

OPEN

Establishing and Coordinating a Nationwide Multidisciplinary Study Group: Lessons Learned by the Dutch Pancreatic Cancer Group

ESTABLISHING A MULTICENTER STUDY GROUP

The DPCG is a nationwide collaboration of surgeons, clinicians from other medical specialties, researchers, nurses, and patient associations involved in pancreatic and periampullary cancers and neoplastic cysts. All 16 hospitals performing pancreatic surgery and several hospitals providing non-surgical care for pancreatic cancer patients in the Netherlands participate. The DPCG was founded with the aim to improve care and survival for patients with pancreatic cancer and built on previous experiences of the Dutch Pancreatitis Study Group.

The first prerequisite is a group of experts who are willing to collaborate within a culture of commitment and mutual trust. All should strongly feel that more will be achieved by collaboration than by competition. Willingness to compromise and take turns in the lead of projects are essential. The board of the study group should facilitate this by showing the right example and arranging transparent regulations supporting the group rather than the individual. Deciding on a group name and logo, soon to be followed by a house style for PowerPoint presentations and a basic website early in the process may seem trivial but are important to promote the “group feeling.” Funding the start-up of such an initiative may be difficult but is essential. The DPCG board approached possible sponsors (industry and patient organizations) to compile a small starting budget. During the first years, a small budget per year was sufficient.

BUILDING A MULTICENTER STUDY GROUP

The three main “platforms” within the DPCG are the plenary study group, and the scientific committee, and the board (Fig. 1). During the four plenary study group meetings per year, new proposals for prospective clinical studies (including randomized trials), and progress of ongoing studies are discussed. Hence, commitment and input from all parties are enhanced. Moreover, new developments in pancreatic cancer from conferences and literature, and the outcome of the surgical and other audits are discussed.

The scientific committee consists of 25 representatives from different specialties, a legal advisor, a clinical epidemiologist and a representative from the patient association. This committee meets four times per year to evaluate research proposals for the use of data from the clinical registries, biobank, and completed trials^{1,2}; advises on scientific activities, including the yearly reporting of the mandatory surgical audit; and assesses research grant applications which are submitted on behalf of the DPCG.

Researchers interested in using data from the registries, biobank, and trials can download a protocol template with instructions from the DPCG-website (www.dpcg.nl) and send the request to the DPCG-coordinator who disperses it before the scientific committee meeting. Subsequently, the researcher is invited to briefly explain his/her proposal at the meeting and take part in the discussion. The proposal may either be approved (with adjustments) or rejected, mostly with the option to resubmit. The aim of the scientific meeting is to promote high-quality research and prevent overlapping initiatives, rather than function as a judgmental organ.

The DPCG board consists of representatives from surgery, medical oncology, gastroenterology, radiotherapy, and the patient association. In their 4-monthly meetings, the board, supported by a PhD-student and the “DPCG-coordinator” (ie, a dedicated research nurse), discusses general issues, governmental and political topics, and finances. All PhD-students involved in the DPCG also meet once per year informally to enhance collaboration. They keep close contacts with each other to exchange ideas and experiences, and establish efficient logistics and workflow across centers.

The daily management, which includes social media, a website, and a 3-monthly newsletter, is done by the DPCG-coordinator together with PhD-students, supervised by the scientific committee and DPCG board. Funding for specific research projects and clinical trials is obtained via regular funding parties; the DPCG functions as a platform, but does not provide funding by itself. DPCG specific activities, such as the salary of the DPCG-coordinator, are mainly funded through donations of patients and their relatives.

DEVELOPMENT OF MULTICENTER STUDIES

Since its establishment in 2011, the DPCG has initiated several multicenter randomized trials, of which 4 have been completed (PREOPANC-1, LEOPARD-1 and -2, and CPR).³⁻⁵ Currently, 4 multicenter randomized trials are ongoing; PELICAN (NTR5517), PREOPANC-2 (NTR7292), PORSCH (NCT03400280), and PACAP-1 (NCT03513705). A study is listed as a “DPCG study” when at least three DPCG centers participate but mostly the vast majority of centers participate.

Besides multicenter randomized controlled trials, several nationwide prospective data registries exist which collaborate under the umbrella of the Dutch Pancreatic Cancer Project (PACAP, www.pacap.nl).¹ PACAP was established in 2013 with funding from

Researchers are increasingly interested in joining forces in multicenter, multidisciplinary study groups as a means to conduct high-quality research, including large randomized trials and prospective cohorts with the aim to improve the quality of care. In the Netherlands, clinical care and research in pancreatic diseases are well-organized within the nationwide Dutch Pancreatitis Study Group and, since 2011, the Dutch Pancreatic Cancer Group (DPCG). The Netherlands has some inherent benefits for multicenter collaboration, including a small and densely populated country (17 million inhabitants), full-time PhD-students working for 3–4 years in clinical research before applying for a residency position, and a healthcare system that pays per diagnosis rather than per intervention allowing for comparisons between procedures/strategies. Aside from this specific situation in the Netherlands, we feel that the presented model of nationwide study groups is also applicable to other regions and countries.

