246). Parents generally have to obtain a prescription from a doctor to purchase the vaccine from a pharmacy and then bring it to a second consultation with a GP to vaccinate the child.

One of the main challenges of the vaccination programme in France comes from decreasing public confidence in vaccination, with important declines observed in the past decade.

Between 2016 and 2018, France was identified as one of the countries in the world with the lowest levels of confidence in vaccination, with 45% of the population reporting low confidence in the safety of vaccines in 2016 (106, 247). A range of reasons can explain this mistrust, such as concerns about vaccine side effects, mistrust of government, health authorities and pharmaceutical companies, or a preference for natural alternatives such as homeopathy (43). These findings led the French health authorities to take important measures to restore and rebuild vaccination confidence, including mass communication campaigns and strategies to raise awareness about the importance of preventing vaccine-preventable diseases. Additionally, 11 childhood vaccines were made mandatory in 2018, following recommendations from a public consultation on strategies to address vaccine hesitancy. These interventions contributed to an observable increase in vaccine confidence in the country since 2018 (107).

3.3 Selection, sampling, and recruitment of participants

Research participants consisted of 15 to 16 year-old girls from different *arrondissements* of Paris and their mothers. Adolescent girls were purposively selected to include a similar number of vaccinated and unvaccinated participants. However, due to the low HPV vaccine

uptake in Paris, only eight vaccinated girls were identified for this study (3 of whom took part in focus groups). The decision to focus on adolescent girls rather than boys or those who identify as non-binary was taken based on the country's official recommendation for HPV vaccination at the time of the study, which was focused on adolescent girls. It is important to note that this decision entails that the findings presented in this thesis may not be as relevant or applicable to these population groups, and further research will need to be completed to fill that gap in countries in which the vaccine is delivered through gender-neutral programmes. These reflections are also applicable to the inclusion of marginalised populations such as racially or ethnically marginalised communities. While adolescents were recruited from all areas of Paris, a multi-cultural and diverse city, purposive sampling was not used to ensure a diverse sample in terms of ethnicity or religious beliefs.

3.3.1 Recruitment for semi-structured interviews

For the semi-structured interviews, adolescent girls and mothers were recruited following a strategy of sampling by theoretical saturation (continuing to recruit participants until no new themes are identified in the data) (238). Saturation was expected to be reached at around 20 interviews for each group (total of 40 interviews).

Recruitment took place in two distinct phases between October 2018 and March 2019. In a first instance, between October 2018 and January 2019, adolescents were approached and asked to participate in the study through their schools. A list of schools in Paris, including public, private and professionals schools (or *lycées* in French) from different *arrondissements*, was developed based on public registers. Particular attention was paid to include a diverse sample of schools in terms of *arrondissements*, socio-economic circumstances and ethnical backgrounds. Consent from school directors was sought to recruit participants from their schools (Appendix C). However, only three school directors out of

150 (contacted across all 20 arrondissement) gave permission to approach adolescent girls in their schools and ask them to participate in the research, leading to four semi-structured interviews (from two schools in the 11th and 15th arrondissement). Only one of the four adolescent girls' mothers accepted to take part in an interview.

In order to recruit more participants, a second recruitment phase took place between February and March 2019. A local research agency specialised in behavioural research (BVA Group) was contracted to recruit an additional 20 adolescent girls and their mothers through their existing panel of potential research participants. This panel is formed of members of the population in France who have agreed to be contacted to take part in various studies. BVA group used baseline information of this panel to screen and identify mothers of 15-16 year old girls living in Paris and invite them and their daughters to take part in the research. A screening question was included to ensure purposive sampling of vaccinated and unvaccinated adolescent girls. Once participants agreed to take part in the research, BVA organised interviews based on the availability of the mothers and the adolescents and contacted the doctoral researcher who then presented herself to participants' homes to conduct the interviews.

3.3.2 Recruitment for natural group discussions

The study aimed to conduct three natural group discussions, each with girls from a different school class (10-15 girls in each group/class). Recruitment took place between October 2018 and January 2019, using the same first phase and approach through schools described for the semi-structured interviews. Out of the three school directors who responded favourably, only one in the 13th arrondissement accepted to organise group discussions. The director put the researcher in contact with a science teacher, who helped organise two group discussions with girls from the same class.

3.3.3 Informed consent procedure for semi-structured interviews and group discussions

During the recruitment phase, all potential participants were handed a study information letter (Appendix C), providing information about the study, confidentiality and anonymity.

Adolescent girls were informed that they first need to seek their parent or guardian consent to participate in the study, in the form of a signed consent form handed over during participant recruitment (Appendix D). If they expressed willingness to take part in the study, they were asked to bring the signed informed consent form with them to the interview/group discussion (signed by themselves and a parent/guardian). Mothers of girls taking part in semi-structured interviews were also contacted to ask whether they are willing to take part in a separate interview and were told they would need to sign a separate consent form for their own individual interview. The consent process was conducted in a private and confidential manner, and no record was kept of individuals who chose not to participate. Before each interview or focus group started, information from the study information letter was summarised verbally and participants were given an opportunity to ask questions. Participants were informed that they can withdraw from the study at any time, even during the interview or group discussion.

3.4 Data collection

3.4.1 Data collection and preparation of documents in French

Conducting a study in a different country poses challenges and possible translation biases both in the data collection and in the data analysis phase (discussed in section 3.5 below). In relation to data collection, this was partly mitigated by not having to use a translator to translate documents or interview conversations themselves, as the doctoral student is fluent in both French and English and trained and experienced in conducting qualitative research. This

means that all the interviews and group discussions were conducted in French, without the risk of losing the trust and rapport between the researcher and the participants by using a translator. In fact, the topic guide, study information sheets and informed consent forms were developed by the researcher in English to facilitate review by the student's English-speaking supervisors and ethical committee. Then, all documents were translated into French by the student, paying attention to medical and health terminology. These documents were then reviewed by the French-speaking supervisors and ethical committee. These documents were used for data collection, with the interviews taking place in French, the student's mother tongue.

3.4.2 Semi-structured interviews

In total, 24 semi-structured interviews were conducted with adolescent girls and 21 interviews were conducted with their mothers (3 mothers declined to participate).

A semi-structured approach was chosen to conduct the interviews, in order to cover predefined topics while providing the necessary flexibility for the discussions to be shaped by interviewees' beliefs and perceptions. Topic guides were developed based on the research questions and objectives (Appendix E) to structure the exchanges with adolescent girls and mothers and cover predetermined questions around HPV vaccination knowledge, beliefs and perceptions as well as decision-making processes, influences and trust. They were piloted with three adolescents (not included in the analysis) to further refine the questions and topics. Basic socio-demographic information (i.e. age, location, nationality, parents' marital status, parents' employment status, number of children/siblings) was also collected at the start of each interview.

Interviews were conducted face-to-face and lasted between 30 minutes to 1 hour. Interviews were conducted at participants' homes or at a private place of their choosing.

Parents/caregivers of adolescent girls were informed that interviews should be conducted in a private manner; no caregiver requested to be present during the interviews.

The interviews were audio-recorded with the use of a digital recorder and with prior approval from participants. At the end of each interview, field notes summarising the discussion were compiled, paying particular attention to the context, quality and feel of the exchange, as well as specific content interviewees emphasised and/or content needing follow-up.

In order to thank them for their time, adolescent girls who accepted to take part in an interview in the first stage of the study recruitment were given an opportunity to enter a lottery to receive a 20€ Amazon voucher. However, in order to comply with the recruitment agency's compensation policy, all participants (mothers and adolescent girls) recruited through BVA during the second stage of recruitment were compensated for their time (20€ each).

3.4.3 Group discussions

Approval from one school to conduct group discussions led to the organisation of two group discussions with 12 girls from the same school class (5 and 7 girls in each group). Similarly to the semi-structured interviews, topic guides were developed based on the study's research questions and objectives (Appendix E). The guides for the group discussions were based on the ones developed and piloted for the semi-structured interviews, focusing on HPV vaccination knowledge, beliefs and perceptions as well as decision-making processes, influences and trust. However, the group discussions mostly consisted of group exercises to facilitate and maximise interaction and obtain more insights on how adolescents talk about HPV among themselves. The activities were developed using literature on group discussion methodologies and the results from the systematic literature review on determinants of HPV

vaccine hesitancy. Basic socio-demographic information was also collected at the start of the group discussions.

The group discussions were conducted face-to-face and lasted around one hour. They were conducted in a private and quiet room at the participants' school. The teacher was not present in this room to respect confidentiality. The group discussions were audio-recorded with the use of a digital recorder and with prior approval from participants. Similarly to the interviews, the researcher compiled field notes summarising both group discussions.

In order to thank them for their time, adolescent girls who accepted to take part in the group discussion were given an opportunity to enter the same lottery as girls from semi-structured interviews to receive a 20€ Amazon voucher.

3.5 Data analysis

Qualitative data can be analysed in various ways, following either a deductive approach in which explanations are derived from pre-existing theories, literature or topic guides, or an inductive one, in which explanations are derived from close readings of the data (238).

Interpretivist approaches to qualitative research tend to focus on inductive analyses, sometimes including elements of deductive analyses. While this thesis' objective of developing a model of adolescent decision-making based on findings emerging from the data would have been more fittingly achieved through a grounded theory approach, timescale and practical constraints related to the requirement for conducting theoretical sampling and recruitment as part of grounded theory approaches means that this was not possible. Instead, this thesis used a thematic framework analysis with some elements of grounded theory incorporated to the analysis.

Thematic framework analyses aim to provide key elements of participants' accounts by mapping content and topics identified across datasets and summarising variations and regularities within the data. It thereby summarises salient issues or typical responses for particular groups of participants which can be useful to general policy and practice-oriented findings (238). As this thesis was not only concerned with what participants say but also why participants have and share certain beliefs, the following elements of grounded theory analysis were incorporated into the thematic framework analysis: an inductive and open process was used to produce as many descriptive and conceptual codes as possible; a constant comparative approach was used to develop categories for coding; memos were used to facilitate reflection and the development of themes from the data; and theory was built from empirical observations in which themes not only summarised the content of interviews but also the concepts that explained the content of participants' accounts. Further details about how inductive and deductive analyses were combined for this thesis are provided in the subsections below.

3.5.1 Transcription of audio-recordings

A French transcription company (AMK France) was contracted to transcribe the audio-recordings from the interviews and group discussions into Microsoft Word documents. Confidentiality rules were strictly respected by replacing personal identifiers such as names with numerical identifiers allocated to each participant (using the letter 'V' for vaccinated adolescents (A) and their mothers (M)) and removing other identifiers such as locations from the transcripts. Additionally, all files were password-protected and secured transfer mechanisms were used to share files between the transcription company and the doctoral student. All files were transcribed in French using a consistent format, with each new speaker starting on a new line, and using other commonly agreed transcript conventions. All

transcripts were reviewed against the audio-recordings by the doctoral student to check for consistency.

3.5.2 Coding and analysis

A codebook approach to thematic analysis was selected to analyse the transcripts from the semi-structured interviews and the group discussions. This approach consists of a cluster of methods that are distinct to reflective thematic analysis in its use of a structured coding framework (248).

The analysis of data (coding and thematic analysis) was conducted in French to prevent losing some of the meaning of data due to words or expressions that may not be translated directly into English. The doctoral researcher, who conducted all interviews in French, used a French transcription company to obtain French transcripts of the interviews. The transcripts were then analysed using a coding tree and themes developed in French. The only step in which data was translated back into English was for the use of quotes provided in this thesis. The student directly translated the quotes into English by paying careful attention to both the literal and conceptual translation of words and expressions. When certain concepts were not easily translated into English, these were explained together with contextual knowledge to limit possible bias in the analysis.

The student first listened to all audio-recordings and read all field notes and transcripts multiple times to familiarise herself with the data, obtain a first understanding of how participants discussed different issues and identify recurrent themes. Analytical memos were created to keep note of any thoughts about the data that could be relevant for the analysis.

While it was originally planned to conduct a separate analysis for the semi-structured interviews and the group discussions, challenges faced in the recruitment phase of this study

meant that only one ‘naturally occurring group’ (one school class) was included in the study. This made the analysis of interactions between adolescent girls difficult and did not allow for comparisons between different groups. For this reason, the transcripts of the group discussions were coded together with the transcripts from the semi-structured interviews. Analytical notes on how different topics were approached and discussed during the group discussions were instead written in the analytical memos and used to enrich the analysis of the findings where possible.

Anonymised transcripts, field notes and analytical memos were imported into the NVivo® software for coding and analysis. All files were stored on a secured server and password-protected computers. An initial coding framework was developed by deductively drawing parent codes from the topic guides, the theoretical background and the analytical memos. This initial coding framework was imported into Nvivo® to facilitate the coding of all transcripts and field notes.

Four transcripts (two mothers and two adolescents) were coded using this initial coding framework, adding additional codes through an inductive process: deriving themes from close readings of the data. The final coding framework was produced based on this additional inductive coding and by categorising, combining and re-organising different codes. The final framework was reviewed by another researcher with experience in qualitative methodologies to enhance its validity and consistency. The framework was then used to code all remaining transcripts and field notes, allowing for codes to be modified, merged or removed to fit more closely with the data during the process. While the same framework was used to code transcripts from both mothers and adolescent girls, transcripts were coded separately to detect differences and similarities early. For example, some codes were only used for adolescents and others were only used for mothers.

A specific Nvivo® function was used to organise codes and themes and to produce a lists of quotes for each code. The quotes or coded excerpts were then compared and analysed to inductively draw a list of themes, using a framework analysis approach to theme development (249). This type of approach recognises the subjectivity and contextual influence of the researchers' analysis (248). In addition to comparing and contrasting all quotes, the analysis included the terminology used by participants, how difficult it might have been to discuss certain issues and the recurrence of those issues in order to build categories and typologies and to start discussing the meaning of the data. Coded excerpts for mothers and adolescent girls were compared at this stage to ensure the themes identified were specific to the type of participant and identify possible differences and similarities between mothers and their daughters. Particular attention was also paid to exchanges between adolescent girls during the group discussions to understand how HPV vaccination is discussed among peers.

Findings were then interpreted within the context of the theoretical background and relevant literature, as well as the social and cultural context during which the interviews and group discussions took place.

3.5.3 Managing the influence of the researcher on qualitative findings

While the interpretivist approach to qualitative methods acknowledges the role and influence of researchers on qualitative data, some small steps were taken to limit this influence. The influence of the interviewer on participants during data collection was partly limited by letting participants decide on the location of the interviews, organising the interviews in private and quiet places, and by the fact that the doctoral student was a young French-speaking woman that participants could relate to more easily. This contributed to building trust and rapport between the researcher and interviewees. Additionally, the role of the

researcher's subjectivity in the analysis of data was partly limited by having a second researcher reviewing the coding framework based on four pilot interviews.

3.6 Structure of this PhD Thesis

The findings of this PhD research are summarised into three chapters (chapter 4-6), focusing on the three first objectives of this research. Each chapter corresponds to one published and peer-reviewed scientific article and therefore comprises of a short introduction, a summary of the methods (similar to the ones presented in this chapter), findings and a discussion. Chapters 7-8 then provide a comprehensive discussion and conclusion based on an interpretation of the findings from the three chapters, with the aim of addressing the fourth objective of this research.

3.7 Ethical considerations

In addition to the confidentiality and anonymity principles described in the previous sections, approval from ethical committees to conduct this qualitative study was sought. The London School of Hygiene & Tropical Medicine's Observational Research Ethics Committee provided approval for this study on the 24th of July 2018 [Ref. 15320-3]. Additionally, approval from a local French Ethical Committee based at Aix-Marseille Université was obtained on the 13th of July 2018 [Ref. 2018-12-07-005]. The study was conducted according to the guidelines of the Declaration of Helsinki.

Chapter 4: “We don’t have the same bodies; we don’t react the same way”: mothers and adolescent girls’ perceptions of the risks and benefits of HPV vaccination in France

RESEARCH PAPER COVER SHEET

SECTION A – Student Details

Student ID Number	315566	Title	Ms
First Name(s)	Emilie		
Surname/Family Name	Karafillakis		
Thesis Title	Adolescent decision-making and Human Papillomavirus vaccination in France		
Primary Supervisor	Heidi J Larson		

If the Research Paper has previously been published please complete Section B, if not please move to Section C.

SECTION B – Paper already published

Where was the work published?	Human Vaccines & Immunotherapeutics, Taylor & Francis		
When was the work published?	03/03/2022		
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion	n/a		
Have you retained the copyright for the work?*	No	Was the work subject to academic peer review?	Yes

*If yes, please attach evidence of retention. If no, or if the work is being included in its published format, please attach evidence of permission from the copyright holder (publisher or other author) to include this work.



SECTION C – Prepared for publication, but not yet published

Where is the work intended to be published?	_____
Please list the paper’s authors in the intended authorship order:	_____
Stage of publication	Choose an item.

SECTION D – Multi-authored work

<p>For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)</p>	<p>I am the first author on this paper, published with 4 other authors. I led the design of the study and methodology for qualitative research, identified and recruited participants, conducted data collection (interviews and focus groups), analysed and interpreted the data, and wrote the manuscript.</p> <p>Other authors provided support and guidance on the design, data collection, analysis and interpretation and revised the manuscript prior to submission.</p>
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SECTION E

Student Signature	
Date	11/03/2022
Supervisor Signature	
Date	18/03/2022

This chapter is the accepted manuscript of an article published by Taylor & Francis in Human Vaccines & Immunotherapeutics on 3 March 2022, available online: Karafillakis E, Peretti-Watel P, Verger P, Chantler T, Larson HJ. “We don’t have the same bodies; we don’t react the same way”: mothers and adolescent girls’ perceptions of the risks and benefits of HPV vaccination in France. Human Vaccines & Immunotherapeutics. 2022. <https://doi.org/10.1080/21645515.2022.2036555>

4.1 Introduction

Despite HPV infection being the most common STI in the world, vaccination against HPV remains highly mistrusted by the public in many countries, including in Europe (88, 107).

While most HPV infections will be cleared out naturally by the immune system, they can sometimes lead to the development of genital warts as well as cervical, anal, oropharyngeal, penile, vaginal, and vulvar cancers (91). Following breast cancer, cervical cancer is the second most common cancer among women aged 15-44 years in Europe in terms of incidence and mortality (88, 92). Evidence has shown that 85% of new cases of cervical cancer in Europe are caused by eight “high-risk” types of HPV, with HPV 16 and 18 alone contributing to an estimated 73% of these new cases (93, 94).

Cervical cancer prevention in Europe consists of routine cytological screening programmes and vaccination of boys and girls before the onset of sexual activity with either a bivalent, quadrivalent or nine-valent vaccine (88, 95, 97). Countries in Europe have had varying degrees of success with HPV prevention, with vaccination coverage rates ranging from 4% in Bulgaria to 94% in Portugal (2018) (250). Despite around 3,000 women being diagnosed with cervical cancer and 1,000 dying from the disease every year in France (251), the country has one of the lowest HPV vaccination coverage in Europe, with only 24% of the targeted population having completed their course of HPV vaccination in 2019 (250). The routine HPV vaccination programme started in France in 2007, targeting 11 to 14-year-old girls with a catch-up campaign for 15 to 19 year-old girls. Boys were only included in the HPV vaccination programme in 2020 (102). Vaccines are available at pharmacies and can be

administered by GPs, paediatricians and gynaecologists. Studies have found low HPV vaccine uptake in France can partly be explained by mothers, young women and adolescent girls having concerns about the risks associated with the vaccines, and questioning their effectiveness and importance (140, 183, 252, 253).

Vaccine intentions have been described as a consequence of one's cognitive and affective perceptions of risks associated with vaccines as well as vaccine-preventable diseases: if the risks of vaccination are perceived to be greater than the risks of the disease it prevents, then individuals will be less likely to vaccinate (6). While information received from doctors, peers or other sources such as the internet allow individuals to assess the risks and benefits of vaccination, the decision-making process is also influenced by individual beliefs and experiences as well as heuristics, trust, emotions, or health literacy (6, 32, 33). The cultural, political, social or economic context in which decisions are made can also shape beliefs and perceptions (254).

Most theories and frameworks related to HPV vaccination have been developed in relation to parental decision-making. However, adolescent perceptions of risks are fundamentally different from those of adults primarily because adolescents tend to overestimate risks, which could be explained by peer influences and emotional reactions to risks (28, 29). While adolescents can have a heightened perception of risks, they also tend to be higher risk-takers than adults, sometimes referred to as the paradox of adolescent risk perception. In fact, adolescents place more weight on perceived benefits than perceived risks when making decisions, even when they overestimate these risks (28). This explains why adolescents might still engage in risky behaviours if they perceive certain benefits associated with the behaviour. Additionally, adolescents sometimes engage in risky behaviours because of the

perception that they are less vulnerable to certain risks as individuals than their peers (28, 31).

While parents often remain key decision-makers for their children's vaccination, adolescents are becoming more engaged in these decisions, with countries such as the UK allowing 12 to 13 year old boys and girls to get vaccinated against HPV without parental consent.

Understanding the way both mothers and adolescent girls perceive the benefits and risks of HPV vaccination and how they may influence each other is therefore important to inform the development of strategies to improve confidence in and uptake of HPV vaccination. The aim of this study is to provide an in-depth exploration and comparison of mothers and adolescent girls' perceptions of the risks and benefits of HPV vaccination in France.

4.2 Methods

Qualitative research, including semi-structured interviews and focus groups, was conducted to explore adolescent girls and their mothers' perceptions around the risks and benefits of HPV vaccination in Paris, France.

4.2.1 Setting, participant recruitment and data collection

Adolescent girls between 15 and 16 years old and their mothers were recruited for this study from different *arrondissements* (local districts) of Paris between October 2018 and March 2019. The study focused on girls as they were targeted by the vaccination programme at the time of data collection, with the age range selected to ensure participants had passed the age at which HPV vaccination is typically offered in France. The study focused on mothers instead of parents or fathers as they are the most common decision-makers for childhood vaccination (255).

In total, 24 adolescent girls (aged 15-16) participated in in-depth interviews and 12 additional girls participated in two focus groups (with 5 and 7 participants in each group). Additionally, 21 in-depth interviews were conducted with mothers (aged 36-55) of the adolescent girls taking part in in-depth interviews (3 mothers of included adolescent girls declined to participate). Participants were purposively selected to target vaccinated and unvaccinated girls. However, due to the low vaccine coverage rates in France, only eight vaccinated girls were identified to take part in this study (five in in-depth interviews and three in focus groups).

Participants were recruited for this study during two distinct phases. In the first phase, adolescents were approached through their schools, or *Lycées*. A list of all *Lycées* in Paris was drawn from public registrars, including public, private and professional and school directors were approached to ask for their consent to recruit girls from their schools. As only four adolescent in-depth interviews and two focus groups were conducted using this recruitment method by January 2019, a second recruitment phase was organised to obtain additional participants between February and March 2019. For the second phase, a local behavioural research agency was recruited to identify and recruit the remaining participants from their existing panel of research participants. The objective was to recruit 20 adolescents and their mothers for in-depth interviews and to conduct 3 focus groups with 8-10 adolescent girls in each group.

All participants were provided with detailed information about the study, including confidentiality and anonymity, in an information letter that was handed out physically or sent by email to them a few days before the interview. This information was summarised verbally before each interview, and participants were reminded that they had the right to withdraw from the study at any time, even during the interview or focus group. After being given an

opportunity to ask questions, adolescent girls and their mothers were then asked to provide written informed consent to take part in the study and for the interviews or focus groups to be audio-recorded. Adolescent girls were also required to provide the written consent from their parent or guardian. In order to thank them for their time, adolescents recruited during the first phase were able to enter a lottery to receive an Amazon voucher while all participants recruited in the second phase were compensated for their time as per the local recruitment agency's practices.

Interviews lasted between 30 and 60 minutes and were conducted in participants' homes or at a private place of their choosing. Focus groups were conducted with girls from the same school class and were therefore conducted in schools, lasting around 60 minutes. All data was collected in French by an experienced researcher fluent in both English and French who also analysed the data in French to prevent losing some of the meaning. Interviews with adolescent girls and mothers were conducted separately and privately, and no parent or guardian asked to be present during the interviews with adolescent girls.

Interviews and focus groups were conducted using semi-structured topic guides that covered predefined topics (Appendix E) while allowing discussions to be shaped by participants' responses. Topic guides focused on knowledge, attitudes and behaviours around HPV vaccination, with a focus on the perceptions and beliefs around the risks and benefits of vaccination. Topic guides were piloted with three adolescent girls who were excluded from the analysis and final number of interviews.

