Process evaluation of the INTENSE study using the Medical Research Council process evaluation framework of complex interventions and the extended Normalisation Process Theory

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Abstract

Introduction

Medication non-adherence is a common issue in the treatment of chronic illnesses. The reported percentages for non-adherence to anti-diabetic medication differ between 7% and 64%. Therefore, researchers have developed a tailored personalised intervention program, focussed on improving medication adherence in people with type 2 diabetes mellitus (T2DM). In the INTENSE study the effectiveness of this intervention will be evaluated. This thesis will focus on the process evaluation of the INTENSE study and the aim of the process evaluation is to identify the facilitators and barriers for implementation of the intervention.

Method

A mixed method design was used to conduct the process evaluation of the INTENSE study. Qualitative data consists of consultations between the pharmacists and the patients and interviews with pharmacists and patients. The OPTION 12 scale was used to measure the level of shared decision-making process during the consultations. A self-composed checklist was used to rate the content of the consultations. The interviews were manually coded by two researchers. In addition, quantitative data, including characteristics of the patients and pharmacists were included in the study.

The Medical Research Council (MRC) process evaluation framework of complex interventions was used to evaluate the fidelity, dose and reach of the intervention program and the extended Normalisation Process Theory (eNPT) was used to assess the engagement of the pharmacists with the intervention.

Results

Almost all items on the self-composed checklist were scored “yes”. The overall OPTION score ranged from 15 to 22, with a mean score of 19.5.

Facilitators for participating in the study were contacting patients through an institution they are familiar with and patients wanting to help with research.

The pharmacists and patients were mostly enthusiastic about the changes the intervention program can bring in the daily life of patients and community pharmacies. This is a facilitator for implementation. Another facilitator is a productive co-operation between the GP and the pharmacy. This can also be a barrier, if the co-operation is unproductive.

There were problems with the recruitment of non-adherent patients for the study, which is an important barrier for the implementation of the intervention. The high workload in community pharmacies, Minddistrict being vulnerable for digital problems and the not complete readiness for use of the study were also considered barriers for implementation.

Conclusion

The content of the consultations was predominantly according the instruction manual. The quality of the shared decision-making process during the consultations was not equal between the consultations.

The recruitment of suitable patients for the intervention program was the most important barrier for implementation. Apart from that, the overall conception is that the intervention really could make a difference in the daily life of patients and the daily life of the community pharmacy if suitable patients can be recruited for the intervention program.

Introduction

Diabetes mellitus (DM) is a common disease (1). According to the International Diabetes Federation, in 2021 there were 537 million adults, aged 20-79 years, with DM. DM is a growing health problem due to the aging population and rising obesity rates. It is expected that by 2045 there will be 783 million people with DM (2, 3). The most prevalent form of DM is type 2 diabetes mellitus (T2DM), which includes over 90% of the cases (1).

In most cases T2DM can be regulated with changes in lifestyle and oral anti-diabetic medication. However, non-adherence is a known problem in the treatment of chronic illnesses. The reported percentages of non-adherence to oral anti-diabetic medication differ between 7% and 64% (2, 4). These rates are wide for example due to the population that is included in the study and the measurement method used to asses non-adherence.

Medication non-adherence is defined as the extent to which patients are unable to follow the recommendations for their prescribed medication. Non-adherence can occur during different stages of treatment, namely (I) a patient may not start their treatment by not filling their prescriptions or by deciding not to take the medication after filling their prescription or (II) a patient might not follow the prescribed dosages, take the medication at the wrong time or discontinue treatment too soon (5). Non-adherence is a serious health issue and it is associated with an increase in morbidity and mortality (2, 6).

There are a lot of factors influencing the adherence of patients, including demographic, social, economic and cultural factors, cognition impairment, knowledge about the disease and the kind of medication (7). The reason for a patient to deviate from the treatment plan may be intentional or non-intentional. Intentional non-adherence means that patient makes an active decision not to follow treatment recommendations, usually after weighting the pros and cons, while unintentional non-adherence is a passive process related to the complexity of the medication regime and the memory of the patient (5).

For the development of an intervention that is aimed at improving adherence, intentional and unintentional non-adherence and factors that influence adherence should be taken into account. Over the years a lot of strategies, single or combined, have been developed that aimed to improve adherence. These strategies vary from complex chronic behavioural management approaches to reminder-based systems (2).

However, according to Blackburn et al. (2013) none of the strategies have resulted in more than small to modest effects on adherence (2). There have been interventions with statistically significant improvement of medical adherence, but the study that found these statistically significant improvements in medical adherence notes that the statistical findings should be interpreted with caution because of the poor quality of the studies (8). This observation is also noted by Blackburn et al. (2013).