No clear guidance exists on how to establish a multidisciplinary study group. In recent years, several members of our group have been asked to share their experiences during (inter-)national meetings. To provide a framework for those interested in multicenter collaboration, we herewith outline the establishment and coordination of the nationwide DPCG, and many of our lessons learned over the past eight years.

O.R.B. and M.G.B. shared senior authorship. Funding was provided by the Dutch Cancer Society [grant number UVA2013-5842]. The authors report no conflicts of interest. Submission category: Surgical perspectives. This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal. Copyright © 2020 The Author(s). Published by Wolters Kluwer Health, Inc. ISSN: 0003-4932/20/27104-e102 DOI: 10.1097/SLA.0000000000003779

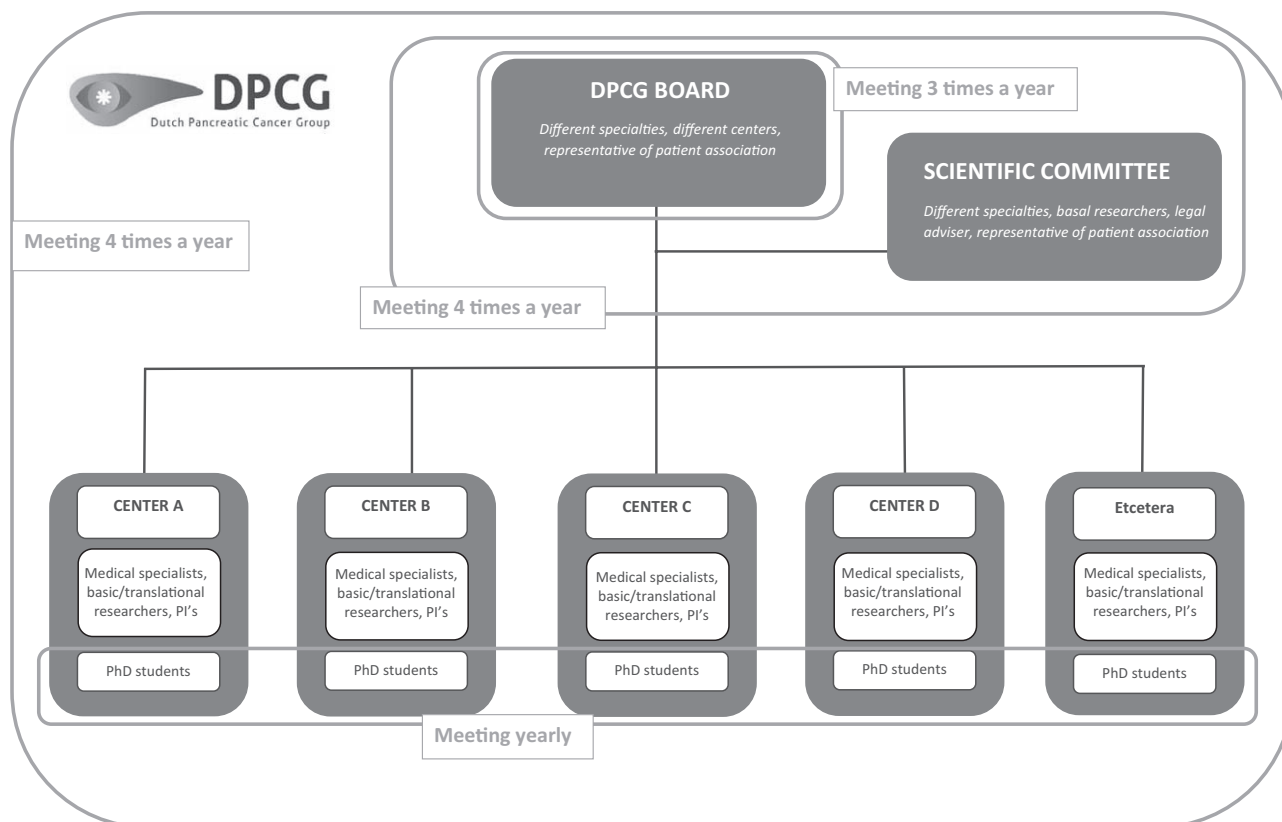


FIGURE 1. Organizational structure of the Dutch Pancreatic Cancer Group.