4.2.2 Data analysis

Audio-recordings from the interviews and focus groups were transcribed by a local transcription company, respecting participants' confidentiality and using secured transfers and password-protected files. Before being imported into Nvivo® for analysis, all data files

including transcripts from interviews and focus groups, field notes and analytical memos were anonymised by removing personal identifiers such names and locations or replacing them with codes ('A' for adolescents, 'M' for mothers, and 'V' for vaccinated participants).

Data on Nvivo® was analysed using a coding framework, first developed by deductively drawing codes from the topic guides, analytical memos and relevant literature and contextual information on HPV vaccination. The coding framework was revised and updated by drawing codes inductively from close readings of the data from four interviews. The final framework, revised by a second researcher, was used to code all transcripts while allowing codes to be modified, merged or removed as required during the analysis. A thematic analysis of codes consisting of an analysis and comparison of coded extracts was performed to draw a list of issues and themes. While transcripts of interviews with mothers and adolescent girls were coded separately, emerging codes and themes were then compared to understand differences and similarities between both groups. This included a comparison of mothers and girls in general and of mothers and girls from the same dyad. Quotes for this article were directly translated into English by the researcher fluent in English and French. Findings were then discussed in relation to existing literature and contextual background information on HPV vaccination in France.

4.2.3 Ethical approval

Ethical approval for this study was obtained from the London School of Hygiene & Tropical Medicine [Ref. 15320-3] and from Aix-Marseille Université [Ref. 2018-12-07-005].

4.3 Results

The thematic analysis identified five key themes: 1) the individuality of perceptions around HPV vaccination risks and benefits; 2) differences in the understanding of what vaccine

safety represents; 3) varied perceptions of vaccine benefits; 4) the influence of emotions on HPV vaccination perceptions; and 5) the influence of perceptions around natural medicine.

Table 1 provides an overview of the sub-themes and perceptions identified for these 5 themes among adolescent girls and/or mothers.

Table 1: Summary of key themes and perceptions among adolescent girls and mothers

	Adolescent girls	Mothers
Individuality of perceptions around HPV vaccination risks and benefits	<ul style="list-style-type: none"> • Individual physical and ideological differences lead to different vaccine risks and benefits • Vaccination need is dependent on personal HPV risk (e.g. sexual activity) • Side effects are given different meaning and value by people • Human bodies respond differently to diseases (i.e. susceptibility) and vaccines (i.e. effectiveness) • Need to develop individualised vaccines, adapted for everyone 	<ul style="list-style-type: none"> • Even a small risk could translate to a risk for their own daughters
	<ul style="list-style-type: none"> • Personal responsibility for contracting HPV (i.e. sexual behaviour, religious beliefs) • Individuals tolerate vaccines differently, affecting individual risks of side effects 	
Differences in the understanding of what vaccine safety represents	<ul style="list-style-type: none"> • Strong trust towards vaccine safety • Vaccine risks relate to vaccines not working or not being injected properly • Vaccines carry minor side effects (e.g. fever, nausea, pain) • More important concerns mirror own mothers' concerns (sometimes word for word) 	<ul style="list-style-type: none"> • Nothing in life comes without risk, including vaccination • Important concerns about vaccine safety (i.e. controversies, ingredients long-term risks) • Vaccines are controversial: lack of scientific consensus around vaccine safety • Conspiracy theories
	<ul style="list-style-type: none"> • n/a 	

Varied perceptions of vaccine benefits	<ul style="list-style-type: none"> • Vaccine benefits relates to reducing risks of disease • Decision-making is based on comparing risks 	<ul style="list-style-type: none"> • HPV vaccination could dilute messages on prevention of other STIs or pregnancy
	<ul style="list-style-type: none"> • For some, the risk of vaccination is worth taking to prevent cancer but for others the risk of vaccination is scarier than the risk of cancer • Permanence of risks associated with vaccination compared to cancer (it cannot be undone) 	
Influence of emotions on HPV vaccination perceptions	<ul style="list-style-type: none"> • Strong positive emotions towards the benefits of vaccination (e.g. security, reassurance, protection) • Minor worries about side effects or fear of needles 	<ul style="list-style-type: none"> • Strong negative emotions towards possible side effects of HPV vaccination • Cancer fears are used to convince parents to accept vaccination • Guilt and shame for not vaccinating daughters • Own or friends' experience with cervical cancer brings out fear but does not always translate to willingness to vaccinate daughters
	<ul style="list-style-type: none"> • Distress about the risk of cancer, perceived as a dangerous and life-threatening disease that can happen to anyone • STIs bring out more emotional reactions than other diseases (e.g. taboos, embarrassment) 	
Influence of perceptions around natural medicine	n/a	<ul style="list-style-type: none"> • Desire to let the body defend itself naturally • France described as a highly medicalised country, with too many vaccines
	<ul style="list-style-type: none"> • The less drugs are used, the better • Preference for natural remedies (sometimes supported by doctors) compared to chemicals in drugs and vaccines 	

4.3.1 Everybody is different: the individuality of perceptions around HPV vaccination risks and benefits

During the qualitative interviews and focus groups, adolescent girls talked about the risks and benefits of HPV vaccination as factors that vary from one individual to the next due to both physical and ideological differences. For some participants, this was explained in terms of the influence of individual values and behaviours. Adolescent girls described the need for

vaccination in relation to their personal risk of contracting HPV and whether or not they were already sexually active: “*Personally, I do not see the use of doing it now, knowing that I do not have sex*” (A2). The role of individual sexual behaviour and personal responsibility for contracting HPV was also discussed by adolescent girls and some mothers, with one girl reporting that young people might benefit from vaccination because they take more risks than adults. One’s religious beliefs was also seen as a factor influencing the risk of contracting HPV by two Muslim mothers and one adolescent girl: “*I am Muslim and in my religion, as I know it’s transmitted sexually, in my religion well, it’s after the wedding... so, I don’t really need it*” (A4). One mother believed that her doctor did not recommend the vaccine because of cultural taboos around sex: “*Maybe they didn’t dare [recommend it] because I’m Arab (...) maybe it’s all this, it’s a taboo for us*” (M24). Finally, girls who took part in focus groups also discussed the individual meaning and value placed on side effects, explaining that some side effects, such as infertility, might be perceived as more or less important by different people.

Additionally, a few girls discussed the risk of getting a disease in relation to natural susceptibility, explaining that people’s bodies are different and that vaccines might therefore only be useful for some people: “*We don’t necessarily have the same physiology (...), there is a possibility that I could get the disease... we are all different, so it could vary with every person, [we could] even have different symptoms...*” (A3). Similarly, adolescent girls stated that vaccines do not offer complete protection and that it would still be possible to contract the disease even after getting vaccinated, with some girls explaining that vaccines might only be effective in certain people: “*I don’t think it can work for everyone (...) we don’t have the same bodies, we don’t react the same way*” (A11).

The belief that individual bodies might react differently to vaccines was also expressed in relation to the risk of possible side effects. However, while some adolescents and mothers explained that the fact that some girls might have bad reactions to vaccination does not mean that they will, some mothers also perceived that every risk that exists could be a risk for their own daughters: *“When they tell you ‘It’s 1 every 10,000’, you think ‘yes, but this 1 in 10,000 exists’, you see? And I’m already someone who is very anxious”* (M19). Some girls and mothers explained that people might tolerate vaccines differently, for example due to pre-existing conditions: *“It happens to, I don’t know, a tiny portion of the population who did [the vaccine] (...). Maybe these people had, I don’t know, medical history that emerged with the vaccine or they were more susceptible to this kind of disease”* (A10). One girl suggested that in order to restore trust in vaccination, vaccines should be ‘individualised’ and adapted for everyone.

4.3.2 What does vaccine safety mean?

Vaccine safety was understood differently by adolescent girls and their mothers in this study. Almost all mothers, including those who vaccinated their daughters, raised concerns about vaccine safety and acknowledged that nothing in life comes without risk. This was not always described in a negative way, as some mothers discussed vaccine risks in a calm, objective manner: *“Whatever medication we take, (...) there are always risks and indeed, we know, it’s part of life. (...) Risk zero does not exist”* (M1V). Mothers expressed concerns about vaccine ingredients and adjuvants such as aluminium and mercury and referred to specific side effects such as auto-immune and neurological complications, arthritis, paralysis, cancer, infertility and multiple sclerosis. Some mothers also expressed concerns about uncertainties around future and long-term risks of vaccination: *“You have to skip at least two generations to see the effects on children... (...) The child is fine, and all at once, poof!”* (M7). Many mothers

also perceived the HPV vaccine as ‘*controversial*’, particularly in comparison to other childhood vaccines and described a lack of scientific consensus around the safety of HPV vaccination, even among doctors and health professionals. Three mothers justified their concerns about HPV vaccination by describing past cases in which drugs were found to cause issues years after they were introduced: “*When I hear: ‘we gave this medicine for X amount of time to women and now, they have this [problem]’. Well, we vaccinated our children and now, they have this... No, I don’t want to do it... Seriously, I’m afraid!*” (M15). Two mothers also described HPV vaccine safety in the context of larger conspiracy theories, for example stating that all manmade products, including shampoos, toothpaste or tampons, are poisonous or believing that the government is trying to ‘*weaken*’ people with vaccines in order to more easily ‘*dominate*’ and ‘*manipulate*’ them.

Contrastingly, most adolescent girls expressed strong trust in the safety of vaccines and rarely described them as controversial. Some believed vaccines are safer in France than in other parts of the world and others placed their trust in the thought that vaccines would not be injected to people if they were not safe. Although some girls acknowledged vaccines can have side effects, they could rarely explain what they were precisely concerned about: “*the problem... I don’t know what the risks of a vaccine are, actually*” (A7). When probed further, many girls were found to understand vaccine risks as ‘the risk of them not working’ or the risk of doctors failing to inject the vaccine properly: “*[the vaccine] can be done incorrectly, and then, well it can become infected (...)* Yes, he could do [the injection] in the wrong place or if the needle is not cleaned properly, or things like that” (A14). Girls that described specific safety concerns often referred to minor and plausible side effects such fever, nausea, pain at the site of injection or allergies. Those who reported more important concerns often mirrored or even repeated their own mothers’ concerns, with one girl particularly affected by online articles about the risks of the HPV vaccine that her mother had shown her: “*I know it’s*

highly controversial (laughs) and even among doctors, there are some who are for it and others who are against. On the internet, you can find anything and everything, so what I remembered first is we don't know whether or not to do it" (A10). Two adolescent girls also discussed the risk of dying after having received the HPV vaccine: *"Every time there is something new, a new vaccine, some people die until they find the real solution. It's the same with vaccines."* (FG02).

4.3.3 HPV vaccine benefits: reducing the risk of disease

Many adolescent girls looked at the benefits of vaccination in terms of 'reducing risks' of diseases and therefore compared the risks associated with the disease to the risks of vaccinating when deciding whether or not to accept HPV vaccination. Most of these girls as well as a few mothers believed that it is worth to 'take the risk' to protect yourself as the risks of cancer and HPV were seen as higher than the risks of vaccination: *"I think I would take [the vaccine] because well it's a serious disease (...). But then, it can harm our body... but since, as they say, it's a risk well, it's better to take the risk"* (A21V). Only two girls and two mothers described the risks of vaccination as being higher, or at least scarier, than the risks of cancer or HPV: *"I would say no because I'm too afraid of what can happen afterwards (...). I wouldn't take the risk, frankly no. Well, obviously, by not taking [the vaccine], I'm also taking a risk, once again, it's paradoxical."* (A10). One girl and one mother also compared the permanence of risks, explaining that risks associated with vaccination are more permanent than the risk of infection and cannot be undone. A couple of mothers also focused on the risk of their daughters becoming pregnant or contracting other STIs such as HIV, and feared that HPV vaccination could dilute messages focusing on these important issues.

4.3.4 From security and reassurance to fear: emotional reactions to HPV vaccination

Discussions around HPV vaccination triggered strong albeit varied emotional reactions among both mothers and adolescent girls. Adolescent girls often used positive emotional language to refer to the benefits of vaccination, reporting feelings of security, reassurance and protection offered by the vaccine: *“I would feel reassured, I wouldn’t be scared to contract the disease, so that’s the most important I think”* (A6). Almost all adolescent girls described HPV vaccination as beneficial and perceived vaccination as an important tool to protect themselves, their partners or the population in general from the risks of diseases. Most girls therefore expressed willingness to get vaccinated, and some questioned why parents would refuse to vaccinate and protect their daughters: *“It’s something that should be done. It’s useless to ask yourself ‘yes or no’ because it’s obviously better to do it”* (A6).

Despite some mothers and girls questioning the need for HPV vaccination, including because of the existence of alternative protection methods such as condoms or screening, both girls and mothers also expressed distress about the risk of contracting HPV and developing cancer. Most of these discussions focused on cancer rather than HPV, with adolescent girls and mothers describing cancer as a serious, dangerous and life-threatening disease: *“It’s important; it’s not something... well it’s not futile. We shouldn’t take it lightly... it could be serious”* (A20). One mother also believed that people’s fears around cancer are being used to convince them to accept vaccination, expressing her own feelings of guilt and shame for not vaccinating her daughter. A few girls and one mother also perceived the risk of developing cancer to be high, expressing concerns that it can happen to anyone, even themselves. Three mothers described their own or their friends’ experience with the detection of pre-cancerous lesions or cervical cancer as tough and scary. However, while one mother explained this experience convinced her to vaccinate her daughter, another one stated: *“no, at no point did I*

say to myself that I was going to vaccinate her because this happened to me. No, I was really disgusted to have it, but..." (M11). Only one mother discussed the benefits of preventing an STI, comparing HPV to AIDS (Acquired immunodeficiency syndrome): *"Even though it's not the same, a sexually transmitted disease to me, I'm referring a bit to AIDS or other [diseases]. Now, if there's a vaccine that [provides] a cure, yes, I would do it, with my eyes closed, without thinking."* (M20). Some participants also believed that discussions around STIs bring more emotional reactions than other infections, including embarrassment and taboos.

Only two girls reported worries about potential vaccine side effects and one girl expressed a fear of needles. In fact, mothers reported more negative emotions towards the risk of side effects following HPV vaccination than their daughters. These emotions were reinforced when discussing the uncertainties surrounding what was still described as a *'new vaccine'*, for which too much remained unknown, including about its effectiveness, safety or long-term risks: *"For me, it's more about whether it will bring other problems, other diseases later. Will we discover [something], in I don't know, 5, 10, 15 years?"* (M9). Some mothers explained that *'new vaccines'* refer to those that were not available when they were children or that have not been tested long enough, perceiving vaccinated girls as guinea pigs: *"I think not enough time has passed, the vaccine is all new, come on our children are not guinea pigs."* (M15).

4.3.5 Perceptions around natural medicine

Almost all mothers as well as a few adolescent girls explained that the less drugs they use, the better it is for their health: *"I had a teacher (...) who told me that it's better to let the disease run its course, and it will go away alone. And it's not by taking medicines all the time that it will go away"* (A17). One girl repeated almost word for word what her mother said during

her own interview: *“The less medication I take and the less I give my daughters, the better I feel”* (M10), *“The less I take them, the better it is, so I prefer to treat myself naturally than with medicines”* (A10). The use of natural remedies, essential oils and homeopathy instead of ‘chemicals’ found in drugs and vaccines was commonly discussed by mothers, who sometimes reported receiving recommendations to use natural remedies from their doctors. Girls also reported a preference for natural remedies or alternatives to vaccines, with a couple stating it would also be better for the environment. In addition to worries about injecting foreign chemicals with vaccination, some mothers were also concerned about allowing the body to defend itself naturally: *“When we are used to receiving too many vaccines, the problem is that the body is not used to protecting itself against infections anymore”* (M9).

Contrastingly to the reported preference for natural medicine and the need to limit the use of drugs, France was also described as a highly medicalised country by two mothers: *“In France, I have to say that we are one of the countries that consume the highest number of drugs. So, I don’t know, maybe people receive too many vaccines, too many drugs”* (M9).

This led to some mothers believing there are too many vaccines, with HPV vaccine described as ‘one too many’. Two mothers also questioned the need to prevent all diseases: *“We will never be able to stop an accident or something like that, so yes I think that it’s ridiculous to do too many vaccines. And even the thought of saying ‘we will protect ourselves against everything’, no, that will never happen”* (M8).

4.4 Discussion

Vaccine hesitancy has sometimes been described as being driven by risk perceptions (43, 256-258) and low uptake of HPV vaccination in France could in part be explained by such perceptions among parents, adolescents, and healthcare professionals (183, 252, 259). As adults and adolescents understand and perceive risks differently, this study provided an in-

depth exploration and comparison of mothers and adolescent girls' understanding of HPV vaccine risks and benefits and their influence on vaccine decisions in France.

4.4.1 Individual differences in vaccine benefits and risks

Among adolescents, the perception that HPV vaccine benefits and risks vary from one individual to another was a strong theme. Adolescents explained that bodies respond differently to both vaccines and diseases, including in terms of vaccine safety (i.e. side effects might not happen to everyone and people might tolerate vaccines differently), vaccine effectiveness (the vaccine might work in some but not others), and risk of disease (i.e. some people are less at risk of HPV). The impact of these views on risk perceptions have previously been described in the context of HIV transmission and protection among adolescents (260), with a lack of previous experience with serious health issues provided as a possible reason for low perceived vulnerability to certain risks (261). Interestingly, findings from our study did not solely reflect a lack of perceived vulnerability by adolescents but a more general perception that medicine should be more personalised to respond to specific individual needs. In such cases, communication strategies focusing on low-level construal messages, such as those using narrative information and stories adolescents can relate to could be more effective to improve vaccine acceptance (262).

Both adolescent girls and mothers also reflected on individual risk behaviours, with religious beliefs discussed as an important factor influencing whether individuals engage in sexual activity and are therefore at risk of catching HPV, confirming findings from previous studies (167, 191, 210, 263). The influence of parental beliefs, values and upbringing on adolescents' perceptions of sexual behaviour and HPV vaccination could constitute an important barrier to vaccine uptake, with possible taboos related to religious convictions hindering communication and engagement of both parents and adolescents (264).

4.4.2 The social construction of vaccine safety perceptions

Vaccine safety is one of the most commonly reported determinants of vaccine hesitancy, with evidence showing individuals may delay or refuse vaccines due to concerns about their safety (6, 43, 265). Most studies have defined and explored perceptions of vaccine safety in relation to the perceived risk of adverse events following vaccination. However, this study has found that vaccine safety can be interpreted and understood differently by individuals. In fact, mothers in this study perceived vaccine safety in relation to the vaccine product itself, discussing concerns and relaying rumours about what they see as a controversial vaccine with important side effects and thinking about long-term effects. Contrastingly, instead of questioning the product, adolescent girls discussed vaccine safety in relation to whether it may be administered or stored incorrectly, for example because of the use of unclean needles and only discussed short-term effects. This supports the theory that adolescents tend to think about risks in the short-term rather than in the longer-term (28).

This distinction could also point to perceptions of vaccine safety being socially constructed, understood and interpreted differently by populations and communities with different cultural and social environments. For instance, adolescent girls in this study also highlighted the impact of social constructionism by explaining individuals place different weight on certain illnesses or conditions, which could influence whether or not they believe they have been affected by a vaccine adverse event. These distinctions in risk and benefit perceptions are important for future research on the determinants of vaccine hesitancy, including in terms of the development of research questions that reflect differences in the understanding of vaccine safety. While health and illness have previously been described as subjective experiences that can be socially constructed (266, 267), more research should be conducted to determine how the occurrence and understanding of perceived and real adverse events following

immunisation may be socially constructed and influenced by social norms, including within different population groups such as fathers, adolescent boys or healthcare professionals.

4.4.3 Controversies and widespread concerns about vaccine safety

Another important difference comes from the nature of side effects believed to be associated with HPV vaccination. While adolescent girls in this study discussed side effects such as fever or allergies, mothers mostly focused on unproven side effects around which rumours and misinformation has been shown to spread on digital and social media. Some mothers for example believed HPV vaccination could lead to multiple sclerosis, reflecting similar discredited rumours around Hepatitis B vaccination in France back in the 1990s (252).

Additionally, most mothers in this study, whether they vaccinated their daughters or not, raised concerns about vaccine safety and admitted that nothing comes without risk. This contrasts to a previous 2012 study (183) and could point to a now widespread belief that vaccines are unsafe in France (106, 247), with mothers no longer questioning whether vaccines can have side effects, but whether their own daughters will suffer from these side effects. Mothers' exposure to a strongly conflicting information environment around vaccination in France could explain their concerns about these unproven side effects and their mistrust of medications in relation to past events that had been mismanaged (252). On the other hand, as adolescent girls expressed low awareness and understanding of HPV vaccination, it could indicate their lack of involvement in decision-making has largely shielded them from exposure to misinformation, even if they use social media more often than their mothers. Yet, some girls reported similar concerns as their mothers, showing the risk of rumours and hesitancy passing from mothers to daughters as they start becoming more involved in decision-making.

4.4.4 Vaccination as a mean of preventing risks

While many girls talked about the importance of vaccination for protection, most of them did so by expressing the importance of preventing the *risks* of disease in comparison to the risks of vaccines, confirming previous evidence showing that individuals are more likely to accept vaccination when they feel at risk or threatened (6). Adolescents have also been shown to overestimate risks and to place more weight on perceived benefits than risks when making decisions (28, 29). Our study shows that the risk of cervical cancer is considered sufficiently important by adolescents to get vaccinated against HPV. However, adolescent girls did not share significant concerns about risks of negative consequences from vaccination as much as their mothers did, and we could not determine whether this would have had an impact on adolescents' decision to get vaccinated. Contrastingly, mothers who also acknowledged the risk of cervical cancer were also negatively influenced by the risk of possible side effects.

Risks were also mostly discussed in relation to cervical cancer rather than STIs, genital warts or HPV infection. The only mother who discussed HPV infection as risky compared it to HIV, showing low perceived severity associated with HPV itself. This highlights the need for communication strategy to focus on cervical cancer as well as the need for strong awareness campaigns on HPV infection, especially if campaigns become more gender-neutral.

4.4.5 Emotional assessments of risks and benefits

While individuals may make decisions by analysing the scientific risks and benefits of vaccination, they will also process risks as feelings, using an instinctive and emotional system to develop a subjective perception of the risks and benefits of vaccination (32, 33, 268, 269). This study found that mothers and adolescent girls both had strong but different emotional reactions to HPV vaccination. Most girls expressed very positive emotions such as security or reassurance in relation to the protection offered by the vaccine, which was less

present among mothers. Vaccination seemed like a natural and obvious behaviour and some girls expressed incredulity at the thought that some parents may refuse them. In addition to the positive feeling of protection offered by the vaccine, both girls and mothers described distress and fear associated with the risk of cancer. Cancer is one of the diseases that provokes anxiety in the general population (270), and despite expressing concerns about cervical cancer, some mothers, including those who experienced precancerous cervical lesion, showed stronger emotions around the perceived risks of HPV vaccination. While this was less commonly reported by girls, this could indicate that vaccination campaigns aiming to elicit fears around the consequences of not vaccinating would resonate less with mothers. More research should be conducted with women who experienced lesions to understand their perceptions of HPV infection, cervical cancer, and vaccination.

In addition to vaccine side effects, fears were also raised in relation to vaccines being unnatural. Despite the fact that the HPV vaccine had been introduced over a decade ago in France, there were also concerns that it was a new vaccine with inherent uncertainty about potential long term effects. Another qualitative study conducted in France found similar results, highlighting the importance of how familiar a vaccine is with how people perceive its risks (252). Stronger support is needed to help navigate the uncertain and conflicting environment around HPV vaccination, particularly for mothers as they decide whether to vaccinate their daughters against HPV.

4.4.6 Strengths and limitations

This study has several limitations that should be taken into account as they could have influenced some of the findings. Participants included in this study came from only one city in France and were mostly unvaccinated against HPV, which could have influenced the themes and issues around risk and benefit perceptions that were identified. Furthermore,

insufficient data on socio-economic demographics was collected to identify possible differences in responses by socio-economic background. Findings could also have been affected by the two methods of recruitment used to identify adolescent girls, including the different compensation mechanisms. While the interviewer was fluent in both French and English, it is possible that some concepts might have been lost in translation. Finally, despite interviews taking place in private, participants may have felt uncomfortable answering some questions, especially with their mothers or daughters in the room next door.

4.4.7 Conclusion

While many studies have been conducted with the aim of exploring factors influencing HPV vaccine perceptions, most of these have focused on parents or mothers, especially in terms of risk and benefits perceptions. This study found that perceptions of HPV vaccination risks and benefits differ between adolescent girls and their mothers. Beyond expected differences in whether vaccines are perceived as safe, beneficial and effective, deeper nuances in how these concepts are understood and applied were identified. Adolescent girls described HPV vaccination in a more beneficial manner, using positive emotions and language to explain their willingness to be vaccinated. Mothers were more impacted by a conflicting information environment surrounding HPV vaccination in France, focusing on concerns about what appeared to be a widespread belief that these vaccines are unsafe. This difference should be further explored, including its impact on strategies to rebuild confidence in HPV vaccination.