A factor contributing to the lack of success of the interventions might be the impersonal nature of the interventions (9). An intervention focussing on the individual needs of patients, taking the underlying reasons for non-adherence into account, might be more effective (9). Therefore, researchers have developed a tailored personalised intervention, focused on improving medication adherence in people with T2DM. The intervention starts with a

questionnaire filled in by patients to find out their specific barriers for medication adherence. A collection of intervention modules to support a patient's adherence is linked to these individual barriers and together with the pharmacist the patient selects the modules they want to use to improve adherence. During the 'improving treatment adherence in people with diabetes mellitus' (INTENSE) study the effectiveness of this personalised intervention will be evaluated in a randomised controlled trial.

The effectiveness of an intervention may not be as expected, which for instance can be caused by weaknesses in the study design or a low degree of implementation (10, 11). A high degree of implementation is vital for a well working intervention and is influenced by intervention-context interactions (10). Hence, studying implementation is important.

The Medical Research Council (MRC) process evaluation framework of complex interventions focusses on implementation, and in particular on the key elements: 'fidelity', 'dose' and 'reach' (10). Fidelity and the adoption of an intervention may vary as a result of the engagement healthcare professionals have with an intervention. The Extended Normalisation Process Theory (eNPT) focusses on this engagement as it is concerned with 'intervention delivery', 'integration' and 'normalisation' (12).
By using the MRC process evaluation framework of complex interventions and the eNPT framework insights can be gained into the constituents of implementation.
In addition to evaluating the effectiveness of the intervention, a process evaluation of the INTENSE study will be executed using the MRC process evaluation framework of complex interventions and eNPT framework to explore the multiple facets of implementation of the intervention into daily pharmacy practice. This thesis will focus on the process evaluation of the INTENSE study and aims to gain insight into the barriers and facilitators of the INTENSE intervention.

Method

Study design

A mixed method design was used to conduct a process evaluation embedded in the INTENSE study. The INTENSE study is a six-month randomised controlled trial to evaluate the effectiveness of a personalised intervention program developed to support patients with T2DM with medication adherence. This study is performed in community pharmacies in the Netherlands and the United Kingdom (UK).

The intervention

A patient fills out a questionnaire which intercepts the patients' personal barriers with taking medication. Based on this questionnaire several intervention modules are selected and are discussed between the patient and the pharmacist during a consultation. During this consultation the patient and the pharmacist decide which modules they want to use according to a shared decision-making process. The available intervention modules are: brief messaging, medication schedule, reminder messaging, clinical medication review, medication dispensing system, smart messaging, unguided web-based self-help application for low mood (Minddistrict) and referral to a general practitioner.

Evaluation of the program

During the randomised controlled trial semi-structured interviews were conducted with patients and pharmacists in the UK to evaluate the intervention program, including its setup and the experiences of the pharmacists and patients with the intervention program. More details about the study protocol of the INTENSE study can be found in the publication describing the design of the study (13).

Data from the consultations between pharmacists and patients, which are part of the intervention program, the data from the interviews mentioned above, and the quantitative data from the pharmacists' and patients' characteristics were used to perform the process evaluation. The Medical Research Council (MRC) process evaluation framework of complex interventions was used to evaluate the fidelity, dose and reach of the intervention program and the extended Normalisation Process Theory (eNPT) was used to assess the engagement of the pharmacists with the intervention.

Frameworks for process evaluation

MRC process evaluation framework of complex interventions

The MRC process evaluation framework of complex interventions was used to evaluate implementation, focussing on the key elements: fidelity, dose and reach. Fidelity describes whether the intervention is delivered as intended. Dose describes the quantity of the intervention delivered and received and reach describes if the intended population comes in contact with the intervention and how (10).

eNPT

The eNPT framework explains and characterizes the executed actions of the health care providers in the implementation of an intervention (14, 15). The framework consists of four main constructs. The first one is potential, which focusses on the commitment of the health care providers to deliver the intervention in the way it was intended. The level of commitment is determined by the change valence and the change efficacy. The change valence is whether health care providers value the change the intervention can bring, and the change efficacy is how the health care providers perceive the feasibility of the changes.

The second construct, capability, focusses on the possibilities presented by the intervention. It includes how health care providers will adjust when organizing an intervention (workability) and how health care providers perceive implementation of the intervention to the wider social system (integration).

The third one, capacity, focusses on the structure into which the intervention will be implemented. The implementation depends on the co-operation between health care providers.

Potential, capability and capacity form the context for the fourth construct, contribution. It comprises the enactment of the intervention, the ways in which health care providers comprehend the intervention and their role in delivering it, and reflexive monitoring of its effects (12).

