



Effects of an online tailored intervention on HPVvaccination decision making among mothers of girls invited for HPV-vaccination

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Abstract

In 2009, the Dutch government implemented a HPV-vaccination programme for girls of 12 years of age. Because the HPV-vaccination uptake was low and mothers indicated a need for a more personal and interactive communication, an online tailored intervention with virtual assistants has been developed to help mothers make an informed decision about the vaccination of their daughters and to increase the HPV-vaccination uptake. In this study we examine the effectiveness of this online tailored intervention on vaccination uptake, informed decision making (IDM) and social-psychological determinants of HPV-vaccination. We also examine subgroup differences of effects for ethnicity, religion, education level, sample and intention at baseline.

This study consisted of a randomized control trial. Participants were recruited through Praeventis (naturalistic sample; N = 36,000) and three Panels (controlled sample; N = 2,483). After giving informed consent (N = 8,062), mothers were randomly assigned to the intervention condition (N = 3,995, the online tailored education) and the control condition (N = 4,067). The effects of the online tailored intervention were tested on vaccination uptake (primary outcome) and IDM (three measures), decisional conflict, intention, attitude, attitude certainty, risk perception, anticipated regret, subjective norm, habit, self-efficacy and relative effectiveness (secondary outcomes; assessed before the intervention (baseline) and after the intervention (follow-up)). Moderation effects for subgroups (ethnicity, religion, education level, sample and intention at baseline) on the effects of the intervention were also tested. The effects were tested with multiple regression analyses with covariates (linear and logistic).

We performed an Intention to treat analysis.

Results showed no effect on HPV-vaccination uptake, but a significant positive effect of the intervention on informed decision-making, decisional conflict, and on almost all determinants of HPV-vaccination uptake. Effects did not differ between subgroups for ethnicity, religion, educational level and sample. HPV-vaccination acceptability increased more among mothers with an initial negative intention and decisional conflict was reduced more among hesitant mothers. We found no adverse effects of the intervention.

The online tailored intervention has great potential in improving HPV-vaccination acceptability, making of informed decisions and reducing decisional conflict among mothers of girls invited for the HPV-vaccination and is ready for implementation and dissemination. Future research has to focus on improving the HPV-vaccination uptake through optimizing the online tailored intervention and structural barriers.

1. Introduction

Cervical cancer has been found as the second most common cancer in women worldwide (Walboomers et al, 1999; Schiffman, Castle, Jeronimo, Rodriguez, & Wacholder, 2007). In the Netherlands, research has shown that every year 600 new cases of cervical cancer arise, and for 200 to 250 women the disease has fatal consequences (Health council of the Netherlands, 2008). Persistent infection with human papillomavirus (HPV) is a major cause of cervical cancer (Bosch, Lorincz, Munoz, Meijer & Shah, 2002; Parkin, 2006). HPV is transmitted through sexual contact, and most women get infected with HPV without any symptoms and disease development. To decrease cervical cancer cases, a HPV-vaccine was developed (Bosch et al., 2002; Health council of the Netherlands, 2008). The HPV-vaccine was developed to prevent infection with HPV-types 16 and 18, which causes 70% of the cervical cancer cases. The vaccine is considered to have an effectiveness of 90-99% in protecting against the pre-stage phase of cervical cancer that is caused by these types of HPV and persistent infection (Health council of the Netherlands, 2008). In 2009, the HPV-vaccine was introduced in the Netherlands for girls of 12 years of age, and got included in the National Immunization Program. Twelve-year-old girls were the target of the HPV-vaccination in order to prevent an infection with HPV before they become sexually active. The HPV-vaccination consists of two injections, the second injection is provided 6 months after the first one (Health council of the Netherlands, 2008). Together with the invitation, girls and their parents received universal education about the HPV-vaccination consisting of an information pamphlet, and a reference to a website for more information (www.rijksvaccinatieprogramma.nl/De_vaccinaties/HPV). The vaccine was organized by the regional "Public Health Service" (GGD) and the information and education was coordinated by the "National Institute for Public Health" (RIVM).

The general uptake of childhood vaccines is usually 92-99% (van Lier et al., 2016). The Health Council estimated that it is feasible that 85% of the girls would get the HPV-vaccine (Health council of the Netherlands, 2008). Considering the effectiveness (90-99%), the coverage (70%) and the estimated vaccination uptake (85%), the HPV-vaccine would have an effectiveness of 54% in protecting against cervical cancer (Health council of the Netherlands, 2008). Rondy, van Lier, van de Kassteele, Rust, & de Melker (2010) expected that the uptake for the HPV-vaccination would be lower (70%) than the health council's estimation (85%; Health council of the Netherlands, 2008) and than usually reached for childhood vaccinations (i.e., 95%; van Lier et al., 2016), because it was a new vaccine, for a new age group, for girls only and targeting a sexual transmitted infection (Rondy et al., 2010). However, up until now the actual HPV-vaccination uptake was even lower (61%; van Lier et al., 2016).

To provide leads for future education to increase the HPV-vaccination uptake, van Keulen et al. (2010a; 2010b; 2013a; 2013b) examined factors that contribute to the HPV-vaccination decision making among invited girls and their mothers as well as preferences for future education. Van Keulen et al. (2010a; 2013a; 2013b) found that mothers played an important role in their daughter's decision

making process regarding the HPV-vaccination. Van Keulen et al. (2013a) found that socialpsychological determinants largely contributed to the HPV-vaccination decision making and accounted for 85% of the variance of the decision to vaccinate (van Keulen et al, 2013b). Several determinants contributed significantly to HPV-vaccination intention. These factors were: risk perception regarding not having received the HPV-vaccination, attitude, outcome expectations (positive and negative), anticipated regret having received or not having received the HPVvaccination, beliefs, relative effectiveness of the HPV vaccination, confidence in responsible authorities, subjective norms, descriptive norms, information processing, habit strength, ambivalence, decisional conflict and opinion about alternatives. Factors that were not found to be related with the HPV-vaccination intention were: knowledge, risk perception regarding having received the HPVvaccination, self-efficacy and past cancer experience (van Keulen et al., 2013a). These findings are important for and should be addressed in future communication strategies to increase the HPVvaccination uptake. Van Keulen et al. (2013a) found that the most important determinants were attitudes, beliefs, subjective norms, habit strength, risk perception and anticipated regret. Mothers were more willing to vaccinate their daughter against HPV when they had a more positive attitude and more positive beliefs (e.g. the belief that the vaccine is safe and effectively protects against cervical cancer) about the vaccination, perceived a more positive attitude about the vaccination among people in their surroundings, and perceived getting the HPV-vaccine as an obvious choice. The vaccination was more accepted if the risk of getting cervical cancer was perceived as higher without the HPVvaccination. Mothers were also more inclined to receive the HPV-vaccination of their daughters if they anticipated more regret if their daughters would not receive the HPV-vaccination and would develop cancer later in life (van Keulen et al., 2013a).

Van Keulen et al. (2013a) found that half of the mothers (50%) did not acquire or process detailed information about the HPV-vaccination after receiving the universal education, and 25% still felt ambivalent after their decision about the HPV-vaccination of their daughter. This indicates that mothers make their decision to vaccinate on unstable grounds, which makes them vulnerable for counter arguments (van Keulen et al., 2010b). Timmermans (2013) described that risks and side effects of a vaccine are heavily considered in the decision to vaccinate. Because of this and exact information about the risks is not clearly available, people become suspicious and are extra susceptible for doom-scenario's that spread around quickly, especially through the internet (Timmermans, 2013). However, Informed decision-making (IDM) is expected to make mothers less vulnerable for counter arguments (Paulussen, Hoekstra, Lanting, Buijs & Hirasing, 2006). Informed decision making is defined as: 'a decision that is based on sufficient knowledge, consistent with the decision-maker's attitudes and behaviourally implemented' (O'Conner & O'Brien-Pallas, 1989). It is important for the decision-maker to make a deliberated decision through active processing (van den Berg, Timmermans, ten Kate, van Vugt & van der Wal, 2006). Nowadays, people are expected to take more control over their decisions, have more autonomy and responsibility. Making an informed decision enables people

to make a decision that is in line with their goals, increasing their self-esteem and sense of autonomy (Timmermans, 2013). Rimer, Briss, Zeller, Chan, & Woolf (2004) described that an informed decision, that is consistent with the individual's values and preferences, leads to satisfaction with decisions and a reduction in decisional conflict. Decisional conflict is closely related to informed decision making, and is defined as a state where someone feels uncertain in their decision of what action they should take. It is often experienced when a decision involves risk or uncertainty about the outcome. There are several factors that contribute in experiencing decisional conflict, such as: lack of information about alternatives and the consequences of these alternatives, unclear values, not having the needed skills to make a decision, emotional distress and feelings of being pressured by the views of others that are important to you (O'Connor, 1995). O'Connor (1995) states that it is important to reduce decisional conflict, because it increases the likelihood that someone makes an effective decision that is in line with his or her values and behaviourally implemented (informed choice). A reduction in decisional conflict leads to less uncertainty and quicker decision making (O'Connor, 1995).

Mothers indicated their need for more interactive, personal communication about the HPVvaccination (Van Keulen et al., 2010b). Therefore, in order to improve HPV-vaccination uptake and decision making, future education needs to target mothers of invited girls, needs to be interactive and personal, needs to reduce ambivalence and address social-psychological determinants.

This led to the development of an online tailored intervention about the HPV-vaccination for mothers of invited girls. A computer tailored intervention is widely available and can reach large groups of people in a cost-effective manner (Krebs, Prochaska and Rossi, 2010). Therefore, they can have a substantial impact at population level (Noar et al., 2007). Based on previous research of van Keulen et al. (2010a; 2013a; 2013b), social psychological determinants that were selected as targets for the intervention were: HPV-vaccination intention, attitude, risk perception, anticipated regret, outcome beliefs (e.g., beliefs about the effectiveness and safety of the HPV-vaccination), subjective norms, habit, and relative effectiveness of the HPV-vaccination. The goal of the online tailored intervention is to improve HPV vaccination uptake, and improve informed decision making, reduce decisional conflict and positively effect the determinants of HPV-vaccination in 2015 (girls who were born in 2002).

The online tailored intervention is tailored, the computer will generate individual feedback, and the intervention is interactive, as it is delivered by two virtual assistants. Tailored education was used because it suited the need of mothers for more personal communication about the HPV-vaccination (Van Keulen et al., 2010a; 2010b). Tailoring is defined as "any combination of information or change strategies intended to reach one specific person, based on characteristics that are unique to that person, related to the outcome of interest, and have been derived from an individual assessment" (Kreuter & Skinner, 2000, p. 1). Tailored interventions have shown to be more effective

compared to generic interventions in improving health behaviours (Krebs et al., 2010; Lustria, Noar, Cortese, van Stee, Glueckauf and Lee, 2013). The positive aspect of tailoring is that they engage people more effectively. Tailored interventions improve exposure (attention) and intensive information processing, are more appreciated, more likely to be read and remembered, help in building selfefficacy and are viewed as personally relevant (Lustria et al., 2013; Brug, Campbell, & van Assema, 1999, Krebs et al., 2010; Brug, Oenema, & Campbell, 2003; Ruiter, Kessels, Jansma, & Brug, 2006). Personal relevance is very important because when a message is seen as personally relevant, someone will feel more involved and will be more motivated to listen to the information (improve the amount of cognitive processing effort). Eventually this leads to higher receptiveness of persuasion to perform the targeted behavior (Lustria et al., 2013; Brug et al., 1999). Previous research on online tailored interventions to increase HPV-vaccination uptake is scarce. Paiva, Lipschitz, Fernandez, Redding and Prochaska (2014) examined the feasibility and acceptability of a computer-tailored intervention about the HPV-vaccination among college aged women. The intervention had a significant positive effect on HPV-vaccination intention, however HPV-vaccination behaviour was not measured. Bennet et al. (2015) evaluated the effect of an online tailored educational intervention on knowledge, intention and the uptake regarding the HPV-vaccination among female students aged 18 to 26 years. They only found a significant increase in knowledge in both the intervention and the control group, but no effects on intention and uptake. This could indicate that an increase in knowledge only is not enough for behavioural change. Ratanasiripong, Cheng and Enriquez (2013) confirmed that indeed knowledge is not directly linked to intention to vaccinate and actual vaccination uptake and, as mentioned before, van Keulen et al. (2013a) also found that knowledge is not a determinant for HPV-vaccination intention. Gerend, Sheperd and Lustria (2013) found that an intervention that was tailored to an individual's perceived barriers for HPV-vaccination increased the intention to vaccinate compared to the control group that did not receive the additional tailored information. Hopfer (2012) studied the effect of an intervention that made use of a combined peer-expert (combination of information given by a peer and an expert) video that was culturally tailored. The participants in the intervention condition showed double as high in vaccination uptake compared to the control group. Again, personal relevance was an important factor that led to the higher uptake according to Hopfer (2012) and increase in intention according to Gerend et al. (2013). These interventions were all aimed at college students, but the effectiveness of an online tailored intervention for mothers with daughters born in 2002 has not been investigated.

