Patient Information Sheet for participation in medical- scientific research

Pancreatic head removal (Whipple) via (robotic-)keyhole or open surgery (DIPLOMA-2)

Official title: Minimally invasive versus open pancreatoduodenectomy for pancreatic and periampullary tumors (DIPLOMA-2)

Introduction

Dear Sir/Madam,

With this information letter we would like to ask you if you would like to participate in medical scientific research. Participation is voluntary. You are receiving this letter because you will soon be undergoing a Whipple operation (medical term: pancreatoduodenectomy/pancreatic head resection). You will read about what kind of research it involves, what it means for you, and what the benefits and drawbacks are. It is a lot of information. Would you like to read through the information and decide if you want to participate? If you want to participate, please fill out the form found in Appendix C.

Ask your questions

You can make your decision with the information you find in this information letter. In addition, we encourage you to:

- Ask questions of the researcher giving you this information.
- Talk to your partner, family or friends about this study.
- Ask questions of the independent experts, P.J. Tanis / Antonino Spinelli.

1. General information

288 subjects from 8 European countries will participate in this study. This study was set up by the Amsterdam UMC, in collaboration with the Poliambulanza Foundation hospital in Brescia, Italy. The medical ethics review committee of the Amsterdam UMC, location AMC and Poliambulanza Foundation hospital have approved this study. General information about the review of research can again be found in the brochure 'Medical scientific research'.

2. Purpose of the study

Your doctor has advised you to undergo the so-called Whipple surgery. The most common reasons for having this operation are tumors or cysts (also called "fluid bladders") in the head of the pancreas, in the duodenum or in the bile ducts. Usually, this (gastric sparing) Whipple surgery was performed by open surgery. Open" in this case means that an incision of about 15-25 cm is made in your abdomen through which the surgeon can access the affected organs. During Whipple surgery, the surgeon removes the duodenum, pancreatic duct, gallbladder and part of the bile ducts. After these tissues are removed, new connections are made between the intestines, stomach, pancreas and bile ducts. Whipple surgery is a major operation and therefore people are always looking for ways to improve it. For some years now, there has also been the possibility of performing the Whipple operation via keyhole surgery (using the operating robot). Surgeons in your hospital are already trained and experienced in this operation, but no studies have ever been done to find out whether this method is actually better than the traditional open operation. Therefore, we would like to compare these two methods in a scientific study. After keyhole surgery, patients often recover faster and are hospitalized for a shorter period of time.

3. Why this study?

The DIPLOMA-2 study investigates in patients undergoing Whipple surgery whether they recover faster after keyhole surgery than after open surgery, and whether there are an equal number of complications after keyhole surgery compared to open surgery.

Usually, Whipple surgery is performed via open surgery. Nowadays, with the development of new techniques, it is also possible to perform this operation through keyhole surgery (using the operating robot). However, it is not yet clear which operation is better, which is why we would like to investigate. In the DIPLOMA-2 study we try to show that keyhole surgery, compared to open surgery, leads to a faster recovery after surgery, without more complications. A possible disadvantage of the (robotic) keyhole surgery may be that the surgery itself may take longer because it may be technically more difficult for the surgeon to remove the tumor or cyst with keyhole surgery. Also, the cost of the surgery may be higher.

4. What participating means

How long does the study last?

Are you participating in the study? The DIPLOMA-2 study consists of a short-term study (6 months) and a long-term study (up to 3 years after surgery).

Step 1: Are you suitable to take part in the study?

We first want to know if you are suitable to participate. Therefore, the investigator will do a number of tests:

- Physical examination: your weight and height will be measured to determine your 'Body mass index (BMI)'. If this number is higher than 35, you cannot participate in the study.
- Imaging examination. A CT scan has already been (or will be) done to see if the abnormality in the pancreas has not grown into the surrounding blood vessels or if there are any metastases. If this is the case, you cannot participate in the study.

Step 2: The operation

For this study, we make 2 groups:

- Group 1 (66% of the participants). The people in this group will have the keyhole surgery.
- Group 2 (33% of the participants). People in this group will have the open surgery.