Chapter 5: *‘I trust them because my mum trusts them’*: exploring the role of trust in HPV vaccination decision- making among adolescent girls and their mothers in France

RESEARCH PAPER COVER SHEET

SECTION A – Student Details

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Thesis Title	Adolescent decision-making and Human Papillomavirus vaccination in France		
Primary Supervisor	Heidi J Larson		

If the Research Paper has previously been published please complete Section B, if not please move to Section C.

SECTION B – Paper already published

Where was the work published?	Vaccine, Elsevier		
When was the work published?	25 January 2022		
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Have you retained the copyright for the work?*	No	Was the work subject to academic peer review?	Yes

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SECTION D – Multi-authored work

<p>For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)</p>	<p>I am the first author on this paper, published with 4 other authors. I led the design of the study and methodology for qualitative research, identified and recruited participants, conducted data collection (interviews and focus groups), analysed and interpreted the data, and wrote the manuscript.</p> <p>Other authors provided support and guidance on the design, data collection, analysis and interpretation and revised the manuscript prior to submission.</p>
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SECTION E

Student Signature	
Date	11/03/2022
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Date	18/03/2022

This chapter is the accepted manuscript of an article published by Elsevier in Vaccine on 25 January 2022, available online: Karafillakis E, Peretti-Watel P, Verger P, Chantler T, Larson HJ. 'I trust them because my mum trusts them': Exploring the role of trust in HPV vaccination decision-making among adolescent girls and their mothers in France. Vaccine. 2022;40 (8):1090-1097. <https://doi.org/10.1016/j.vaccine.2022.01.028>

5.1 Introduction

Vaccination has often been described as one of the most important public health achievements of the 20th century (4, 27). Yet, in a context where scientific knowledge is regularly being questioned by the public, some parents are becoming increasingly hesitant to vaccinate their children (256, 271). In 2016, France was identified as the country with the lowest level of confidence in vaccination in the world, building upon decades of erosion of public trust resulting from controversies around vaccines and government health decisions (106, 247).

Consequently, France also has one of the lowest HPV vaccine uptake rates in Western Europe, with only 32.7% of adolescent girls vaccinated with two doses in 2020 (girls born in 2004, at 16 years old) (100, 105). In France, the vaccine is recommended and prescribed by family doctors or paediatricians to girls aged 11 to 14 years old, with a catch-up campaign for those aged 15 to 19 (102). Since 2020, the vaccine is also recommended to boys of the same age. Despite evidence showing the effectiveness of the HPV vaccine in preventing cervical cancer (272), mothers in France are hesitant to accept the vaccine because of concerns about vaccine safety or insufficient protection provided by the vaccine (184, 252, 256).

While mothers are the primary decision-makers around childhood vaccination and parental consent is required for vaccination, the role and influence of adolescent girls in HPV vaccination decision-making is increasingly being recognised (80, 252).

5.1.1 The role of trust in vaccination decision-making

While vaccination decisions have often been described as the main consequence of an individual's representation of the risks and benefits of vaccination, these representations are also shaped by societal issues such as trust (4, 5, 27, 43, 252). Trust expressed towards products (i.e. vaccines), providers (i.e. healthcare professionals) and policy-makers (i.e. health systems, governments, scientists) can constitute levers of vaccine acceptance (273). Trust in information around vaccination does not only depend on information about the risks and benefits of vaccination but also on those who produce and share that information (273).

In comparison to confidence that is expressed in 'systems' that protect against uncertainty, trust is interpersonal and is typically expressed in individuals, groups or institutions and therefore depends on the parties' behaviours as well as their moral and affective competence (58). Parents have therefore traditionally placed their trust in proximal sources such as doctors and health professionals rather than more distant ones such as health authorities (231, 255). Less evidence exists around who adolescents place their trust into as their contribution to vaccination decision-making has been more limited.

However, individuals are increasingly questioning the trustworthiness of scientific experts and information, which could be a consequence of the fragmentation of information: as information is now available from a multitude of sources, individuals are able to pick the ones that confirms their pre-existing beliefs (274). This can lead to individuals turning to alternative sources of information such as peers or the internet, potentially exposing them to information discouraging vaccination (51, 71). While adolescents' use of the internet and social media is more frequent than other population groups (275) and they often have more close knit relationships with their peers, the full impact of these issues on their perceptions of vaccination remains uncertain.

In fact, the role of trust in HPV vaccination decision-making, particularly among adolescents, has not been studied extensively (273). Studies have shown that while trust increases with age, it stabilises in adolescence and can play a key role in vaccination decision-making for adolescents (276, 277). Understanding who they place their trust in for issues such as vaccination and how this compares to their mothers and influences the dynamics of decision-making is therefore essential. In fact, while adolescents need parental consent to get vaccinated, their beliefs and confidence can sometimes influence parents' decisions as was seen in Ireland or Colombia, where vaccine coverage dropped following reports of alleged vaccine side effects and anxieties among adolescents. Adolescence is also the first time individuals might be involved in vaccination decision-making, which could influence their future confidence in vaccination as the adults and parents of tomorrow. This study aims to explore the role of trust in HPV vaccination decision-making among mothers and adolescent girls in France, with the objective of answering the following questions: 1) how does trust in HPV vaccines, vaccine providers and policy-makers influence decision-making around HPV vaccination; and 2) how can trust in alternative sources of information (e.g. internet, family, peers) be characterised?

5.2 Methods

A qualitative methodology was employed to explore the role of trust in HPV vaccination decision-making among mothers and adolescent girls in France through semi-structured interviews and focus groups.

5.2.1 Setting and study participants

In order to obtain a diverse sample, the study was conducted within different *arrondissements* (local districts) of Paris, a city with varied socio-economic, religious and cultural backgrounds, as well as varying levels of confidence in vaccination.

Research participants consisted of vaccinated and unvaccinated 15-16 year old girls to target adolescents who had passed the age of receiving the vaccine (while still available for the catch-up campaign) and their mothers. Mothers were selected for this study as they are the most common household decision-makers around health and vaccination in France.

5.2.2 Data collection

Data collection was conducted in two stages between October 2018 and March 2019. In the first stage, adolescents were approached through their schools, based on a comprehensive list of *Lycées* (public, private and professionals) obtained from public registers, and with prior approval from school directors. Adolescent girls who took part in the study were asked to contact their mothers to invite them for a separate interview. As this method only yielded 4 interviews and 2 focus groups with adolescents and one interview with a mother, a second stage of data recruitment was organised using an existing panel of a local research agency specialised in behavioural research (BVA Group). The agency identified 20 mothers and their own daughters to take part in the study.

A total of 24 in-depth interviews were conducted with adolescent girls and 21 with mothers (three mothers were unavailable to take part in an interview). Two focus groups were conducted with 5 and 7 girls in each group, both groups comprising of girls from the same school class. The decision to combine semi-structured interviews with focus groups for adolescents was made to ensure conversations happened both in a private setting, in which

girls might feel less intimidated and embarrassed to share their views on a vaccine against an STI, and in a natural peer setting (schools), to capture how social group dynamics may influence individual perceptions and how adolescents talk about HPV and vaccination among their peers. Only 5 girls included in the in-depth interviews and 3 in focus group discussions were vaccinated against HPV.

Interviews (30-60min) were conducted in participants' homes, or at a private place of their choosing and focus groups (60min) took place in schools. Parents/caregivers were informed that interviews with adolescents would be conducted in a private manner. Interviews, audio-recorded with prior approval from participants, were conducted by the main researcher, fluent in both English and French and experienced in qualitative research. Topic guides, piloted with three participants (excluded from the analysis), focused on decision-making processes and trust but also included questions around knowledge, beliefs and perceptions about HPV vaccination as well as the influence of different sources of information about the vaccine. While the themes covered in the topic guides were the same for all interviews and focus groups, small adaptations were made for the topic guides with mothers and the guides for focus groups.

A few days before the interview, participants were handed a study information letter (with information about the study, confidentiality and anonymity), which was summarised verbally by the researcher at the beginning of each interview. Informed consent was required for all participants, with adolescents also required to obtain written consent from their parent or guardian. Participants were given an opportunity to ask questions and were informed of their right to withdraw from the study at any time.

Adolescents in the first stage of data collection were given the opportunity to enter a lottery to receive an Amazon voucher to thank them for their time, while participants (adolescents

and mothers) recruited in stage two were compensated for their time as per the recruitment agency's compensation policy.

5.2.3 Data analysis

The researcher compiled field notes and analytical memos summarising the discussions, paying particular attention to the content, context, quality and feel of the exchange. Audio-recordings from the interviews and focus groups were transcribed by a local transcription company, respecting strict confidentiality rules by removing identifiers such as names or locations and using secured transfers with password-protected files. In this manuscript, each interview was allocated a letter (A for adolescent and M for mothers, FG for adolescents in focus groups) and a number, with vaccinated individuals complemented by the letter V (e.g. A5V). Transcripts were reviewed against the audio-recordings by the researcher and imported into NVivo® together with field notes and analytical memos.

An initial coding framework was developed by deductively drawing codes from the topic guides, theories around trust and decision-making and the analytical memos (238). Four adolescent transcripts were coded using this framework, adding additional codes using an inductive process through close readings of the data. The revised framework was reviewed by a second researcher to enhance the validity and consistency of the codes and the final coding framework was used for the remaining transcripts. During the process, some codes were modified, merged, or removed to fit more closely with the data. Coded extracts were compared and contrasted to develop a list of themes, paying particular attention to the terminology used by participants to build categories and typologies and to start discussing the meaning of the data (278). Transcripts were coded separately for mothers and adolescent girls to allow the analysis to pick up differences and similarities, and the themes identified as well as the language used by participants were compared between mothers and adolescent girls.

Key themes were then identified across all interviews and focus groups. Those results were finally analysed within the context of existing literature and theory on decision-making and trust as well as the social and cultural context in which the study took place. In order to avoid losing some of the meaning of data due to translation issues, data analysis was conducted in French, with results written up in English and quotes translated by the main researcher.

5.2.4 Ethical approval

Ethics approval for this research was obtained from the London School of Hygiene & Tropical Medicine [Ref. 15320-3] and from Aix-Marseille Université [Ref. 2018-12-07-005].

5.3 Results

The thematic analysis identified four key themes and a range of sub-themes across all semi-structured interviews (mothers and adolescents) and focus groups: uncertainty around a mistrusted vaccine, navigating mistrust and influences from a negative information environment, the importance of trust and deferring decision-making to those perceived as more knowledgeable, and trusting oneself in the context of external influences on HPV vaccination decision-making. Table 2 provides a summary of the key characteristics of participants included in this research, together with their numerical identifier.

Table 2: Participant characteristics

	Adolescents, n=36	Mothers, n=21
Data collection method	24 semi-structured interviews 12 focus groups	21 semi-structured interviews
Age	15 year old: n=20 (55.6%) 16 year old: n=14 (38.9%) n/a: n=2 (5.6%)	30-39 year old: n=1 (4.8%) 40-49 year old: n=16 (76.2%) 50-59 year old: n=4 (19.0%)
Vaccination status	Vaccinated: n=8 (22.2%) Unvaccinated: n=28 (77.7%)	
Arrondissement	3: n=1 (2.8%) 5: n=1 (2.8%) 10: n=2 (5.6%) 12: n=4 (11.1%)	3: n=1 (4.8%) 5: n=1 (4.8%) 10: n=2 (9.5%) 12: n=3 (14.3%)

	13: n=3 (8.3%) 14: n=1 (2.8%) 15: n=3 (8.3%) 17: n=1 (2.8%) 19: n=8 (22.2%) 20: n=7 (19.4%) n/a: n=5 (13.9%)	13: n=0 (0%) 14: n=0 (0%) 15: n=1 (4.8%) 17: n=1 (4.8%) 19: n=2 (9.5%) 20: n=5 (23.8%) n/a: n=5 (23.8%)
Marital status		Divorced/separated: n=3 (14.3%) In partnership: n=6 (28.6%) Married: n=11 (52.4%) Single: n=1 (4.8%)
Employment		Yes: n=18 (85.7%) No: n=3 (14.3%)
Number of children (total)		1: n=2 (9.5%) 2: n=10 (47.6%) 3: n=5 (23.8%) 4: n=2 (9.5%) 6: n=2 (9.5%)

5.3.1 Uncertainty around a mistrusted vaccine

HPV vaccination: a mistrusted and controversial vaccine?

While adolescent girls were rarely involved in HPV vaccination decision-making, mothers described decision-making as a difficult experience. This partly came from perceptions that HPV vaccination was different from other vaccines, less trusted and more controversial, thereby requiring more time to make what mothers qualified of as a ‘*serious decision*’. In French, mothers used the expression ‘*pas anodin*’ to refer to their mistrust of the vaccine, which means both that it is not insignificant and that it does not come without risks.

Some mothers and adolescent girls believed that researchers, experts or doctors may not trust the vaccine and its safety either: “*There is a real debate among doctors (...) if all scientists had said, this vaccine is great, it works all the time, I think doctors would have said ok, we do it*” (A10). Exposure to questioning of vaccination, sometimes among experts, led to the feeling that it was a controversial vaccine. One mother called for the vaccine to be made

mandatory to relieve parents from this difficult decision: “*At least, [if it was mandatory], I wouldn't be the one imposing it, it would be the State*” (M14).

Uncertainty and decision-making

For some mothers, the feeling of uncertainty remained years after first being told about the vaccine, sometimes even after having vaccinated their daughters. Some explained that they were not entirely convinced of their decision from the beginning, while others reported influence from mothers who refused the vaccine and media controversies. One woman also expressed remorse for not vaccinating her daughter, feeling her daughter might blame her in the future: “*It's not a decision I am proud of. I'm not serene. I tell myself, my daughter will always be able to blame me if something happens to her*” (M16).

For some, a highly trusted vaccine

A small number of mothers but most adolescent girls expressed strong trust in the vaccine or talked about HPV vaccination as a straightforward decision, referring to the importance of disease prevention and the feeling of protection associated with the vaccine: “*I don't think it's useful to talk about it, I think we have to do it (...) it's obviously better to do it*” (A6).

5.3.2 Navigating mistrust and influences from a negative information environment

Participants who received information about HPV vaccination were often forced to navigate a mistrusted information environment, exposed to conflicting and negative information: “*It's terrible, to do it or not to do it? It's terrible, but both, both are terrible. You read things on both, and you're wrong. You do it, and then she gets cancer, for sure. You don't do it, and then she gets cancer, for sure. What do you do, what do you do then?*” (M14). Girls expressed the suspicion that any type of information can be manipulated, including social media and the internet as well as mainstream media, the news or even teachers and doctors.

One mother described this mistrust as a French cultural trait, where citizens question everything. Findings are discussed in further details below by information sources and format.

Information on the internet and social media

Mothers who stated looking for additional information about HPV vaccination used search engines on the internet, official or medical websites or social media and forums. A couple of mothers explained that people often look for information that confirms their own beliefs: *“I think that on the internet, there is so much information that in general, you will look for information that confirms and feeds your own beliefs”* (M14). Online information was generally negative, recommending people not to accept the vaccine or discussing alleged side effects of the vaccine. Although girls did not report seeing information on social media, they believed it would be the best channel to reach their generation, particularly Instagram and Snapchat. While some mentioned the use of sponsored ads that can reach large numbers of users, one girl saw them as less trustworthy due to their commercial nature. Instead, many girls believed that influencers such as celebrities or public figures could have a strong impact by sharing their personal experiences: *“An influencer has a large number of followers, so we know that if she is giving us that message, it comes from her heart and it’s to warn us”* (A23V).

However, despite using it, mothers and adolescent girls were extremely judgmental and mistrustful of information available on the internet and social media, describing it as too personal or negative: *“I don’t read Doctissimo [French forums on health and well-being], because it’s not, well, it’s the worst (...). People only share negative experiences”* (M13V). Some mothers used very strong emotional language around social media, talking about it as ‘atrocious’, ‘depressing’ or ‘alarming’, with one mother explaining that information on

social media can trigger uncontrollable doubt and anxiety: “*It completely reactivated my uncertainty. I told myself: ‘Damn, what should I do in the middle of all of this?’ (...)* Even if it’s not rational, it prompts something intimate and dramatic” (M19).

Information in the media

Mothers were also exposed to negative information about vaccination in the mainstream media on television, radio or magazines and the feminine press: “*It really impacted me, hearing about negative consequences of this vaccine on the radio*” (M1V). One woman described being strongly affected by an article in a national newspaper reporting alleged side effects of the vaccine: “*I remember really alarmist articles with terrible things, multiple sclerosis. I remember in [a newspaper], the testimony of a mother that had innocently vaccinated her daughter and then of course, always the stories of doubt in the medical profession, that denies it.*” (M19).

Information from schools

Although adolescent girls did not report receiving information from schools, both girls and mothers believed it would be a trustworthy mean of informing girls. Visits from external speakers, for example during sexual health classes, or discussions with school nurses were seen as appropriate ways of informing adolescents around HPV vaccination. Mothers explained that information would be more objective in schools and it would allow more serious and informed discussions with their daughters at home.

The importance of how information is presented

In addition to the sources of information, the way in which information is presented was also seen as important by mothers and adolescent girls. While most girls expressed a preference for information around HPV vaccination to be presented in the form of personal testimonies,

particularly through videos, mothers showed a small preference for statistical facts, expressing distrust of subjective opinions. Adolescents raised the importance of understanding people's experiences, describing personal stories as more trustworthy as well as more touching, memorable and meaningful than data: *"I would be more interested in their experiences, as numbers (...) don't tell you how they lived it, how it happened"* (A15).

A need for more information

A large number of participants reported a lack of information about HPV vaccination, with mothers raising the need for more in-depth information, particularly from their doctors, and girls showing a complete lack of awareness about HPV and cervical cancer: *"I'm surprised, well, I'm shocked (...) we discover new viruses every day, but the fact that this was a virus that already existed and that I just didn't know about it, it surprises me"* (A3).

5.3.3 Blind trust and deference to epistemic authority

Deferring decision-making to those with more expertise and knowledge, also referred to as epistemic authorities, was a recurring theme, with girls deferring the decision to their mothers and mothers placing their trust in their doctors. However, the nature of the trusting relationship between girls and mothers and mothers and doctors was relatively different.

Adolescent girls' trust in their mothers

Adolescent girls' decisions and opinions around HPV vaccination were strongly influenced by their mothers, described as reassuring '*protectors*', while involvement of fathers in decision-making was not reported. Despite interviews being conducted in private, some girls shared the same arguments, and sometimes the same language, as their mothers but without necessarily understanding what they meant. One girl repeated some of the concerns her mother had about vaccination but was not able to explain what she was concerned about

specifically, and instead asked the interviewer why her mother did not want her to get vaccinated. Adolescent girls passively followed their mothers' decisions and opinions showing blind but strong trust. A lack of alternative positive influencers about HPV vaccination was identified, related to a lack of information provided from schools, doctors or other networks. Mothers expected their daughters to trust and listen to them. In the case of vaccine hesitant mothers, this created a barrier, where girls would be '*protected*' from the vaccine by their mothers, remaining ignorant but '*safe*'.

Doctors: a strong trust relationship with mothers

Mothers showed very strong trust in their doctors and often deferred HPV vaccination decision-making to them: "*We don't ask ourselves too many questions, we trust the medical body*" (M1V). While some described trust as a consequence of expertise and scientific knowledge, others believed these traits could lead to arrogance and disrespect: "*Doctors in France, I don't know if it's different elsewhere, they always have a very professional side, as "what we say, it's the truth, etc." They think we don't know anything*" (M10). Instead, many mothers described trusting doctors who know them for a long time and who have a reassuring, comforting presence. The way the vaccine was offered was particularly important, with mothers valuing doctors who listened to them and explained or advised rather than pressured or judged them: "*He tells me "I suggest this", I suggest. I think it's really good. Other doctors will tell you, "Ok, we have to do this vaccine" and they give you the prescription. There is a difference between suggesting and giving*" (M7).

Doctors' personal beliefs around vaccination and their intentions as to whether they would vaccinate their own daughters was important for mothers, who described doctors in their parenting role as even more reliable, trustworthy and honest: "*This was the argument that convinced me: if she, as a doctor, would vaccinate her daughter, well then I will vaccinate*

mine” (M22V). Similarly, some mothers expressed strong trust in friends or family members working in the medical environment as they were seen as more objective: *“It has a lot of weight, the fact that doctors, in their personal lives, don’t vaccinate their daughters. (...) They are well informed, if they don’t do it, there must be a reason”* (M16).

High trust in doctors also meant that some mothers did not vaccinate their daughters because their family doctors had not recommended the vaccine or recommended against it, sometimes because of concerns about side effects. Some mothers believed their doctors lacked information: *“And my doctor, what’s strange, is that he doesn’t talk about it; and the paediatrician either. So, I tell myself, it’s, strange, I feel like in France, it’s not something really developed”* (M8). Mothers and girls were also surprised and conflicted when hearing contradictory opinions from different doctors: *“It’s even more perturbing when doctors can’t agree, how can we make a decision if even doctors don’t know whether or not it should be done?”* (A10).

While many girls expressed trust in their doctors around health and HPV vaccination, they did not report a significant direct influence from their doctors in the same way as mothers. Some girls reported that their doctors had not discussed the vaccine with them, and instead only addressed their mothers. Others explicitly explained they would follow their mothers’ advice over their own doctors’ advice: *“If the doctor would recommend it to me? I would still say no, because my mum decided, and I trust her, so the doctor wouldn’t change my mind”* (A7).

Trust in health authorities: a more complex relationship

While mothers described trusting health authorities, they also described events that made them question their trustworthiness, such as beliefs that the hepatitis B vaccine caused multiple sclerosis, concerns about the way the H1N1 vaccination campaign was handled, or

reports of the blood contamination scandal of the 1980s: “*I remember we had the blood contamination scandal, it was just a catastrophe. They killed many, many people. And they know the blood was contaminated, it didn’t bother them. They were high-level people. So yes, I think that, if it happened once, it can happen a second time*” (M9). These type of events tainted mothers’ trust in official sources. Some also discussed reluctantly feeling it is better to trust experts, or feeling ‘*naïve*’ for trusting them. While adolescent girls’ trust in health authorities was generally more positive, some relied on their mothers to assess whether or not they should place their trust in them: “*I trust them because my mum trusts them*” (A13V). Some mothers also discussed financial or objectivity concerns around health authorities and pharmaceutical companies.

5.3.4 Trusting oneself in the context of external influences and social norms

Both mothers and girls described the importance of trusting oneself while acknowledging the sometimes unavoidable influence of others around them. One girl described decision-making around HPV vaccination as a process entirely dependent on external influences: “*It’s a question of influence: (...) If I had only seen doctors who had told me yes, I would have done it; and if I had only seen doctors who had told me no, I wouldn’t have done it but because I heard from both, I’m in the middle, asking myself what do I do?*” (A10).

Influences from friends and family

Influences from family and friends were mostly discussed in a positive way by mothers and girls, reflecting a need to hear a range of opinions as well as an opportunity to obtain more information. Many mothers reported hearing negative stories, views or controversies about the vaccine from their friends, instilling doubt and anxiety in their decision.

Mothers and girls also acknowledged that their friends often shared the same beliefs and values as them, which could explain why influences are reported in a positive way: “*with my friends, we more or less have the same thoughts, it’s a little, we’re not connected but often, on topics, we have the same opinion*” (A5V).

Social influences and social norms

Social norms were important, as one mother explained that diverging from group opinions was frowned upon and others described worries about being judged for their decisions. One mother also described taking the decision to vaccinate their daughters as a group decision with her friends, following one of her friend’s diagnosis with cervical cancer. Guilt and anxiety was also found to be associated with the social meaning of good parenting, particularly in the face of cancer: “*There’s always that moralising aspect of telling myself, oh my god, I might be putting my daughter in danger, I’m really an unworthy mother*” (M14).

Being wary of others’ opinions and prioritising one’s own intuition

Despite acknowledging influences from others, some mothers showed a wariness of others’ beliefs and perceptions: “*I listen to what people say and I look around to see what others do, but I make my own opinion. I try to not be influenced.*” (M22V). Both mothers and adolescent girls described HPV vaccination as a personal decision, despite mothers making the decision for their daughters, stressing the importance of one’s own intuition, beliefs and decision: “*If friends told me, we don’t want to get vaccinated against this, I would tell them it’s a shame, and well it’s their decision. (...) It wouldn’t influence my decision in the sense that, I already know what I think and nobody will change my mind*” (A22V). Some girls also described their own role as influencers, and the importance of warning their friends about the danger of diseases, explaining they may try to convince others around them like their friends to get vaccinated against HPV: “*It’s cancer (...) I think it’s our role to warn others, it’s an*

important topic so we need to discuss it with our friends. Maybe they don't know [about it]. (...) It's true that maybe I should have talked to friends about it, and they would have talked to other friends and more people would have been aware and would have gotten vaccinated" (A24).