Besides tailoring, the online tailored intervention also made use of virtual assistants, which suited the need of mothers for more interactive communication about the HPV-vaccination (van Keulen et al., 2010a; 2010b). A virtual assistant is a type of 'embodied agent', which is a computer program that has a life-like visual appearance and is presented on computer screens (van Vught, 2008). Virtual agents resemble humans not only in visual appearance but also in the use of interactive conversation with the users of the programme. They can also tailor the response to the user by information that was obtained by previous interaction with the user (Hertzum et al., 2002). A virtual assistant is used to support people in information-seeking and decision-making in computerized programmes. It is used to help navigate people through a programme in an effective and pleasant way. This increases the likelihood of satisfaction with the programme (Hertzum, Andersen, Andersen, & Hansen, 2002). The beneficial aspect of using a virtual assistant instead of a text and picture-based website is that it improves recall of information previously presented (Beun, Vos, &Witteman, 2003), transfer of learning (Atikinson, 2002), the learning amount (Baylor, 2009), self-efficacy expectations, literacy and behaviour change (Jin, 2010; Blanson Henkemans et al., 2008; Blanson Henkemans et al., 2009). For example, Bickmore, Pfeiffer and Paasche-Orlow (2009) examined the benefits of using a virtual assistant in online interventions. They emphasize the positive effects of two-way communication (verbal and non-verbal communication, interactive, dynamical assessment and repeat information if necessary). Verbal and non verbal communication allows to maximize comprehension and establish trust and satisfaction. Using a virtual assistant allows the participant to take as much time as they need and repeat information as many times as they need until they fully understand the information. The virtual assistant provides information in a simple speaking style and focuses on the information found most important by the participant.

The effectiveness of an online tailored intervention about the HPV-vaccination with virtual assistants for mothers with daughters born in 2002, has not been investigated before. Therefore, we will focus in this study on the effects of the online tailored intervention among mothers of daughters invited for HPV-vaccination. The first aim of this study is to examine the effects of the online tailored intervention on the primary (HPV-vaccination uptake) and secondary outcomes (informed decision making, decisional conflict and the social psychological determinants of HPV-vaccination uptake). Some factors were not a target in the intervention but were measured for research in this study (e.g., self-efficacy).

To identify the need for further development of the online tailored intervention, the second aim of this study is to examine which subgroups benefit most by the online tailored intervention. Krebs et al. (2010) and Lustria et al. (2013) also emphasized this need for future research in their meta-analyses. We will examine this for socio-demographic factors (ethnicity, religion and educational level), baseline intention and sample.

Lustria et al. (2013) described possible moderators of effectiveness of online tailored interventions in their meta-analysis. They found that online tailored interventions were most successful when it targeted the general population, compared to minority groups in the population. They also described that beliefs about health, disease and treatment in ethnic and racial minority groups differ from the general population, which influences the efficacy of the online tailored intervention. Krebs et al. (2010) did not find differences between socio-demographic factors (age, ethnic minority and gender) in effectiveness of online tailored interventions. In the meta-analysis of Noar et al. (2007) of tailored health interventions, socio-demographic factors (gender, age and race)

did not influence effectiveness, but tailoring on these factors added value to other tailoring techniques used in interventions. Resnicow, Soler, Braithwaite, Ahluwalia and Butler (2000) described that the cultural, social, historical, environmental, and psychological factors that influence the desired health behaviour may differ greatly among different ethnicities and that people from different ethnic backgrounds may benefit from different approaches in interventions. Brug and van Assema (2000) described in their study that computer-tailored nutrition education may only be effective for highly educated participants. Other research of Preston, Baranowski and Higginbotham (1988) found that health communication in general was more effective for highly educated people. Research on the possible moderation effect on the effectiveness of online tailored interventions of religion have not been done yet, but more research on educational level and religion has been addressed by multiple studies as implication for future research (Krebs et al., 2010; Lustria et al., 2013).

Additionally, research on a moderation effect of having a certain intention before participating in an online tailored intervention on the effectiveness of the intervention, has not been done yet either. Brug et al. (2000) did describe that computer-tailored nutrition education only work for people who are already motivated to change. People who are not motivated experience no "need to change" and subsequently do not have a reason to participate in an intervention (may not complete a survey and may not read and process tailored feedback; Brug et al., 2003). Based on this finding, we might carefully expect that people who have a more positive intention are motivated and subsequently benefit more of the online tailored intervention. However, we do not know for sure if a certain baseline intention influences the effect of the online tailored intervention and for which baseline intention, the online tailored intervention had the most positive effects. This additional research on baseline intention.

In the findings, mentioned above, we found that there is a lack of research on moderation effects of religion and baseline intention, limited findings on educational level and variability in findings for ethnicity. However, previous research (Krebs et al., 2010; Lustria et al., 2013; Noar et al., 2007; Resnicow et al., 2000; Preston et al., 1988; Brug et al., 2003) does indicate that sociodemographic factors and baseline intention might be important to consider in developing an online tailored intervention. Therefore, we want to explore which socio-demographic and baseline intention subgroups will benefit most from the online tailored intervention in this study. This means that we have no explicit hypotheses about which socio-demographic and baseline intention subgroups will benefit most from the online tailored intervention.

We also examine the effects of the online tailored intervention among a controlled (for efficacy testing) and a naturalistic (for effectiveness testing) sample and which sample benefits the most of the intervention. Efficacy testing is used as a measure of the treatment's ability to produce the desired effect under controlled circumstances (Ernst & Pittler, 2006). Effectiveness testing measures what the actual effect of the treatment will be when it would be implemented in society (Ernst & Pittler, 2006). The controlled sample (efficacy testing) are represented by panel members; they are

perceived as more used to online measurement and education than the naturalistic sample (effectiveness testing; i.e., participants from Preaventis, that is, the Dutch vaccination register; van Keulen, 2013a). We therefore expect that the online tailored intervention will be more effective for the controlled sample.

1.1. Theoretical and practical significance

Online tailored intervention about the HPV-vaccination is currently not widely available, but may promote informed decision making, reduce decisional conflict and have positive effects on HPV-vaccination uptake and the social-psychological determinants. The effects on uptake are important because it leads to a decrease in the amount of cervical cancer cases, because of the high effectiveness of the HPV-vaccination (90-99%; Health council of the Netherlands, 2008). Research about the effectiveness of online tailored intervention for mothers of girls to be invited, has not been done before. If effective, the intervention is going to be embedded by the RIVM in the communication about the HPV-vaccination and disseminated throughout the Netherlands.

1.2. Research questions and hypotheses

The research questions are: (1) What is the effectiveness of the online tailored intervention on HPV-vaccination uptake of participants' daughters (primary outcome), on the mothers' informed decision making, decisional conflict and social-psychological determinants (secondary outcomes) regarding the HPV-vaccination of their daughter? (2) How does the effectiveness of the online tailored intervention on primary and secondary outcomes differ for subgroups with regard to ethnicity, religion, educational level, sample and intention at baseline towards getting the HPV-vaccination?

We expect more positive effects on primary (i.e., a higher HPV-vaccination uptake) and secondary outcomes (e.g., a more informed decision, less decisional conflict, a more positive attitude) among participants in the experimental condition compared to the control condition.

Because of its explorative nature, we do not have hypothesis about which subgroup for ethnicity, religion, educational level and intention at baseline, benefit most from the online tailored intervention. Furthermore, we expect that the online tailored intervention will be more effective for the controlled sample compared to the naturalistic sample, because the controlled sample is expected to be more used to online measurement and education.

2. Method

2.1. Research design

The study was approved by the ethical committee of the VU Medical Center in Amsterdam, and registered at the Dutch Trial Register NTR4935. The study was executed between January and March, 2015. We used a randomized controlled trial (RCT) to examine the effects of the online tailored intervention. Participants were randomly allocated to one of two conditions: (1) control condition, and (2) experimental condition. Participants in the experimental condition were invited to

visit the online tailored intervention. The primary outcome (HPV-vaccination uptake) was assessed through the HPV-vaccination status that was registered in Praeventis, the Dutch National Immunization Register. This register is used to invite 12-year old girls from the Netherlands to participate in the HPV-vaccination program. The complete vaccination-uptake data was available 18 months after the baseline measurement (July 2016), in order to provide all girls the opportunity to finish the vaccinations. Secondary outcomes were assessed at baseline (i.e., before the first vaccination was received) and follow-up (i.e., right before or during the first vaccination round, which was 2 months after baseline), for both conditions using online surveys.

2.2. Participants

Mothers were invited when they had a daughter that was born in 2002; these girls were invited for the HPV-vaccination round in 2015. The controlled sample was invited by email, and consisted of participants randomly drawn from internet panels (i.e., Veldkamp BV, Intromarkt GFK and NGO FlyCatcher). The controlled sample (N = 2,483) was stratified by region. The panel members received a small financial reimbursement for every finished survey. An extra financial reimbursement was given, when mothers had finished both surveys and for the intervention group, when they had finished both surveys and visited the online tailored intervention. The amount of money that was given to the mothers is based on the length of the intervention and surveys and depended on the standards from the different panels. The goal of the financial reimbursement in panels was to ensure high response levels of the panels. The financial reimbursements were provided by the panels. The naturalistic sample (N = 36,000) was invited by mail, and consisted of participants randomly drawn from the Dutch National Immunization Register (Praeventis). Mothers in this sample were not rewarded for their participation, because this would not be part of the intervention if implemented in the future.

After mothers consented to participate in the study and approved for the request of their daughters HPV-vaccination status from Praeventis, they were randomly assigned to the experimental or control condition.

In figure 1, an flow-chart provides an overview of the recruitment and response. We invited 38,483 mothers to participate in the intervention. There were 9,124 participants randomly assigned to a condition at T0. From these participants there were 8,593 (94%) that completed the baseline survey and 4,678 (51%) completed the follow-up survey (T1, 8 weeks after baseline). There was information of 8,062 mothers available for data-analysis.

Besides drop-out there were also participants that were excluded (N = 1,067) because they did not meet the inclusion criteria of being a female, between the age of 24 and 62 years old and having a daughter born in 2002. Another reason for being excluded was if they were found to be duplicates across the controlled sample (panels) and the naturalistic sample (Praeventis).

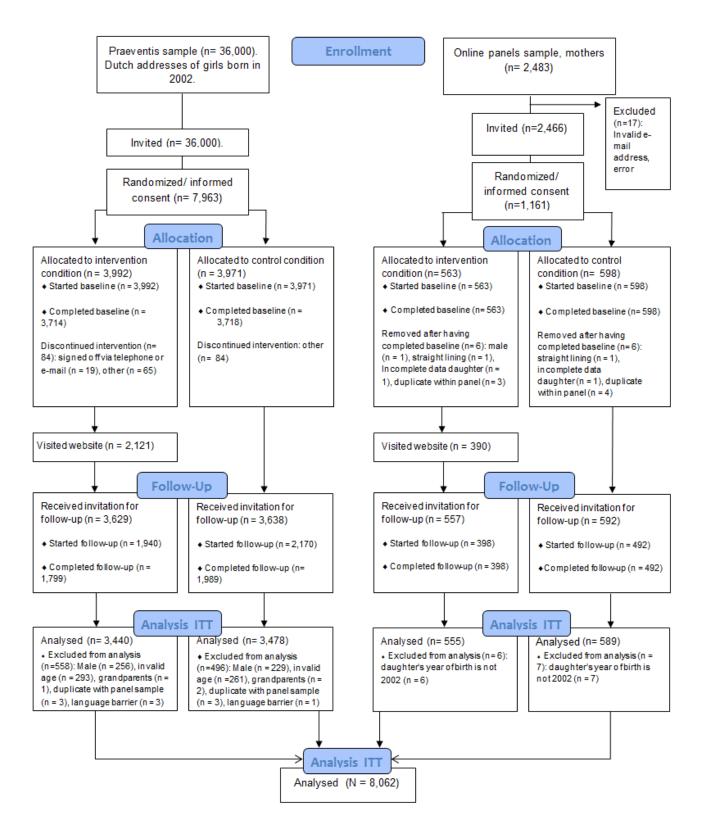


Fig. 1. Flow diagram of the recruitment and response of study participants. *Participants could be excluded based on multiple criteria (e.g., a male with an invalid age). Therefore, the total amount of Praeventis participants excluded differed from the sum of separate criteria for exclusion.

2.3. Procedure

The study was performed in 2015, before the first HPV-injections started.