Lottery determines your operation. You will not be told before surgery whether you will have (robotic) keyhole surgery or open surgery, and after surgery a large bandage will be placed on your abdomen to ensure that you cannot see which operation you have had. Once you have recovered sufficiently (about the 5th day after surgery) from the surgery, the doctor will tell you which type of surgery you had and the bandage will be removed. In both groups, you will undergo Whipple surgery and the exact same tissue will be removed. The differences between the surgeries are explained below.

<u>Group 1: the Whipple via (robotic) keyhole surgery.</u>

The patients in this group will be operated through keyhole surgery. This keyhole surgery is performed under general anesthesia and carbon dioxide (gas) will be used to inflate the abdomen, as in all keyhole surgeries. There will be 5 to 6 small incisions in your abdominal wall during this surgery. Through each incision, the surgeon inserts a tube into the abdomen that connects to a controllable robot. Through a camera in one of the tubes, the surgeon can see what is happening in the abdomen. So in this operation, the surgeon and assistants must look at a screen to remove the duodenum, part of the pancreas and part of the bile ducts through a small incision. The surgeon performs this operation by using the steerable robotic arms and where he is assisted by a second surgeon who operates various special instruments outside the abdomen with his hands.

<u>Group 2: the Whipple via open surgery.</u>

Patients in this group will be operated on via open surgery. This involves making a 15-20 cm incision in the abdominal wall, just below the rib arch or in the middle of the abdominal wall, under general anesthesia. Through this opening, the surgeon can remove the duodenum, part of the pancreas and part of the bile ducts and make the new connections.

NB: In every keyhole surgery (group 1), there is a small change (<10%) that due to unexpected circumstances, the surgeon has to decide that the surgery can only be performed or finished via open surgery. In this case, the surgery will be performed according to group 2.

Step 3: examinations and measurements

Before the examination, you will have the usual tests:

- Imaging studies: CT scan, scheduled before surgery.

If you are participating in the study, we will do the following additional examinations:

- (Online) questionnaires.

Before surgery, you will be given a questionnaire. The questions are about your quality of life. During your hospitalization you will be asked to write down how much pain you have once a day. After surgery, we will send you an online questionnaire 5 times (after 2 weeks, after 3 months and after 6 months, and then after 1 and 3 years). The questions will also cover your recovery and quality of life. It will take you about 30 minutes to complete these questionnaires. If desired, this questionnaire can also be completed on paper, and returned via mail.

- Fitbit™ sports watch

Before the operation you will receive a Fitbit™ sports watch. We ask you to wear it immediately (at least 2 weeks) before surgery, until 3 months after surgery. In the meantime, you may only take off the sports watch for recharging (1x per week, preferably at night). The screen will be shielded during this period. You can keep the Fitbit™ watch afterwards, you don't have to return it.

Step 4: aftercare

What is different from regular care?

There is not much different in this study than in regular care. The checkups and examinations that are part of this study will be no different or more frequent than you would get if you were not participating in the study.

5. What is expected of you?

In order for the examination to go well, it is important that you keep the following appointments:

- You will not also be participating in any other medical scientific research during this study.
- You will wear the Fitbit™ sports watch in the manner explained to you by the researcher.
- You will complete the (online) questionnaires. If you prefer a paper version, return it by mail.
- You come to each appointment.
- You will contact the researcher in these situations:

- You are admitted to or treated in a hospital.
- You suddenly experience problems with your health.
- You no longer wish to participate in the study.
- Your phone number, address, or e-mail address changes.

Can you be pregnant during the study?

Women who are pregnant cannot participate in this study.

Pregnant?

Will you become pregnant during the study? Please let the researcher know right away. In consultation with the medical examiner, you should stop the study as soon as possible.

What assessments will be done in the study, different to the normal treatment?

If you decide to participate in this study, you will be asked to record how much pain you have once a day during your hospitalization. After your discharge from hospital you will also be asked to complete an (online) questionnaire 5 times. This questionnaire is about your recovery and quality of life after surgery and takes about 30 minutes each time to complete. Preferably, it can be completed on paper, and returned by mail.