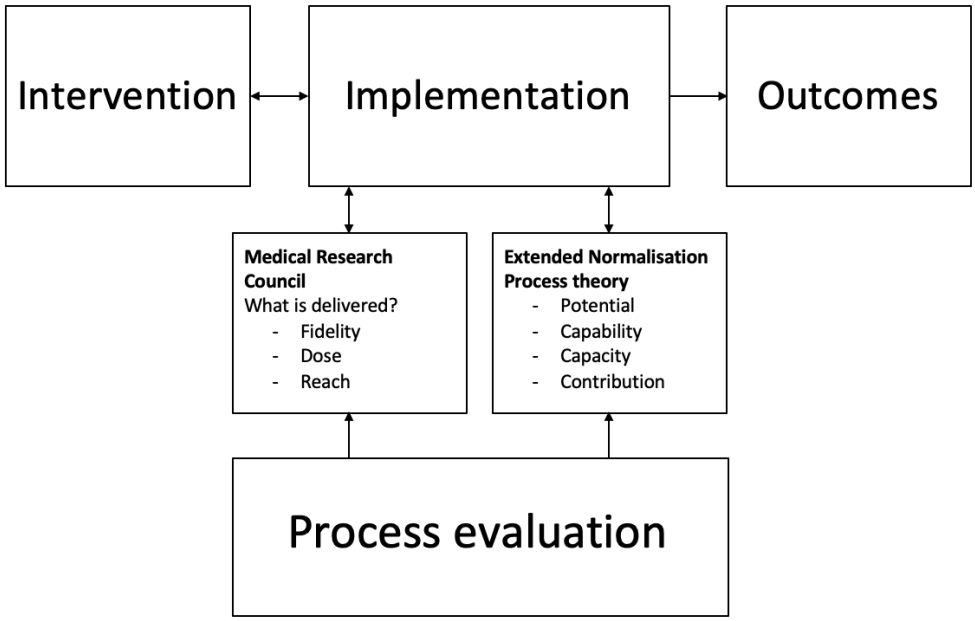

Figure 1: Visual presentation of the process evaluation

Data collection

Quantitative data

Quantitative data including patients' age and gender and the pharmacists' gender and years in their current role was collected.

Qualitative data

Consultations

Four face-to-face consultations from the Dutch branch, which lasted between 11 and 54 minutes (mean 26 minutes), were audiotaped and transcribed verbatim.
Two transcribed consultations, which lasted between 5 and 15 minutes (mean 10 minutes), and a summary of a consultation from the UK branch of the study were also included.

Interviews

Eight semi structured interviews, four with patients and four with pharmacists, were conducted and audio recorded in the UK. A topic guide was used when the interviews were conducted. The topic guide for the interviews with the pharmacists was based on the eNPT framework. The interviews with the patients lasted between 9 minutes and 32 minutes (mean 20 minutes) and the interviews with the pharmacists lasted between 20 minutes and 31 minutes (mean 23 minutes). The interviews were audiotaped and transcribed verbatim. The transcriptions of the interviews were supplied to the Netherlands.

Data analyses

Quantitative data

Quantitative data are presented using descriptive statistics.

Qualitative data

Consultations

The revised Observing Patients Involvement (OPTION) 12 item instrument was used in this study for the assessment of shared decision making in the audio-recorded consultations

(16). This scale consists of 12 items and there are 5 score options, range 0-4, with 0 = "the behaviour is not observed", 4 = "the behaviour is observed and executed to a high standard" (16). The scale has been developed to rate the extent of shared decision making for health decisions. The OPTION 12 scale was chosen because it represents a complete communication procedure focused on shared decision making. Moreover, the OPTION 12 scale is the most commonly used observer scale to assess shared decision making and it has been described as a reliable and validated instrument in literature (16, 17, 18,). Two researchers (MvdK, MG) rated the consultations individually. Additional notes could be made. Subsequently the OPTION 12 scales filled in by the researchers were compared and in case of disagreement discussed until consensus was reached. The OPTION 12 scale is presented in table 2.

In addition, a self-composed checklist was used to rate the content of the consultations. This checklist consists of 5 items. The score options are "yes" and "no". The items are based on the discussion points named in the instruction manual provided to the community pharmacies and are presented in table 3. The discussion points were predetermined by the researchers as points that should be discussed during the consults. The checklists were filled in by the researchers separately. Additional notes could be made outside the checklist as well and the separately filled in checklists were also compared with each other and in case of disagreement discussed until consensus was reached.

Thereafter, the consultations were assessed to gain insight about the fidelity (whether the intervention was delivered as intended) and the dose delivered (quantity of intervention delivered).

Interviews

The transcripts of the interviews with the pharmacists and patients were manually coded by the two researchers (MvdK, MG) separately. The differences in coding were discussed until consensus was reached. After that, the codes were transferred to the software program MAXQDA 2020. Next the codes were grouped into categories. During a final check some minor adaptations to the codes were made, and a couple of codes were merged. The process of coding was inductive.

Coded sections of the interviews were used to assess the fidelity, dose and reach of the intervention. Subsequently coded sections of the interviews with the pharmacists were used to gain insight into the constructs of eNPT. For an overview of the components of both frameworks, including which kind of codes were linked to which components, see table 1.