In January 2015, the first invitations for the baseline measurement were sent to all participants. It existed of a link to a secured website, information about the study and a unique log-in code to enter the baseline survey and the follow-up survey. For the participants in the intervention condition the same code was used to enter the online tailored feedback. Access to the survey was given once the informed consent was signed, which explained the assurance of privacy, that their responses were confidential and that they could withdraw at any time. Two weeks after the baseline measurement, a reminder was sent to all participants to increase the response rate.

Four weeks after the baseline measurement (two weeks after the reminder), participants from the intervention condition received an invitation by email to visit the online tailored education. Mothers were given the opportunity to visit the online tailored intervention more than once and were able to visit the online tailored intervention until the invitation of the follow-up was sent out. A reminder was sent to participants in the intervention condition, one week after the first invitation to visit the online tailored intervention.

Two weeks after the first invitation for the online tailored intervention (six weeks after baseline), the follow-up measurement was sent to participants through email. One week after this invitation a reminder was sent for the follow-up survey.

The participants in both the intervention and control group received the universal information about the HPV-vaccination as part of the regular invitation for the HPV-vaccination, including an information pamphlet, and a reference to the website for general information about the HPV vaccine.

2.4. Materials and measurements

The **online tailored intervention** consisted of a website that provides tailored and interactive feedback provided by two virtual assistants. It has been developed using the Intervention Mapping Protocol (Bartholomew, Parcel, Kok, Gottlieb, & Fernández, 2011), computer-assisted tailoring (Kreuter & Skinner, 2000) and Theory of Planned Behaviour (Azjen, 1991). The Health Belief Model (Becker, 1974) and Social Cognitive Theory (Bandura, 1986), were used as theoretical frameworks for strategies used in the intervention. A user centered design was used to adjust the intervention to the mother's wishes. First, there were three static experimental pre-tests used to find empirical support for the used intervention strategies to be effective. Followed by three focus group phases to test interactive prototypes to aim at matching the preferences of the target group. After every phase, mothers were asked to give their evaluation. Based on these evaluations, adjustments were made which eventually resulted in the online tailored education as it is now.

The intervention targeted determinants that influence HPV-vaccination uptake, which were identified in previous research (Van Keulen et al., 2010a; 2013a; 2013b). We used two virtual assistants: 'Petra', who represents a mother and 'Dokter de Vries', who represents a doctor. 'Petra'

guides mothers through the website and gives information about the website itself (i.e., how it works and where information can be found). 'Dokter de Vries' gives tailored feedback and information based on answers the mother gave on questions regarding the HPV-vaccination (e.g. risk perception). Previous research (Hopfer et al., 2012; Durantini et al., 2006) found that the combination of a peer and expert delivering information was very effective. Both methods alone did not show significant effects on HPV-vaccination uptake (Hopfer et al., 2012).

The online tailored intervention consists of four components: (1) two-sided information about the HPV-vaccination with regard to facts and myths, effectiveness of the HPV-vaccination, the chance of getting HPV and cervical cancer, working method, other mothers opinions, importance of young age vaccination, side effects of the HPV-vaccination, ways to protect against cervical cancer, path from HPV infection to cervical cancer), (2) a decisional balance: Mothers were presented with a list of pros and cons of the HPV-vaccination by 'Petra'. Based on pros and cons mothers marked as most important, they were presented with a visual balance. The balance showed where mothers were standing on a scale of "not wanting to vaccinate my daughter" to "wanting to vaccinate my daughter". In this same menu there was a 'value clarification' tool to help mothers weigh up their personal values. Mothers were asked about their most important values in life and were then asked to relate these to the HPV-vaccination, (3) practical information: Here, information was provided with regard to how and where to receive the HPV-vaccine and strategies to talk with their daughter and/or partner about the vaccination and (4) frequently asked questions (see Appendix 1 for examples of the online tailored education).

Feedback was tailored in three ways. First, tailoring was used to provide mothers with tailored feedback on answers they gave to questions in the first menu. Statements that could be 'facts and myths' were given and depending on their answer, 'Dokter de Vries' responded on the correctness or the misunderstandings and provided more information (e.g., mothers who perceived the chance of HPV infection when not vaccinated, as low. The feedback that was presented was that this chance is actually high. If mothers answered with perceiving the chance of HPV infection when not vaccinated as high, they received feedback that showed them they were correct). Second, the decisional balance was used to provide tailored feedback with regard to choice for or against the HPV-vaccination based on which pro's and con's were most important to mothers. The third use of tailoring was by means of presenting mothers their progress in the intervention. They could see what components they had finished and were addressed (by 'Petra') which components still had to be done.

2.4.1 Primary outcome measures

Table 1 gives an overview of the outcomes that were measured.

HPV-vaccination-uptake was measured by requesting the HPV-vaccination uptake from 'Praeventis' after the HPV-vaccination round. Vaccination-uptake was dichotomized into having received one or two injections (1=vaccinated) versus having received no injection (0=not vaccinated). This is done because we expected the largest differences between these two groups on HPVvaccination determinants, which was confirmed by our data.

2.4.2 Secondary outcome measures

Secondary outcomes were assessed by two online surveys (i.e., at baseline and follow-up). Scores on items were combined into one scale when they had enough internal consistency (Cronbach's alpha > 0.60) and had a good coverage of content (Schmitt, 1996).

Informed Decision Making (IDM)

Three measures were used for IDM.

IDM outcome was measured in two ways (dichotomous and continuous) by means of the Multi-dimensional Measure of Informed Choice (MMIC; Marteau, Dormandy, & Michie, 2001). The MMIC (Marteau et al., 2001) is an assessment of the combination of attitude, knowledge and the actual behavior. We added a continuous measure because a dichotomous measure is somewhat rigorous, with a continuous measure we are able to determine the amount of IDM on a scale from 0 (not informed) to 48 (most informed). Correlation analyses showed a high correlation between the dichotomous and the continuous measure (r = .78). In the dichotomous IDM measure, a choice was considered informed (1) when it consisted of either sufficient knowledge (higher than the baseline mean score), a positive attitude (higher than 4 on a 7-point scale) and having received one or two HPV-injections; or sufficient knowledge, a negative attitude (lower than 4 on a 7-point scale) and having received no HPV-injections. Any other combination was considered as an uninformed choice (0). See Table 1, for information on how the two IDM outcome measures were constructed.

The third IDM measure, IDM process, was constituted from the subscale 'Informed Choice' of the Decision Evaluation Scales (DES; Stalmeier et al., 2005). This subscale consists of five items that are on a seven-point Likert-scale (e.g., 'I can make a well informed decision.'; 1 = completely disagree to 5 = completely agree). A higher score represented a better informed choice. The internal consistency was high (Cronbach's alpha = .88).

Decisional conflict

Decisional conflict was measured with the uncertainty subscale of the Decisional Conflict Scales (DCS; O'Connor, 1995). It consisted of 3 items that are on a seven-point Likert-scale ranging from completely disagree (= 1) to completely agree (= 7). Higher scores represent lower decisional conflict. An item example is: 'I felt sure what to choose'. The internal consistency was high (Cronbach's alpha = .94).

Social-psychological determinants

The social psychological determinants that were selected for this study are: HPV-vaccination intention, attitude towards the HPV-vaccination, attitude certainty towards the HPV-vaccination, risk perception (having received the/no HPV-vaccination), anticipated regret about rejecting the HPV-vaccination, beliefs about the HPV-vaccination, subjective norms towards the HPV-vaccination, habit

strength towards the HPV-vaccination, self-efficacy expectations towards the HPV-vaccination, knowledge about the HPV-vaccination and relative effectiveness of the HPV-vaccination.

The scales of the determinants all had a sufficient internal consistency (Cronbach's alpha > .60; see Table 1 for more information about the determinants). Cronbach's alpha was used for scales consisting of more than 2 items and Pearson r was used for scales consisting of 2 items.

Measure	Item	Answer options	Scale (minimum to maximum value)	Number of items	Cronbach's alpha (α) or Pearson's r (r) ²	Reference
<i>Primary outcome</i> HPV-vaccination uptake	Uptake of the HPV-vaccination is obtained through data from Praeventis.	0 = 0 injections 1 = 1 or $2injections$	n/a	n/a	n/a	
Secondary outcome IDM outcome (dichotomous)	An informed decision is made when: - the knowledge score was higher or equal to the mean of knowledge at baseline, the attitude score (without attitude certainty) was higher than 4 and the HPV- vaccination has been received. - the knowledge score was higher or equal to the mean of knowledge at baseline, the attitude score (without attitude certainty) was lower than 4 and the HPV- vaccination has not been received. Any other combination was categorized as 'no informed decision'.	0 = no informed decision 1 = informed decision	n/a	n/a	n/a	Marteau et al. (2001) ; Michie, Dormandy , and Marteau (2002) ; Van der Pal, Otten, and Detmar (2010)
IDM outcome (continuous)	Attitude was recoded from 0-7 to -3 (negative) – 3 (positive attitude) and HPV-uptake was recoded from 0 or 1 to -1 (no injection) or 1 (1 or 2 injections). Level of consistency was measured by multiplying the scores for attitude with those for HPV-uptake(-3 = low consistency; 3 = high consistency). Consistency was then recoded from -3 to 3 into 0 (low) to 6 (high). Knowledge scores (-8 = low; 8 = high) lower or equal to zero were considered insufficient (0 = no/insufficient knowledge; 8 = high knowledge). The level of IDM outcome was determined by multiplying the scores for knowledge with those for consistency.		0 = not/ least informed decision to 48 = most informed decision	n/a	n/a	Marteau et al. (2001) ; Michie et al. (2002) ; Van der Pal et al. (2010)
IDM process	 I can make a well informed decision; I know the pro's and con's of getting the HPV-vaccination or not getting the HPV-vaccination; I am satisfied with what I know now about the HPV-vaccination; I want clearer advice ^d; I want more information about 	1 = completely disagree to 7 = completely agree	1 = bad informed choice to 7 = good informed choice	5	.88 (α)	Stalmeier et al. (2005)

Table 1 Overview of primary and secondary outcome measures.

	the decision ^d .					
Decisional Conflict about the HPV- vaccination	As regards the HPV- vaccination, - I felt sure what to choose; - The decision was relatively easy to make; - I was clear about the best choice for my daughter.	1 = completely disagree to 7 = completely agree	1 = high to 7 = low decisional conflict	3	.94 (α)	O'Connor (1995)
HPV-vaccination intention	Are you planning on getting your daughter vaccinated against HPV? How big is the chance that you	1 = definitely not to = 7 = definitely yes 1 = very low	1 = negative intention to vaccinate to 7 = positive intention to vaccinate	2	.92 (r)	Van Keulen et al. (2013a); Van Keulen et al. (2013b)
	will get your daughter vaccinated?	to $7 = $ very high				
Attitude towards the HPV- vaccination	Vaccinating my daughter against HPV is	 1 = very undesirable to 7 = very desirable; 1 = very bad to 7 = very good; 1 = very negative to 7 = very positive; 1 = very unimportant to 7 = very important. 	1 = negative to 7 = positive attitude	4	.98 (α)	Paulussen, Lanting, Buijs, and Hirasing (2000)
Attitude certainty towards the HPV- vaccination	How certain are you about your opinion on the HPV-vaccination?	1 = very uncertain to 7 = very certain	n/a	1	n/a	Paulussen et al. (2000)
Risk perception (having received no HPV- vaccination)	Imagine that your daughter was not vaccinated against HPV. The chance that my daughter will get cervical cancer is	1 = very small to 7 = very large	1 = low to 7 = high risk perception (having received no HPV vaccination)	1	n/a	Paulussen et al. (2000); Reiter et al. (2009)
Risk perception (having received the HPV- vaccination)	Imagine that your daughter was vaccinated against HPV. The chance that my daughter will get cervical cancer is	1 = very small to 7 = very large	1 = low to 7 = high risk perception (having received the HPV vaccination)	1	n/a	Paulussen et al. (2000); Reiter, Brewer, Gottlieb, McRee, and Smith (2009)
Anticipated regret about rejecting the HPV- vaccination	Imagine your daughter has not received the HPV-vaccination and she gets cervical cancer in the future. How much would you regret your decision to let her receive no vaccination?	1 = no regret and 5 = very much Regret	n/a	1	n/a	Van Keulen et al. (2013a); Van Keulen et al. (2013b)
Beliefs about the HPV-vaccination	- If the government offers the vaccination, I assume it will be	1 = completely disagree to 7 =	1 = negative to 7 = positive beliefs	7	.85 (α)	Reiter et al. (2009);

	 safe; Our government shows responsibility for the health of the Dutch population by introducing the HPV- vaccination; The HPV-vaccination was only introduced because the pharmaceutical industry will earn a lot of money from it ^d; There is too little known about whether the HPV-vaccination effectively protects against cervical cancer ^d; There is too little known about the detrimental side effects of the HPV-vaccination ^d; My daughter is too young to receive the HPV-vaccination ^d; My daughter does not need the vaccination because she is not yet sexually active ^d. 	completely agree	about the HPV vaccination			Gerend, Weibley, and Bland (2009)
Subjective norms towards the HPV- vaccination ^c	Normative beliefs Regarding the HPV- vaccination of your daughter, what is your expectation on the opinion of Social referents: partner, daughter Motivation to comply How motivated are you to comply with the opinion of?	-2 = certainly not vaccinating to 2 = certainly vaccinating, 3 = not applicable; Not applicable was recoded into '0' 1 = not at all to 5 = very much	-20 = negative to 20 = positive	2	.64 (<i>r</i>)	Reiter et al. (2009)
Habit strength towards the HPV- vaccination	Letting my daughter receive the HPV- vaccination is something I do - automatically - without thinking	1 = completely disagree to 7 = completely agree	1 = weak habit strength to 7 = strong habit strength	2	.78 (<i>r</i>)	Verplanke n and Orbell (2003)
Self-efficacy expectations towards the HPV- vaccination	To what extend would you succeed in dealing with the following statements? - Guiding my daughter in the decision regarding the HPV- vaccination - Having a good talk with my daughter about the HPV- vaccination - Having a good talk with my partner* about the HPV- vaccination - Motivating my daughter to have herself vaccinated - Getting the actual HPV- vaccination / two injections with my daughter	1 = I would certainly not succeed to 7 = I would certainly succeed	1 = low self- efficacy to 7 = high self-efficacy	4 /5	.82 (α)	
Knowledge about the HPV- vaccination ^a	 HPV is sexually transmittable; Condoms fully protect against HPV; My daughter is obliged to get the HPV-vaccination when she is invited; You will always notice when 	-1 = incorrect 0 = don't know 1 = correct	-8 = incorrect 8 = correct	8	n/a	Van Keulen et al. (2013a); Van Keulen et al.