5.4 Discussion

This study explored the role of trust in decision-making processes around HPV vaccination among mothers and adolescent girls in France. Trust has been described as a means of reducing uncertainty and facilitating decision-making (24, 65, 255). In this study, HPV vaccination was described by mothers as a highly difficult decision that requires time and serious consideration, which could indicate important trust issues. Four key themes were identified: 1) uncertainty around a mistrusted vaccine, 2) navigating mistrust and influences from a negative information environment; 3) the importance of trust and deferring decision-making to epistemic authorities; and 4) trusting oneself in the context of external influences on HPV vaccination decision-making.

5.4.1 HPV vaccination: a mistrusted and controversial vaccine

Mothers' description of the HPV vaccine as 'controversial' and their tendency to distinguish it from other childhood vaccines could be a consequence of years of criticism and questioning of the vaccine by some public figures and members of the medical community in the French media (252). While this was not visible among adolescent girls in this study, it is possible that long-term exposure to such controversial information, especially when children are growing up could have long-lasting effects on who adolescents place their trust into. The vaccine has also been described in this study and others as eliciting mistrust because of a perceived lack of scientific evidence around its safety and effectiveness (252, 279). This feeling was

reinforced when mothers and girls received conflicting advice from doctors or experts which could result in long-term trust erosion and delays in HPV vaccine acceptance (47, 280).

In response to growing childhood vaccine hesitancy in France, authorities made 11 childhood vaccines mandatory in 2018. While HPV vaccination was not part of these 11 vaccines, it would be interesting to conduct further research to understand the possible impact of such legislation on parental attitudes, especially as one mother reported reassurance associated with mandated vaccines.

5.4.2 Deferring vaccine decision-making: the central role of health professionals and mothers

Strong trusting relationships between parents and healthcare professionals can help alleviate doubts and concerns around vaccination (281). When making decisions around HPV vaccination, mothers in this study were found to place their trust in doctors, confirming findings from previous research (154, 252, 279). Doctors' trustworthiness was described as a consequence of their expertise and scientific knowledge as well as personal and long-term relationships, confirming findings from a previous study showing that trust in proximal actors is stronger than trust in more distant actors (255). Consequently, mistrust was expressed towards doctors who judged or pressured mothers into accepting vaccination. The characterisation of trust based on personal relationships was also highlighted by the desire to know whether doctors would vaccinate their own children and by mothers seeking advice from doctors in their personal networks to obtain what they described as more trustworthy and honest guidance. These findings highlight the need to strengthen dialogues between parents and healthcare professionals, with a focus on listening and understanding of parental concerns, for example through motivational interviewing techniques (282) or presumptive recommendation approaches (283).

However, strong trust in doctors can constitute a barrier to vaccination if doctors themselves are hesitant to vaccinate their patients against HPV. A survey conducted in France showed that a substantial proportion of GPs express low confidence in the vaccine due to concerns about the risks and benefits of HPV vaccination and questioning of its utility (184). These findings explain why mothers in our study commonly reported not having received a recommendation to vaccinate or having received a recommendation against HPV vaccination by doctors. Mothers' inability to rely on doctors to help navigate decision-making around HPV vaccination could increase their uncertainty and hesitancy to vaccinate their daughters.

While adolescent girls also expressed some trust in healthcare professionals, they were less influential than mothers in their decision-making. Deferral of decision-making to epistemic authorities is common, with doctors often playing this role for health-related decisions (284), as was seen with mothers in this study. While adolescents are known to rely on their parents for important decisions (285), this study showed that their trust in mothers could make adolescents disregard guidance received from healthcare professionals. If mothers who question HPV vaccination are the only source of information for adolescent girls, this could contribute to the creation of a future generation of vaccine hesitant individuals. Mothers have been shown to play a key role in transmitting their own health behaviours, beliefs and values to their children (80). Furthermore, the lack of awareness about HPV vaccination among adolescent girls identified in this study highlights the urgency of informing girls outside the home, such as in schools as they were seen as a highly trusted environment by both mothers and girls. Finding more opportunities for adolescents to meet with their doctors and discuss HPV vaccination could also help build a stronger relationship between doctors and adolescent girls.

5.4.3 Characterisation of trust towards the government and health authorities

Trust expressed towards governments, health authorities or scientific experts was more nuanced than trust in healthcare professionals. While both mothers and adolescent girls described trusting health authorities, mothers also criticised the management of previous events in France. Interestingly, and perhaps because adolescent girls were too young to remember these events, their trust in health authorities was stronger. These events have previously been described as influential in parental hesitancy to vaccinate (252), confirming the notion that a health system's past performance can influence public trust in institutions, particularly around their competency and ability to deliver similar interventions or programmes (273). This context of mistrust of authority combined with the perception that scientific expertise should be trusted and listened to led to what some mothers described as 'reluctant trust' (62). Rebuilding trust in authorities may take a long time, but should start with an acknowledgment of previous mistakes and a review of lessons learnt from past events.

5.4.4 Trustworthiness of different sources of information and the importance of trusting oneself

Trust is relied on to determine which experts to believe, especially when they offer conflicting recommendations (64). This study confirms previous findings that while mothers and adolescent girls mistrust online information, this does not prevent them from accessing it (252, 286). This could be a consequence of the mistrust expressed towards official sources of information as well as evidence of the important role of the internet in today's information environment. However, internet and social media can facilitate the spread of misinformation and information discouraging vaccination, especially as individuals tend to engage more commonly with negative rather than positive information online (287). Mothers in this study

reported being affected by information discouraging vaccination online, as well as in mainstream media such as national television and radio or the feminine press which could have contributed to their uncertainty and hesitancy to accept HPV vaccination. Additionally, despite adolescents describing social media as an essential tool to inform young people, they also raised the concern that all information can be manipulated. This could be an effect of a generation growing-up in a world constantly discussing the effects of misinformation (288), leading to adolescents becoming more suspicious, even when information comes from credible sources. Exploring the impact of this change in attitudes towards information is essential to prepare and adapt communication strategies. Improving education on the evaluation of information as well as providing information through additional trusted sources, such as schools, will also be important to restore confidence in HPV vaccination.

Despite accepting information from others, most particularly female peers (255), both mothers and adolescent girls raised the importance of making decisions around HPV vaccination independently, free of external influences. The uncertainty and low awareness identified around HPV vaccination could mean that the desire to remain in control of decision-making is associated with psychological empowerment rather than health literacy or conviction in one's own decision-making capacities (289). Empowering adolescent girls to make decisions about HPV vaccination could be particularly important as they expressed strong certainty about the benefits of the vaccine and its essential role in preventing cancer.

5.4.5 Limitations

There are some limitations to this study. Due to the low HPV vaccine uptake rates in France, only a small number of vaccinated participants were included in the study, which could have skewed some of the findings. The study was also conducted in Paris, which may not be representative of the rest of France and only included mothers which may have limited

findings from families in which fathers or other guardians are responsible for vaccination decision-making. The two recruitment and compensation mechanisms may have also affected the results. The fact that the interviews were conducted in French and reported in English could mean some concepts might have been lost in translation. This was partly mitigated by the researcher, fluent in English and French, analysing data in French and explaining concepts that could not be easily translated in more details.

5.4.6 Conclusion

This study found that HPV vaccination decision-making in France is a complex and uncertain process, which could be a consequence of erosion of trust in the vaccine, healthcare professionals, health authorities and information itself. As HPV vaccination has now become available to boys, these dynamics will need to be explored further among all adolescents, with future quantitative research also needed to provide more representative and generalizable findings. Furthermore, a controversial environment and healthcare professionals' own uncertainty and failure to recommend HPV vaccination could also lead mothers to question the trustworthiness of the vaccine. This study therefore highlights the need for further research to evaluate the effects of long-term trust building strategies focusing on HPV vaccination, vaccine providers, policy-makers and other sources of information.

Chapter 6: The role of maturity in adolescent decision-making around HPV vaccination in France

RESEARCH PAPER COVER SHEET

SECTION A – Student Details

Student ID Number	315566	Title	Ms
First Name(s)	Emilie		
Surname/Family Name	Karafillakis		
Thesis Title	Adolescent decision-making and Human Papillomavirus vaccination in France		
Primary Supervisor	Heidi J Larson		

If the Research Paper has previously been published please complete Section B, if not please move to Section C.

SECTION B – Paper already published

Where was the work published?	Vaccine, Elsevier		
When was the work published?	02/09/2021		
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion	n/a		
Have you retained the copyright for the work?*	No	Was the work subject to academic peer review?	Yes

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Where is the work intended to be published?	_____
Please list the paper's authors in the intended authorship order:	_____
Stage of publication	Choose an item.

SECTION D – Multi-authored work

<p>For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)</p>	<p>I am the first author on this paper, published with 4 other authors. I led the design of the study and methodology for qualitative research, identified and recruited participants, conducted data collection (interviews and focus groups), analysed and interpreted the data, and wrote the manuscript.</p> <p>Other authors provided support and guidance on the design, data collection, analysis and interpretation and revised the manuscript prior to submission.</p>
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SECTION E

Student Signature	
Date	11/03/2022
Supervisor Signature	
Date	18/03/2022

This chapter is the accepted manuscript of an article published by Elsevier in Vaccine on 2 September 2021, available online: Karafillakis E, Peretti-Watel P, Verger P, Chantler T, Larson HJ. The role of maturity in adolescent decision-making around HPV vaccination in France. Vaccine. 2021;40 (39):5741-5747. <https://doi.org/10.1016/j.vaccine.2021.08.096>

6.1 Introduction

Mothers across the world, play a caregiving and protective role for children and are primarily responsible for household health-related decisions (79, 80). As family health managers, they play a key role in teaching children healthy behaviours such as nutrition, hygiene and vaccination, with children commonly assuming the behaviours, beliefs and values of their mothers (80, 255, 290).

Some mothers delay or refuse vaccination for their children, questioning the necessity, effectiveness and safety of vaccines (43, 265). Increasing exposure to unverified and often negative information on the internet and social media, together with contextual and historical factors such as poor government management of previous health crises, including lack of transparency breeding distrust, have contributed to the decrease of public confidence in vaccination in some communities (273, 287). In some cases, this has led to important drops in vaccination coverage rates and the resurgence of vaccine-preventable diseases, as observed in recent measles outbreaks (291, 292).

6.1.1 Decision-making and public questioning of HPV vaccination

Vaccination against HPV has elicited particularly strong concerns among parents, in part due to widespread controversies around the vaccine's safety that circulated in some countries (293, 294). France has one of the lowest HPV vaccination rates within Europe, with parents citing concerns about possible side effects and insufficient protection provided by the vaccine as reasons for refusal (100, 184, 252, 295).

Compared to many countries in which HPV vaccination is administered in schools, the vaccine is administered by family doctors in France, targeting 11 to 14 year old girls as well as 15 to 19 year old girls as part of a catch-up campaign (102). While there is no international agreement on the age at which adolescents are considered to be competent to make medical decisions, including vaccination, legal majority is often used as a threshold in European countries (83). Minors under 18 years old in France are unable to be vaccinated against HPV without their parents' consent, which is often given implicitly (102). Yet, studies have shown that adolescents as young as 11 years old could be competent to make informed decisions, including participation in clinical trials and acceptance of medical treatments (83-85). While adolescents' competence is task and context specific, adolescents in some countries are increasingly being given a more active role in providing their consent to receive HPV vaccination. In the UK, the Gillick competency tool is used by health professionals to assess the competency of adolescents to provide consent for vaccination (81, 82). This allows adolescents to be vaccinated even if their parents have not provided written consent, whether for logistical or for ideological reasons (81, 82).

However, involving adolescents in vaccination decision-making could include various challenges. Adolescents' competency to make health decisions depends on a variety of factors, including their maturity level and ability and readiness to assume responsibility for health and life decisions over time.

6.1.2 The role of maturity in adolescent decision-making

Maturity is defined differently across legal, social, psychological, sexual or public health contexts. In this paper, we use Cauffman and Steinberg's definition of maturity, in relation to judgement in decision-making (86). While their definition was proposed in the context of legal decisions, it has previously been applied to health (296, 297) and refers to essential

factors influencing vaccine decision-making. They define maturity of judgment in decision-making in relation to three key psychosocial factors: responsibility, temperance and perspective (86). Responsibility refers to the development of a sense of personal identity, leading to health autonomy and the ability to make decisions independently, resisting external pressure to act in a way that may go against one's own values (86). Rather than simply disregarding the advice of others, it is about understanding how others can influence one's own beliefs and behaviour and knowing where and when to turn for advice (86, 87). Temperance is the ability to control one's emotions and impulses, avoiding rash decisions and evaluating situations before making a rational and informed decision (83, 86, 87, 298). Perspective is the acknowledgement of the bigger context in which decisions are made, for example by understanding short- and long-term consequences of decisions or by being able to see how one's decision may affect others (83, 86, 299). It also refers to the understanding of why others make certain decisions and the influence of larger forces that cannot always be controlled such as the role of social institutions (86).

These factors can define how adolescents make decisions, including around HPV vaccination, although they will also depend on the nature of the situation and the context in which a decision is being made (83, 86). Maturity should be understood as a continuum rather than a binary concept, which means that children of the same age may have different levels of maturity as they progress differently through physical, neurodevelopmental, psychological and social changes (8, 86). Furthermore, while adolescents may be mature enough to make decisions in certain areas, they could be less competent in others (83). Intellectual maturity may not automatically imply emotional or social maturity; for instance, while adolescents may understand medical information, they have been shown to be more likely than adults to be influenced by their emotions when making decisions (83, 87). The age at which HPV vaccination is given in France corresponds to major life and social changes

and school transitions, as adolescents move from primary school (ages 6-11) to middle school (ages 11-15). The impact of this transitional period between childhood and adulthood is not negligible, as adolescents reach an age when they seek greater independence from parents while experiencing closer relations with peers, which could have important implications for health decision-making (9).

6.1.3 Aim and rationale

In this paper, we explore the role of maturity in adolescents' involvement in the decision-making process about being vaccinated against HPV in France. This understanding can provide insights into adolescents' interactions with their mothers during the decision-making process as well as insights on how mothers' concerns about vaccination could shape their daughters' current and future beliefs and perceptions of vaccination. These findings could provide valuable information for the development of policies on adolescent consent for vaccination.

6.2 Methods

Qualitative semi-structured interviews and focus group discussions with adolescent girls and their mothers were conducted in France to explore the role of maturity in decision-making around HPV vaccination.

6.2.1 Data collection

Between October 2018 and March 2019, 24 in-depth interviews and two focus groups (with 5 and 7 participants in each group) were conducted with adolescent girls (aged 15-16) and 21 in-depth interviews were conducted with their mothers. Participants were purposively selected to include both vaccinated and unvaccinated girls from different districts in Paris.

However, only eight vaccinated girls were identified for this study, three of whom took part in focus group discussions.

Participants were identified using two recruitment methods. Adolescents were first approached through public, private and professional *Lycées* (high schools), with prior approval from the school directors. However, as only four adolescent interviews and two focus groups were conducted using this recruitment method, a local research agency specialised in behavioural research (BVA Group) was contracted to identify additional participants. All participants received a study information letter that described the study objectives and stated how interviewees' confidentiality would be protected. Adolescent girls and their mothers were required to provide written informed consent to take part in the study. Adolescents were also asked to obtain written consent from their parents.

Interviews (30-60min) and focus groups (60min) were conducted in French by an experienced qualitative researcher who is fluent in English and French. The interviews were conducted in participants' homes or at a private place of their choosing and the focus groups took place in schools with girls from the same school class. Interviews and focus group discussions were audio-recorded with prior approval from all participants. All interviews were conducted privately; no caregiver requested to be present during the interviews with adolescents. Adolescents recruited through schools entered a lottery to receive an Amazon voucher to thank them for their time, while all participants recruited through the research agency were compensated for their time.

Topic guides for the interviews and focus group discussions (Appendix E) were designed to cover predetermined questions around HPV vaccination knowledge, decision-making processes and influences, and beliefs and perceptions, while remaining sufficiently flexible to

allow discussions to be shaped by the participants' responses. The topic guides were piloted with three adolescent girls (excluded from the analysis).

6.2.2 Data analysis

This study used a codebook approach to thematic analysis, as described by Braun and Clarke as a cluster of methods distinct to reflective thematic analysis in its use of a structured coding framework (248). Transcripts from the interviews and focus group discussions, field notes and analytical memos were imported into Nvivo® for analysis. All data files were anonymised to ensure confidentiality, removing personal identifiers such as names and locations and using numerical codes to refer to participants (using the letter 'V' to indicate vaccinated individuals). All files were stored on a secure server and password-protected computers. Analysis was conducted in French to avoid losing the meaning of data, with quotes for this paper directly translated into English for write-up by the researcher fluent in both languages.

Data was analysed using a coding framework, developed by deductively drawing parent codes from the topic guides, existing literature and contextual background information and the analytical memos. The coding framework was tested on four transcripts and finalised using an inductive process to derive additional codes. The final framework used to code remaining transcripts was reviewed by a second researcher, allowing some codes to be modified, merged or removed during the analysis.

Transcripts from interviews with mothers and adolescent girls and focus groups with adolescent girls were coded separately to detect differences and similarities in the coding phase. Coded excerpts as well as the language used by participants was then compared between mothers and adolescent girls, with particular attention paid to exchanges between

adolescent girls during the focus group to understand how HPV vaccination is discussed among peers.

Codes were analysed by inductively drawing a list of issues and themes from a comparison and analysis of coded excerpts. These themes were then analysed in the context of literature on adolescent decision-making, following a framework analysis approach to theme development (249). This type of analytical approach also recognises the researchers' subjectivity in analysis and the contextual aspect of knowledge (248).

6.2.3 Ethical approval

This study obtained ethical approval from the London School of Hygiene & Tropical Medicine [Ref. 15320-3] and from Aix-Marseille Université [Ref. 2018-12-07-005].

6.3 Results

HPV vaccination was generally discussed by participants as a decision that should involve girls and mothers. However, perceptions about the extent to which adolescent girls should be included in the decision varied widely between and within families. Both mums and girls spontaneously referred to '*maturity*', *independence and responsibility* as key factors influencing the role adolescents should have in decision-making: "*It depends on everyone's maturity, because some people can be convinced of their decision at a certain age but (...) without necessarily having enough hindsight*" (A19). While none described what they meant by the term '*maturity*', differences in maturity levels were used to explain why some adolescent girls might be involved in HPV vaccination decision-making and others may not. The word '*immature*' was never used and involvement in decision-making was instead described as a process that evolves together with maturity. Some adolescents described their own process of change and perception of becoming more mature: "*My mentality also*

changed a lot in comparison to before. Now, I ask myself a lot more questions, while before, it was 'I have to do it, so I do it'" (A3).

Five key themes were identified through the thematic analysis, organised and described in further details below according to Cauffman and Steinberg's definition of factors influencing maturity. The themes 'adolescents' role in decision making', 'recognising the influence of others' and 'adolescent girls' understanding of HPV vaccination' relate to 'responsibility'. The theme 'impulsive and emotional decisions' related to temperance, and the theme 'understanding the broader context in which decisions are made' relates to 'perspective'.

6.3.1 Adolescents' role in decision making

Adolescent girls' involvement in HPV vaccination decision-making was mostly described by mothers in terms of 'passive obedience', with one mother explaining that her daughter would hand over all responsibility to her without understanding what decisions such as vaccination mean (M14). Similar to childhood vaccination, girls followed their parents' decisions without taking into consideration their own values or preferences, sometimes without being aware of which vaccine they received: *"My parents take me [to get vaccinated] but I don't know what I'm vaccinated against (...) So, I really don't know whether I received [the HPV vaccine] or not"* (A2). Some girls not only followed their parents' decisions, but repeated the concerns expressed by their mothers, without always understanding them. Although this was in part explained as part of a strong relation of trust, girls also thought that their parent's life experience made them more capable of reflecting on the decision: *"I think parents' advice is to be taken into account because they are adults, they have life experience"* (A10). While some girls explained feeling mature, health was seen as an area remaining under parental responsibility. A couple of girls preferred to distance themselves from decisions that could

carry possible risks: *“I prefer to let my mum decide for me, because if something happens to me, I don’t want to be responsible”* (A15).

Mothers also discussed HPV vaccination as their responsibility, sometimes preventing their daughters from taking part in the decision: *“I did it early to take the decision instead of her, and I assume that completely; for me it’s the mother’s role.”* (M1V). Doctors seemed to share that perspective, as girls explained they rarely discussed HPV vaccination directly with them: *“He said ‘on this day, I would like you to come back to get a vaccine’, but then he explained everything to my mum”* (FG2). One mother believed that involving her daughter in this decision would represent ‘*cowardice*’ and not ‘*assuming your role as a parent in decision making*’, stressing that *“the responsibility could place a weight on her shoulders”* (M16).

Despite most girls and mothers agreeing that the decision should remain the responsibility of parents, some participants believed that girls should also be involved in the decision to some extent. Having an informed discussion about the vaccine and HPV infection and cervical cancer was described as important by both mothers and adolescent girls. A few girls also believed that as the vaccine concerns their own bodies, they should make the final decision, showing a sense of personal identity and separate self: *“It concerns girls, not parents. They won’t be the ones who have to live with the vaccine, or who have to get vaccinated. Girls, not parents should decide”* (A20). The age for legal maturity and parental consent was also questioned by mothers, who acknowledged that today’s adolescents are becoming mature earlier and suggested that new legislation around access to health could reflect these changes: *“Maybe if there was a legislation to allow girls who would like to get vaccinated to do it without their parents’ consent. I mean, for abortions, young people can do it without their parents’ consent. So, there is a whole procedure that is already in place.”* (M24). A couple of mums also described trying to empower their daughters in relation to their own health,

explaining that HPV vaccination could be a good opportunity to help them become more mature: *“I try to make her more independent. Well, it even goes beyond health; it’s more... yes, in terms of autonomy.”* (M11).

6.3.2 Recognizing the influence of others

When reflecting about HPV vaccination, the role and influence of others in decision-making was discussed differently by adolescent girls, which could indicate different maturity levels. Although some girls understood the influence others such as friends, experts or figures publicly discussing vaccination may have on their own decisions, others referred to themselves as stubborn or not easily influenced: *“I like to make decisions myself. (...) If the advice fits me, I follow it, if it doesn’t, I don’t follow it. I follow my own mind”* (A3). One girl also reported doing the opposite of what people tell her, almost describing an act of teenage rebellion: *“Most of the time, when people tell me something, I do the opposite (...) when I want something, I really want it so even if I listen to what they tell me... (...) I’m quite stubborn actually”* (A11). Girls who understood the influence of others often grounded their responses in more reflection and explained their decisions would depend on whom they talk to.

6.3.3 Adolescent girls’ understanding of HPV vaccination

Maturity in decision-making was described by both mothers and adolescents in relation to the understanding of what HPV vaccination represents, with many describing adolescent girls as too young to be responsible for the decision: *“I don’t think she has perspective, well she cannot understand and could refuse because of opposition [to her parents] or because she doesn’t like injections, or because she doesn’t understand the importance of this decision”* (M13V). While some participants were aware of the benefits of protection against cancer or the understanding of the possible risks associated with vaccination, some mothers also

described maturity in relation to a girl's awareness of sexual health: "*she isn't in this type of thing, and she doesn't have the consciousness of all these [issues], what is an STI... She's millions miles away from all of this*" (M11). This was only described by one adolescent girl: "*We're not going ask a 10 year-old to choose whether she wants to get vaccinated, because she doesn't have the maturity to understand what it consists of. But I think we should talk more to girls, especially as they engage in sexual intercourse earlier now, so they should be warned before it happens*" (A24).

Many adolescent girls were not aware of HPV vaccination, and showed limited understanding around HPV infection, cervical cancer and HPV vaccination. They often explained this by a lack of access to information rather than unwillingness to become more informed. In fact, many girls explained that they would need more information before being able to decide whether to accept the vaccine, showing an understanding of the need to evaluate situations before making decisions. Girls not only explained they would do their own research before making a decision, but also described an assessment of where to find trustworthy information. The importance of obtaining advice from others was raised, especially those with more expertise such as doctors or those with previous experience with vaccination, such as older sisters.