Table 1 Framework process evaluation with components of the MRC process evaluation framework of complex interventions and eNPT. *The table shows an example of the kind of codes used to gain insight into the components of the frameworks*

Theory	Component	Description	Codes related to
The MRC process evaluation framework of complex interventions	Fidelity	Was the intervention delivered as intended?	E.g. shared decision making, provision of information, problems with intervention

	Dose delivered	Quantity of the personal intervention program delivered	E.g. problems with intervention
	Dose received	Quantity of personal intervention program received The engagement of participants with the intervention	E.g. effort, reason for participating,
	Reach	Whether the intended audiences come in contact with the intervention and how	E.g. way of contact, patient suitability, selection process
Extended Normalisation Process Theory	Potential	Commitment of pharmacist to deliver the intervention in the right way Change valence and change efficacy	E.g. effectiveness, usefulness, impact
	Capability	Workability and experiences of pharmacists with the intervention	E.g. time investment, workload, larger scale, opinions
	Capacity	Structure into which the intervention will be implemented and changes that are needed in the working processes	E.g. points of improvement, future of the intervention, co-operation, communication with GP
	Contribution	Distribution of tasks Comprehension of the intervention and the role in delivering it	E.g. role of pharmacist, responsibility, activities

Results

Consultations

Six transcribed consultations (four from the Dutch branch and two from the UK branch) of pharmacists with patients and one summary of a consultation performed in the UK were included in this study.

The patients (N = 7) had the following demographics: five male patients and two female patients. Their ages range between 57 and 74 years old (mean 68 years old).

OPTION scores

The summary of the consultation was excluded from the OPTION scores, because it contained insufficient information to fill out the OPTION 12 scale.

The overall OPTION score ranged from 15 to 22, with a mean total score of 19.5 (SD= 2.74; maximum total score 48). None of the items of the scale for any of the consultations were scored as 4, the maximum score option, or scored as 2.

Four items were scored the same over all consultations, namely items 2, 3, 4 and 10. The behaviour described by item 2 ('The clinician states that there is more than one way to deal with the identified problem ('equipoise')') and 4 ('The clinician lists 'options', which can include the choice of 'no action'') were noticed in all the consultations to a good standard (score 3) and these items had the highest mean scores. The behaviour described by item 3 ('The clinician assesses the patient's preferred approach to receiving information to assist decision making') and 10 ('The clinician elicits the patient's preferred level of involvement in decision making') was scored 0, thus the lowest mean score, in all the consultations, meaning the behaviour was not observed at all. An overview of the mean scores per item are presented in table 2.

Table 2: OPTION scores. *Score range 0-4: 0 = "the behaviour is not observed", 4 = "the behaviour is observed and executed to a high standard" (16)*

#	OPTION ITEM	MEAN (SD)
1	The clinician draws attention to an identified problem as one that requires a decision-making process	2.50 (1.22)
2	The clinician states that there is more than one way to deal with the identified problem ('equipoise')	3.00 (0.00)
3	The clinician assesses the patient's preferred approach to receiving information to assist decision making	0.00 (0.00)
4	The clinician lists 'options', which can include the choice of 'no action'	3.00 (0.00)
5	The clinician explains the pros and cons of options to the patient (taking 'no action' is an option)	0.67 (0.52)
6	The clinician explores the patient's expectations (or ideas) about how the problem(s) are to be managed	0.83 (0.41)
7	The clinician explores the patient's concerns (fears) about how problem(s) are to be managed	2.00 (1.10)
8	The clinician checks that the patient has understood the information	2.33 (1.03)
9	The clinician offers the patient explicit opportunities to ask questions during the decision-making process	0.67 (1.21)
10	The clinician elicits the patient's preferred level of involvement in decision making	0.00 (0.00)
11	The clinician indicates the need for a decision-making (or deferring) stage	2.67 (0.82)
12	The clinician indicates the need to review the decision (or deferment)	1.83 (1.33)
	Mean	1.63 (1.13)

The consultations conducted in the UK scored lower, respectively 15 points and 18 points, than the consultations conducted in the Netherlands, respectively 22, 21, 22 and 19 points, on the OPTION 12 scale.

The researchers had a high amount of disagreement in OPTION scores. They disagreed on 31 of 72 items (12 items x 6 consultations), an agreement of 56.9%, however consensus was reached easily.

Checklist scores

Three consultations (two from the Dutch branch and one from the UK branch) scored "yes" on all the options. The other three consultations scored "no" on item 2 ('The pharmacist discusses the purpose of the consultation with the patient.') and one of these consultations also scored "no" on item 3 ('The pharmacist discusses the answers of the Adapted QBS questionnaire with the patient.'). The percentages of the individual items scored "yes" can be seen in table 3. The summary of the consultation conducted in the UK did not contain enough information to fill out the complete checklist, but items 2, 3 and 4 were scored "yes" with the information at hand. The results from the summary were excluded from table 3.

Table 3: Self-composed checklist scores. *Percentage of the individual items scored "yes"*

Item	**Percentage scored "yes" (out of six)**
The pharmacist uses Castor during the consultation.	100%
The pharmacist discusses the purpose of the consultation with the patient.	50%
The pharmacist discusses the answers of the Adapted QBS questionnaire with the patient.	83%
The pharmacist discusses the interventions the patients qualifies for.	100%
The pharmacist discusses with the patient which interventions the patient wants to use.	100%

As can be derived from the results of the self-composed checklist, most of the items described in the study protocol were discussed during the consultations. The personalised interventions were offered to the patients, which were done so as a result of the completed Adapted QBS questionnaire.