	 you are infected by HPV; Only women can get infected by HPV; Women who received the HPV-vaccination are still advised to participate in the cervical cancer screening in the Netherlands; The HPV-vaccination fully protects against cervical cancer; My daughter does not need to get the HPV- vaccination if she is already sexually active. 					(2013b)
Relative effectiveness of the HPV vaccination ^b	How would you rate the effectiveness of the following methods of preventing cervical cancer: • having safe sex • having sex with only one person in a lifetime • participating in the cervical cancer screening • having a healthy lifestyle (e.g. not smoking) • the HPV vaccination Participants rated the effectiveness of each method	1 = not at all effective to 10 = very effective	-9 = HPV vaccination least effective to 9 = HPV vaccination most effective	5	n/a	Van Keulen et al. (2013a); Van Keulen et al. (2013b)

Notes n/a = not applicable; 1. All scores on scaled items that showed sufficient internal consistency (Cronbach's alpha \geq .78 / Pearson's r \geq .64) were averaged into a scale; 2. Cronbach's alpha was used for scales consisting of more than 2 items, and Pearson's r was used for scales consisting of 2 items; a) Knowledge is not a scale because the answer on one item does not predict the answer on other items; the items were summed up to present a sum score of knowledge; b) The difference between the rated effectiveness of the HPV vaccination and the most effective alternative represented the relative effectiveness score (-9 = HPV vaccination least effective to 9 = HPV vaccination most effective); c) The subjective norms score was first computed by multiplying normative beliefs and motivation to comply for each social referent, and then by summing up the multiplications of the social referents; d) These items were reverse coded; *Only applicable if mother indicated that she had a partner.

2.4.3. Socio-demographic variables

Socio-demographic variables age, country of birth, religion and educational level, were assessed at baseline. For ethnicity the answer options that were given were: Netherlands, Germany, Belgium, Indonesia, Surinam, Dutch Antilles/Aruba, Turkey, Morocco and other. It was then divided in two categories: The Netherlands versus other. This coding was done because, in this sample, only 6.97% (562) of 8,062 participants were born in a different country than the Netherlands. Religion was also divided in two categories: having a protestant Christian religion or not. First mothers answered a question about what religion they identify with, with the answer options: Protestant Christian, Roman Catholic, Islam, Judaism, Buddhism, Hinduism, no religion and other, please specify. We made this division based on previous research indicating that, in the Netherlands, people with a Protestant religion refrain more from vaccination compared to the other (non) religious groups (van Keulen, 2013a; 2013b). Educational level was assessed as the highest education that has been completed, and divided into low (no education, primary school and MAVO/VMBO), intermediate (HAVO, VWO and MBO) and high (HBO and university).

2.4.4. Baseline intention

In order to examine differences in effectiveness moderated by intention before the intervention, we divided intention in three groups: (1) Mothers with a negative intention (baseline scores lower than half the standard deviation below the mean score that was centered for intention), (2) mothers who were hesitant (scores between half the standard deviation below the centered mean and half the standard deviation above the centered mean of intention) and (3) mothers who had a positive intention (scores higher than half the standard deviation above the centered mean of intention).

2.5. Statistical analysis

To describe the baseline sample, we used descriptive statistics.

The effects of the online tailored intervention and subgroup differences were examined using intention-to-treat (ITT) analyses. Using ITT increases power and it decreases the risk for bias that is caused by selective drop-out (van Buuren, 2012). In the ITT the missing data was predicted using multiple imputation by chained equations (van Buuren, 2012; White, Royston, and Wood, 2011). By doing this, we generated 15 imputed data-sets using the predictive mean matching algorithm in IBM statistical package SPSS (version 23). The results of these 15 imputed datasets were then pooled together by using the rules Rubin (1987), described in his book. To check for convergence of the imputations we inspected the iteration plots. We also performed complete case (CC) analyses to check if there were differences between the results of the ITT and CC analyses. Additionally, drop-out analyses were done to see if drop-out was selective. In the drop-out analysis, a p-value of .002 was used as the criterium for significance (bonferroni corrected alpha = .05/21 factors = .002). IBM statistical package SPSS (version 23) was used to perform the analyses of the data.

To check for baseline differences between intervention and control conditions, chi-square tests (for categorical variables) and independent t-tests (for continuous variables) were used.

The effects of the online tailored intervention were examined by logistic (for dichotomous variables, e.g., HPV-vaccination uptake) and linear regression analyses (for continuous variables, e.g., intention). The outcome at the follow-up measurement was used as the dependent variable (e.g., intention at T1), and the outcome at baseline (T0) and condition (experimental versus control condition) as the independent variables. A p-value of .003 was used as the criterium for significance (bonferroni corrected alpha = .05/17 outcomes = .003). The effect size measure in logistic regression analyses was the odds ratio. The odds ratio was classified in three categories: a small effect (1.5), a medium effect (3.5) and a large effect (9) (Cohen, 1988). In linear regression analyses the effect size was calculated in R (RDevelopment, C. O. R. E. TEAM 2009.). Here we calculated the Cohen's f^2 (R²AB = R²A/1 - R²AB) for hierarchical regression analyses (Cohen, 1988) to indicate the effect sizes (ES). They were interpreted in three categories: small (0.02), medium (0.15) and large (0.35; Cohen, 1988).

To examine which subgroups benefit most of the online tailored intervention, we performed moderation analyses. Subgroup differences were examined by adding the subgroup factor (i.e., ethnicity, religion, education level, sample or intention) and the two-way interaction term (i.e., condition * subgroup factor) to the regression analyses mentioned above. We used a p-value of .003 as the criterium for significance (bonferroni corrected alpha = .05/17 outcomes = .003).

Assumptions of linear regression analyses were checked and met. These were linear relationship between the independent and dependent variables, independent errors, homoscedasticity, multicollinearity and normal distribution. The dependent variables are continuous variables and the independent variables are continuous or dichotomous (Field, 2013).

The assumptions for logistic regression analyses, linearity between the independent variables and the Log odds and independence of errors were also checked and met (Field, 2013).

3. Results

3.1. Descriptive statistics

Table 2 provides a description of the baseline sample. The mean age of the participants was 44 years old (SD = 4.25). Compared to the Dutch population, the sample consisted of more mothers that were born in the Netherlands (76% versus 93%; Centraal Bureau voor de Statistiek, 2016a), more highly educated mothers (34% versus 45%; Centraal Bureau voor de Statistiek, 2016b), more mothers who had a daughter that obtained the HPV-vaccination (61% versus 75%, van Lier et al., 2016). The sample was comparable with the Dutch population with regard to religion (19% Protestant versus 16% in the Dutch population; Centraal Bureau voor de Statistiek, 2015). At baseline, mothers appeared to have a relatively positive intention towards letting their daughter receive the vaccination (M = 5.35, SD = 1.69).

There were no baseline differences on socio-demographic variables (p < .05) between the intervention and control condition.

Variables	Intervention	Control	Total	X^2
	(N = 3,995)	(N = 4,067)	(N = 8,062)	
Age	43.70 (4.27)	43.58 (4.22)	43.64 (4.25)	
				0
Country of birth	$N_{missing} = 4$	$N_{missing} = 4$	$N_{\text{missing}} = 8$.05 ^a
The Netherlands	93.1%	93.0%	93.0%	
Other	6.9%	7.0%	7.0%	
Religion	$N_{\text{missing}} = 7$	$N_{\text{missing}} = 6$	$N_{\text{missing}} = 13$.72 ^a
Religion	r missing - /	Tymissing – O	1.0 missing -1.0	.12
Protestant	18.9%	18.1%	18.5%	

Table 2 Sample description (N = 8,062)

Not Protestant	81.1%	81.9%	81.5%
Educational Level	$N_{missing} = 4$	$N_{\text{missing}}=3$	$N_{missing} = 7$ 7.59 ^a
Low	14.7%	13.3%	14.0%
Middle	45.5%	42.7%	43.1%
High	41.8%	44.0%	42.7%

Notes. In case of missing values, the number of missing values (Nmissing) was presented; a) all chi-square outcomes between the socio-demographic variables and condition were not significant (p > .05).

Drop-out analyses showed a higher drop-out among mothers from the intervention group (b = .29, p < .002), a non-Dutch ethnicity (b = ..33, p < .002), with a low education (b = ..23, p < .002, b = ..27, p < .002; compared to a middle or high education), who were not making an informed decision (b = ..01, p < .002), had a positive attitude (b = .08, p < .002), had a higher risk-perception if their daughter was vaccinated (b = .11, p < .002), had a lower self-efficacy (b = ..10, p < .002), were in the Praeventis sample (b = -1.03, p < .002) and there was more drop-out among mothers who had daughters who were not vaccinated against HPV (b = ..24, p < .002).

3.2. Research question 1: Effects of online tailored intervention on primary and secondary outcomes

Table 2 shows an overview of the effects of the online tailored intervention on primary and secondary outcomes.

The hypothesis that the online tailored intervention was more effective than universal education on the primary outcome and secondary outcomes was partly accepted. No significant effects were found for the primary outcome, HPV-vaccination uptake. The experimental (73.3%) and control group (72.8%) did not differ on HPV-vaccination uptake (OR = 1.03, p = .60).

However, the online tailored intervention had significant effects on most of the secondary outcomes. Significant effects were found on Informed decision making outcome (dichotomous) (b = .25 (.06), p < .003), Informed decision making (continuous) (b = 1.72 (.27), p < .003), Informed decision making process (IDM process; b = .60, p < .003), intention (b = .18 (.03), p < .003), Attitude (b = .15 (.03), p < .003), Attitude certainty (b = .17 (.03), p < .003), beliefs (b = .12 (.02), p < .003), Decisional conflict (b = .21 (.04), p < .003), risk perception of parents if their daughter would obtain the HPV-vaccination (b = -.11 (.03), p < .003), subjective norm (b = .82, p < .003), Habit (b = .14 (.04), p < .003), Relative effectiveness (b = .46 (.07), p < .003) and knowledge (b = .35 (.05), p < .003). All significant effects on the primary and secondary outcomes that were found were small to medium (Cohen's f^2 were .06 or smaller, and odds ratio (OR) for informed decision making was 1.28).