the Dutch Cancer Society (KWF) and contains clinical data, patient-reported outcomes and biomaterials. Clinical data are collected within the Netherlands Cancer Registry and the Dutch Pancreatic Cancer Audit (DPCA), a mandatory audit in which nearly 150 variables are collected per pancreatic resection.⁶ Patient-reported outcomes are collected from patients with pancreatic or periampullary carcinoma from almost 50 centers. Biomaterials from resection specimens are collected in the Dutch Pancreas Biobank (www.pancreasparel.nl) in collaboration with the Parelsnoer Institute which provides the infrastructure, logistics, and a legal/ethical framework for nationwide biobanking.²

When designing multicenter studies, the first and foremost advice is to actively involve all specialties, researchers of several centers, and patient advocates in an early stage. This in contrast to the situation where a small (often monocenter/monodisciplinary) group designs a trial and convinces other centers and specialties to participate in “their” trial. The board and scientific committee stimulate trials for each disease stage (ie, resectable, locally advanced, metastatic cancer), and aim to prevent competing trials

although this may occur, especially in case of small phase I/II trials of innovative therapies.

AUTHORSHIPS

In many collaborative groups, authorship is a recurring topic. To maximize transparency, authorship regulations are specified in detail in each DPCG study protocol, under the premise that the International Committee of Medical Journal Editors guidelines are leading.⁷ Authors are identified from each participating center already during the design phase of the protocol to allow for broad discussion and input. Naturally, all authors are also required to deliver input during the study and during the stage of analyses and writing of the manuscript. When a potential author would not meet the International Committee of Medical Journal Editors criteria, he/she is listed as a collaborator. The senior authorship position(s) are reserved for the principal investigator(s). First authorship(s) are usually for the PhD student(s) who was/were responsible for daily management, data collection and the first draft of the manuscript. The other authorships are for the researchers from the different participating centers and often based on the number of contributed samples/patients (eg, 0–50 patients 1 authorship, 50–100

patients 2 authorships, etc); these authors are usually listed in alphabetical order.

DIFFICULTIES AND MISTAKES

Over the years we experienced a lot of difficulties and clearly made several mistakes. Also within our group, competition between centers has been an issue. We feel that there is no simple solution. To prevent discussions on authorships, we define authorship positions in great detail in the study protocol, before the actual start of a study. Also, to prevent discussions on positions in boards and committee; regular rotations of board and committee positions (and predefined periods) helps to overcome these issues. Also, a culture in which these kind of feelings (eg, a center feels disadvantaged) can openly be discussed eventually improves collaboration.

Funding is one of the most important ongoing problems. The principal investigator of each DPCG study is responsible for obtaining sufficient funding through regular channels. Because of the collaboration and steady results over the years, the DPCG as a group has become more interesting for funding parties. Moreover, because of the already established logistics, we aim to perform trials

more efficiently (and less costly) using the “trials within cohorts” design in the PACAP cohort and “registry-based randomized trials” within the DPCA.⁸ We hope that these developments will secure our position to perform clinically relevant randomized trials in years to come.

AMBASSADOR'S ROLE

Apart from scientific activities, a nationwide study group will automatically receive an “ambassador's role” and become involved in education. For instance during the introduction of new (surgical) techniques a centrally coordinated initiative for safe implementation could have a strong effect on quality control. As an example, the DPCG initiated the LAELAPS projects for safe implementation of laparoscopic and robotic pancreatic surgery.^{9,10} The DPCG also plays a central role in overseeing several aspects of clinical care. For example, after the LEOPARD-2 trial questions were raised about the safety of laparoscopic pancreatoduodenectomy, after which all DPCG surgeons decided to stop performing these procedures in the Netherlands. The DPCG facilitates and participates in the development of nationwide guidelines on pancreatic cancer and coordinates a nationwide expert panel. The DPCG also (co-)organizes several scientific and social activities, and functions as a point of contact for those interested in organizing pancreatic cancer-related activities in (collaboration with) the Netherlands.

THE FUTURE

For the future, advanced trial logistics and sustaining financial support are probably the most relevant challenges. To face these challenges, the DPCG is working with novel trial designs; multiple parallel “trials within cohorts” in the PACAP cohort,^{1,8} “registry-based randomized trials” within the DPCA, and “stepped-wedge” trials for implementation of new standards of care. Additionally, it may soon be impossible to run multicenter trials in a single country because of the growing required sample sizes (less incremental yield due to continuously improving outcomes). This development may drive further international collaboration between multicenter study groups. For example, the DPCG endorses the European Consortium on Minimally Invasive Pancreatic Surgery (www.e-mips.com) which is running

the DIPLOMA trial (ISRCTN44897265), and has joined forces with the German StuDoQ registry on pancreatic surgery. These types of collaborations are likely to provide a further quality impulse in the coming years and are welcomed by the DPCG.