The researchers reached a higher amount of agreement with the checklist in comparison with the OPTION 12 scale. They scored the consultations the same for 18 of the 25 items (5 consultations x 5 items), an agreement of 72.0%.

Interviews

The coding of the interviews was discussed between the researchers. They agreed largely on which parts of the interview needed coding, however the labels of the coding sometimes differed, mostly in choice of words. After discussion between the researchers, consensus was reached for the labels.

The interviewee were four pharmacists and four patients. Three of the pharmacists are female, one is male. The time they have been working in their current role ranges from 1 to 13 years. The patients are all male and their ages range between 65 and 74 years old (mean 70 years old).

Fidelity

The personalised interventions were discussed with the patients during the consultations. This contributes to the fidelity. However, as is clear from the results from the OPTION 12 scale but also from the interviews with patients, the quality of the shared decision-making process varies.

"yes it was ok because she's got quite a friendly voice and um she's just checking everything's ok and I'm doing all right and what my opinion is so it's not a problem" – Patient, male, 65 years old

"oh right she probably talked me into it um I just assumed it was all part of this research … so that's probably why I agreed to it"…"I didn't say no I don't want that but I'll do this no I said um yes I'm willing to have a go at anything if it helps research" - Patient, male, 73 years old

The first patient clearly states the pharmacist asked his opinion, which implies that there was room for shared decision making. The second patient however feels like he was talked into it, which implies that in his case it was not a shared decision-making process. That is not in line with the INTENSE study protocol which clearly states that the consultations should contain a shared decision-making process. However, the fact that the patient says he said yes to everything to help the research, might mean a decent shared decision-making process was in fact conducted.

The provision of information lacked in some parts, for example it was not clear for a patient that he could not reply to the brief messages. The provision of information about Minddistrict was not complete either, because one patient did not know it was a program to support people with low mood.

"yes in my opinion I wasn't quite aware of that side [the online application being related to low mood/mood] much" – Patient, male, 65 years old

The information provided influenced the expectation the patient had with the program.

"but I was surprised because I didn't realise it [Minddistrict] was going to go into my mood depression and relaxation I thought it was just about taking tablets I take and if I get any side effects that I don't think I was told about the mood and relaxation part which seems to be quite an important part of the survey" – Patient, male, 65 years old

Thus, the information provision for the personalised interventions was not optimal.

Minddistrict was discussed in more detail during the interviews, because there were some problems with the digital aspect of the program. Examples of these problems include the computer shutting down and problems with logging in into the program. The computer shutting down is however not a problem of Minddistrict itself. The logging in problems settled down after the patient figured out how the program worked.

"once it [Minddistrict] got going it was ok but when it started I seemed to have a lot of emails all in one go and that did confuse me um I don't know if that was a mistake or how it

was meant to be um but after I did the first one I realised how it was going to work and I adapted to the routine so it was once it was started I was ok" – Patient, male, 65 years old

So, the problems with Minddistrict did not seem to have affected the fidelity.

Dose

The interventions introduced to the patients during the consultations influenced the dose delivered positively. However, as described earlier, one patient was not able to take part in Minddistrict, because of problems with his computer. This influenced the dose received by the patient negatively.

One patient received every intervention module he was offered, which is described in the Fidelity section. Another patient only received Minddistrict, this was the only module discussed in the interview. This influenced the dose received by the patient positively.

One interviewee did not receive any of the personalised interventions.

"And if I understand correctly, you're not receiving any additional interventions? Because you're fully adherent to your medications? Is that correct?" – Researcher

"That's correct yes." – Patient, male, 68 years old

This patient also talks about the fact that he is fully adherent to his medication. More about the suitability of the patients for the intervention program can be read in the Reach section.

Most patients wanted to have the medication review. Three patients from the consultations conducted in the Netherlands got a medication review right after the consultation and the other one made an appointment for it during the consultation. The medication review was mentioned by a patient as the most helpful intervention module.
As described earlier one patient took part in all the interventions he was offered because he wanted to help the research. This was a reason for more patients to participate in the study. Their willingness to help research or the healthcare system had a positive influence on the engagement patients had with the study.

"Then I thought, well, I might as well help if it helps people to understand about medications, diabetes, high blood pressure. Let's give it a go. Basically." – Patient, male, 68 years old

Aside from the engagement with intervention program as a whole, the engagement with Minddistrict was also good. Although some patients got bored with the content of the program, they were committed to finish it, because they thought it might help someone.

"I think I guess halfway through I wondered why am I doing this [Minddistrict] and then but I persevered you know … I persevered because I thought well it may be helping someone at the end of the day" – Patient, male, 73 years old

The patients were positive about using the supporting programmes in the future.