Before surgery:

You will be asked to complete an (online) questionnaire about your functioning and quality of life (approximately 30 minutes). You will be given a Fitbit™ watch that performs various measurements that are important for the study. We therefore ask you to wear the watch immediately, up to 3 months after surgery, and to take it off only for recharging (1x per week). The screen will be shielded during this period. You may keep the Fitbit™ watch afterwards, you do not have to return it.

During hospitalization:

You will be asked daily to indicate how much pain you are in (about 1 minute each time)

2 weeks, 3 and 36 months after surgery:

You will receive an (online) questionnaire about your quality of life (about 20 minutes each time).

6 months after surgery:

You will receive an (online) questionnaire about treatment after surgery, hospitalizations and body image after surgery. (approx. 20 minutes)

The total time burden for participation in the study is thus approx. 2-2.5 hours.

6. Possible side effect or complications

As with any abdominal surgery, there is a risk of hitting organs or tissues in the abdomen. However, these are the same in both ways of Whipple surgery: the (robotic) keyhole surgery or the open surgery are therefore associated with the same risks. The surgeon will discuss these with you. If you have any questions about this, you can always contact the researcher, your doctor or the independent physician. You can find the contact information at the end of this form.

7. Possible advantages and disadvantages?

The possible advantages of the (robotic) keyhole surgery are the smaller surgical wound and faster recovery. The possible advantage of the open surgery is that this procedure is standard, has already been performed many times and is easier to perform. A possible disadvantage of the open surgery is that this procedure is often accompanied by more blood loss than the keyhole surgery. Another disadvantage of open surgery is the larger surgical wound with a potentially higher risk of scar rupture and adhesions. The results of this have been extensively studied scientifically.

If you do not want to participate, or if you want to stop participating in the study

The decision to participate in the study is yours. Participation is voluntary. If you do not want to take part, you will be treated for your pancreatic cancer in the usual way, using standard, open Whipple surgery and there will be no consequences for the doctor-patient relationship. If you do participate, you can always change your mind and stop, even during the study. You will then be treated as usual and there will be no consequences for the doctor-patient relationship. You do not have to explain why you are stopping. We do ask you to report this to the researcher immediately. The data collected up to that point will be used for the study. If there is new information about the new study that is important to you, the investigator will let you know. You will then be asked if you want to continue participating.

8. End of the study

The researcher will let you know if there is new information about the study that is important to you. The researcher will then ask you if you want to continue participating.

In these situations, the study stops for you:

- All the studies according to the schedule are over and all the questionnaires have been completed at the times previously mentioned
- The end of the whole study has been reached.
- You want to stop the study yourself. This is possible at any time. Report this immediately to the researcher. You do not have to tell the researcher why you are stopping. You will then receive the usual treatment, namely open Whipple surgery without the keyhole surgery. The medical examiner will still invite you for a follow-up check-up.

- The medical examiner thinks it would be better for you to stop. The investigator will still invite you for a follow-up check.
- One of the following authorities decides that the research should be stopped:
  - The Amsterdam UMC / Fondazione Poliambulanza Brescia
  - The government or
  - The medical-ethical committee that evaluates the research.

What happens if you stop with the study?

The researchers use the data collected up to the moment of stopping.

The entire study ends when all participants are finished.

9. What happens after the study has finished?

Will you receive the results of the study?

Once the study is over, the results of the study will be analyzed and incorporated into a scientific article. This scientific article will be submitted for publication to one of the medical journals, so that surgeons worldwide will be aware of the outcome of this study. If you wish, we can inform you about this personally.

10. Use and storage of your personal data

Are you participating in the study? Then you also give permission to collect, use and store your data. Each test subject will be given a code that will match with the data. Your name and other personal data will be omitted.

What data do we keep?

We keep these data:

- your name
- Your gender
- your address
- your date of birth
- data about your health
- (medical) data we collect during the study

Data collected by the Fitbit™ Activity Tracker:

- Number of steps taken per day
- Distance covered per day
- Measurements of intensity of activity

- Minutes of rest per day
- Heart rate

Why do we collect, use and store your data?

We collect, use and store your data to answer the questions in this study. And to publish the results.