Marin Strijker, MD✉

Tara M. Mackay, MD

Department of Surgery, Cancer Center Amsterdam, Amsterdam UMC, University of Amsterdam, Netherlands
✉m.strijker@amsterdamumc.nl

Bert A. Bonsing, MD, PhD

Department of Surgery, Leiden University Medical Center, Leiden, Netherlands

Marco J. Bruno, MD, PhD

Department Gastroenterology and Hepatology, Erasmus MC, Rotterdam, Netherlands

Casper H. J. van Eijck, MD, PhD

Department of Surgery, Erasmus MC, Rotterdam, Netherlands

Ignace H. J. T. de Hingh, MD, PhD

Department of Surgery, Catharina Hospital, Eindhoven, Netherlands

Bas Groot Koerkamp, MD, PhD

Department of Surgery, Erasmus MC, Rotterdam, Netherlands

Hanneke W. van Laarhoven, MD, PhD

Department of Medical Oncology, Cancer Center Amsterdam, Amsterdam UMC, University of Amsterdam, Netherlands

I. Quintus Molenaar, MD, PhD

Hjalmar C. van Santvoort, MD, PhD
Department of Surgery, Regional Academic Cancer Center Utrecht, UMC Utrecht Cancer Center and St Antonius Hospital, Utrecht, Netherlands

Geertjan van Tienhoven, MD, PhD

Department of Radiotherapy, Cancer Center Amsterdam, Amsterdam UMC, University of Amsterdam, Netherlands

Johanna W. Wilmink, MD, PhD

Department of Medical Oncology, Cancer Center Amsterdam, Amsterdam UMC, University of Amsterdam, Netherlands

Sako Zeverijn, MBA

Living With Hope Foundation,
Utrecht, Netherlands

Olivier R. Busch, MD, PhD

Marc G. Besselink, MD, PhD✉

Department of Surgery,

Cancer Center Amsterdam,

Amsterdam UMC,

University of Amsterdam, Netherlands

✉m.g.besselink@amsterdamumc.nl

on behalf of the Dutch Pancreatic Cancer Group

REFERENCES

1. Coebergh van den Braak RRJ, van Rijssen LB, van Kleef JJ, et al. Nationwide comprehensive gastro-intestinal cancer cohorts: the 3P initiative. *Acta Oncol.* 2018;57:195–202.
2. Strijker M, Gerritsen A, van Hilst J, et al. The Dutch pancreas biobank within the Parelstoer Institute: a nationwide biobank of pancreatic and periampullary diseases. *Pancreas.* 2018;47:495–501.
3. Versteijne E, van Eijck CH, Punt CJ, et al. Pre-operative radiochemotherapy versus immediate surgery for resectable and borderline resectable pancreatic cancer (PREOPANC trial): study protocol for a multicentre randomized controlled trial. *Trials.* 2016;17:127.
4. de Rooij T, van Hilst J, van Santvoort H, et al. Minimally invasive versus open distal pancreatectomy (LEOPARD): a multicenter patient-blinded randomized controlled trial. *Ann Surg.* 2019;269:2–9.
5. van Hilst J, de Rooij T, Bosscha K, et al. Laparoscopic versus open pancreatoduodenectomy for pancreatic or periampullary tumours (LEOPARD-2): a multicentre, patient-blinded, randomised controlled phase 2/3 trial. *Lancet Gastroenterol Hepatol.* 2019;4:199–207.
6. van Rijssen LB, Koerkamp BG, Zwart MJ, et al. Nationwide prospective audit of pancreatic surgery: design, accuracy, and outcomes of the Dutch Pancreatic Cancer Audit. *HPB (Oxford).* 2017;19:919–926.
7. International Committee of Medical Journal Editors (ICMJE). Defining the Role of Authors and Contributors. Available at: <http://www.icmje.org/recommendations/browse/roles-and-responsibilities/defining-the-role-of-authors-and-contributors.html>. Accessed July 23rd, 2019.
8. Gal R, Monninkhof EM, van Gils CH, et al. The Trials within Cohorts design faced methodological advantages and disadvantages in the exercise oncology setting. *J Clin Epidemiol.* 2019;113:137–146.
9. de Rooij T, van Hilst J, Boerma D, et al. Impact of a nationwide training program in minimally invasive distal pancreatectomy (LAELAPS). *Ann Surg.* 2016;264:754–762.
10. de Rooij T, van Hilst J, Topal B, et al. Outcomes of a multicenter training program in laparoscopic pancreatoduodenectomy (LAELAPS-2). *Ann Surg.* 2019;269:344–350.