6.3.4 Impulsive and emotional decisions

Adolescence was also seen as a period of change, when decisions are sometimes highly volatile. A few girls changed their mind repeatedly as the interview progressed. One explained that her responses cannot be seen as certain because adolescent girls change their minds based on the situations they are in, from one day to the next: "*Opinions change all the time. (...) the fact that you ask me all these questions, I answer them, but I know, myself, personally, I really know that it's probably going to change. Maybe one day, I will finally*

have a response” (A3). While for some girls, this could be a sign of impulsive decision-making, it could also be a sign of maturity, showing that adolescents take into account different influences before making decisions: *“If I still don’t want to get vaccinated then I won’t do it and if I received information that convinced me to get vaccinated, then I would do it”* (A21V). This can be particularly difficult in a controversial context, as adolescents explained they received conflicting advice from doctors and mothers described the vaccine as highly controversial.

In comparison to mothers, girls seemed calmer when discussing HPV vaccination, less influenced by emotions and impulses. While mothers showed strong fears about the safety of HPV vaccination and discussed the vaccine as highly controversial, girls were convinced of the protection offered by the vaccine, expressing positive feelings of security, reassurance and tranquillity associated with a vaccine that prevents cancer. Girls also explained that as they become more mature, they have less emotional reactions to decisions. For example, not being afraid of needles was associated with *‘growing up’*, with most girls describing their experience of vaccination as a stress-free one.

6.3.5 Understanding the broader context in which decisions are made

HPV vaccination was discussed in the context of the general public’s decisions around vaccination with girls describing public controversies around vaccination: *“It’s controversial. Of course! If it wasn’t, we would have done, or we wouldn’t have... but we would be asking ourselves the questions, we wouldn’t be here to talk about it. I think that’s what differentiate it from other vaccines, yes”* (A10). However, attitudes towards parents who might be hesitant to vaccinate their children were varied. Some girls expressed incomprehension and strong criticism of parents who might not want to vaccinate their daughters and protect them against diseases: *“If parents don’t want her to get vaccinated, it’s not normal”* (A23V). Others,

despite disagreeing with anti-vaccine views, expressed an understanding of the reasons for their hesitancy: *“I know there are controversies around vaccines, saying that they don’t necessarily work or they cause other diseases or complications, or that we would catch the diseases when receiving the vaccine, but I do not believe all of this”* (A24). Finally, some girls, especially those with mothers with anti-vaccination views, expressed worries about the controversies around HPV vaccination.

Adolescent girls discussed HPV vaccination with both a short- and long-term outlook, particularly in relation to the prevention of HPV infection and cervical cancer. In fact, while most girls described the importance of the prevention of cancer in the long-term, some girls also believed that it was too early for them to get vaccinated as they were not sexually active yet: *“If you don’t have sex when you’re 15 years old, well, I don’t see why you would do a vaccine that protects against sexually transmitted diseases”* (A2). One girl also discussed the permanence of the decision to accept a vaccine: *“I think that there is more of a preventive nature in saying no than if I say yes when, well, once we have said yes, in fact, it’s a little irreversible. We can’t, we can’t go back, so I would say no”* (A10).

A few unvaccinated and vaccinated girls also discussed the act of vaccinating themselves as a social one and a way of protecting others, such as their sexual partners or the greater community. Finally, some adolescent girls also understood the role of social institutions in their decision, mentioning that vaccines can be trusted because they are produced by experts and health authorities whose role is to protect populations.

6.4 Discussion

This study explored the role of maturity in adolescent decision-making around HPV vaccination in France. Adolescent girls’ involvement in decision-making was found to be a

process that evolves together with maturity, with important differences identified in maturity levels and participation in decision-making from one family to the next. While some girls described childlike traits such as doing the opposite of what they are being told or making impulsive decisions without understanding the role and influence of others on their own decisions, others reported going through more rational decision-making processes. These differences could be a consequence of adolescents progressing towards maturity at different speeds and could be influenced as well as influence relationships between adolescents and their mothers (300, 301). In fact, some adolescents described their life as a period of change, explaining that as they become more mature, they start asking more questions and become less emotional when making decisions. For example, while many studies have previously reported strong fears of needles among adolescents (218, 279, 302), participants in this study reported being less anxious about needles than they used to be when they were younger, associating overcoming their fears with progressing towards adulthood.

In contrast to more mature adolescents, some girls described their decision-making process as highly volatile, explaining that their decisions would be influenced by the information they receive and the people they speak to, with some girls even repeatedly changing their mind about HPV vaccination during the interview. This could suggest these adolescent girls were less emotionally mature, making decisions emotionally or impulsively rather than rationally (86). However, some mothers expressed even more emotional reactions to HPV vaccination than their daughters, confirming the theories that adults often make decisions, including in relation to vaccination, using an intuitive, rapid and sometimes emotional system rather than a more analytical one (34, 268). Adolescence is not only a period of change for adolescents themselves but also for their mothers, and the impact of these changes on the role of emotions in mothers' decision-making should be explored further. Adolescents' volatile decisions and uncertainty may also reflect the controversial environment in France where the adolescent

girls grew up, surrounded by information questioning the safety and value of HPV vaccination, including from medical sources and the mainstream media (252). More research is needed to understand the long-term effect of low public confidence in vaccination on adolescents' future views on vaccination, especially in the current context of misinformation spreading on social and digital media (288).

In fact, adolescent girls expressed strong, albeit varied, opinions about vaccine hesitant individuals in France. Some girls in this research were highly critical of those they labelled as "anti-vaccine", questioning why parents, even their own, would refuse protecting their children against diseases. Others expressed concerns and worries about the controversies and uncertainties around HPV vaccination. More importantly, some adolescent girls also discussed their own mothers' hesitancy towards vaccination, repeating their concerns without necessarily understanding them. Adolescence is an important stage during which health behaviours and beliefs develop, often being passed down from parents (80, 303). As future parents and vaccinators, adolescence is the first time girls are asked to face a decision about vaccination and the influence of vaccine hesitant mothers could have longer term impacts on the girls' future vaccine confidence (255).

Furthermore, most girls in this study described their role in HPV vaccination decision-making as one of passive obedience. Health, and more specifically vaccination, was described as being the responsibility of parents, confirming findings from previous research (302, 304, 305). While some girls wished for more involvement in decision-making, most of them followed their parents' decisions. Our findings suggest that adolescents' lack of involvement in decision-making may be related to societal restrictions and social norms rather than solely a lack of maturity. In fact, girls in the study explained receiving little information about HPV vaccination, and being ignored by their doctors who discussed the

vaccine directly with their mothers. Only one mother in this study described HPV vaccination as an opportunity to start empowering girls to become more autonomous in health decisions. Similarly, some mothers preferred to avoid talking about the vaccine with their daughters because of personal concerns about vaccination or because of the conviction that girls are too young to be involved in such decisions. The decision of vaccine hesitant mothers to exclude girls from discussions about the vaccine were previously observed in another study in the United States (306). Girls' exclusions from decision-making means that any positive views towards vaccination or desire to protect themselves from cervical cancer may not influence their mothers' decisions.

As parental consent constitutes a potential barrier to optimal vaccination uptake and mothers' hesitancy towards HPV vaccination is particularly high in France, engaging adolescent girls in decision-making could be beneficial to improving HPV vaccine uptake (252, 301, 305). Allowing adolescents to participate in healthcare decisions has not only been shown to make them more autonomous and responsible, but also to help adolescents make better and more informed decisions about sexual health (187, 306, 307). Additionally, adolescent girls in this study as well as in others have reported a desire to become more informed and more involved in decision-making, while showing a strong interest in HPV and cervical cancer (304, 305, 308). Yet, most of them reported not having received any information from their teachers at school or from school nurses about the vaccine. Improving communication and education strategies targeted at adolescents is therefore essential to improve their understanding of what vaccination represents and increase their autonomy in vaccination decision-making, especially as awareness was found to be particularly low in this study.

Furthermore, as adolescents were found to progress at different speeds towards maturity, a one-size-fits-all approach to adolescent involvement in shared decision-making may not be

appropriate and more individualised approaches may be required. In the UK for instance, adolescent self-consent for HPV vaccination is possible but healthcare professionals are required to use the Gillick competency tool to evaluate their ability to understand what vaccination involves and their competency to make decisions autonomously (309).

Adolescent self-consent comes with important challenges however, such as the risk of straining family relationships by allowing adolescents to override their vaccine-hesitant parents and the difficulty healthcare professionals may face in assessing adolescents' autonomy (81, 301). This is particularly true as some parents' hesitancy in France comes from controversies that surrounded the Hepatitis B vaccination campaign, previously provided in schools (256). Focusing on gradually engaging adolescents in their own care and encouraging the development of their responsibility and autonomy instead may be more appropriate in countries without self-consent legislation already in place (301).

6.4.1 Study limitations

This study provides a valuable analysis of the role of maturity in adolescent decision-making around HPV vaccination. However, some results have to be interpreted with caution. As this was an exploratory study, maturity was not measured against any tools and findings focused on thematic analysis instead. Further research could explore associations between maturity levels, assessed through such scales, and willingness to accept HPV vaccines. All adolescent girls included in this study were from Paris, and most of them were not vaccinated against HPV, which could have skewed some of the findings. Data was collected with 15 to 16 years old girls, to obtain a sample of girls who had passed the age of being offered the vaccine. While our findings around maturity may not apply to younger girls, they provide important information around the possible involvement of older girls in decision-making. The use of two different recruitment methodologies may also have influenced the final sample of

participants included in the study. Girls who accepted to take part in the study may have been more mature than those who refused, influencing some of the findings. Findings from this study are only applicable to adolescent girls: no interviews were conducted with adolescent boys as they were included in the HPV vaccination programme in France in 2020, after data for this study was collected. Future research could explore the differences in the role of maturity among boys and girls in HPV vaccination decision-making.

6.4.2 Conclusion

This study found that adolescent girls in France were rarely included in HPV vaccination decision-making, despite their interest in HPV and cervical cancer and their desire to be involved in discussions with their mothers and doctors. While adolescent girls and mothers described involvement in decision-making as a process that evolves together with maturity, adolescents were often prevented from taking part in decisions by their mothers, doctors, and a lack of information. As some adolescents showed signs of maturity of decision-making, strategies should be developed to increase their gradual engagement in their own care, including in vaccination. This is especially important in a context where mothers are refusing or delaying HPV vaccination due to low confidence in vaccination.

Chapter 7: Discussion

This chapter provides a summary of key findings of this PhD research, reflections on the dynamics of adolescent vaccination decision-making, and consideration of the psychosocial factors influencing adolescent girls' decision-making with regards to HPV vaccination in France. Based on these findings, a model of adolescent vaccination decision-making is proposed and implications for future research are discussed. Finally, limitations of the research are outlined.

7.1 Summary of key findings

The overall aim of this research was to identify and characterise the psychosocial factors influencing adolescent girls' decision-making with regards to HPV vaccination in France, one of the countries with the lowest levels of public confidence in vaccination. A systematic literature review conducted as part of this research (Chapter 2) found that populations in Europe have important concerns around HPV vaccination, with common reports of issues around the quantity and quality of information, worries about the potential side effects of the vaccine, and mistrust of health authorities, healthcare professionals and new vaccines. Determinants of confidence in HPV vaccination differed by country and population group, highlighting the need for local listening and understanding of the reasons driving public questioning around HPV vaccination. While other frameworks on parental or adult decision-making around vaccination have been developed, less evidence exists on adolescents, despite their increasing role in vaccination decision-making around vaccines like HPV and considering their development into the parents of tomorrow. The qualitative research focused on key factors influencing vaccination decision-making: risk-benefit perceptions (chapter 4),

trust and information (chapter 5), and adolescents' involvement in decision-making in relation to maturity (chapter 6).

Vaccine decision-making is strongly influenced by **individuals' cognitive and emotional appraisal of the risks and benefits of vaccination**. This research (Objective 1, Chapter 4) found that adolescent girls and their mothers have different perceptions of the risks and benefits of HPV vaccination. While adolescent girls placed more weight on the perceived benefits of vaccination than their possible risks, highlighting the importance of preventing cervical cancer and HPV, their mothers often focused on the risks of vaccination. This was also confirmed by the different emotional reactions and language used around HPV vaccination by mothers and girls. The understanding of what vaccine safety represents was particularly distinct, as mothers widely focused on controversial and possible long-term side effects and adolescents discussed short-term or local side effects or concerns about doctors not injecting the vaccines properly. This could be explained by mothers' exposure to a conflicting information environment while adolescents were being shielded by a lack of involvement in decision-making and limited exposure to information about HPV vaccination. Finally, adolescents also highlighted physiological (e.g. immune system), behavioural (e.g. sexual behaviour) and ideological (e.g. values, religious beliefs) differences between individuals that can influence the possible risks and benefits of vaccination. Adolescents sometimes believed this meant they were not particularly at risk of vaccine side effects, but mothers still perceived every risk as a possible risk for their own daughters.

Public **trust in vaccines, providers, policy-makers and information** can be important levers of vaccine confidence and acceptance. This research (Objective 2, Chapter 5), observed that an erosion of trust in HPV vaccination, experts and health authorities, and in information itself led to mothers describing decision-making as a complex and uncertain

process. While strong trust in medical professionals was observed among both mothers and adolescent girls, this did not always lead to vaccine acceptance: mothers explained closely following their doctors' recommendations and advice, which meant that some did not vaccinate their daughters because their doctors had not recommended or recommended against HPV vaccination. This conflicting advice generated mistrust of the vaccine. Adolescent girls' trust in the vaccine, providers, and policy-makers was generally high. However, their trust in their own mothers was more important which meant that they would prioritise their mothers' decisions over doctors' recommendations. This could lead to lower confidence in situations where mothers are vaccine hesitant, especially as adolescents reported a lack of exposure to positive sources of information from doctors, schools or the media. Finally, adolescent girls raised the concept of 'fake news' when they expressed mistrust of information in general, as they explained that any information, even when coming from trustworthy sources, could be manipulated.

Mothers remain responsible for vaccination decisions in most households and parental consent is required for HPV vaccination in France, although adolescents can engage in decision-making by sharing their views and preferences and influence their mothers' decisions. However, their **capacity to contribute to decision-making depends on their level of maturity and their autonomy in health**. This research (Objective 3, Chapter 6) confirmed that maturity is not binary and adolescents progress towards maturity at different speeds. While some adolescent girls expressed childlike characteristics such as making impulsive decisions, others showed more rational decision-making based on reflection and an understanding of the context in which they make decisions and the external influences on their decisions. In relation to HPV vaccination, most adolescents passively followed their parents' decisions, without engaging in decision-making. Yet, this could have been due to a lack of awareness as adolescent girls expressed a desire for more information and

involvement in discussions, which, rather than a lack of maturity, could indicate that adolescents are excluded from participating in decisions (i.e. by mothers, doctors).

Furthermore, while adolescents described a volatile decision-making process, influenced by information, emotions and others around them, mothers had stronger emotional reactions to HPV vaccination.

7.2 Reflections on the dynamics of adolescent vaccination decision-making

Vaccination decision-making cannot be characterised by a linear succession of steps that individuals follow when they are faced with the decision to accept or refuse a vaccine. This research has shown that it is complex, influenced by a range of factors and dynamics often occurring simultaneously and influencing each other.

Based on the findings from this research, a model of adolescent vaccination decision-making was developed (Objective 4, see Figure 5), reflecting on the dynamics influencing decision-making among adolescent girls. The model aims to provide a theoretical explanation of the different factors influencing adolescent decision-making and how they interact or influence each other.

7.2.1 Development and description of the model

The success of health promotion programmes, including strategies and interventions to increase vaccine confidence and uptake in various populations, is dependent on the use and application of evidence. In the field of vaccination, health behaviour models that explain why individuals engage in certain behaviours have been essential for the development of strategies to improve parents' beliefs and confidence in vaccination as well as their acceptance and uptake of vaccines (18).

Vaccination decision-making varies tremendously from one population to another, with pregnant women, healthcare professionals, parents or adults from different backgrounds or countries being influenced by different factors when deciding whether or not to accept a specific vaccine (4). Yet, these differences in health behaviour can usually be explained by similar models: while individuals might have different concerns about vaccine safety or might respond to differently to social norms, the dynamics and overall influence of these factors on health decisions will remain the same (only the strength or direction of influence might change).

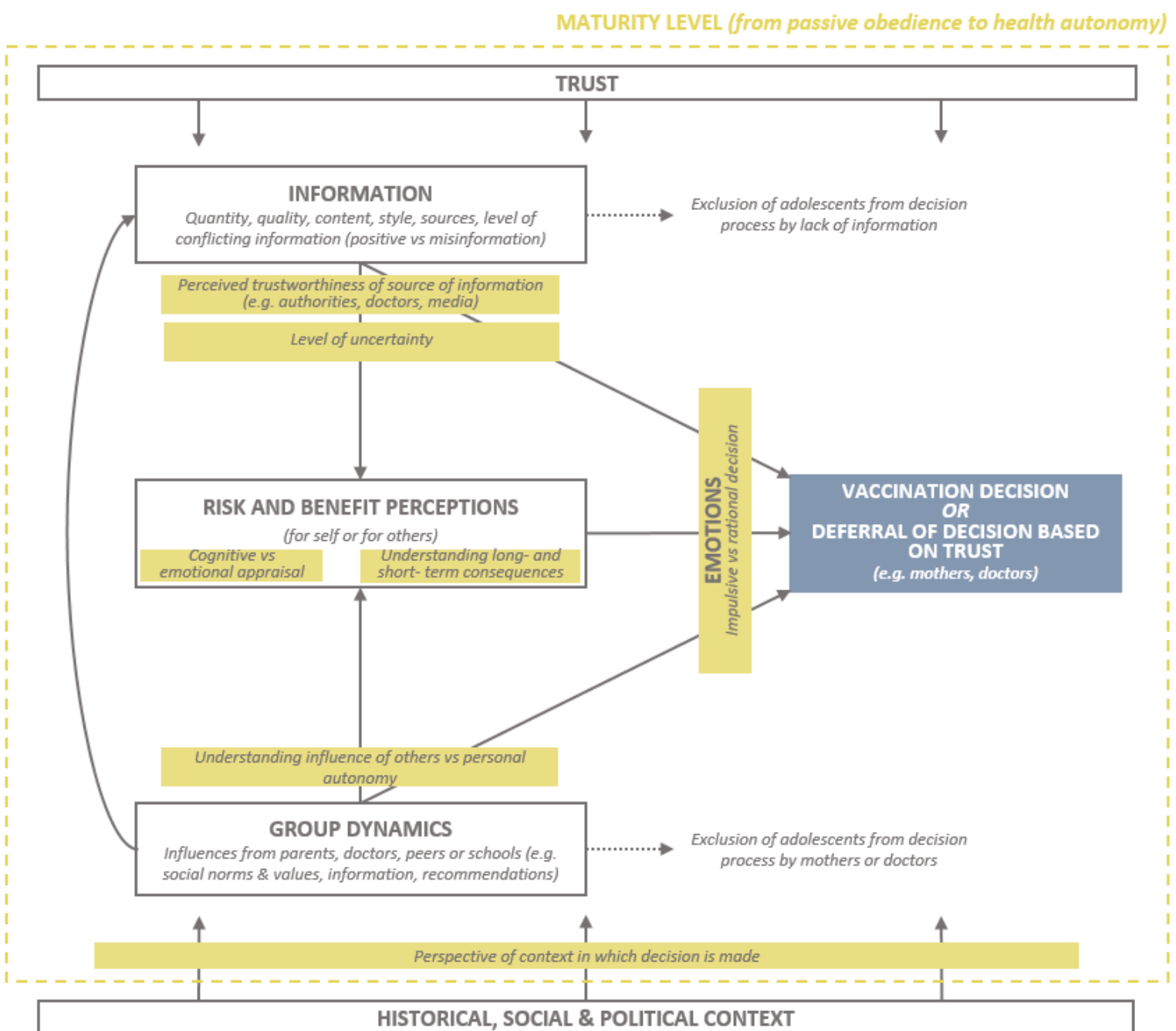
However, the context of adolescence poses different challenges. In fact, adolescents have been shown to make decisions in completely different ways than adults, with their decision-making processes evolving together with their maturity (86). Yet, comprehensive behaviour models for vaccination decision-making among adolescents are lacking. As adolescents are not only becoming more involved in vaccination decisions but also are also forming their beliefs and future behaviours as the parents of tomorrow, this highlights the need for the development of adolescent-specific health behaviour model focusing on vaccination.

The model proposed in this chapter was developed based on a qualitative exploratory study with adolescents, using the specific example of HPV vaccination in France. The study was designed with the objective of identifying the psychosocial factors influencing adolescents while making decisions about vaccination, exploring in details what type of factors played an important role in their decisions, as well as how they related to and influenced each other.

The qualitative analysis focused on identifying key themes that are known to influence vaccination decisions (i.e. risk and benefit perceptions, information, trust, group dynamics and maturity), while allowing more themes to be identified directly from the data. These are described in more details in the results chapter of this thesis. However, in order to create the

model, an overarching thematic analysis was conducted. This involved the re-organisation of all codes identified in the analysis through the use of post-it-notes, allowing the researcher to pay particular attention to the relationships and direction of influences of each theme identified (238). This method allowed the development of a model grounded in the data from this study, described in further details below.

Figure 5: Model of adolescent vaccination decision-making



The model shows that adolescents' vaccination decisions are influenced by five core factors (black boxes): 1) perceptions of the risks and benefits of vaccination, 2) information, 3) group dynamics, 4) trust, and 5) the historical, social and political context. The impact of these five core factors on vaccination decisions is shaped by psychosocial factors characterising adolescents' maturity of judgment (yellow boxes). The model further acknowledges that adolescent vaccination decision-making occurs in the context of maturity, with different levels of maturity (from passive obedience to health autonomy) influencing how adolescents experience and go through the decision-making process. Finally, the model shows that while some adolescents will make vaccination decisions themselves, others will defer decision-making to someone they trust (e.g. mothers or doctors).

All of the elements of the model are grounded in data from this study and can be linked to specific chapters of this thesis. For instance, adolescents' appraisal (cognitive and emotional) of short- and long-term risks and benefits of vaccination for themselves and for others and its direct influence on vaccination decision-making is described in further details in Chapter 4. The role of information and the impact of trustworthiness of the source of information as well as the concept of uncertainty stemming from conflicting information is discussed in Chapter 5, focusing on trust. This is also where further data on the influence of trust on decision-making is discussed in details, including trust in vaccines, healthcare providers, health authorities and information. Group dynamics are discussed in various sections of the results chapters, with Chapter 4 for instance covering the influence of religious beliefs and social norms and Chapter 5 discussing the role of trust in group dynamics (i.e. responding to recommendations from doctors or parents), social norms, making decisions in the context of social influences, and the understanding of how others influence our own decisions. The influence of context is also discussed in various chapters, with for example data on the social context discussed as part of Chapter 4 in relation to the culture of over-use of medication in

France and the preference for natural alternatives or the influence of religious beliefs. Data on the influence of the historical and political context is discussed in relation to mismanagement of previous health crises by health authorities in Chapter 5. The concept of maturity and its influence on adolescents' vaccination decision-making at various levels, including for example the transition from passive obedience to health autonomy or the role of impulsive vs rational decision-making is described in all chapters but specifically in Chapter 6. Finally, the exclusion of adolescents from decision-making by a lack of information or by mothers or doctors is described in Chapter 5 and the deferral of decision-making to others (e.g. mothers, doctors) is a concept described both in Chapter 5 and Chapter 6.

The various elements of this model are discussed in further details below.

7.2.2 Vaccination decisions and deferral of decisions

When making complex decisions and assessing risks and benefits of interventions or technologies such as vaccination, we often rely on those with knowledge and expertise in the field (64). However, relying on information provided by those experts can become complicated when they express differing views and assessments of risks and benefits. In such cases, social trust is determines which experts to listen to (64). This is not a spontaneous process, but a dynamic one as it can take years for individuals to find someone they can place their trust into (255). In this research, social trust was not only used to identify trustworthy sources of information but in some cases to defer the decision-making process to others who are deemed more capable to make the decision. While adolescents expressed strong trust in their doctors, they mostly deferred their decisions to their mothers (compared to mothers who themselves deferred decisions to their doctors). This could lead to challenges, as adolescents with vaccine hesitant mothers then not only remain unvaccinated but may also be influenced by some of their mothers' concerns or mistrust of vaccines. The distinction between decision-

making and deferring decisions to others in the proposed model is important as efforts to improve confidence in and uptake of vaccination will need to address both those deferring decisions and those making decisions on their behalf.

7.2.3 Maturity

One of the key findings from this research was the central role played by maturity in adolescent decision-making. In a first instance, maturity levels can determine whether or not adolescents are included in the decision-making process. As adolescents evolve from passive obedience to full healthcare autonomy, they become more involved in decisions around their own health, including vaccination. Even if they are not legally able to get vaccinated without their parents' consent, they can still be involved in discussions around HPV vaccination or given full decision-making capacity by their parents. Their maturity levels can determine whether they take part in decisions but also whether they are excluded from decision-making by others who believe they are not mature enough such as their mothers or doctors (discussed further in the sections below). Additionally, taking part in health decisions such as HPV vaccination can also be seen as an opportunity for adolescents to become more mature and autonomous.