To further clarify the above mentioned results, we describe what exactly happened from pretest to post-test, comparing the experimental and control group. More participants in the experimental group (N = 990) made an informed choice, on post-test compared to pre-test, than participants in the control group (N = 767). Participants in the experimental group (M difference = 7.16) increased more in making an informed choice from pre-test to post-test compared to participants in the control group (*M difference* = 5.33), on a scale from 1 to 48. Participants in the experimental group (*M difference* = 1.68) increased more from pre-test to post-test in IDM process compared to participants in the control group (*M difference* = 1.06), on a scale from 1 to 7. Participants in the experimental group (*M* difference = .24) increased more from pre-test to post-test in intention towards the HPV-vaccination compared to participants in the control group (M difference = .07), on a scale from 1 to 7. Participants in the experimental group (*M difference* = .19) got a more positive attitude, from pre-test to post-test, towards the HPV-vaccination compared to participants in the control group (*M difference* = .03), on a scale from 1 to 7. Participants in the experimental group (*M difference* = .54) increased more in attitude certainty, from pre- to post-test, and were more certain about their opinion compared to participants in the control group (*M difference* = .39), on a scale from 1 to 7. Participants in the experimental group (*M difference* = .28) increased more, from pre-test to post-test, in having positive beliefs about the HPV-vaccination compared to participants in the control group (*M difference* = .16) on a 7 point scale. Participants in the experimental group (M difference = 1.05) reported more decrease in decisional conflict, from pre-test to post-test, compared to participants in the control group (M difference = .84), on a scale from 1 to 7. Participants in the experimental group (M difference = .84).13) decreased more, from pre-test to post-test, in risk perception if not vaccinated compared to participants in the control group (*M difference* = .02), on a scale from 1 to 7. Participants in the experimental group (*M difference* = 1.37) increased more in having a positive subjective norm compared to participants in the control group (*M difference* = .54) on a scale from -20 to 20. Participants in the experimental group increased (M difference = .23) more, from pre-test to post-test, in having a strong habit strength compared to participants in the control group (M difference = .10) on a 7 point scale. Participants in the experimental group increased (*M difference* = .62) more in perceiving HPV-vaccination as most effective to prevent cervical cancer compared to participants in the control group (*M difference* = .17) on a scale from -9 to 9. Lastly, participants in the experimental group (*M difference* = 1.35) increased more, from pre-test to post-test, in knowledge compared to participants in the control group (*M difference* = .99). Participants could score between -8 and 8.

The online tailored intervention had no significant effect on risk perception of mothers if their daughter did not obtain the HPV-vaccination, anticipated regret and self-efficacy.

Results of the ITT analyses were confirmed by CC analyses. However additionally, CC analyses did show a significant effect on anticipated regret and self-efficacy.

	Control (N =	4,067),	Intervention (N = 3,995),		
	Mean (SD) of	r	Mean (SD) or	r		
	percentage (N	J)	percentage (N	J)		
	Pre-Test	Post-Test	Pre-Test	Post-Test	B (standard	Cohen's
					error)	f^2 or OR
Primary outcome						
HPV-vaccination uptake						
Has received no HPV-		27.2%		26.7%		
injection (reference)		(1106)		(1066)		
Has received one or two		72.8%		73.3%	.03 (.05)	1.03
HPV-injections		(2961)		(2929)		
Secondary outcomes						
Informed decision-making:						
outcome (dichotomous)						
Not informed (reference)	66.1%	47.3%	67.3%	42.5%		
	(2689)	(1924)	(2689)	(1699)		
Informed	33.8%	52.7%	32.7%	57.5%	.25 (.06)*	1.28
	(1376)	(2143)	(1306)	(2296)		
Informed decision-making:	18.95	24.28	18.69	25.85	1.72 (.27)*	.007
outcome (continuous) (0-48)	(11.45)	(11.82)	(11.21)	(12.30)		
Informed decision-making:	3.56 (1.37)	4.64 (1.34)	3.56 (1.40)	5.11 (1.28)	.47 (.04)*	.038
process (1-7)						
Decisional conflict (1-7)	4.33 (1.74)	5.17 (1.45)	4.33 (1.75)	5.38 (1.36)	.21 (.04)*	.008
Intention (1-7)	5.35 (1.70)	5.42 (1.97)	5.35 (1.69)	5.59 (1.87)	.18 (.03)*	.006
Attitude (1-7)	5.19 (1.46)	5.22 (1.57)	5.18 (1.45)	5.37 (1.51)	.15 (.03)*	.006
Attitude certainty (1-7)	5.14 (1.54)	5.53 (1.42)	5.16 (1.51)	5.70 (1.34)	.17 (.03)*	.007
Beliefs (1-7)	4.21 (.72)	4.37 (.80)	4.19 (.73)	4.47 (.81)	.12 (.02)*	.010
Risk perception not vaccinated	3.73 (.98)	3.70 (1.05)	3.74 (0.98)	3.77 (1.08)	.06 (.02)	.001
(1-7)						
Risk perception vaccinated	2.76 (1.06)	2.74 (1.08)	2.77 (1.07)	2.64 (1.10)	11 (.03)*	.004
(1-7)						
Anticipated regret (1-5)	3.68 (1.27)	3.50 (1.33)	3.71 (1.25)	3.59 (1.31)	.07 (.03)	.001
Subjective Norm (-20 – 20)	5.92 (7.90)	6.46 (9.46)	5.88 (7.81)	7.25 (9.20)	.82 (.20)*	.004
Habit (1 – 7)	4.26 (1.79)	4.36 (1.82)	4.28 (1.78)	4.51 (1.83)	.14 (.04)*	.004
Relative Effectiveness (1-10)	-2.01 (2.24)	-1.84 (2.36)	-1.97 (2.22)	-1.35 (2.27)	.46 (.07)*	.015
Self-Efficacy (1-7)	6.24 (.76)	6.24 (.78)	6.27 (.73)	6.29 (.75)	.04 (.02)	.001
Knowledge $(-8 - 8)$	4.42 (2.16)	5.41 (2.09)	4.40 (2.14)	5.75 (2.09)	.35 (.05)*	.009

Table 2 Effects of online tailored intervention (N = 8,062)

Notes. * p < .003 (Bonferroni: 0.05 / 17 factors). A higher score means a higher X (e.g., more positive attitude) except for decisional conflict; here, a higher score means less decisional conflict; OR > 1: the higher the score on a factor, the higher the outcome of IDM / chance of the daughter being vaccinated; OR < 1: the higher the score on a factor, the lower outcome of IDM / the chance of the daughter being vaccinated.

3.3. Research question 2: Subgroup differences

Table 3 (country of birth), 4 (religion), 5 (educational level), 6 (sample) and 7 (intention) show an overview of subgroup differences in the effect of the online tailored intervention. There were no significant subgroup differences between primary and secondary outcome measures for country of birth (all p's > .08) and religion (all p's > .08). For educational level, we found an interaction effect of educational level and relative effectiveness (b = .59, p < .003). The online tailored intervention was more effective on perceived relative effectiveness of the HPV-vaccination among mothers with a high educational level than mothers with a low educational level. The effect size here was also found to be small (Cohen's $f^2 = .005$).

Our hypothesis that the online tailored intervention would be more effective for participants from the controlled sample (Panels) is rejected. No difference in effect on the primary and secondary outcomes were found between the controlled and naturalistic samples (all p's > .04; table 6).

Baseline intention significantly moderated the intervention effects on decisional conflict, intention, attitude, subjective norm and relative effectiveness (see Table 7). The online tailored intervention had a more positive effect on intention and relative effectiveness for mothers with a negative intention compared to mothers who were hesitant (intention: b = -.26 (.08), p < .003; relative effectiveness: b = -.39 (.12), p < .003) or positive (intention: b = -0.40 (.08), p < .003; relative effectiveness: b = -.53 (.12), p < .003) at baseline. This was also found for the outcomes attitude and subjective norm but here only compared to mothers who were positive (attitude: b = -.21 (.06), p < 0.003; subjective norm: b = -1.64 (.43), p < .003) at baseline. The intervention also showed a positive interaction effect on decisional conflict for mothers with a hesitant intention (b = .26 (.08), p < .003). There were no significant differences found between mothers who were in doubt and mothers who had a positive intention (p's > .004).

	Control (N =	4,067),	Intervention (N = 3,995),	Country of	
	Mean (SD) or	ſ	Mean (SD) or	r	birth	
	percentage (N	J)	percentage (N	J)		
	Pre-Test	Post-Test	Pre-Test	Post-Test	B (standard	Cohen's
					error)	f^2 or OR
Primary outcome						
HPV-vaccination uptake						
Has received no HPV-		27.2%		26.7%		
injection (reference)		(1106)		(1066)		
Has received one or two HPV-		72.8%		73.3%	.26 (.16)	1.29
injections		(2961)		(2929)		
Secondary outcomes						
Informed decision-making:						
outcome (dichotomous)						
Not informed (reference)	66.1%	47.3%	67.3%	42.5%		
	(2689)	(1924)	(2689)	(1699)		
Informed	33.8%	52.7%	32.7%	57.5%	05 (.26)	1.28
	(1376)	(2143)	(1306)	(2296)		
Informed decision-making:	18.95	24.28	18.69	25.85	.07 (1.46)	.003
outcome (continuous) (0-48)	(11.45)	(11.82)	(11.21)	(12.30)		
Informed decision-making:	3.56 (1.37)	4.64 (1.34)	3.56 (1.40)	5.11 (1.28)	.08 (.13)	.002
process (1-7)						
Decisional conflict (1-7)	4.33 (1.74)	5.17 (1.45)	4.33 (1.75)	5.38 (1.36)	11 (.13)	.001
Intention (1-7)	5.35 (1.70)	5.42 (1.97)	5.35 (1.69)	5.59 (1.87)	.07 (.12)	.000
Attitude (1-7)	5.19 (1.46)	5.22 (1.57)	5.18 (1.45)	5.37 (1.51)	01 (.10)	.000
Attitude certainty (1-7)	5.14 (1.54)	5.53 (1.42)	5.16 (1.51)	5.70 (1.34)	27 (.19)	.001
Beliefs (1-7)	4.21 (.72)	4.37 (.80)	4.19 (.73)	4.47 (.81)	.05 (.07)	.000
Risk perception not vaccinated	3.73 (.98)	3.70 (1.05)	3.74 (0.98)	3.77 (1.08)	17 (.10)	.004
(1-7)						
Risk perception vaccinated	2.76 (1.06)	2.74 (1.08)	2.77 (1.07)	2.64 (1.10)	04 (.11)	.001
(1-7)						
Anticipated regret (1-5)	3.68 (1.27)	3.50 (1.33)	3.71 (1.25)	3.59 (1.31)	.01 (.10)	.001
Subjective Norm (-20 – 20)	5.92 (7.90)	6.46 (9.46)	5.88 (7.81)	7.25 (9.20)	37 (.74)	.001
Habit (1 – 7)	4.26 (1.79)	4.36 (1.82)	4.28 (1.78)	4.51 (1.83)	02 (.14)	.000
Relative Effectiveness (1-10)	-2.01 (2.24)	-1.84 (2.36)	-1.97 (2.22)	-1.35 (2.27)	.39 (.23)	.002
Self-Efficacy (1-7)	6.24 (.76)	6.24 (.78)	6.27 (.73)	6.29 (.75)	.12 (.08)	.002
Knowledge $(-8 - 8)$	4.42 (2.16)	5.41 (2.09)	4.40 (2.14)	5.75 (2.09)	.09 (.30)	.008

Table 3 Moderation effects of Country of birth on primary and secondary outcomes (N = 8,062)

Notes. * p < .003 (Bonferroni: .05 / 17 factors). A higher score means a higher X (e.g., more positive attitude) except for decisional conflict; here, a higher score means less decisional conflict; OR > 1: the higher the score on a factor, the higher the outcome of IDM / chance of the daughter being vaccinated; OR < 1: the higher the score on a factor, the lower outcome of IDM / the chance of the daughter being vaccinated.