"What do you think about using these supporting programmes in the future?" – Researcher

"*Um as I say I think they're probably a good idea"* – Patient, male, 73

Reach

The patients in the UK were approached for the research through a letter sent to them by the GP. They felt like that was a good approach, because they know the GP and if the letter would come from INTENSE, they would not trust it.
In the UK the GP was in charge of the recruitment of non-adherent patients. One pharmacist however was not positive about the fact that the recruitment was conducted by the GP.

"Well, this is where I think the study went massively behind. Because it was, the way it was written was it had to be the GP surgery that recruited the patients? And that's where it fell down." – Pharmacist, male, 1 year in current role

There were multiple problems with the selection process in the UK. One pharmacy was not able to continue with the study, because it took too much time to improve the search to identify suitable patients. Another issue was the actual recruitment of suitable patients. The pharmacists and the patients both felt that the right patients were not selected for the study. The pharmacists thought the patients selected for the study were adherent with their medication or they at least thought other patients, who were not selected, needed more support than the ones selected for the study. The patients felt like they were adherent with their medication and didn't need support with adherence.

"the patients that I think was recruited to us actually were quite compliant with their own medications" – Pharmacist, female, 10 years in current role

"I don't know whether I'm the sort of person they want to do this survey because although I have diabetes 2 I keep it under control I don't have a lot of health issues I don't have hypo's" – Patient, male, 65 years old

Potential

The pharmacists were enthusiastic about the effects the intervention program could bring the patient. They felt like it could really make a difference in supporting the patients with their non-adherence, but also make a difference for the pharmacy.

"making the pharmacist being more vigilant um we've like how the patient is taking the things and how it's affecting them so it's taking the pharmacy to the front so in this sense I think it's really positive for the patient and for the pharmacy" – Pharmacist, female, 13 year in current role

They were also enthusiastic about the module Minddistrict, as they felt it might change the mindset of the patients.
They recognized the effect brief messages could have on patients, however, there was concern about the brief messages being sustainable for a long period of time.

"I'm not really sure what impact brief messages that's great on a day-to-day basis but is that something that can continue long-term I'm not sure um" - Pharmacist, female, 10 years in current role.

Capability

As can be read earlier, the pharmacists were definitely engaged with taking part in the study and using the intervention program. However, there are components of the intervention program that need improvement. One pharmacist felt the study was not completely ready to use.

"I think it probably would have been easier if it was a more sort of established study and model." – Pharmacist, female, 11 years in current role

Another pharmacist felt the study set-up was not good.

"I think the study wasn't set up to fail. But the process kind of put it in a bad situation, that it was always going to struggle." – Pharmacist, male, 1 year in current role

These statements were connected to the problems with the selection procedure, which were described earlier.
The problems with the selection of patients was even the reason one pharmacy could not start with the intervention program, because they never came further than the selection.

Apart from the selection problems of the study, time also has had an influence on the workability of the intervention program. The intervention program is a tailored personalised intervention and it takes time to perform the intervention. This time might not be available in community pharmacies, as they already have a lot of work and not enough time.

"So you don't really have the time or the inclination to go looking for more work." – Pharmacist, female, 11 years in current role

The pharmacists have ideas to improve the workability of the intervention. Most of these ideas are associated with the problems with the selection process. One pharmacist mentions it's important to figure out the recruitment process first. This is the first step for a good execution of the intervention program.

As previously mentioned, the pharmacists were mostly positive about the intervention modules. Although there was concern about the interventions being digital, because the target population for the intervention program is predominantly of older age and they might have problems with the fact that the intervention modules are mostly online.

"…they have got probably an old age or they are not as skills as probably we are with online things" – Pharmacist, female, 13 years in current role

The pharmacists do however think the intervention program can, with a few changes, be used on a larger scale in the future.

"so about using in the future routine delivery by the pharmacy and using it by patients and for it to be delivered to a large number of patients um do you think that would be possible" – Researcher

"yes why not yes" – Pharmacist, female, 10 years in current role

Capacity

The effectiveness of the intervention is linked to the co-operation of the GP and the pharmacy, because they both play an important role in the selection of suitable patients. The collaboration between the GP and the pharmacy is something that goes well in some practices, but not in others.

One pharmacist was for example not satisfied with the work of the GP in relation to the recruitment of patients:

"even if the surgery did do a good job, and I don't think they did" – Pharmacist, male, 1 year in current role

Another pharmacist is positive about the contact between the pharmacy and the GP.

"in our case we have got a very very intimate relationship with the doctors" – Pharmacist, female, 13 years in current role

This pharmacist however mentions that the relationship her pharmacy has with the GP is unique and most pharmacies do not have a close relationship with the GP. That has a negative effect on their co-operation.

Communication and co-operation between the GP and the pharmacy is thus something where there is room for improvement, as the pharmacist believes it will beneficial.