In addition to influencing the role of adolescents in vaccination decision-making, maturity levels can also influence how adolescents decide whether or not to get vaccinated. In fact, many of the psychosocial factors characterising maturity of judgment can shape the influence of information, risk-benefits, group dynamics, trust or contextual factors on vaccination decisions (see yellow boxes in the model). For example, individuals are known to make decisions in a rational and/or an impulsive way, with rationality and control of ones' emotions seen as a sign a mature decision-making (86). In fact, previous studies have shown that adolescents often make more spontaneous, reactive or impulsive decision due to

instinctive reactions and anticipatory emotions (e.g. anxiety, fear) to risk and uncertainty (28, 36). As adolescents become more mature and progress into adulthood, their decisions become less volitional (30). Differences were observed among adolescents in this research, with some discussing vaccination as a rational decision and others showing more signs of impulsive decisions, influenced by emotions or others around them. This suggests that adolescents evolve towards maturity and adulthood at different speeds, emphasising the need for individualised approaches to adolescent involvement in decision-making.

Other psychosocial factors influencing maturity of judgment that are related to vaccination decision-making include the cognitive and emotional appraisal of information and risks and benefits, capacity to understand long-and short-term consequences of decisions, capacity to understand the influence of others on our own decisions, personal autonomy in decision-making, and perspective of the context in which decisions are made. These are discussed in further details in the corresponding sections below.

7.2.4 Risk and benefits of vaccines

The notion that individuals make vaccination decisions based on their perceptions of the risks and benefits of vaccines is central to many models of vaccine decision-making, and has been studied extensively. In some models, such as the one developed by Betsch et al. (6), benefits are discussed in terms of ‘risks of diseases’ to highlight the focus of decision-making on an assessment of the risks of vaccinating vs the risks of not vaccinating. While this was in part supported by this research, showing that fears and anxiety about the ‘risk of cancer’ can be central to decision-making, distinguishing between risks and benefits is particularly important in the context of adolescence. In fact, adolescents had highly positive attitudes towards vaccination and emphasized the importance of prevention and protection. This confirms previous evidence stating that adolescents tend to place more weight on benefits than on risks

when making decisions (28) but contradicts the belief that short-term benefits such as peer acceptance are more influential than long-term ones such as cancer prevention (28, 30).

The importance of benefit perceptions was also reflected in the positive language and emotions that adolescents used around vaccination, especially when compared to mothers who showed more negative emotions related to the risks of vaccines. In fact, mothers appraised risks and benefits of vaccines more emotionally than adolescents, which would suggest that making emotional decisions in relation to vaccination is less related to maturity than to the complex nature of vaccination decisions themselves.

Risks and benefits of HPV vaccination are also perceived in relation to oneself or to the wider community, including loved ones such as partners. Europe has mostly been described as an individualistic culture, in which vaccination decisions are made to prevent diseases (or risks of vaccines) in the person who gets vaccinated (310). Yet this research found that adolescents are also influenced by the importance of protecting others, which could be a sign of the socialisation process they are going through at that age and influences from the school environment. Similarly, adolescents emphasised the long-term benefits of vaccination (i.e. cancer prevention) over the short-term possible negative consequences of vaccination (i.e. side effects), which has also been defined as a sign of mature decision-making (86).

7.2.5 Information

Information can influence vaccination decisions in many ways, from the quality, quantity and content of the information received, to the style of messaging (e.g. narrative vs statistics) or the sources and channels of information (311-314).

Adolescents in this study reporting having little information about HPV vaccination overall, limiting their ability to contribute to the decision-making process. Adolescents and mothers

in this study highlighted the important role of schools in providing this information which could improve adolescents' health literacy and appraisal of information (and misinformation) as well as influence their values, beliefs and decision-making processes. Low engagement of adolescents through communication campaigns at schools, doctors or mass media campaigns can create important barriers and an imbalance in exposure to positive vs negative information. For example, adolescents with vaccine hesitant mothers might be solely exposed to negative information about vaccination, which could have damaging effects on their own levels of confidence in vaccination.

This is particularly important as mothers reported having to navigate a conflicting information environment around vaccination, sometimes provoking strong emotional reactions such as anxiety or creating a feeling of uncertainty in decision-making which can affect trust in vaccines, vaccine providers or authorities. This can be further reinforced if conflicting information is received from trusted and respected figures such as doctors or peers with a medical background.

Uncertainty is also influenced by the perceived trustworthiness of the sources of both positive and negative information: the higher the trust in those recommending vaccines and the lower the trust in alternative sources of misinformation, the less uncertainty and risk of refusing vaccines. This was seen among adolescents, who were less exposed to misinformation but also showed strong trust in doctors, health systems, health authorities and experts.

Interestingly, both mothers and adolescents expressed strong trust in doctors, particularly those they have known for a long time and who treat them with respect or do not judge them. Yet, while this trust translated to mothers following their doctors' advice and recommendations (even when they would recommend against vaccination), this was not

always the case for adolescents who valued trust in their own mothers more than trust in their doctors.

Finally, misinformation often comes from the internet or social media. Yet trustworthiness of the internet is a complex issue that can be difficult to assess, as the internet is just a channel for different sources of information including experts and doctors as well as those with less technical knowledge on vaccination such as influencers or contributors to forums (315). As most mothers and adolescents in this study and in a previous study conducted in France (252) stated not trusting ‘the internet’ but then still showed signs of influences from information found online, this distinction requires further exploration.

7.2.6 Group dynamics

While personal autonomy in decision-making is a sign of maturity, understanding the influence of others on our own decisions has also been defined as a characteristic of maturity in decision-making (86). This conflict can be seen in how vaccination decision-making is approached, as individuals can show a desire to remain in control of their decisions and to trust themselves above all, while at the same time acknowledging the influence of group dynamics from peers such as family members, friends, or colleagues as well as doctors or schools.

These individuals can have a direct influence on decision-making by sharing information, personal experiences or recommendations with adolescents or an indirect one by transmitting certain values or norms. In this research, direct influence from mothers and doctors were most commonly reported (as discussed in the previous section on information), with some of them also excluding adolescents from taking part in the decision-making process due to perceptions they were not mature enough to make such important decisions. However, parents have been shown to underestimate their children’s maturity, which could mean that

adolescents are left out of discussions and their autonomy in health is delayed even when they are mature enough (316). This could indicate the need for a stronger role from health authorities and medical practitioners in involving adolescents in decision-making.

As adolescents in this research did not report discussing vaccines among their peers, indirect group influences were less commonly observed among adolescents. This could be due to the lack of awareness observed among adolescents or the individualised focus of the vaccination programme in France, with vaccines being administered through individual doctors' appointments rather than through schools. Instead, the influence of social norms and values were reported by mothers who discussed the meaning of good parenting and perceived judgment from peers. Additionally, both mothers and adolescent girls reported selecting peers based on shared values and beliefs. Peer pressure and social norms have previously been established as important factors influencing vaccine decisions (317-320); if individuals cluster with others with similar beliefs and attitudes to vaccination, this could create difficulties in addressing or improving vaccine confidence unless entire communities are targeted by similar communication and engagement strategies. This is also important in relation to ideological or religious communities, as this study confirmed that certain values held by such communities, for example around sexual health, can influence decision-making among both adolescents and mothers.

7.2.7 Trust and context

Some elements, such as trust or the context in which decisions are made can be seen as overarching, influencing vaccination decision-making at various levels. For instance, trust in family members or friends can affect how one reacts to group dynamics, or trust in health authorities, experts or governments can influence one's assessment of information and thus

their perceptions of risks and benefits. Additionally, individuals sometimes defer decision-making to those they have particularly strong trust in (e.g. mothers).

Similarly, the context in which decisions are made can greatly influence how people make decisions about vaccination, for instance by determining who people place their trust into, levels of information and misinformation, or levels of uncertainty. Contextual factors that could influence decisions include for example historical events such as the management of previous health crises by the government and health authorities, political discourses on vaccination, or social and cultural traits. Additionally, whether or not individuals understand the influence of this context on their decisions can also ultimately play a role in their attitudes to vaccination. This has also been identified as a sign of maturity (86) and was observed to some extent among both mothers and adolescents in this research.

The overarching influence of trust and context on vaccination decision-making is particularly difficult to address when aiming to improve confidence in vaccination. It not only requires long-term strategies and efforts at multiple levels across various disciplines, but also entails a stronger understanding of the specific dynamics of vaccination decision-making in various populations, communities or countries (321).

7.3 Implications for future research

The findings from this PhD research have highlighted some implications for future research in the field of vaccine confidence and vaccine decision-making in the context of adolescence. While some of these are discussed in the individual discussions of the three results chapters, this section focuses on the wider implications, focusing specifically on the model of adolescent vaccination decision-making described above and how it can be used to inform the

development of more specific tools to assess vaccine confidence and behaviours among adolescents.

The model was designed with the aim of providing an overview of the different factors influencing adolescent decision-making and more research should also be conducted focusing on interventions that can be developed to address different elements of the model and improve vaccine confidence and uptake. This is particularly important for the novel elements of this model, such as maturity. While interventions may not be able to change one's level of maturity in decision-making, they could instead focus on involving and supporting adolescents in vaccination decision-making.

The model and findings from this study more broadly also provide important lessons for the development and evaluation of communication strategies to increase vaccination confidence and uptake. For instance, the challenge of the conflicting information environment points to the need for unified and coordinated communication coming from a wide range of sources, including doctors and health authorities, schools, mass and social media as well as peer groups. This would provide a more consistent positive narrative around vaccination, and could also counteract some of the negative information adolescents might receive from their parents. Similarly, a mix of scientific or statistical information with more narrative and storytelling formats should be considered. The protective and positive language used by adolescents around vaccination also suggests the importance of providing positive information around the benefits of vaccination such as the prevention of diseases. Such communication strategies and interventions should be evaluated further in the context of adolescence to fully understand their impact on vaccination beliefs and behaviours at different ages.

As this research was an exploratory study, further testing and evaluation of the model of adolescent decision-making is required. Additional quantitative studies could for example be conducted to validate some of the elements and associations described in the model, as well as to develop a better understanding of the strength and relative importance of each component of the model. Furthermore, similar exploratory studies or quantitative surveys should be conducted in various contexts (e.g. different settings, countries or vaccines) to identify possible additional components and to refine the model further. This is also important as some elements of the model such as maturity are highly influenced by cultural and contextual aspects.

In fact, the concept of maturity as an essential element influencing adolescents' participation in vaccination decision-making and their final decisions is relatively new and warrants further research. More specifically, studies should be replicated with adolescent girls and boys at different ages, including younger ones who are directly targeted by HPV vaccination programmes, to understand how decision-making evolves at different stages of maturity. The use of maturity scales could help define this impact in a more reliable and validated manner.

As most adolescents in this study did not have an active role in decision-making, it would also be important to explore whether adolescents' involvement in vaccination decision-making could impact vaccination uptake rates, adolescent's confidence in vaccination in the short- and long-term (as the parents and adults of tomorrow), and adolescents' health autonomy.

While many studies have already been conducted on the role of risk and benefit perceptions on vaccination decisions (43), this research found evidence of a social construction of risks. More research should therefore be conducted to improve our comprehension of how vaccine safety is understood by different populations, which could influence the type of questions

researchers ask around ‘vaccine safety’ in the future. This study also confirmed the effects of navigating a controversial information environment on vaccination decisions among mothers, but findings among adolescents were less clear due to their lack of awareness around HPV vaccination. Future studies should look at the effects of growing up in a controversial and uncertain environment, as well as the influence of mothers’ hesitancy on adolescents’ current and future acceptance of vaccination.

As this controversial environment often comes from misinformation circulating online, more efforts should also be directed at understanding the effects of trust and mistrust in the internet. Studies, including this one, often show that individuals do not place their trust in the internet or social media for vaccination decisions (231). However, there is a gap in evidence showing how individuals trust different sources of information on the internet: would individuals still say they mistrust the internet in relation to posts or articles written by doctors or scientific experts? In order to fully understand the impact of the internet and social media on our decision-making processes, these questions need to be addressed.

The process of deferring decision-making to trusted individuals (e.g. mothers or doctors) could also be further explored, including the challenges raised when these trusted individuals are hesitant themselves. The concept of reluctant trust has been explored previously (62), and more research could help understand whether we defer decision-making reluctantly or whether there is a more positive relationship between trusted and trusting parties.

The influence of other individuals on our decisions around vaccination also warrants further research. While studies have looked at the role of social norms and the effect of group dynamics on our decisions, these have mostly been conducted among parents, with little evidence existing for adolescents (317-320). This was not studied in depth in this research due to a lack of awareness among adolescents, but could be explored further in future

research, looking at questions such as how adolescents cluster with friends with similar values and beliefs (and the impact on vaccination confidence), or how they are influenced by peer pressure or social norms.

Finally, data for this PhD research was collected before the COVID-19 pandemic. Studies have shown that the pandemic may have had various consequences on vaccination confidence, due to the increase in the circulation of misinformation, a possible increase in health and vaccination literacy in the general population, or other factors such as changes in trust in governments and health authorities (322-324). Additionally, adolescents have been targeted by COVID-19 vaccination campaigns, with some countries allowing them to get vaccinated without their parents' consent. The effects of the pandemic on adolescents' decision-making processes should therefore be evaluated further.

7.4 Study limitations

This PhD study provides a valuable exploration of adolescent girls' decision-making processes around HPV vaccination in France. The findings from this qualitative research should be viewed and interpreted in light of several limitations.

Qualitative research is often criticised for being too anecdotal and subjective. While participants' accounts may not provide data as generalizable or reliable as quantitative studies that focus on providing the frequency of certain beliefs or behaviours in a specific population, they allow in-depth understanding and exploration of these beliefs and behaviours. Findings from this research should nevertheless be interpreted with caution, as the study was conducted in Paris and additional themes might have been identified if participants from other regions had been included. Reliability of study findings was guaranteed by developing and implementing good fieldwork, data collection and analyses practices, including by

analysing the entire data set comprehensively. Furthermore, all interviews and focus groups were audio-recorded and all procedures and methods used to collect and analyse data were clearly reported to ensure transparency. Reliability of study findings might have also been affected by the fact that all interviews and focus groups were conducted and analysed in French but reported back in English. This could have resulted in some concepts being lost in translation, which was limited by providing explanations of concepts not easily translated into English and by the fact that the doctoral student is fluent in both English and French. Finally, in order to ensure the validity of the study, findings were analysed and interpreted together with sufficient context, for example by including evidence from the data using quotes and citations or by analysing deviant cases to prevent the reporting of only the most noteworthy or remarkable findings.

The influence of the interviewer on participants during semi-structured interviews and focus groups should also be discussed. In qualitative research, the researcher has a non-negligible influence on the findings and content of the interviews due to their presence during the discussions and the structure of the interviews themselves. In this study, this was partly limited by letting participants decide on the location of the interviews, organising the interviews in private and quiet places, and by the fact that the doctoral student was a young French-speaking woman. Despite this, most interviews were conducted at participant homes, which could have made participants feel uncomfortable answering some questions, knowing their mothers or daughters was in the room next door.

Focus group discussions were also organised to allow adolescents to talk about HPV vaccination, which could be seen as a sensitive topic, among themselves in a natural and comforting environment. This helped adolescents feel more confident and open when sharing their views in front of a stranger. However, conducting the focus groups in schools rather

than in more informal, relaxed atmospheres might have influenced some of the content of the discussions. Although some resistance from parents was expected in relation to the participation of their daughters to this study as they are minors, all parents gave their consent for their daughters to take part in the study and none requested to be present during the interviews.

Findings from this study could have also been influenced by the small number of vaccinated participants identified and included in the study, a consequence of the low HPV vaccination uptake rates in France. Similarly, it is possible that participants who accepted to take part in this study had different views on vaccination or were more mature than those who refused. Using two methods of participant recruitment may have mitigated these limitations, but may also have generated other types of limitations and selection biases, especially as different compensation mechanisms were used. Furthermore, the restriction of the sample to adolescent girls aged between 15 and 16 years old means that findings cannot be applied to younger girls (main recipients of the vaccine) or boys who have now also been added to the vaccination programme: this is particularly important in relation to findings around maturity, as it evolves with age. Similarly, the exclusion of fathers or other guardians responsible for vaccination decision-making could have limited some of the findings from this research.

Finally, the model of vaccination decision-making developed as part of this PhD research was based on an exploratory study, meaning that some factors influencing decision-making may have been missed due to the context and location in which the qualitative studies took place as well as the focus of discussions during interviews. For example, certain factors such as access or knowledge were not specifically studied. While these constitute limitations to this research, they also open the way for future research on this topic to further evaluate and validate the proposed model of decision-making.

Chapter 8: Conclusion

Adolescents have an essential role to play in vaccination programmes. In countries where adolescents are legally allowed to get vaccinated without their parents' consent, their decisions could contribute to higher vaccination coverage rates, while in other countries, their inclusion in discussions and in the decision-making process could influence their parents' decisions. The COVID-19 pandemic has also revealed that adolescents can be highly engaged in their own care, and allowing them to take part in vaccination decisions could also impact their future confidence in and acceptance of vaccination as the parents and adults of tomorrow.

Yet, insufficient evidence exists on adolescent decision-making processes for vaccination. Drops in the coverage rates of certain adolescent vaccines, such as HPV, have been observed in various countries due to the spread of concerns, rumours and anxiety among adolescents and parents, highlighting the need for a stronger understanding of adolescent decision-making processes. This PhD thesis proposes a new model of adolescent vaccination decision-making based on factors and dynamics identified through an exploratory qualitative study.

Similarly to adult decision-making, the model acknowledges the important role of risk-benefits perceptions, group dynamics, information, trust and the context in which decisions are made. Yet adolescents experience and are influenced by these factors differently than their parents, which supports the need for adapted and targeted strategies to improve their confidence in vaccination. For example, adolescents in this study perceived and understood the risks and benefits of vaccination differently to their mothers, showing more positive and less emotional reactions. They were also shown to place their trust in vaccines, information, doctors and health authorities differently than mothers, often prioritising trust in their own mothers. These findings raise questions about how much their mothers' perceptions and

sometimes concerns will influence adolescents' own beliefs as they start becoming more involved in vaccination decisions. Additionally, due to a lack of information targeted at adolescents and consequently a lack of awareness about HPV vaccination, the effect of certain elements such as group dynamics or public controversies remain unclear and warrant further evaluation.

An innovative element of this model of vaccination decision-making, specific to adolescents, relates to the role of maturity, both in terms of influence on the extent of their participation in the decision process and on their vaccination decisions. This research found that despite showing signs of maturity, adolescents remained excluded from vaccination decision-making due to barriers imposed by mothers, doctors, and a lack of information. Further evidence is needed on individualised approaches to involve adolescents in discussions around HPV vaccination, especially as taking-part in decision-making was seen as a possible opportunity to increase adolescents' health autonomy in preparation for future important health decision. Maturity was also found to play an important role in how adolescents contemplating HPV vaccination approached vaccination decision-making at various stages (e.g. risk-benefit perceptions, information appraisal, etc.). Interestingly, adolescents in this study sometimes made more rational and less impulsive or emotional decisions than their mothers. Although more research is needed to understand this difference, this could point to the important role of emotions and the sometimes anxiety-inducing environment surrounding vaccination decisions. Understanding the process and the causes of this shift from rational to emotional decisions is essential for the successful implementation of vaccination programmes.

This research proposes one of the first model of vaccination decision-making adapted to adolescents. Future research should aim to evaluate and validate the model, while also answering some key remaining questions such as the impact of growing up in a controversial

environment on adolescents' maturity and decision-making process. Additionally, the recent COVID-19 pandemic has had unexpected consequences on vaccine confidence and decision-making, for example in relation to health literacy, public perceptions of the safety and importance of vaccination, as well as trust in governments, health authorities and health professionals. Furthermore, adolescents in many countries have been more empowered to take control over their own health and the question of how to address adolescent vaccination has resurfaced. While this research can help address and understand some of these changes, their impact on vaccination decision-making among parents and adolescents and on the role of adolescents' maturity on decision-making remains to be seen.

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APPENDICES

APPENDIX A: Permissions and right to reproduce

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Article DOI: 10.1080/21645515.2018.1564436

Author name: Emilie Karafillakis, Clarissa Simas, Caitlin Jarrett, Pierre Verger, Patrick Peretti-Watel, Fadia Dib, Stefania De Angelis, Judit Takacs, Karam Adel Ali, Lucia Pastore Celentano & Heidi Larson

Journal title: Human Vaccines & Immunotherapeutics

Volume number: 15

Issue number: 7-8

Year of publication: 2019

Name: Emilie Karafillakis

Street address: 43B Moray Road

Town: LONDON

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Article DOI: 10.1080/21645515.2022.2036555

Author name: E Karafillakis, P Peretti-Watel, P Verger, T Chantler & HJ Larson

Journal title: Human Vaccines & Immunotherapeutics

Volume number: *

Issue number: *

Year of publication: *

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APPENDIX B: Supplementary materials for chapter 2

8.1.6 Supplementary material 1: Critical assessment of studies

Critical assessment of studies with qualitative data

Legend: Insufficient/No = **L/N**; Reasonable = **R**; Good/Yes = **G/Y**; Cannot say = **?/N/A**

* Mixed-method studies

Global rating calculation: Calculation based on responses to each of the questions and qualitative appraisal of each paper

	Was there a clear statement of the aims?	Is a qualitative methodology appropriate?	Was the research design appropriate?	Was the recruitment strategy appropriate?	Was data collected to address the research issue?	Was the relationship with participants considered?	Have ethical issues been taken into consideration?	Was data analysis sufficiently rigorous?	Is there a clear statement of findings?	Global rating for paper
Brabin2007*	Y	Y	?	Y	Y	?	?	Y	Y	R
Camano2017	Y	Y	Y	Y	Y	Y	Y	Y	Y	G
Craciun2012	Y	Y	?	Y	?	?	?	?	Y	R
Fidalgo2013	Y	Y	?	?	?	?	?	N	Y	I
Gordon2011	Y	Y	Y	Y	Y	?	Y	?	Y	G
Gottvall2013	Y	Y	?	Y	Y	Y	Y	Y	Y	G
Gottvall2011	Y	Y	Y	Y	Y	?	Y	Y	Y	G
Grandahl2014(a)	Y	Y	Y	Y	Y	?	Y	Y	Y	G
Grandahl2012	Y	Y	?	Y	Y	?	Y	Y	Y	G
Gray2014	Y	Y	Y	Y	Y	?	Y	?	Y	G
Haesebaert2012*	Y	Y	?	Y	Y	?	?	?	?	I
Hilton2011(a)	Y	Y	Y	Y	Y	Y	Y	Y	Y	G
Hilton2011(b)	Y	Y	?	Y	Y	?	?	?	Y	R
Hofman2013	Y	Y	?	Y	Y	N	Y	Y	Y	R
Hutton2009	Y	Y	?	Y	Y	N/A	N/A	?	Y	R
Jackson2016	Y	Y	Y	Y	Y	Y	Y	Y	Y	G
Karamanidou2016	Y	Y	Y	Y	Y	Y	Y	Y	Y	G
Kennedy2014	Y	Y	Y	Y	?	?	Y	?	?	I
Klotzler2012	Y	Y	?	Y	Y	?	Y	?	Y	R
Lasset2014*	Y	Y	?	Y	Y	?	Y	Y	Y	R
Lutringer2011(a)*	Y	Y	Y	?	?	?	?	N	Y	R
Lutringer2011(b)*	Y	Y	?	Y	?	?	?	N	Y	I
Marlow2009(a)	Y	Y	Y	Y	Y	Y	Y	?	Y	G
Martin2011	Y	Y	Y	Y	Y	Y	Y	Y	Y	G
Martinez2016	Y	Y	Y	Y	Y	?	Y	Y	Y	G
McSherry2012	Y	Y	Y	Y	Y	Y	Y	Y	Y	G
Morison2015*	Y	Y	Y	Y	Y	?	N	Y	Y	G
Mortensen2010(a)*	Y	Y	Y	Y	Y	Y	Y	Y	Y	G
Mupandawana2016	Y	Y	Y	N	Y	?	Y	N	Y	I
Noakes2006	Y	Y	Y	?	?	?	?	?	Y	R
Oscarsson2011	Y	Y	?	Y	Y	Y	Y	Y	Y	G
Oscarsson2012	Y	Y	Y	Y	Y	Y	Y	Y	Y	G
Pop2015	Y	Y	Y	Y	Y	Y	Y	?	Y	G
Salad2015	Y	Y	Y	Y	Y	Y	Y	Y	Y	G