	Control (N =	4,067),	Intervention	(N = 3,995),	Religion	
	Mean (SD) o	r	Mean (SD) o	r		
	percentage (N	(V	percentage (N	N)		
	Pre-Test	Post-Test	Pre-Test	Post-Test	B (standard	Cohen's
					error)	f^2 or OR
Primary outcome						
HPV-vaccination uptake						
Has received no HPV-		27.2%		26.7%		
injection (reference)		(1106)		(1066)		
Has received one or two HPV-		72.8%		73.3%	.17 (.12)	1.19
injections		(2961)		(2929)		
Secondary outcomes						
Informed decision-making:						
outcome (dichotomous)						
Not informed (reference)	66.1%	47.3%	67.3%	42.5%		
	(2689)	(1924)	(2689)	(1699)		
Informed	33.8%	52.7%	32.7%	57.5%	.04 (.14)	1.04
	(1376)	(2143)	(1306)	(2296)		
Informed decision-making:	18.95	24.28	18.69	25.85	43 (.68)	.000
outcome (continuous)(0-48)	(11.45)	(11.82)	(11.21)	(12.30)		
Informed decision-making:	3.56 (1.37)	4.64 (1.34)	3.56 (1.40)	5.11 (1.28)	07 (.09)	.000
process (1-7)						
Decisional conflict (1-7)	4.33 (1.74)	5.17 (1.45)	4.33 (1.75)	5.38 (1.36)	16 (.09)	.001
Intention (1-7)	5.35 (1.70)	5.42 (1.97)	5.35 (1.69)	5.59 (1.87)	.08 (.08)	.002
Attitude (1-7)	5.19 (1.46)	5.22 (1.57)	5.18 (1.45)	5.37 (1.51)	.10 (.07)	.002
Attitude certainty (1-7)	5.14 (1.54)	5.53 (1.42)	5.16 (1.51)	5.70 (1.34)	06 (.12)	.000
Beliefs (1-7)	4.21 (.72)	4.37 (.80)	4.19 (.73)	4.47 (.81)	01 (.04)	.001
Risk perception not vaccinated	3.73 (.98)	3.70 (1.05)	3.74 (0.98)	3.77 (1.08)	09 (.07)	.001
(1-7)						
Risk perception vaccinated	2.76 (1.06)	2.74 (1.08)	2.77 (1.07)	2.64 (1.10)	.05 (.08)	.000
(1-7)						
Anticipated regret (1-5)	3.68 (1.27)	3.50 (1.33)	3.71 (1.25)	3.59 (1.31)	01 (.07)	.002
Subjective Norm (-20 – 20)	5.92 (7.90)	6.46 (9.46)	5.88 (7.81)	7.25 (9.20)	.46 (.51)	.004

Table 4 Moderation effects of religion on primary and secondary outcomes (N = 8,062)

Habit (1 – 7)	4.26 (1.79)	4.36 (1.82)	4.28 (1.78)	4.51 (1.83)	03 (.08)	.002
Relative Effectiveness (1-10)	-2.01 (2.24)	-1.84 (2.36)	-1.97 (2.22)	-1.35 (2.27)	04 (.12)	.001
Self-Efficacy (1-7)	6.24 (.76)	6.24 (.78)	6.27 (.73)	6.29 (.75)	.04 (.04)	.001
Knowledge $(-8 - 8)$	4.42 (2.16)	5.41 (2.09)	4.40 (2.14)	5.75 (2.09)	20 (.12)	.001

Notes. * p < .003 (Bonferroni: .05 / 17 factors). A higher score means a higher X (e.g., more positive attitude) except for decisional conflict; here, a higher score means less decisional conflict; OR > 1: the higher the score on a factor, the higher the outcome of IDM / chance of the daughter being vaccinated; OR < 1: the higher the score on a factor, the lower outcome of IDM / the chance of the daughter being vaccinated.

Table 5 Moderation effects of education level on primary and secondary outcomes (N = 8,062)

	Control (N =	4,067),	Intervention ((N = 3,995),	Education	level			
	Mean (SD) o	r	Mean (SD) of	r	Low –		Low -		
	percentage (N	1)	percentage (N	percentage (N)		Intermediate		High	
	Pre-Test	Post-Test	Pre-Test	Post-Test	В	Coh	В	Coh	
					(standard	en's	(standard	en's	
					error)	f^2	error)	f^2	
						or		or	
						OR		OR	
Primary outcome									
HPV-vaccination									
uptake									
Has received no		27.2%		26.7%					
HPV-injection		(1106)		(1066)					
(reference)									
Has received one or		72.8%		73.3%	.02 (.15)	1.02	11 (.16)	.89	
two HPV-injections		(2961)		(2929)					
Secondary outcomes									
Informed decision-									
making: outcome									
(dichotomous)									
Not informed	66.1%	47.3%	67.3%	42.5%					
(reference)	(2689)	(1924)	(2689)	(1699)					
Informed	33.8%	52.7%	32.7%	57.5%	13 (.23)	.88	26 (.22)	.77	
	(1376)	(2143)	(1306)	(2296)					
Informed decision-	18.95	24.28	18.69	25.85	-1.01		-1.34 (.97)	.021	
making: outcome	(11.45)	(11.82)	(11.21)	(12.30)	(.96)				
(continuous) (0-48)									
Informed decision-	3.56 (1.37)	4.64 (1.34)	3.56 (1.40)	5.11 (1.28)	01 (.12)		04 (.13)	.006	
making: process (1-7)									

Notes. * p < .003 (Bonferroni: .05 / 17 factors). A higher score means a higher X (e.g., more positive attitude) except for decisional conflict; here, a higher score means less decisional conflict; OR > 1: the higher the score on a factor, the higher the outcome of IDM / chance of the daughter being vaccinated; OR <1: the higher the score on a factor, the lower outcome of IDM / the chance of the daughter being vaccinated. The reference category is a low educational level.

Table 6 Moderation effects of sample on primary and secondary outcomes (N = 8,062)

	Control (N = 4,067), Mean (SD) or percentage (N)		Intervention (N = 3,995), Mean (SD) or percentage (N)		Sample	
	Pre-Test	Post-Test	Pre-Test	Post-Test	B (standard	Cohen's
					error)	f^2 or OR
Primary outcome						
HPV-vaccination uptake						
Has received no HPV-		27.2%		26.7%		
injection (reference)		(1106)		(1066)		
Has received one or two HPV-		72.8%		73.3%	09 (.14)	.91
injections		(2961)		(2929)		

Secondary outcomes

Informed decision-making:

Not informed (reference)	66.1%	47.3%	67.3%	42.5%		
	(2689)	(1924)	(2689)	(1699)		
Informed	33.8%	52.7%	32.7%	57.5%	.01 (.15)	1.01
	(1376)	(2143)	(1306)	(2296)		
Informed decision-making:	18.95	24.28	18.69	25.85	.80 (.73)	.003
outcome (continous) (0-48)	(11.45)	(11.82)	(11.21)	(12.30)		
Informed decision-making:	3.56 (1.37)	4.64 (1.34)	3.56 (1.40)	5.11 (1.28)	.04 (.09)	.005
process (1-7)						
Decisional conflict (1-7)	4.33 (1.74)	5.17 (1.45)	4.33 (1.75)	5.38 (1.36)	07 (.08)	.005
Intention (1-7)	5.35 (1.70)	5.42 (1.97)	5.35 (1.69)	5.59 (1.87)	.11 (.08)	.002
Attitude (1-7)	5.19 (1.46)	5.22 (1.57)	5.18 (1.45)	5.37 (1.51)	.06 (.07)	.002
Attitude certainty (1-7)	5.14 (1.54)	5.53 (1.42)	5.16 (1.51)	5.70 (1.34)	.06 (.10)	.001
Beliefs (1-7)	4.21 (.72)	4.37 (.80)	4.19 (.73)	4.47 (.81)	.02 (.05)	.003
Risk perception not vaccinated	3.73 (.98)	3.70 (1.05)	3.74 (0.98)	3.77 (1.08)	12 (.06)	.001
(1-7)						
Risk perception vaccinated	2.76 (1.06)	2.74 (1.08)	2.77 (1.07)	2.64 (1.10)	04 (.07)	.002
(1-7)						
Anticipated regret (1-5)	3.68 (1.27)	3.50 (1.33)	3.71 (1.25)	3.59 (1.31)	.06 (.06)	.000
Subjective Norm (-20 – 20)	5.92 (7.90)	6.46 (9.46)	5.88 (7.81)	7.25 (9.20)	.35 (.48)	.001
Habit (1 – 7)	4.26 (1.79)	4.36 (1.82)	4.28 (1.78)	4.51 (1.83)	05 (.09)	.001
Relative Effectiveness (1-10)	-2.01 (2.24)	-1.84 (2.36)	-1.97 (2.22)	-1.35 (2.27)	.08 (.14)	.002
Self-Efficacy (1-7)	6.24 (.76)	6.24 (.78)	6.27 (.73)	6.29 (.75)	02 (.04)	.000
Knowledge $(-8 - 8)$	4.42 (2.16)	5.41 (2.09)	4.40 (2.14)	5.75 (2.09)	.27 (.13)	.003

outcome (dichotomous)

Notes. * p < .003 (Bonferroni: .05 / 17 factors. A higher score means a higher X (e.g., more positive attitude) except for decisional conflict; here, a higher score means less decisional conflict; OR > 1: the higher the score on a factor, the higher the outcome of IDM / chance of the daughter being vaccinated; OR < 1: the higher the score on a factor, the lower outcome of IDM / the chance of the daughter being vaccinated.

Table 7 Moderation effects of baseline intention on primary and secondary outcomes (N = 8,062)

	Negative - Hesitant	Negative - Positive	Hesitant - Positive	
	Beta (standard	Beta (standard error)	Beta (standard error)	
	error)			
Primary outcome				
HPV-vaccination uptake				
Has received no HPV-injection				
(reference)				
Has received one or two HPV-	21 (.13)	.01 (.18)	.22 (.18)	
injections				

Secondary of	utcomes
--------------	---------

Informed decision-making: outcome

Not informed (reference)			
Informed	.18 (.15)	.09 (.15)	10 (.14)
Informed decision-making: outcome	.92 (.69)	1.03 (.65)	.11 (.65)
(0 - 48)			
Informed decision-making: process	.22 (.08)	.001 (.09)	22 (.07)
(1 - 7)			
Decisional conflict (1 - 7)	.26 (.08)*	.04 (.07)	.22 (.08)
Intention (1 - 7)	26 (.08)*	40 (.08)*	14 (.07)
Attitude (1 - 7)	17 (.06)	21 (.06)*	04 (.06)
Attitude certainty (1 - 7)	04 (.04)	02 (.04)	23 (.08)
Beliefs (1 - 7)	04 (.04)	02 (.04)	.02 (.04)
Risk perception not vaccinated (1 -	.04 (.07)	.09 (.07)	.05 (.06)
7)			
Risk perception vaccinated	.04 (.06)	06 (.07)	10 (.07)
(1 - 7)			
Anticipated regret (1 - 5)	03 (.07)	.02 (.07)	.04 (.06)
Subjective Norm (-20 - 20)	-1.18 (.47)	-1.64 (.43)*	46 (.37)
Habit (1 - 7)	.08 (.08)	.06 (.08)	01 (.07)
Relative Effectiveness (1 - 10)	39 (.12)*	53 (.12)*	14 (.11)
Self-Efficacy (1 - 7)	00 (.05)	.03 (.04)	.03 (.05)
Knowledge (-8 - 8)	01 (.13)	13 (.12)	11 (.12)

Notes. * p < 0.003 (Bonferroni: 0.05 / 17 factors). A higher score means a higher X (e.g., more positive attitude) except for decisional conflict; here, a higher score means less decisional conflict); OR > 1: the higher the score on a factor, the higher the outcome of IDM / chance of the daughter being vaccinated; OR <1: the higher the score on a factor, the lower outcome of IDM / the chance of the daughter being vaccinated. In the first two columns, the reference category is those with a negative intention. For a comparison between those in doubt (reference category) and a positive attitude, see column three.

4. Discussion

The first aim of this study was to examine the effects of the online tailored intervention on primary (i.e., HPV-vaccination uptake) and secondary outcomes (i.e., informed decision making, decisional conflict and determinants of HPV-vaccination behaviour). It was expected that the online tailored intervention would lead to an increase of the uptake of HPV-vaccination, making a more informed decision, less decisional conflict and positive effects on determinants of HPV-vaccination behaviour (e.g., more positive attitude, more positive beliefs, etc.).

Unfortunately the study did not find any significant effect of the online tailored intervention on the HPV-vaccination uptake. This was also found by Bennet et al. (2015), but not by Hopfer (2012), who both studied the effects of online tailored intervention on specifically HPV-vaccination. An explanation for this non significant effect might be that the overall sample in this study showed a high percentage of HPV-vaccination uptake in both the intervention as well as in the control condition (about 73%) compared to what is measured within the general Dutch population by van Lier et al. (61%; 2016). This could mean that we had a selective sample in this study. Hopfer (2012) used cultural tailoring through a narrative approach based on the 'culture-centric narrative theory' of Larkey and Hecht (2010). Culturally adjusted prototypical HPV decision stories of the targeted college female students were used in her study. The health messages were also adjusted for implicit cultural values. Cultural tailoring might have been important for the effects Hopfer (2012) found for HPV-vaccination uptake. However, it should be addressed that in her study, HPV-vaccination uptake was measured through self-report, which has previously found to be more susceptible for response error (Baker, Stabile and Deri, 2004). Another explanation for the non significant effect on HPV-vaccination uptake could be explained through the process evaluation of the online tailored intervention, which was done parallel to this study by Hofstra (In Preparation). The intervention might have an indirect effect on HPV-vaccination uptake through exposure. The process evaluation study found that exposure to the intervention had a significant positive effect on HPV-vaccination uptake. The more a mother completed the intervention, the higher the HPV-vaccination uptake (Hofstra, In Preparation). Not finding an effect on HPV-vaccination uptake could also be because of structural barriers, such as the organisation of the HPV-vaccination itself. The HPV-vaccination is free until a daughter is 16 years of age and is delivered in a group approach (Health council of the Netherlands, 2008). It was found that there was a higher uptake (75%-87%) of the HPV-vaccination in countries who used an individual school-based approach, such as the United Kingdom (Kessels, Marshall, Watson, Braunack-Mayer, Reuzel, & Tooher, 2012). Individual school-based delivery makes use of individual consultation with the youth health professional at school. This approach provides more opportunity for personal interaction and is promising because of the high reach it has and because it has been found very effective in uptake for other vaccinations (Shah, Gilkey, Pepper, Gottlieb, & Brewer, 2014). Besides, this approach has been shown to be suitable for girls with a higher risk for HPV (girls from ethnic minority families with a low social economical status; Shah et al., 2014).