How do we protect your privacy?

To protect your privacy, we code your data. On all your data, we put only this code. The key to the code stays with the researcher. When we process your, we always use only that code. Even in reports and publications about the research, no one can retrieve that it was about you.

To access your Fitbit data, you will be asked to authorize a third party, FitabaseServices, owned and operated by Small Steps Labs LLC, via an online form. Fitabase is a research platform that collects data from Fitbit™ Activity trackers for study purposes. Principal Investigators will authorize Fitabase to collect and store your Fitbit data, and connect Fitabase to your Fitbit account. This account will use your identical code and will not contain any personally identifiable information. This is done to collect you information for the study of your physical activity after surgery. When the study has completed, all your data will be deleted from Fitabase.

Who can see your data?

Some people do have the ability to see your name and other personal information without a code. These are people who check that the researchers are conducting the study properly and reliably. These individuals can access your data:

- Members of the committee that monitors the safety of the research.
- An auditor who works for the researcher.
- National and international supervisory authorities. For example, the Health Care Inspectorate.

These people will keep your data confidential. We ask you to give us permission to see them.

How long will we keep your data?

Research data will be kept for a period of 15 years after completion of the research.

May we use your data for other research?

Your data may also be of interest to other scientific research in the field of pancreatic surgery after this study has ended. For this purpose, your data will be kept for 15 years. In the consent form you can

indicate whether this is okay with you. You do not give permission? Then you can still participate in this research. You will receive the same care.

What happens in case of unexpected findings?

During the study, we may happen to find something that is important to your health or the health of your family members. The researcher will then contact your family doctor. You will then discuss with your family doctor what should happen. You give your consent with the form to inform your general practitioner or specialist.

Can you withdraw your permission for the use of your data?

You can withdraw your permission for the use of your data at any time. However, please note: if you withdraw your consent and researchers have already collected data for a study, they may still use these data. If so, they may still use this data.

Where can you find more information about the study?

You can find more information about the study on the following website(s). www.ClinicalTrials.gov and/or www.clinicaltrialsregister.eu.

11. Compensations or costs for participating

There are no additional costs or fees associated with this study for you.

12. Insurance for Study Subjects

Your hospital has insurance covering damage caused by the regular provided care. This insurance also covers damage caused by the research, since it contains non-experimental treatments.

13. We inform your family doctor

The researcher will send your primary care physician a letter to let them know you are participating in the study. This is for your own safety, for example to ask about your medical history or the medicines you are taking.

14. Questions?

Please direct questions about the study to the research team. Would you like advice from someone who has no interest in it? Then go to the independent doctor, P.J. Tanis or A. Spinelli. He knows a lot about the research, but does not cooperate with this research.

Do you have a complaint? Discuss it with the researcher or the doctor treating you. Would you rather not? Then go to the Complaints Committee your local hospital.

15. How do you consent to the study?

You can first think about the research at your leisure. Then you can tell the researcher if you understand the information and whether or not you want to participate. Do you want to participate? If so, fill out the consent form that accompanies this information letter. You and the researcher will both receive a signed version of this consent form.

Thank you for your time.

Attachments to this information

A. Contact information
B. Schedule research actions
C. Informed consent form
D. <<< center specific insurance information and complaints committee >>>

Attachment A: contact information

Research team

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<<< local coordinator details >>>>