"if all the pharmacists had the same relationship with the GP's [as we do] that would be incredible for the patient and that would be incredible for the GP's to" – Pharmacist, female, 13 years in current role

Contribution

The GP was in charge of the recruitment of patients and as described earlier this was not something that went smoothly. One pharmacist mentioned that it would have been helpful to have a meeting with the GP and the pharmacy team to discuss who would commit to what part of the intervention setup. Another pharmacist felt it should have been the task of the pharmacy, because they would be more committed to recruit patients. He also thought of easy ways to contact the patients, for example with a note included with their medication.

"I would 100% would have put the pharmacy in charge of recruitment" – Pharmacist, male, 1 year in current role

The pharmacists also didn't exactly know the activities the medical team fulfils in improving the medication adherence of patients. They are not aware of the activities of the GP.

"to be fair I'm not I don't really know how they work" – Pharmacist, female, 13 years in current role

The pharmacists also didn't know how the GP could help with supporting patients with adherence as the workload is high for the GP too.

"I'm not sure how they could help cos they're overrun to be honest so I'm not sure" – Pharmacist, female, 10 years in current role

One pharmacist mentioned that outside of this study, generally the GP does not actively search for non-adherent patients. She believes it's something the pharmacy identifies.

The role of the pharmacy's employees in supporting non-adherent patients is limited. The involvement asked of them is to notify the patients that the pharmacists want to have a talk with them. The talk itself and the clinical part of the job falls under the responsibility of the pharmacists. Having the time to give attention to individual patients is however an important factor. If there was more time, that could make a difference in supporting the patients.

"I think it's really taking the time to sit and make that your focus and priority for a patient will help bring forward you know, to bring to the surface [problems with medication]" – Pharmacist, female, 11 years in current role

Furthermore, the pharmacists believe the identification of the non-adherent patients should be a joint responsibility between the pharmacy's team and the GP's team.

"I think it's a shared responsibility between the patient and their carers." – Pharmacist, female, 11 years in current role

An overview of the facilitators and barriers is presented in table 4.

Table 4 An overview of facilitators and barriers

Facilitators for participating in the study	Patients wanting to help with research
	Contacting patients through an institution they are familiar with
Facilitators for implementation	Pharmacists and patients being enthusiastic about the effects the intervention program can bring
	Productive co-operation between the GP and the pharmacy
Barriers for implementation	Minddistrict being a digital program and thus being vulnerable for problems with the technique
	Problems with the selection process
	Recruitment of eligible patients is difficult
	Workload and available time in the community pharmacy

	The readiness for use of the study
	Unproductive co-operation between the GP and the pharmacy

Discussion

In this thesis the consultations between pharmacists and patients and the interviews with the pharmacists and the patients, together with the quantitative data were used to conduct a process evaluation. The process evaluation used the key elements of the MRC process evaluation framework of complex interventions framework and the constructs of the eNPT framework to gain insight into the facilitators and barriers for the implementation of the intervention program.

Most of the important discussion points were covered during the consultations, which ensures that the fidelity of the consultations is decent. However, the purpose of the consultation should have been discussed more extensively in some cases. Some consultations barely touched on the purpose of the consultation and only briefly explained what they were going to do during the consultation.

The shared decision-making process is an important part of the intervention program and should be clearly recognizable in the consultations. The checklist scores show that shared decision-making process indeed was conducted during the consultations, which positively influences the fidelity. However, the quality of the shared decision making was not consistent over the six consultations, as reflected by the OPTION scores. A possible explanation for this is that the trainings for the pharmacists related to the INTENSE program did not contain an element about shared decision making. For some pharmacists the shared decision-making process might therefore not have been a priority. Moreover, not all pharmacists have the same skills and some pharmacists might be better in communication than others. Another reason for the fluctuating quality of shared decision-making process might be the different durations of the consultations. Namely, previous research has found that the time of a consultation is related to the quality of shared decision making (19). This might also explain why the consultations conducted in the UK were found to have a shared decision-making process with a lower quality than the consultations conducted in the Netherlands, as the duration of the consultations conducted in the UK was shorter.

Introducing the personalised interventions to the patients contributes to the dose of the intervention delivered. This however does not mean the dose has also been received. There were some problems with Minddistrict related to the fact that it's an online module. A digital module is vulnerable because of computer or internet problems. These are the exact problems that occurred when patients wanted to use Minddistrict. Computer problems are not an issue of the intervention program itself, but it did influence the dose received by patients negatively. Namely, one patient couldn't use Minddistrict, because his computer crashed.

The engagement with the study was good. An important reason for the patients to participate in the study, but also to continue with the study, was to contribute to research. This has been proven before to be an important reason to participate in studies (20). However, when the intervention program is implemented, the reason to participate in the study, namely to help with research, will not contribute to engagement with the intervention, because it is not performed within research anymore. Then the engagement

with the intervention program might decrease. Therefore, it is important to try to convince non-adherent patients that the intervention program could really have a positive impact on their health. That might help to convince people to engage with the intervention program.

The medication review was received by most patients. One patient thought it was the module that was most helpful. That's not surprising, as research has shown it can improve adherence, positively impact the appropriateness of prescribing and it even potentially reduces emergency department visits (21). Besides, the medication review is an intervention were the pharmacists are really involved in their patients' health and that is beneficial for patients' outcome (22).