The online tailored intervention did show an increase on both Informed decision making outcome (continuous and dichotomous) as well as informed decision making process. This means that the mothers were making a more informed choice after receiving the online tailored intervention (intervention condition; IDM continuous measure). The study showed that an informed decision was made by more mothers in the intervention condition compared to mothers in the control condition (IDM dichotomous measure). Beside this, positive effects were found for decisional conflict, intention, attitude, attitude certainty, beliefs, risk perception if vaccinated, subjective norms, habit strength, relative effectiveness and knowledge for mothers in the intervention condition. Mothers who were assigned to the intervention condition and received the online tailored education showed less decisional conflict, had a higher intention to vaccinate, had a more positive attitude, were more certain about their opinion, had more positive beliefs regarding the HPV-vaccination, perceived the risk that their daughter would get cervical cancer after HPV-vaccination lower, had more positive subjective norms, had a stronger habit strength, rated the effectiveness of HPV-vaccination to prevent cervical cancer as more effective compared to other alternatives (e.g. participating in the cervical cancer screening; having safe sex) and had more knowledge of HPV and the HPV-vaccination than mothers who were assigned in the control condition. Other research on online tailored interventions found similar results on an increase in HPV-vaccination intention (Gerend et al., 2013, Hopfer, 2012; Paiva et al., 2014) and knowledge (Bennet et al., 2015).

There were no intervention effects found on the perceived risk of mothers, that their daughter would get cervical cancer without the HPV-vaccination, the regret they anticipated to feel when their daughter would get cervical cancer after not being vaccinated and self-efficacy. In this study, mothers perceived risk of getting cervical cancer when not vaccinated was higher than the risk a girl actually has of getting cervical cancer (integral cancer centre, 2013). The intervention provided mothers with the right information about the risk a girl has to get cervical cancer when not vaccinated. Because this information showed a lower risk than the mother initially thought, it is not likely that the intervention will increase their risk perception. Anticipated regret was only addressed indirectly in the online tailored intervention. This might explain why there was no significant effect on anticipated regret. This was done because mothers indicated, in the pilot studies, that directly mentioning that getting the HPV-vaccination could reduce anticipated regret, enhanced feelings of resistance. The non-significant results for self-efficacy could be because of a ceiling effect at baseline. Self-efficacy was scored very high at the baseline measure (mean score of 6.27 on a 7 point scale), and a further increase in self-efficacy is not realistic.

In addition to the main effects, the effect the intervention had on habit strength was interesting. The intervention appeared to have a positive effect on habit. Habit in letting their daughter receive the HPV-vaccination was operationalized with two items: (1) something mothers did naturally and (2) something they did without thinking. A positive effect on the second item would be in contrast with the aim of trying to get mothers to actively process information to make an informed decision. Secondary analysis among the two items separately showed that there was only an effect on the first item (something they did naturally). This means that the intervention increased perceiving HPV-vaccination as more naturally. The term 'Habit', might not be the appropriate choice for this item. Habit is usually used when we speak of repetitive behavior (Verplanken & Orbell, 2003). Vaccination uptake can be a repetitive behavior but HPV-vaccination uptake is not (two injections).

The results of this study suggest that the online tailored intervention does have a positive influence, as we have hoped and hypothesized, on IDM, decisional conflict and a great amount of the social-psychological determinants of HPV-vaccination intention. This suggests that this intervention has great potential in increasing HPV-vaccination intention and in helping mothers to make a well informed choice and decrease uncertainty in making this choice. With intention being a very important

predictor of actual behaviour (Fishbein and Azjen, 2010), these findings are very important because it shows the possibility of increasing the low HPV-vaccination acceptability.

The second aim of this study was to examine which subgroups (ethnicity, religion, educational level, sample and intention at baseline) benefit the most by the online tailored intervention.

No moderation effects were found for ethnicity and religion and only one effect for educational level on the effects of the intervention. Because there was only one significant interaction effect found for educational level, the effect should be carefully interpreted because it could be a case of coincidence. Finding no difference in effects of the online tailored intervention for the sociodemographic factors, suggests that the online tailored intervention is effective for the broad Dutch population, for people with different cultural backgrounds, religious beliefs and people from all educational levels.

We expected that there would be a difference between the naturalistic (Praeventis) and the controlled sample (Panels). The finding that there was no difference in effectiveness of the online tailored intervention between these groups can be perceived as something positive. Besides being effective in controlled circumstances, the online tailored intervention also produced the desired effect under naturalistic circumstances, what stimulates implementation in society (Ernst & Pittler, 2006).

There were differences between mothers with a different baseline intention (negative vs. hesitant vs. positive intention). HPV-vaccination acceptability increased more among mothers with an initial negative intention and decisional conflict reduced more among hesitant mothers. Most importantly, we did not find adverse effects of the intervention, mothers did not become more negative. Finding that mothers with an initial negative and hesitant intention benefit most of the online tailored intervention and that mothers only become more positive is promising for future adaptation of the intervention.

4.1. Limitations and Strengths

However, this study had the following limitations. Drop-out was high in this study and the drop-out seemed to be selective. Mothers who dropped out were different from mothers who completed the intervention. For example, mothers with daughters who did not vaccinate against HPV showed a higher drop-out compared to mothers in the control condition. A high drop-out rate and the fact that there's a difference between participants who had complete data and participants who dropped out (selective drop-out) is seen in more tailored interventions (computerized and non computerized; Blanson Henkemans et al., 2009; Bennet et al., 2015; Gagnon, Godin, Alary, Bruneau, & Otis, 2010). However, we found no difference between ITT and CC analyses. Therefore, it seems unlikely that the effects of the intervention were because of selective drop-out.

Effect sizes on all significant outcomes were small. This was also found in other metaanalysis (computerized and tailored: Krebs et al., 2010; tailored: Noar et al., 2007; computerized: Webb, Joseph, Yardley and Michie, 2010), which suggests that small effect sizes are common in online and/or tailored interventions. Noar et al. (2007) and Webb et al. (2010) described that more extensive use of theoretical concepts in an intervention appeared to increase effectiveness. Especially when the concepts include attitude, self-efficacy, stage of change, processes of change and social support. Messages that increase positive views and confidence towards the health behaviour were more effective than messages raising threats of a disease or death (Noar et al., 2007). The combination of using an expert and a peer virtual assistant has been shown to be very effective in previous studies (Duranti, Albarracin, Mitchell, Earl, & Gillette, 2006; Hopfer, 2012). Our study did use most of these aspects, but nevertheless had small effect sizes. Despite the small statistical effect sizes in this study, we still interpreted them as important on population level. Small effects can be of significant importance on a big population sample like the one for HPV-vaccination (Webb et al., 2010).

However, it is important to find ways to increase the effect size. Rimer & Kreuter (2006) described that tailoring could enhance motivation in four ways: 1) content should be matched to an individual's needs and interests, 2) information should be provided in a meaningful context, 3) using design and production elements to capture attention and 4) providing information in the preferred amount, type and channels of delivery of the individual. If all four aspects are addressed in tailoring, the tailored intervention would be very effective. Additionally, it appeared to be that in process of achieving behaviour change, different stages of readiness (precontemplation, contemplation, action and maintenance) require different messages. For example, if a mother is unaware, it is important to capture attention. If a mother is aware but not yet sure about taking action and performing the behaviour, it is important to use persuasion and address attitude. Different stages do not only require different approaches but also differ in delivery method (computerized or not). Rimer & Kreuter (2006) describe that tailoring on stages of readiness could have great beneficial effects on improving the effectiveness of a tailored intervention. Because HPV-vaccination uptake is not a behaviour that has to be maintained and mothers have to make the decision one time (unless if there are other younger daughters in the family), the maintenance and action phase can be combined (Paiva et al., 2014). Paiva et al. (2014) found evidence that an intervention, tailored on the different stages of change has positive effects on the acceptability and feasibility of the HPV-vaccination. Using a strategy that takes readiness to change into account, makes it able to reach all participants at all stages of change (Rimer & Kreuter, 2006; Paiva et al, 2014).

Rimer &Kreuter (2006) also described that tailoring on age, race, sex, reading level or learning style and other attributes might lead to outcomes with a high effect size. Especially, cultural tailoring has been addressed by multiple studies and appeared to add value to other tailoring techniques (Noar et al., 2007; Hopfer , 2012; Fu, Bonhomme, Cooper, Joseph, & Zimet, 2014; Resnicow et al., 2000). Just like tailoring on different stages of change it is found that people from different ethnic backgrounds may benefit from different approaches (Resnicow et al., 2000). The cultural, social, historical, environmental, and psychological factors that influence the desired health behaviour may differ greatly among different ethnicities. One factor might be of great influence in one culture but not in another one (e.g., more sensitive for an adult opinion versus a peer opinion; Resnicow et al., 2000). Fu et al. (2014) emphasized the differences in subjective norms and beliefs between people with different ethnic backgrounds. Additionally, Durantini et al. (2016) described that if the virtual agent is tailored to demographic and behavioural similarities it would facilitate behaviour change significantly, which was also confirmed by Noar et al. (2007).

Using a narrative approach appeared to be positive in increasing the effectiveness of an intervention in certain subgroups (Kreuter et al., 2010; Hopfer, 2012). An informational approach presents participants with information using arguments and reasons to convince them to present a certain behaviour. In contrast to a narrative approach, in which stories are used to engage participants and demonstrate the behaviour that is desired (Kreuter et al., 2010). The advantages of using a narrative approach is that it better reaches people who are less involved, more resistant, are in the early stages of behaviour change and have limited knowledge about the issue of not performing the desired behaviour (Hopfer, 2012). However, previous research for development of the online tailored intervention used in this study showed that an informational approach for risk was more effective (Pot et al., Resubmitted).

Another limitation of this study was that the sample is not representative of the general Dutch population. HPV-vaccination uptake was relatively high in both the experimental as the control group. The finding that there was selective drop-out among mothers who did not let their daughter receive the vaccination confirms this conclusion. Besides, the sample consisted of mothers with a high self-efficacy at baseline and was overrepresented by highly educated mothers, and mothers with a Dutch nationality. This all negatively influences the generalizablity of this study. However, the moderation analyses for the socio-demographic subgroups did not show that there was a difference in the effectiveness of the intervention between the subgroups. Still, it is important to increase the reach to the underrepresented groups to be able to draw conclusions from moderation analyses for subgroups.

The effect of the intervention is not measured on the long-term. This is not necessary for the desired outcome of increasing the HPV-vaccination uptake, because uptake almost immediately follows after the intervention. However, previous research found a decrease in effect after intervention completion (Krebs et al., 2010) or no significant effect on the long term on behaviour change (Gagnon et al., 2010; Bennet et al., 2015; Fu et al., 2014). These findings might be important for mothers with multiple daughters, who will have to make the decision to vaccinate again, and in considering if mothers would not regret their decision after vaccinating or not vaccinating their daughter. For behaviour change it is important that the significant effects of the study will maintain over time (Bennet et al., 2015).

Strengths of the current study were the use of a Randomized controlled design (RCT), the large sample size, that we used an objective measure to measure the effects on HPV-vaccination uptake (i.e., derived from Praeventis, the national vaccination register) which is less susceptible for response error (Baker, Stabile and Deri, 2004). Another strength is that the study addressed an

extensive amount of determinants that were found to have a significant impact on HPV-vaccination intention in previous research by Van Keulen et al. (2013a; 2013b), more determinants were addressed than in other studies (Bennet et al., 2015; Hopfer, 2012; Gerend et al., 2013). The possibility of using a naturalistic sample is a big strength of this research because it gives the opportunity to examine how the online tailored intervention would work in real life. The finding that there was no difference in effectiveness of the online tailored intervention between the naturalistic and controlled sample is very promising. Also, the use of a continuous measure for IDM gives us more detailed information about how informed a mother was, instead of rigorously categorizing mothers in making an informed decision or not (dichotomous), which was also recommended by others in previous research (e.g., van den Berg et al., 2006).

4.2. Recommendations for future research and implementation

The findings of this study suggest that the online tailored intervention has great potential to increase the HPV-vaccination uptake intention and acceptability, making informed decisions and decrease decisional conflict mothers reported to have before. Therefore, implementation of the online tailored intervention with the peer and expert virtual assistants is recommended.