Stretch2009	Y	Y	?	Y	Y	?	Y	Y	Y	G
Todorova2014	Y	Y	?	?	?	?	?	?	Y	I
Waller2006	Y	Y	Y	Y	Y	?	?	Y	Y	G
Williams2011	Y	Y	?	Y	Y	?	?	?	Y	I

Critical assessment of studies with quantitative data

Legend: Weak = **W**; Moderate = **M**; Strong = **S**; Not applicable = **N/A**

* Mixed-method studies

Global rating calculation: Weak = two or more WEAK ratings; Moderate = one WEAK rating; Strong = no WEAK rating

	Selection bias	Study design	Confounders	Blinding	Data collection methods	Withdrawal and dropouts	Global Rating for paper
Abram2012	W	W	W	M	W	N/A	W
Baglioni 2014	W	W	W	M	M	N/A	W
Bakogianni 2010	W	W	M	M	W	N/A	W
Bianco2014	W	W	S	M	M	N/A	W
Blodt2012	M	W	S	M	M	N/A	M
Bouvret2015	M	W	W	M	W	N/A	W
Brabin2006	W	W	S	M	M	N/A	W
Brabin2007*	W	W	S	M	M	N/A	W
Brabin2008	M	M	S	M	S	M	S
Brabin2009	W	W	W	M	M	N/A	W
Collange2016	S	W	S	M	M	N/A	M
Dahlstrom2010	S	W	S	M	W	N/A	W
D'Hauwers2013	W	W	W	M	W	N/A	W
Di Giuseppe2008	M	W	S	M	M	N/A	M
Donders2008	S	W	S	M	M	N/A	M
Esposito2007	M	W	S	M	M	N/A	M
Firenze2015	M	W	S	M	M	N/A	M
Forster2010	M	W	S	M	S	N/A	M
Forster2015	M	W	S	M	M	N/A	M
Gefenaite2012	W	W	S	M	M	N/A	W
Gesouli2010	M	W	W	W	W	N/A	W
Giambi2014	W	W	W	M	M	N/A	W
Giambi2011	M	W	S	M	M	N/A	M
Giuliani2015	M	W	W	M	S	N/A	W
Gottvall2009	M	W	W	M	M	N/A	W
Grandahl2014(b)	S	W	S	M	M	N/A	M
Haesebaert2012*	W	W	S	M	M	N/A	W
Hofman2014(a)	W	W	W	M	S	N/A	W
Hofman2014(b)	W	M	S	M	S	M	M
Korfage2008	W	W	S	M	W	N/A	W
Kuitto2010	M	W	W	M	W	N/A	W
Lasset2014*	W	W	S	M	W	N/A	W
Lenselink2008	W	W	W	M	S	N/A	W

Lutringer2011(a)*	M	W	W	W	W	N/A	W
Lutringer2011(b)*	M	W	S	M	M	N/A	M
Maier2015	M	W	S	M	S	N/A	M
Mammas2016	M	W	S	M	W	N/A	W
Marek2011(a)	M	W	S	M	M	N/A	M
Marek2011(b)	S	W	S	M	M	N/A	M
Marlow2007(a)	W	W	S	M	M	N/A	W
Marlow2007(b)	W	W	S	M	S	N/A	W
Marlow2008	M	W	S	M	M	N/A	M
Marlow2009(b)	S	W	S	M	S	N/A	M
Medeiros2013	M	W	W	M	M	N/A	W
Michail2014	M	W	S	M	W	N/A	W
Morison2010*	W	W	S	M	M	N/A	W
Mortensen2015	M	W	M	M	M	N/A	M
Mortensen2010(a)*	M	W	S	M	S	N/A	M
Mortensen2010(b)	M	W	S	M	M	N/A	M
Nadarzynski2015	M	W	S	M	M	N/A	M
Napolitano2016	M	W	S	M	M	N/A	M
Navarro2015	M	W	S	M	W	N/A	W
Navarro2014	M	W	M	M	S	N/A	M
Papagiannis2013	M	W	S	M	W	N/A	W
Paul-Ebhohimhen2010	W	W	W	M	W	N/A	W
Pelullo2012	M	W	S	M	S	N/A	M
Perez2014	W	W	W	M	M	N/A	W
Piana2009	W	W	W	W	W	N/A	W
Remschmidt2014	W	W	S	M	W	S	W
Sabiani2012	S	W	W	W	W	N/A	W
Sacks2014	M	W	S	M	M	N/A	M
Sadlier2016	M	W	M	M	M	N/A	M
Sotiriadis2016	M	W	S	M	W	N/A	W
Stocker2013	W	W	S	M	M	N/A	W
Stretch2008	W	W	M	M	W	N/A	W
Sundstrom2010	W	W	S	M	W	N/A	W
Tisi2015	W	W	W	M	W	N/A	W
Tozzi2009	M	W	M	M	W	N/A	W
van der Berg2010	W	W	S	M	M	N/A	W
Verger2015	M	W	S	M	S	N/A	M
Voidazan2016	M	W	S	M	W	N/A	W
Woodhall2007	W	W	S	M	W	N/A	W

8.1.7 Supplementary material 2: Study characteristics

Article	Year of study	Country	Data collection	Participants	Study conducted after the introduction of HPV vaccine (year introduced)?
Parents					
Haesebaert2012(183)	2008	France	Mixed methods (interviews and questionnaires)	Mothers	Yes (2007)
Tozzi2009(152)	2007	Italy	Questionnaires	Mothers	No (2008)
Craciun2012(154)	2010-2012	Romania	Qualitative interviews and focus groups	Mothers	Yes (2008)
Abram2012(181)	2010	Romania	Questionnaires	Mothers	Yes (2008)
Navarro2015(138)	2010-2011	Spain	Cross-sectional	Mothers	Yes (2007)
Waller2006(168)	2005	UK	Qualitative focus groups	Mothers	No (2007)
Marlow2007(a)(192)	2006	UK	Questionnaires	Mothers	No (2007)
Marlow2007(b)(193)	2006	UK	Questionnaires	Mothers	No (2007)
Marlow2009(a)(210)	2008	UK	Qualitative interviews	Mothers from ethnic minorities	Yes (2007)
Gordon2011(156)	2010	UK	Qualitative interviews	Mothers from Jewish Orthodox communities	Yes (2007)
Baglioni 2014(147)	2012	Italy	Questionnaires	Parents	Yes (2008)
Bianco2014(177)	N/A	Italy	Questionnaires	Parents	Yes (2008)
Giambi2014(129)	2012	Italy	Cross-sectional	Parents	Yes (2008)
Gefenaite2012(128)	2009	Netherlands	Questionnaires	Parents	No (2010)
Hofman2014(a)(188)	2009	Netherlands	Discrete choice experiment	Parents	No (2010)
Hofman2014(b)(130)	2009-2011	Netherlands	Questionnaires	Parents	(2010)
van der Berg2010(146)	2009	Netherlands	Cross-sectional	Parents	No (2010)
Lenselink2008(325)	N/A	Netherlands	Questionnaires	Parents	(2010)
Hofman2013(162)	2008	Netherlands	Qualitative focus groups	Parents	No (2010)
Voidazan2016(326)	2014	Romania	Cross-sectional	Parents	Yes (2008)
Dahlstrom2010(186)	2007	Sweden	Population based survey	Parents	No (2008)
Gottvall2013(158)	2012	Sweden	Qualitative interviews	Parents	Yes (2008)
Grandahl2014(a)(159)	N/A	Sweden	Qualitative interviews	Parents	Yes (2008)
Brabin2006(153)	2005	UK	Questionnaires	Parents	No (2007)
Brabin2008(125)	2007	UK	Questionnaires	Parents	No (2007)
Stretch2008(173)	2007-2008	UK	Questionnaires	Parents	Yes (2007)

Morison2015(208)	2007	UK	Mixed methods (questionnaire)	Parents	No (2007)
Brabin2007(219)	N/A	UK	Mixed methods (interviews and questionnaires)	Parents	No (2007)
Hutton2009(207)	N/A	UK	Qualitative open questionnaire	Parents	Yes (2007)
Noakes2006(203)	N/A	UK	Qualitative focus groups	Parents	No (2007)
Mupandawana2016(202)	N/A	UK	Qualitative interviews	Parents from African origins	Yes (2007)
Mortensen2010(b)(137)	2010	Denmark	Questionnaires	Parents of boys (boys vaccination)	Yes (2008)
Tisi2015(143)	2011	Italy	Questionnaires	Parents of boys (boys vaccination)	Yes (2008)
Mortensen2015(131)	N/A	UK, Germany, France, Italy	Questionnaires	Parents of boys (boys vaccination)	Yes (2007, 2007, 2007, 2008)
Adolescents					
Stocker2013(197)	2010	Germany	Questionnaires	Adolescent girls (14-18)	Yes (2007)
Klotzler2012(171)	2009	Germany	Qualitative interviews	Adolescent girls (13-17)	Yes (2007)
Mammas2016(133)	2008-2014	Greece	Cross-sectional	Adolescent girls (11-16)	Yes (2008)
Firenze2015(213)	2013	Italy	Cross-sectional	Adolescent girls (14)	Yes (2008)
Navarro2014(194)	2010-2011	Spain	Cross-sectional	Adolescent girls (15)	Yes (2007)
Camano2017(170)	2013	Spain	Qualitative focus groups	Adolescent girls (18)	Yes (2007)
Brabin2009(187)	2007-2008	UK	Questionnaires	Adolescent girls (12-13)	No (2007)
Forster2010(126)	2009	UK	Questionnaires	Adolescent girls (16-17)	Yes (2007)
Forster2015(127)	2011-2013	UK	Questionnaires	Adolescent girls (15-16)	Yes (2007)
Marlow2009(b) (191)	2007	UK	Questionnaires	Adolescent girls (16-19)	Yes (2007)
Paul-Ebhohimhen2010(172)	2008-2009	UK	Questionnaires	Adolescent girls (<18)	Yes (2007)
Sacks2014(141)	2011	UK	Questionnaires	Adolescent girls (13-19)	Yes (2007)
Hilton2011(b)(218)	2009-2010	UK	Qualitative focus groups	Adolescent girls (12-18)	Yes (2007)
Williams2011(169)	2009	UK	Qualitative interviews	Adolescent girls (17-18)	Yes (2007)
Marek2011(b)(148)	2009	Hungary	Nationwide survey	Adolescent boys and girls (12-19)	No (2014)
Maier2015(132)	2015	Romania	Cross-sectional	Adolescent boys and girls (16-18)	Yes (2008)
Gottvall2009(149)	2008	Sweden	Cross-sectional	Adolescent boys and girls (15-16)	Yes (2008)
HCWs					
Bouvret2015(176)	2015	France	Questionnaires	GPs	Yes (2007)
Collange2016(184)	2014	France	Cross-sectional	GPs	Yes (2007)
Verger2015(327)	2013-2014	France	Cross-sectional	GPs	Yes (2007)
Piana2009(195)	2008	France	Questionnaires	GPs	Yes (2007)
Lasset2014(124)	2007-2010	France	Mixed methods (interviews and questionnaires)	GPs	Yes (2007)

Lutringer2011(b)(209)	2007-2008	France	Mixed methods (interviews and cross-sectional)	GPs	Yes (2007)
Martinez2016(217)	N/A	France	Qualitative focus groups	GPs	Yes (2007)
Lutringer2011(a)(211)	2007-2008	France	Mixed methods (interviews and cross-sectional)	Gynaecologists	Yes (2007)
D'Hauwers2013(185)	2006, 2012	Belgium and Netherlands	Cross-sectional	HCWs	No and Yes (2007 and 2010)
Todorova2014(206)	2010-2013	Bulgaria	Qualitative interviews	HCWs	No and Yes (2012)
Karamanidou2016(201)	N/A	Greece	Qualitative interviews	HCWs	Yes (2008)
McSherry2012(165)	N/A	Ireland	Qualitative interviews	HCWs	Yes (2008)
Perez2014(214)	2013	Spain	Cross-sectional	HCWs	Yes (2007)
Kuitto2010(199)	2008-2009	Germany	Questionnaires	HCWs (including data for GPs, gynaecologists)	Yes (2007)
Papagiannis2013(144)	2011-2012	Greece	Cross-sectional	Medical students	Yes (2008)
Oscarsson2011(166)	2010	Sweden	Qualitative interviews	Midwives at youth clinics	Yes (2008)
Esposito2007(175)	2006	Italy	Cross-sectional	Paediatricians	No (2008)
Grandahl2014(b)(212)	2013	Sweden	Cross-sectional	School nurses	Yes (2008)
Gottvall2011(157)	2010	Sweden	Qualitative focus groups	School nurses	Yes (2008)
Stretch2009(161)	2007-2008	UK	Qualitative interviews	School nurses	Yes (2007)
Hilton2011(a) (205)	2008-2009	UK	Qualitative interviews	School nurses	Yes (2007)
Nadarzynski2015(145)	2014	UK	Questionnaires	Sexual healthcare professional (MSM vaccination)	Yes (2007)
Young adults					
Napolitano2016(151)	2015	Italy	Cross-sectional	Young men (14-24)	Yes (2008)
Blodt2012(179)	2010	Germany	Questionnaires	Young men and women (18-25)	Yes (2007)
Martin2011(221)	N/A	UK	Qualitative focus groups	Young men and women (20-24)	N/A (2007)
Pelullo2012(216)	2011	Italy	Cross-sectional	Young men and women (lesbians, gay men, bisexual) (26)	Yes (2008)
Di Giuseppe2008(178)	2007	Italy	Cross-sectional	Young women (14-24)	No (2008)
Mortensen2010(a)(182)	2009	Denmark	Mixed methods (focus groups and questionnaires)	Young women (16-26)	Yes (2008)
Michail2014(136)	N/A	Greece	Cross-sectional	Young women (17-24)	N/A (2008)
Oscarsson2012(204)	2009	Sweden	Qualitative interviews	Young women (17-26)	Yes (2008)
Remschmidt2014(139)	2013	Germany	Questionnaires	Young women (18-25)	Yes (2007)
Bakogianni2010(180)	N/A	Greece	Questionnaires	Young women (18-25)	Yes (2008)
Giambi2011(223)	2008-2009	Italy	Questionnaires	Young women (18-26)	Yes (2008)

Gray2014(200)	N/A	UK, Spain, Bulgaria	Qualitative focus groups	Young women (18-26)	Yes (2007, 2007, 2012)
Adults					
Medeiros2013(135)	2007-2008	Portugal	Questionnaires	Men and women (17-35)	Yes (2007)
Sundstrom2010(198)	2007	Sweden	Population based survey	Men and women (18-30)	No (2008)
Giuliani2015(189)	N/A	Italy	Questionnaires	Men attending sexual health clinics (24-46)	Yes (2008)
Sadlier2016(196)	2014	Ireland	Questionnaires	Men who have sex with men (18+)	Yes (2008)
Jackson2016(163)	2013-2015	UK	Qualitative interviews and focus groups	Travelling and gypsy communities	Yes (2007)
Donders2008(190)	2007	Belgium	Questionnaires	Women	Yes (2007)
Sotiriadis2016(142)	2005-2010	Greece	Questionnaires	Women	No and Yes (2008)
Marlow2008(134)	2008	UK	Questionnaires	Women (16+)	Yes (2007)
Gesouli2010(222)	2008	Greece	Questionnaires	Women (18-65)	Yes (2008)
Pop2015(215)	2005-2013	Romania	Qualitative interviews	Women (20-78)	No and Yes (2008)
Korfage2008(150)	N/A	Netherlands	Questionnaires	Women (30-62)	No (2010)
Grandahl2012(160)	2011	Sweden	Qualitative focus groups	Women immigrants (18-60)	Yes (2008)
Mix					
Woodhall2007(220)	2005	Finland	Questionnaires	Parents, adolescent boys and girls (15)	No (2013)
Kennedy2014(164)	2008-2010	UK	Qualitative interviews and focus groups	Parents, adolescent girls (12-15), HCWs	Yes (2007)
Sabiani2012(140)	2009-2010	France	Questionnaires	Women, adolescent girls (15-45)	Yes (2007)
Marek2011(a)(174)	2009	Hungary	Questionnaires	Young men and women (18+), parents	No (2014)
Fidalgo2013(155)	N/A	Switzerland	Qualitative interviews	Young women (16-20), HCWs	Yes (2008)
Salad2015(167)	N/A	Netherlands	Qualitative interviews and natural groups	Young women (17-21), mothers from Somali communities	Yes (2010)

APPENDIX C: Study information letters

8.1.8 Information letter for school directors

The following is an English translation of the French information letter for school directors

Information letter for school directors

Adolescent decision-making and HPV vaccination in France

The study principle investigator, Emilie Karafillakis, has invited you to participate in the doctoral research project called: “Adolescent decision-making and HPV vaccination in France”. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and to talk to others about the study, if you wish. Do not hesitate to ask Emilie for further information.

Purpose of the study

This study is being conducted as part of a student’s doctoral research. The student, Emilie Karafillakis, is supervised by Aix-Marseille University and the London School of Hygiene & Tropical Medicine. Her research aims to understand how and why adolescent girls’ make decisions about Human Papillomavirus (HPV) vaccination. We are inviting 15-16 year old adolescent girls living in Paris to take part in interviews or focus groups. We are contacting a number of school directors from different arrondissements of Paris to ask them permission to invite adolescent girls attending their schools to take part in the study.

What will happen during the research?

If you agree for your school to take part in this study, 15-16 year old adolescent girls will be contacted at your school and invited to take part in the study. Emilie will give them information about the study and if they are interested to participate, they will be asked to sign an informed consent form. The study will consist of individual interviews that will take about one hour or focus groups with girls from the same school class that will take about an hour and a half. In the interview/focus groups, Emilie will ask them questions about how they feel about HPV vaccination. For example, what they believe are the benefits and risks of getting HPV vaccination. Their views are very important and what they tell us will help understand concerns girls might have about the vaccine. The student will take notes and with their permission, the interview/focus group will be audio-recorded.

What are the possible benefits of taking part?

Taking part in the study is unlikely to benefit your school or the adolescent girls directly. However, the information they share with us will help understand concerns girls might have.

What are the possible disadvantages and risks of taking part?

This study has no foreseen disadvantages or risks. The girls might feel uncomfortable about talking about their experiences but they will be reassured that they can stop at any time or refuse to answer certain questions.

What are your rights as a participant in this research?

Your school and the girls' participation in this study is entirely voluntary. If you are interested in taking part in the study, we will go through this information letter with you and give you the opportunity to ask any questions you may have. Before the study starts we will ask you to sign a consent form to indicate that you are giving us permission to contact girls in your school. Girls will also be given an information sheet and will be asked to sign an informed consent form if they agree to take part in the study. They will also need their parents' approval.

This research follows the French Public Health Code (Title II of the First Book on biomedical research), more information is available on the website Legifrance (www.legifrance.gouv.fr). The principal investigator of this study is Emilie Karafillakis, a PhD student supervised by Professor Patrick Peretti-Watel from Aix-Marseille Université and Professor Heidi Larson, from the London School of Hygiene & Tropical Medicine.

Will information shared by adolescent girls remain confidential?

Yes. Any information they share with us during the course of this study will be kept strictly confidential and we will not tell anyone about their participation in this study or the name of the schools that participated in the study. The interviews/focus groups will be conducted by Emilie, who does not work at your school, nor with health authorities. Interview and focus group transcripts will be made anonymous and stored securely in line with Research Ethics Committee guidelines. Where appropriate, anonymised quotes from the interviews may be used in publications or reports to illustrate certain points but it will not be possible to identify who the quotes come from: utmost care will be taken to ensure that no individual or organisation can be identified.

What will happen to the results of the research study?

The results of this study will be written up in a doctoral thesis, which will be shared with researchers based at the London School of Hygiene & Tropical Medicine, Aix-Marseille University and INSERM. We will also publish findings from our research in academic journals and might use it for teaching. We may be asked to comment on our research and

findings by representatives of the media. You, your school, and the girls will not be identified in any report, publication or media communications.

Expenses and payments

You, your school, and the girls should not incur any expenses from taking part in this study since the interviews will take place at their home, school or at places convenient for them.

This study is being realised by Emilie Karafillakis, the University Aix-Marseille and the London School of Hygiene & Tropical Medicine.

It was given a favourable ethical opinion by the Aix-Marseille University Ethics Committee and the London School of Hygiene & Tropical Medicine Research Ethics Committee. You can contact them by email on ethics@lshtm.ac.uk.

Contact details

[removed]

Thank you for considering taking part in this study. If you decide to take part, please keep a copy of this information letter

8.1.9 Information letter for participating adolescent girls

The following is an English translation of the French information letter for adolescent girls

INFORMATION LETTER FOR ADOLESCENTS

Adolescent decision-making and HPV vaccination in France

My name is Emilie Karafillakis, I am a PhD student and I would like to invite you to take part in my doctoral research: “Adolescent decision-making and HPV vaccination in France”

- The person responsible for data collection and management for this research is Emilie Karafillakis, from the London School of Hygiene & Tropical Medicine, London, Keppel Street, London, WC1E 7HT UK (emilie.karafillakis@lshtm.ac.uk)
- The delegate for data protection is the Observational Research Ethics Committee from the London School of Hygiene & Tropical Medicine (ethics@lshtm.ac.uk)

Presentation of the research project:

I am supervised by Aix-Marseille Université Aix-Marseille and the London School of Hygiene & Tropical Medicine in the United Kingdom. The methodology for this research protocol have been submitted and authorised by the Ethics Committees of Aix-Marseille Université and the London School of Hygiene & Tropical Medicine, whose missions are to verify the required conditions to protect and respect your rights.

This research aims to understand what you think about cervical cancer, and its prevention with vaccination. I would like to know how you make decisions with regards to vaccination, whose advice you follow, and how you speak about vaccination with your friends and your family. There are no right or wrong answers.

Presentation of the research protocol:

I would like to talk to you for about an hour, at a time and place of your choosing. We will talk about your opinions of cervical cancer, human papillomavirus (HPV) and its vaccine. If accept to participate in the study, you will still be able to change your mind and stop the interview without having to give a reason. You can also refuse to answer any questions.

I would like to take note and with your permission, the interview will be recorded.

I confirm that I will only keep the most relevant information, related and restricted to what is needed for this research. This means that I will only keep the information useful to my research.

The nature of information that will be used:

The legal basis for the collection of information and its processing in the context of this research is Article 6 (a) of the General Data Protection Regulation (GDPR), entered into force on May 25, 2018.

Information collected as part of this research include:

- Information on health
- Name, surname
- Age
- School name
- Number and age of siblings
- Contact details

Confidentiality:

Your participation in this study is entirely voluntary. At any moment, you can withdraw from the study or refuse to respond to a specific question or share specific information or belief that might make you feel uncomfortable without having to justify yourself.

The information you share will be used in an anonymous way for the findings of this research and it will never be possible to link responses with participants.

The information collected will be stored on a computer and anonymised (using initials and the date of the interview), using a system only known by myself. Your participation in this study will remain entirely confidential.

We will never store your name in a file and information used for this study will always be anonymised.

If you tell me something that could make me worried about your safety or the safety of someone, I am obliged to inform my superior, after discussing this with you.

People with access to your information:

I will be the only one with access to data before it is anonymised.

Results from this study will be written up in a doctoral thesis that will be shared with researchers from the London School of Hygiene & Tropical Medicine, the Aix-Marseille University and INSERM. Results from the research will also be published in academic journals and may be used for teaching.

Anonymous citations might be used in publications or reports to illustrate specific points. We will ensure that no individual or organisation can be identified from these citations.

It is possible that I may be invited to comment on my research and my findings by media representatives.

You will not be identified in any report, publication or communication.

Your rights:

In accordance with the provisions of the law relating to data processing and freedoms (law n ° 78-17 of January 6, 1978 modified by law n ° 2004-801 of August 6, 2004) and of regulation n ° 2016/679, known as general data protection regulation (GDPR), you have a right of access, rectification, opposition and erasure.

These rights can be exercised with the Data Protection Officer (DPD contact).

In accordance with article L1122-1 of the Public Health Code, you will be informed, at your request, of the overall results of the study by contacting Emilie Karafillakis.

You can contact the Ethics Committee of Aix-Marseille University and the Ethics Committee of the London School of Hygiene & Tropical Medicine by email for more information at: ethics@lshtm.ac.uk

Contact details:

[removed]

If you decide to take part, please keep a copy of this information letter

8.1.10 Information letter for participating mothers

The following is an English translation of the French information letter for mothers

INFORMATION LETTER FOR MOTHERS

Adolescent decision-making and HPV vaccination in France

The principal investigator, Emilie Karafillakis, has invited you to participate in the doctoral research project: “Adolescent girl decision-making and HPV vaccination in France”

- The person responsible for data collection and management for this research is Emilie Karafillakis, from the London School of Hygiene & Tropical Medicine, London, Keppel Street, London, WC1E 7HT UK (emilie.karafillakis@lshtm.ac.uk)
- The delegate for data protection is the Observational Research Ethics Committee from the London School of Hygiene & Tropical Medicine (ethics@lshtm.ac.uk)

Presentation of the research project:

This study is being conducted as part of a students’ doctoral research.