Independent doctors

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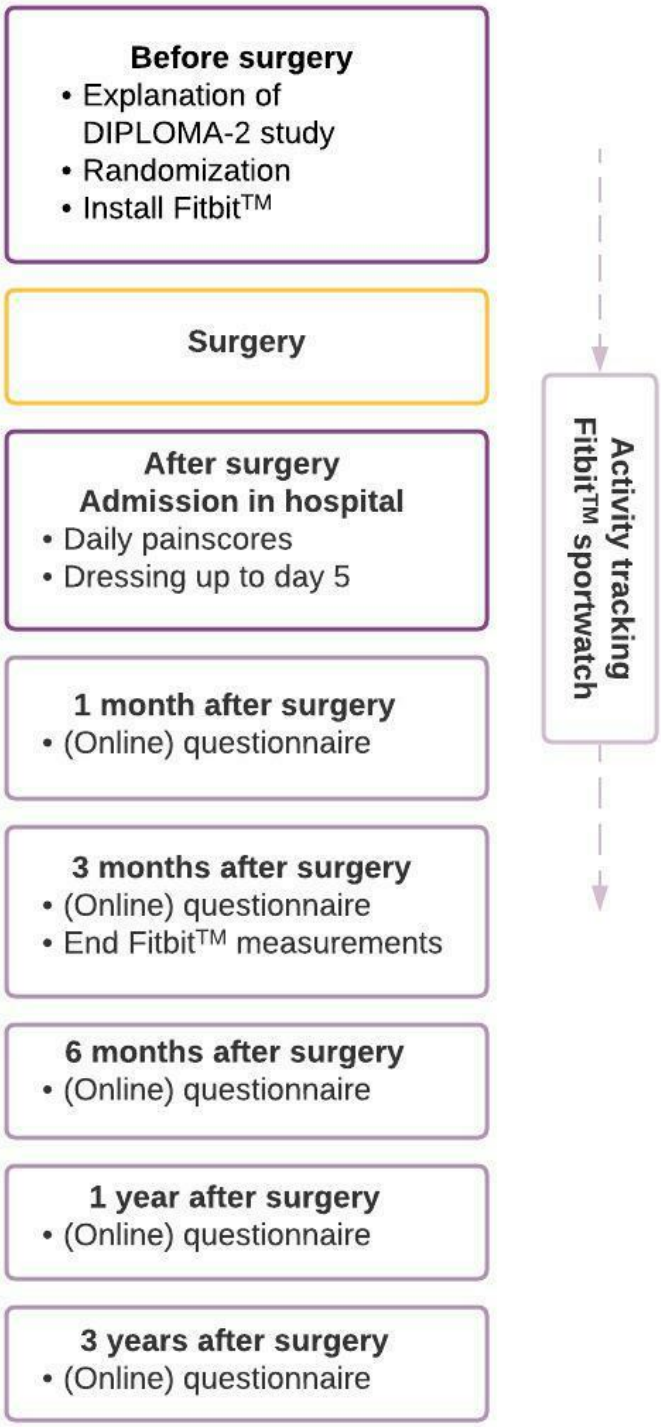
Attachment B: Schedule research actions



Attachment C: Informed Consent Form – for patient

Pancreatic head removal (Whipple) by (robot-)keyhole or open surgery (DIPLOMA-2)

- I read the information letter. I was also able to ask questions. My questions were answered well enough. I had enough time to decide whether to participate.
- I know that participation is voluntary. I also know that I can decide at any time not to participate in the study after all. Or to stop. I do not have to say why I want to stop.
- I give the researcher permission to let my primary care physician know that I am participating in this study.
- I give the researcher permission to give my GP or specialist information about unexpected findings from the study that are important to my health.
- I give the researchers permission to collect and use my data. The researchers will do this only to answer the research question of this study.
- I know that for the purposes of monitoring the study, some people will be able to see all of my data. Those people are listed in this information letter. I give these people permission to see my data for this audit.
- I give permission for my data to be kept at the research site for 15 years after this study.

I agree to wear a Fitbit sports watch during the study period and know that Google in the U.S. may be able to use the encrypted data for commercial purposes, outside of European privacy rules. I give permission to use my Fitbit data to be stored in the Fitabase data collection system.	Yes ☐	No☐
I give permission to keep my data to use it for other research, as stated in the information letter.	Yes ☐	No☐
I give permission to approach me again for a follow-up study, after the study.	Yes ☐	No☐

- I wish to participate in this study.
-

Subject's Name:

Signature: Date : __ / __ / __

I certify that I have fully informed this subject about the aforementioned study.

If any information becomes known during the study that could affect the subject's consent, I will inform him/her in a timely manner.

Name of investigator (or his/her representative):

Signature: Date: __ / __ / __

Additional information was given by (if applicable):

Name:

Position:

Signature: Date: __ / __ / __

The subject will receive a complete information letter along with a signed version of the consent form.