We do have some recommendations for future research to promote implementation and dissemination. To prevent overrepresentation of certain groups in the sample and high baseline scores, it is important to get a sample that is more representative for the general Dutch population. Further research on finding other ways of recruitment might be a solution for this problem. Future research should aim at reaching mothers with a low education, that are not Dutch-native, who were initially more negative (compared to the current sample) and mothers who were less likely to let their daughter receive the HPV-vaccination. Our finding that mothers who were negative or hesitant benefit most of the online tailored intervention confirms that future research should focus on those mothers. Hopfer (2012) suggests that interventions aimed at reaching minority groups need to identify vaccine messages that work most effectively with these groups.

As mentioned before, research on process evaluation of the online tailored intervention found that the amount of completion of the intervention had positive effects on IDM, HPV-vaccination intention and HPV-vaccination uptake, which means that the higher rate of completeness a mother had, the more positive effects the online tailored intervention had. Increasing exposure would be a promising goal to increase completeness of the intervention and eventually the HPV-vaccination uptake. However, it is important to first identify characteristics of interventions that are associated to more exposure, this was also recommended by Brouwer et al. (2011).

Previous research (Rimer & Kreuter, 2006; Hopfer 2012; Noar et al., 2007; Hopfer , 2012; Fu et al., 2014; Resnicow et al., 2000; Paiva et al., 2014; Kreuter et al., 2010) suggests that adaptation of tailoring in the online tailored intervention is a possible way to increase the effectiveness of the intervention. Different tailoring variables, strategies and different message formats are a better fit

along the behavioral pathway (Rimer & Kreuter, 2006), and works different for every individual. Tailoring on the different stages of change shows promising results and future research should aim at identifying an individual's stage of change and examining what variables, strategies and message formats optimize effectiveness of the online tailored intervention (for what stage). Despite that we found no difference in effectiveness of the intervention in specific subgroups of participants, we need to be careful with generalizing the results of this study to the general population (i.e., Dutch mothers of girls aged 12 years) because we were not able to check the representativeness of the sample (overrepresentation in the sample). Because of the above mentioned caution needed for interpreting the results and because of previous research that found that cultural tailoring adds value to other tailoring techniques (Noar et al., 2007; Hopfer, 2012; Fu, Bonhomme et al., 2014; Resnicow et al., 2000), we recommend that future research should also be done on the effects of cultural tailoring. Examining what leads to great effectiveness in people from different cultures and using this in the development of the intervention could add value to the already effective tailoring strategies used in the online tailored intervention. Because of the contradictory findings on the use of an informational or narrative approach, it is important to continue research on the effects of these different approaches. Future development of the online tailored intervention could emphasize more on the role of the mother like virtual assistant 'Petra'. Using a narrative approach with this virtual assistant, might have a positive effect on the HPV-vaccination uptake. Combination of a peer and expert delivery method is still very important, because both methods alone did not show significant effects on HPV-vaccination uptake (Hopfer, 2012). To summarize, research on how and under what circumstances tailoring is effective and how the effects can be optimized on different aspects for different individuals should be done in future research. For further development of the online tailored intervention, future research needs to explore a much wider range of tailoring strategies, formats, effects, and mechanisms for effectiveness.

It is clear that the use of a tailored intervention might be an effective way to change behaviour (Krebs et al., 2010; Lustria et al., 2013; Hopfer, 2012). However it is important to consider that the provision of tailored information in an online intervention alone might not be enough to lead to change. There are many other factors, which a person cannot control and which are not changeable by (tailored) information, that are determinants for the health behaviour. Structural barriers (e.g. organisation of the HPV-vaccination) are very important in why someone is not able to perform a certain health behaviour (Rimer and Kreuter, 2006). Especially the mode of delivery of the HPV-vaccination is of great influence. Because previous research (Kessels et al., 2012) found higher HPV-vaccination rates in countries who used an individual school-based approach, revising the current group-based approach would be beneficial in improving HPV-vaccination uptake. More research needs to be done on how effective a school-based approach will be in the Netherlands.

Although no difference between parents opinions were found by van Keulen et al, (2013a), they did find that both parents played the most important role in the decision to vaccinate. Future

implementation might benefit in also addressing fathers. Additionally, the daughters role in the decision making should not be underestimated (Keulen et al., 2013a) and therefore should be included in future implementation of the online tailored intervention. Other countries such as: The United States, Australia, Austria and the United Kingdom (Garland, Molesworth, Machalek, Cornall and Tabrizi, 2015; personal communication, L. A. Markle-Hamilton, 1 june 2016) also target or plan to target boys in HPV-vaccination programmes because there are different HPV types (6, 11, 16 and 18) that can lead to more types of cancer than only cervical cancer (e.g. vaginal, vulvar, anal, penile, and head and neck cancer and genital warts; Marty, Roze, Bresse, Largeron and Smith-Palmer, 2013). When and if the Netherlands will implement a HPV-vaccination programme that protects for more types of HPV which also protects boys for HPV related diseases, it will be important for future development and implementation of this online tailored intervention to add boys as one of the target groups.

4.3. Conclusion

This study provides relevant information about areas of research on online tailored intervention to increase HPV-vaccination uptake, which is not widely available. The online tailored intervention has great potential in improving HPV-vaccination acceptability, making of informed decisions and reducing decisional conflict among mothers of girls invited for the HPV-vaccination and is ready for implementation and dissemination. Future research needs to focus on improving the HPVvaccination uptake. This can be achieved in optimizing the online tailored intervention by addressing tailoring (e.g., stages of change, cultural and message delivery), finding a representative sample for Dutch population and increase exposure, but also by optimizing additional factors (e.g., organization of the HPV-vaccination).

Acknowledgements

Petra Oomen (RIVM) and the panels (Veldkamp BV, Intromart GFK and NGO Flycatcher) helped with data collection. ZonMw (The Netherlands Organisation for Health Research and Development) supports this study (grant-number: 50-51515-98-259).

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Appendices

Appendix 1: Intervention screenshots

	Informatie HPV-inenting	Afwegen voor- en nadelen				Veelgestelde vrage
	Stelling	Uw antwoorden			Hoe belangrijk is dit voor u?	sorring hit.
	Mijn dochter is te jong om ingeënt te worden tegen HPV.	Eens	Neutraal	Oneens	**	OEEN NUMBER
-	Als mijn dochter zich laat inenten tegen HPV, dan zal zij in de toekomst onveilig vrijen.	Eens	Neutraal	Oneens	***	VOLGENDE
	Als de overheid meisjes laat inenten tegen HPV dan ga ik er vanuit dat de inenting veilig is voor mijn dochter.	Eens	Neutraal	Oneens	***	Voor/nødelen toevoegen
	Mijn dochter is nog niet seksueel actief, dus hoeft ze van mij de HPV- inenting niet te krijgen.	Eens	Neutraal	Oneens	***	
(the	Mijn dochter is al een tijd lang seksueel actief is, dus heeft het geen zin meer om haar te laten inenten tegen HPV.	Eens	Neutraal	Oneens	***	
	De HPV-inenting verkleint de kans dat mijn dochter later baarmoederhalskanker krijgt.	Eens	Neutraal	Oneens	***	2.F
MAG 1	De meeste moeders in mijn omgeving laten hun dochter ook inenten tegen HPV.	Eens	Neutraal	Oneens	***	
	Mijn dochter wil zich niet laten inenten.	Eens	Neutraal	Oneens	***	Ŷ







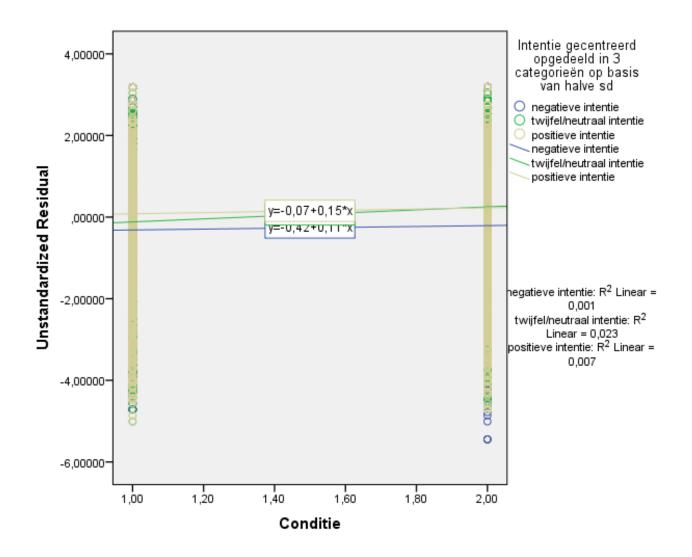




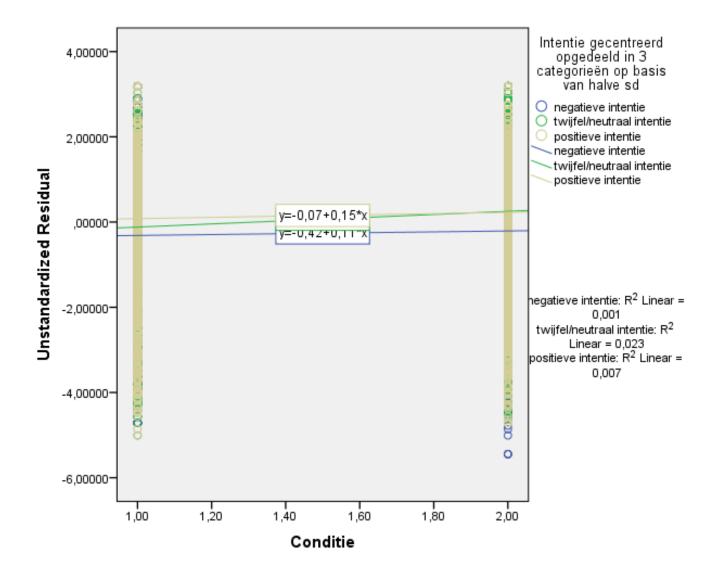


Appendix 2: Graphs of Intention moderation analyses

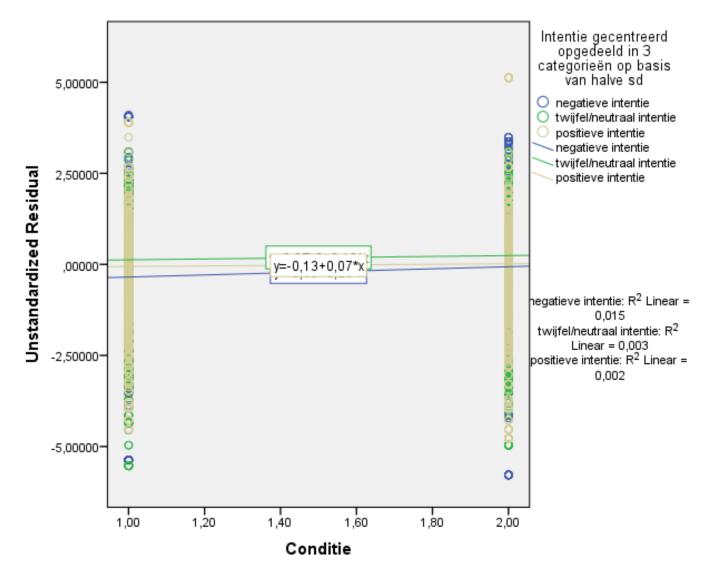
Decisional conflict



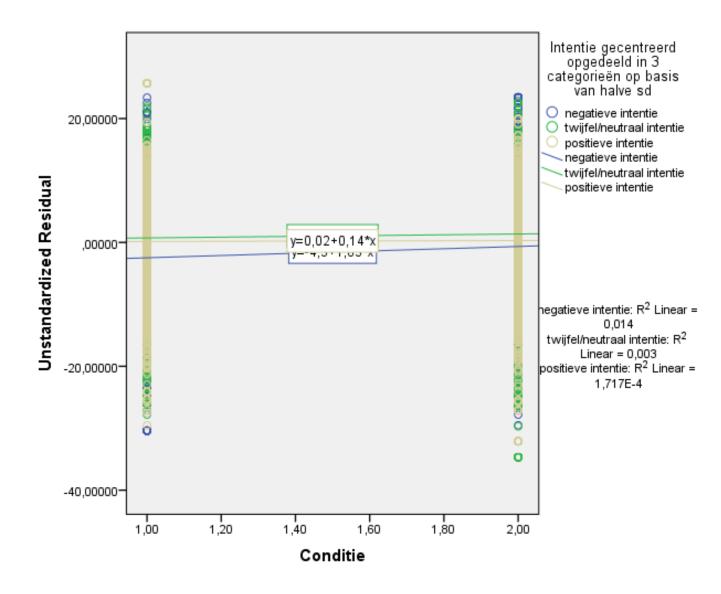
Intention







Subjective norm



Relative effectiveness