The student, Emilie Karafillakis, is supervised by Aix-Marseille Université Aix-Marseille and the London School of Hygiene & Tropical Medicine in the United Kingdom. The methodology for this research protocol have been submitted and authorised by the Ethics Committees of Aix-Marseille Université and the London School of Hygiene & Tropical Medicine, whose missions are to verify the required conditions to protect and respect your children and their rights.

This research aims to understand how and why adolescents make decisions about vaccination against Human Papillomavirus (HPV) in Paris, France. The research will also try to understand how adolescents discuss vaccination among themselves and with their mothers.

Presentation of the research protocol:

If you accept and give approval for your daughter to take part in this study, Emilie will arrange to meet you at a time and location suitable for you. You will take part in an individual interview that will last for about 60 minutes. During the interview, Emilie will ask you questions on what you think of HPV vaccination. For example, what are, according to you, the benefits and the risks of the vaccine? Your views are important and what you share with us will help us understand concerns mothers may have about the vaccine.

Emilie will take notes and with your permission, the interview will be recorded.

Emilie confirms that she will only keep the most relevant information, related and restricted to what is needed for this research.

The nature of information that will be used:

The legal basis for the collection of information and its processing in the context of this research is Article 6 (a) of the General Data Protection Regulation (GDPR), entered into force on May 25, 2018.

Information collected as part of this research include:

- Information on health
- Name, surname
- Age
- School name
- Number and age of children
- Marital status
- Employment
- Contact details

Confidentiality:

Your participation in this study is entirely voluntary. At any moment, you can withdraw from the study or refuse to respond to a specific question or share specific information or belief that might make you feel uncomfortable without having to justify yourself.

The information you share will be used in an anonymous way for the findings of this research and it will never be possible to link responses with participants.

The information collected will be stored on a computer and anonymised (using initials and the date of the interview), using a system only known by the researcher. Your participation in this study will remain entirely confidential.

We will never store your name in a file and information used for this study will always be anonymised.

People with access to your information:

Emilie Karafillakis will be the only one with access to data before it is anonymised.

Results from this study will be written up in a doctoral thesis that will be shared with researchers from the London School of Hygiene & Tropical Medicine, the Aix-Marseille University and INSERM. Results from the research will also be published in academic journals and may be used for teaching.

Anonymous citations might be used in publications or reports to illustrate specific points. We will ensure that no individual or organisation can be identified from these citations.

It is possible that I may be invited to comment on my research and my findings by media representatives.

You will not be identified in any report, publication or communication.

Your rights:

In accordance with the provisions of the law relating to data processing and freedoms (law n ° 78-17 of January 6, 1978 modified by law n ° 2004-801 of August 6, 2004) and of regulation n ° 2016/679, known as general data protection regulation (GDPR), you have a right of access, rectification, opposition and erasure.

These rights can be exercised with the Data Protection Officer (DPD contact):
ethics@lshtm.ac.uk

In accordance with article L1122-1 of the Public Health Code, you will be informed, at your request, of the overall results of the study by contacting Emilie Karafillakis.

You can contact the Ethics Committee of Aix-Marseille University and the Ethics Committee of the London School of Hygiene & Tropical Medicine by email for more information at:
ethics@lshtm.ac.uk

Contact details:
[removed]

If you decide to take part, please keep a copy of this information letter

APPENDIX D: Informed consent form

8.1.11 Informed consent forms for participants (adolescent girls and mothers)

The following is an English translation of the French informed consent forms distributed to adolescent girls and mothers

Informed consent form (in 2 copies) Cervical cancer prevention with vaccination

The person responsible for data collection and management for this research: Emilie Karafillakis, London School of Hygiene & Tropical Medicine, Keppel Street, London, WC1E 7HT UK (emilie.karafillakis@lshtm.ac.uk)

The delegate for data protection is the Observational Research Ethics Committee from the London School of Hygiene & Tropical Medicine (ethics@lshtm.ac.uk)

Emilie Karafillakis, from Aix-Marseille University and the London School of Hygiene & Tropical Medicine, principal investigator, asked me to participate in the research entitled "Adolescent girl decision-making and HPV vaccination in France".

I have read the information letter explaining the research protocol mentioned above. I was able to ask all the questions I wanted, I received appropriate answers.

I understood that this research aims to understand how and why adolescent girls make decisions about human papillomavirus (HPV) vaccination in Paris, France and how adolescent girls discuss vaccines with each other and with their mothers.

The person responsible for data collection and management undertakes to collect only data that is relevant, adequate and limited to what is necessary with regard to the purposes of the research.

This data comprises of:

- Health Information
- Name, surname
- Age
- Name of school
- Number of siblings (and age)
- Contact information

I have noted that the data collected during this research will remain strictly confidential. This data will be anonymized as part of the research and the file will be kept for the time of the analysis and accessible only to the researcher. Only Emilie Karafillakis will have access to information before it is anonymised.

I accept the computerized processing of my personal data in accordance with the provisions of law n° 2004-801 of August 6, 2004 relating to the protection of persons and modifying law n° 78-17 of January 6, 1978 relating to computing, files and freedoms.

I have noted that I will be able to exercise my right of access and rectification, opposition and erasure guaranteed by regulation 2016/679, known as the general data protection regulation in accordance with the provisions of articles 15, 16,17 and 21 of the same regulation.

I understood that I could refuse to participate in this study without consequence for me, and that I could withdraw my consent at any time (before and during the study) without having to justify myself and without consequence.

The implementation of this processing is carried out under the responsibility of the researcher.

The researcher confirms the implementation of an impact analysis relating to data protection, in particular to cover the risks to the rights and freedoms of the persons concerned and to have implemented the appropriate technical and organizational measures in order to guarantee a level of security appropriate to the risks identified.

Finally, the researcher certifies that the data collected is not subject to any transfer to a country outside the European Union.

Given the information that has been transmitted to me, I freely and voluntarily agree to participate in the research entitled: “Decision-making of adolescent girls and vaccination against HPV in France”.

Initials:.....

My consent does not release the investigator from her responsibility towards me.

Signed in..... (city), on (Date)

In two original copies

Research participant

Surname, Name

Signature:

(Preceded by the words: Read, understood and approved)

Principal investigator

Surname, Name

Signature:

8.1.12 Informed consent forms for legal guardians of participating adolescent girls

The following is an English translation of the French informed consent forms distributed to the legal guardians of adolescent girls participating in this study

Information notice for legal guardians of a minor

You have been invited you to consider the participation of your child to the doctoral research: “Adolescent girl decision-making and HPV vaccination in France”

- The person responsible for data collection and management for this research is Emilie Karafillakis, from the London School of Hygiene & Tropical Medicine, London, Keppel Street, London, WC1E 7HT UK (emilie.karafillakis@lshtm.ac.uk)
- The delegate for data protection is the Observational Research Ethics Committee from the London School of Hygiene & Tropical Medicine (ethics@lshtm.ac.uk)

Presentation of the research project:

This study is being conducted as part of a students’ doctoral research.

The student, Emilie Karafillakis, is supervised by Aix-Marseille Université Aix-Marseille and the London School of Hygiene & Tropical Medicine in the United Kingdom. The methodology for this research protocol have been submitted and authorised by the Ethics Committees of Aix-Marseille Université and the London School of Hygiene & Tropical Medicine, whose missions are to verify the required conditions to protect and respect your children and their rights.

This research aims to understand how and why adolescents make decisions about vaccination against Human Papillomavirus (HPV) in Paris, France. The research will also try to understand how adolescents discuss vaccination among themselves and with their mothers.

Presentation of the research protocol:

If you give approval for your daughter to take part in this study, Emilie will arrange to meet her at a convenient time and location. They will take part in an individual interview that will last for about 60 minutes. During the interview, Emilie will ask her questions on what they think of HPV vaccination. For example, what they believe are the benefits and the risks of the vaccine, or if she decided to get vaccinated and why? Her views are important and what she shares with us will help us understand concerns adolescent girls may have about the vaccine.

Emilie will take notes and with her permission, the interview will be recorded. She will ask you whether you would also like to take part in an individual interview. Individual interviews with mothers are conducted separately. No information shared by adolescents will be share with mothers (and vice-versa).

Emilie confirms that she will only keep the most relevant information, related and restricted to what is needed for this research.

The nature of information that will be used:

The legal basis for the collection of information and its processing in the context of this research is Article 6 (a) of the General Data Protection Regulation (GDPR), entered into force on May 25, 2018.

Information collected as part of this research include:

- Information on health
- Name, surname
- Age
- School name
- Number and age of siblings
- Contact details

Information that adolescents share with Emilie for this research will help to understand concerns adolescents may have about HPV vaccination.

Your child will be able, at any time, to withdraw from the study or to refuse to answer to a specific question or to give information or opinions that may make her feel uncomfortable.

Information provided by adolescents will be used in an anonymous way for this research and it will never be possible to link responses to your child.

The information collected will be stored on a computer and anonymised (using initials and the date of the interview), using a system only known by the researcher.

We will never store your child's name in a file and information used for this study will always be anonymised.

People with access to your information:

Emilie Karafillakis will be the only one with access to data before it is anonymised.

Your child's rights:

In accordance with the provisions of the law relating to data processing and freedoms (law n ° 78-17 of January 6, 1978 modified by law n ° 2004-801 of August 6, 2004) and of regulation n ° 2016/679, known as general data protection regulation (GDPR), you have a right of access, rectification, opposition and erasure.

These rights can be exercised with the Data Protection Officer (DPD contact):
ethics@lshtm.ac.uk

In accordance with article L1122-1 of the Public Health Code, you will be informed, at your request, of the overall results of the study by contacting Emilie Karafillakis.

We invite you to talk about this document with your child and your peers.

If you give approval for your daughter to take part in this study, please send back this document, signed, to Emilie Karafillakis: Emilie.karafillakis@lshtm.ac.uk. You can also give this signed document to your daughter before her interview, so that she can hand it to Emilie in person or contact Emilie by phone (*number removed*).

I give my consent for my daughter to take part in the study “Adolescent girl decision-making and HPV vaccination in France”

I confirm having read and understood the information letter and the aim of this study

SURNAME: **NAME:**

NAME OF YOUR DAUGHTER:

Phone number:

Email:

Signature:

APPENDIX E: Topic guides

8.1.13 Topic guides for semi-structured interviews with adolescent girls

Date: __ / __ / ____

Location of interview: _____

Participant identification number: __

PART A: Consent process:

1. Read the study information letter with the participant, ensure they understand the purpose of the study and give them the opportunity to ask questions
2. If they are happy to take part in the study, ask them to sign the consent form before starting the interview

PART B: Interviewee socio-demographic characteristics

Name of interviewee: _____

Date of birth: __ / __ / ____

Arrondissement: _____

School: _____

Nationality: French / Other: _____

Parents' marital status: Married or cohabiting / Divorced or separated / Widowed

Employment of mother (if applicable): _____

Employment of father (if applicable): _____

Number of siblings (gender, age): _____

PART C: Interview questions

Legend: green=for vaccinated participants, red=for unvaccinated participants

Introduction and HPV infection

1. When you are sick, who takes care of you? Do you take care of yourself or does one of your parent or someone else helps take care of you?
 - *Probe: Do you believe that children your age should have a role in medical decisions?*

- *Probe: Generally, when you go to the doctor, do you go alone or with your parents?*
- 2. What is the most severe disease you have ever had?
 - *Probe: could you share your experience with this condition? Probe about anxiety, risk perceptions*
- 3. Do you sometimes talk about health with friends?
 - *Probe: what topics specifically? How do these conversations make you feel?*
- 4. Can you tell me what you know about the human papillomavirus (HPV)?
 - *Probe: What are symptoms and complications of HPV? Have you heard about the link between HPV and cancer?*
 - *Probe: How can you get HPV and who is more likely to get it?*

HPV vaccination

- 5. Do you know how you can prevent getting infected with HPV?
 - *Probe: Have you ever heard about HPV vaccination?*
- 6. Are you vaccinated with HPV vaccination?
 - *If yes, do you remember how many doses you received?*
 - *If yes, could you describe your experience receiving the vaccine? How did you feel before, during and after you received it?*
 - *If no, do you intend to receive it?*

Decision-making

- 7. How did you come to the decision **to receive/not to receive** the vaccine?
 - *Probe: What could have convinced you **not to get/to get** the vaccine?*
- 8. Who do you think should be involved in decisions about receiving the vaccine?
 - *Probe: Do you think adolescents, mothers or fathers should make the decision?*
- 9. Did you speak with your mother, father, or family about whether or not you should receive the HPV vaccine?
 - *Probe: How do they feel about HPV vaccination?*
 - *Probe: How much did their opinions influence your views/decisions about the vaccine?*
- 10. Did you speak with your friends about whether or not you should receive the HPV vaccine?
 - *Probe: How do they feel about HPV vaccination?*
 - *Probe: How much did their opinions influence your views/decisions about the vaccine?*
 - *Probe: Have your friends made the same decision as you?*
- 11. Do you know anyone who **has not received/has received** the HPV vaccine?
 - *Probe: Why do you think they made this decision?*
 - *Probe: How does that make you feel?*
- 12. Have you spoken about the vaccine with a doctor? Which ones?
 - *Probe: What was his or her advice? How did that make you feel?*
 - *Probe: How do you feel about your doctor? Do you trust what he/she tells you?*
 - *Probe: If he/she were to offer a new vaccine for your daughter today, for example against another type of cancer, how would you react?*

Risks and benefits

13. What do you think **were/would be** your benefits of receiving HPV vaccination?
 - *Probe: How did that influence your decision **to receive/not to receive** the vaccine?*
14. **Have you had or do you think you could have side effects or negative consequences from the vaccine? If you were to vaccinate, do you think you could have side effects or negative consequences from the vaccine?**
 - *Probe: Which side effects/negative consequences?*
 - *Probe: How did that influence your decision **to receive/not to receive** the vaccine?*
15. How certain do you think scientists are that the HPV vaccine is safe? Effective?
 - *Probe: Do you believe there is consensus within the medical community on the safety and effectiveness of the vaccine?*

Information

16. What do you think is the best way to inform young girls about the HPV vaccine?
 - *Probe: Do you think parents and young girls should be informed in the same way or differently?*
 - *Probe: would you trust certain sources of information more than others?*
17. Where have you received information about HPV vaccination from?
 - *Probe: Have you ever seen or heard any reports about HPV vaccination on TV, or on the news?*
 - *Probe: Have you seen any public health campaigns? (at your doctors? At school?)*
 - *Probe: Have you read anything online? Or on social media?*
18. Have you ever anything at school or on social media about HPV vaccination?
 - *Probe: What do you think about the use of social media to research health information? Which platforms? Do you trust them?*

Trust

19. Do you feel confident in the decisions taken by your doctor? For example, when he provides treatment or recommends a specific medication or vaccine?
 - *Probe: Did he ever recommend homeopathy? How do you feel about it?*
20. Do you feel confident in the decisions taken by health authorities, or the ministry of health?
 - *Probe: Do you think they are able to make good decisions with regards to health? Do you think they listen to what parents and adolescents think?*
21. Do you feel confident in the decisions taken by the government in general?
 - *Probe: do you think that the government has adolescents' health at heart when making decisions? Does the government listen to the population?*
22. In general, how much confidence do you have in vaccination?

Part D: Conclusion

23. If you were offered the vaccine today, would you (still) be willing to receive it?
- *Probe: why/why not?*
 - *Probe: What would make you feel differently?*
24. Is there anything else you think is important for us to discuss today? Do you have any questions for me?

8.1.14 Topic guides for semi-structured interviews with mothers

Date: __ / __ / _____

Location of interview: _____

Participant identification number: __

PART A: Consent process:

1. Read the study information letter with the participant, ensure they understand the purpose of the study and give them the opportunity to ask questions
2. If they are happy to take part in the study, ask them to sign the consent form before starting the interview

PART B: Interviewee socio-demographic characteristics

Name of interviewee: _____

Date of birth: __ / __ / _____

Arrondissement: _____

Nationality: French / Other: _____

Marital status: Married or cohabiting / Divorced or separated / Widowed

Employment: _____

Employment of partner/husband (if applicable): _____

Number of children (gender, age): _____

Name of daughter interviewed: _____

PART C: Interview questions

Legend: green=for vaccinated participants, red=for unvaccinated participants

Introduction and HPV infection

1. When your daughter is sick, who takes care of her? Does she take care of herself or do you or someone in the family takes care of her?
 - *Probe: Do you believe that children her age should have a role in medical decisions?*
 - *Probe: Generally, when she goes to the doctor, does she go alone or with you or someone else from the family?*
2. What is the most severe disease she has ever had?

- *Probe: could you share your experience with this condition? Probe about anxiety, risk perceptions*
3. Do you sometimes talk about your daughter's health with friends?
 - *Probe: what topics specifically? How do these conversations make you feel?*
 4. Can you tell me what you know about the human papillomavirus (HPV)?
 - *Probe: How can you get HPV and who is more likely to get it?*
 - *Probe: What are symptoms and complications of HPV? Have you heard about the link between HPV and cancer?*
 5. Do you think your daughter is at risk of getting HPV?
 - *Probe: If she were at risk of getting HPV, do you think it could be dangerous?*

HPV vaccination

6. How can girls and women prevent getting infected with HPV?
 - *Probe: Have you ever heard about HPV vaccination?*
7. Is your daughter vaccinated with HPV vaccination?
 - *If yes, do you remember how many doses she received?*
 - *If yes, could you describe her experience receiving the vaccine? How did she feel before, during and after she received it?*
 - *IF no, why not?*
8. How did you come to the decision *to vaccinate/not to vaccinate* your daughter?
 - *Probe: What could have convinced you *not to vaccinate her/to vaccinate her*?*
 - *Probe: Who are the people who influenced the most your decision?*
9. Who do you think should be involved in decisions about receiving the vaccine?
 - *Probe: How do you think adolescent girls should be involved in the decision? Did you involve your daughter in the decision?*
10. Did you speak with your partner or family about whether or not she should receive the HPV vaccine?
 - *Probe: How do they feel about HPV vaccination?*
 - *Probe: How much did their opinions influence your views/decisions about the vaccine?*
11. Did you speak with your friends about whether or not she should receive the HPV vaccine?
 - *Probe: How do they feel about HPV vaccination?*
 - *Probe: How much did their opinions influence your views/decisions about the vaccine?*
 - *Probe: Have your friends made the same decision as you?*
12. Do you know anyone who *has not received/has received* the HPV vaccine?
 - *Probe: Why do you think they made this decision?*
 - *Probe: How does that make you feel?*
13. Have you spoken about the vaccine with a doctor? Which ones?
 - *Probe: What was his or her advice? How did that make you feel?*
 - *Probe: How do you feel about your doctor? Do you trust what he/she tells you?*
 - *Probe: If he/she were to offer a new vaccine for your daughter today, for example against another type of cancer, how would you react?*

Risks and benefits

14. What do you think **were/would be** your daughter's benefits of receiving HPV vaccination?
 - *Probe: How effective do you think the vaccine is in preventing HPV? Cancer?*
 - *Probe: Are there any other benefits you can think of?*
 - *Probe: How did that influence your decision **to vaccinate/not to vaccinate** your daughter?*
15. **Has your daughter had or do you think she could have side effects or negative consequences from the vaccine? If you were to vaccinate her, do you think she could have side effects or negative consequences from the vaccine?**
 - *Probe: Which side effects/negative consequences?*
 - *Probe: How did that influence your decision **to vaccinate/not to vaccinate** your daughter?*
16. How certain do you think scientists are that the HPV vaccine is safe? Effective?
 - *Probe: Do you believe there is consensus within the medical community on the safety and effectiveness of the vaccine?*

Information

17. What do you think is the best way to inform parents about the HPV vaccine?
 - *Probe: Do you think parents and young girls should be informed in the same way or differently?*
18. Where have you received information about HPV vaccination from?
 - *Probe: Have you ever seen or heard any reports about HPV vaccination on TV, or on the news?*
 - *Probe: Have you seen any public health campaigns? (at your doctors? Your daughter's school?)*
 - *Probe: Have you read anything online? Or on social media?*
19. What did you think about the quality and quantity of the information you have received?
 - *Probe: Did you trust some sources of information more than others?*
 - *Probe: Was there anything else you would have liked to know? Did the information help make you more certain about your decision?*
20. Did you ever see information about HPV vaccination that you did not agree with?
 - *Probe: how did that make you feel?*

Trust

21. Do you feel confident in the decisions taken by your doctor? For example, when he provides treatment or recommends a specific medication or vaccine?
 - *Probe: Did he ever recommend homeopathy? How do you feel about it?*
22. Do you feel confident in the decisions taken by health authorities, or the ministry of health?
 - *Probe: Do you think they are able to make good decisions with regards to health? Do you think they listen to what parents and adolescents think?*
23. Do you feel confident in the decisions taken by the government in general?
 - *Probe: do you think that the government has adolescents' health at heart when making decisions? Does the government listen to the population?*
24. In general, how much confidence do you have in vaccination?

Part D: Conclusion

25. If you were offered the vaccine today, would you (still) be willing to give it to your daughter?
- *Probe: why/why not?*
 - *Probe: What would make you feel differently?*
 - *Probe: Would you accept it for yourself?*
26. Is there anything else you think is important for us to discuss today? Do you have any questions for me?

8.1.15 Topic guides for focus group discussions with adolescent girls

Date: __ / __ / _____

Location of focus group discussion: _____

School: _____

Focus group identification number: _

PART A: Consent process:

1. Read the study information letter with the participants, ensure they understand the purpose of the study and give them the opportunity to ask questions
2. If they are happy to take part in the study, ask them to sign the consent form before starting the discussion

PART B: Participant socio-demographic characteristics

Participant identification number: __

Name of participant: _____

Date of birth: __ / __ / _____

Arrondissement: _____

Nationality: French / Other: _____

Parents' marital status: Married or cohabiting / Divorced or separated / Widowed

Employment of mother (if applicable): _____

Employment of father (if applicable): _____

Number of siblings (gender, age): _____

Vaccinated with HPV: No / 1 dose / 2 doses / 3 doses / Yes, but not sure how many doses

If no, does she intend to receive the vaccine? _____

PART C: Introduction

Ask participants to introduce themselves, by first giving their name, whether or not they received the HPV vaccine, and something surprising about themselves.

PART D: Group discussion

Group task 1:

Hand out cards with groups of individuals who might be at risk from HPV infection (i.e. pregnant women, children, adolescent girls, adolescent boys, older people...).

Ask the participants to sort the cards into groups of differing risk levels. Ensure participants talk to each other, and verbalise their reasoning.

Prompts for general discussion:

- Do you know what HPV is and how it is transmitted? Who is more likely to get it? Do you feel at risk?
- Why do you think the vaccine is offered to adolescent girls?
- What are symptoms and complications of HPV? Have you heard about the link between HPV and cervical cancer?
- Do you think it would be dangerous if you would get infected with HPV infection?

Group Task 2:

Draw two columns on a blackboard, one with the heading “Benefits” and one “Risks”.

Ask participants to agree on a list of benefits and risks of HPV vaccination and decide which goes where as a group. Then, list them in order of importance.

Prompts for general discussion

- What do you think are the benefits of the vaccine?
- What do you think are the risks of the vaccine?
- Have you heard about any potential side effects? Which ones?

Looking at the list, ask participants to select items where they believe they do not have sufficient information about. Then items they believe scientists do not have enough information about.

Prompts for general discussion

- How certain are you that the HPV vaccine is safe/effective?
- How certain do you think scientists are that the HPV vaccine is safe/effective?
- How did/would this influence your decision to receive/not to receive the vaccine? What would/did influence your decision to receive or not to receive the vaccine?
- Who would you trust to give you this information?

Group Task 3:

Show participants four different types of social media reports about HPV vaccination: one describing alleged HPV vaccine side effects, one describing the safety of the vaccine, one describing the danger of HPV infection and related cancers, and one describing the alleged uncertainty around the effectiveness of the vaccine. Make sure the source of each article is clearly readable.

Ask participants to explain how they feel about each article and select the article: 1- they trust the most; 2- makes them feel more certain about the safety and benefits of the vaccine

Prompts for general discussion

- What do you think is the best way to inform adolescent girls or parents about the HPV vaccine?
- Where and when have you received information about HPV vaccination from?
- Did you look for additional information about HPV vaccination yourself? Where?
- When you saw information about HPV vaccination that you did not agree with, how did that make you feel? How did you react?

Conclusion:

Ask if participants would like to add anything to the discussion, or if they have any questions about the study.