The personal aspect is also appreciated by the patients when it comes to communication between pharmacist, GP and patient. For this study, the patients were contacted with a letter by their own GP. This was something the patients appreciated, because they are familiar with the GP. They said that if they were contacted by the research team, they might not have participated as they would not have trusted the letter. So, for patients it is important the letter comes from an institution they are familiar with.
The pharmacists were however not positive about the fact the GP was in charge of recruitment, with one pharmacist in particular. He felt like the GP did not work hard enough to find and recruit eligible patients.
Another problem with the recruitment was the fact that the selected patients were mostly adherent with their medication. This was mentioned by the patients themselves, but also by the pharmacists. Apparently, it was hard to find patients who were eligible for the intervention program. This is a problem that has occurred in other intervention programs supporting adherence as well (20).
It might be more effective to use another method for the recruitment of suitable patients in future research. Another method could for example be to contact all T2DM patients, ask them to fill out a questionnaire and if they want to be contacted for research, and select patients from that group. That way there might be a larger inclusion.

Apart from the selection process, the pharmacists were positive about the intervention program. They felt like it could really make a difference in the lives of the patients, but also in the day to day live in the community pharmacies. They were enthusiastic about Minddistrict as well, as they believed a change in the mindset of patients could be reached because of the intervention module. Pharmacists being enthusiastic about the intervention program is an important facilitator for implementation, because then they might be more inclined to spend time on implementing the intervention.

Another barrier however is the time available in the community pharmacies. The pharmacists mentioned a personalised intervention program might be too time consuming on top of the already high workload. This affects the workability of the intervention negatively. A high workload and a lack of time is a known problem in community pharmacies (23).

Furthermore, in some practices the co-operation between the GP and the pharmacy is a barrier. As can be concluded from the interviews, most pharmacies have a co-operation with the GP that is not productive, for example because the communication between the GP and

pharmacies is predominantly one sided. This can be a barrier for the implementation of the intervention program.

However, some practices have good co-operation and communication, and this has a positive effect on the implementation of new intervention, because if there is trust in each other's capability to perform activities, the workload can be shared. In that case the co-operation is a facilitator for implementation.
The importance of the co-operation relates mostly to the recruitment of eligible patients. Namely, as mentioned by pharmacists, the responsibility for identifying non-adherent patients should be shared between the patient and their health care workers. Since the GP and the pharmacy are involved in the prescription chain, the responsibility to identify non-adherent patients and to support these patients should be for both the pharmacy and the GP. The patients of course have their own responsibility too, because it is their health. However, it might be difficult for patients to ask for help or to admit their non-adherence, because they might feel ashamed about it. This is something that could be deduced from the interviews and consultations. Patients not wanting to admit to non-adherence might be a reason why it was difficult to recruit non-adherent patients for the study, as they might not want to partake in a study focussed on supporting non-adherent patients.

Strengths and Limitations
A strength of this study is the use of the MRC process evaluation framework of complex interventions and eNPT frameworks to gain insight into the facilitators and barriers of implementation. The use of a framework for process evaluations is recommended in literature (24).
Another strength was the fact that the consultations were audio recorded. This gave insight in the content of the consultations, which was important information to measure the fidelity. The absence of audio tapes from the consultations was named as a limitation in another study (20).

A limitation of the research was that score 2 "The clinician asks the patient about their preferred way of receiving information to assist decision" from the OPTION 12 scale was not selected once, because the researchers did not think the score option was suitable. They felt it was more of an OPTION 12 scale item then a score option. This influenced the scores.
Another limitation was that the first item of the self-composed checklist, "The pharmacist uses Castor during the consultation." was hard to score because it was not always clear from audio/transcript.
Moreover, all the interviewed patients were male. This might have affected the results.
Another limitation is that there were only interviews from the UK branch available, what caused that we currently do not have experiences from the Netherlands. It would be interesting to see if a problem with the recruitment of suitable patients occurred in the Netherlands as well, because the way of recruitment in the Netherlands differed from the UK.

Conclusion
The content of the consultations was predominantly in line with the instruction manual. The quality of the shared decision-making process during the consultations varied between the consultations.

This process evaluation gave insight into the facilitators and barriers for implementation of the INTENSE intervention program. Facilitators for being able to conduct the research include the fact that patients want to help with research and contacting the patients for the intervention program by an institution the patients are familiar with.
A facilitator for implementation is the fact that pharmacists believe the intervention can make a positive difference in supporting patients with non-adherence. Barriers include the already high workload in community pharmacies, the digital aspect of Minddistrict, and the recruitment of suitable patients. The identification of eligible patients turned out to be the most important barrier for implementation and was mentioned by both pharmacists and patients.
The co-operation between the GP and the pharmacy can be a facilitator and a barrier, depending on to what extent the co-operation is productive.
The overall conception is however that the intervention really could make a difference in the daily life of the community pharmacy and the daily life of patients if suitable patients can be recruited.

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