



JOIN SCIENCE TO HAVE A SIGNIFICANT IMPACT ON HEALTHCARE

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Interview

Each year, approximately 200 PhD students from Radboudumc defend their PhD thesis and obtain the honorary title of “dr.”, resulting in them finally being able to call themselves “Doctor of Philosophy”. A PhD is a unique academic title that proves that the holder of this title has successfully participated in advanced academic work. It is a good method to distinguish oneself, as it is attempted by comparatively few students after graduation. Moreover, it is a good opportunity to have a significant impact on healthcare, as the holders of this title in the medical sciences have performed work which greatly aids the understanding of human disease and health. Thus, it is no surprise that performing research in the career of the young doctor is becoming more of a rite of passage than an exception.

Philosophiae Doctor

PhD is the Latin abbreviation of “Philosophiae Doctor”. It is an advanced postgraduate degree involving three or more years of independent research on an original topic. A PhD is carried out with the support from one or more expert academic supervisors; the promotor being the principal supervisor. The end result is a thesis that offers a significant original contribution to knowledge leading to innovative implementations or lays down a basis for further research. Often, a PhD-position is obtained by applying for an open position, or internal via previous internships or connections. Here in Nijmegen, it is also possible to compete for a position in a unique way, namely via the PhD research proposal competition. This competition was brought to life by the Radboud University and Radboud university medical center in 2009. It offers master students the possibility of designing their own PhD, which is a unique opportunity in the sense that the students have the chance to devise and write their own PhD research project, in collaboration with a department of the Radboud university medical center. Students who win the competition receive a grant which is sufficient to carry out their self-written project for the next three or four years. Currently, each year, five to six students can start their own PhD project. But what does doing a PhD entail? Editors of RAMS interviewed three winners of the PhD competition from previous years, Thijs Landman (2017), Daan Viering (2018) and Jeroen Slaats (2016), to find out how they value performing a PhD and how they perceived their road to their self-written PhD-research.

Choosing a field of interest

It can be difficult to decide in which department and research topic you would like to do a PhD in but knowing the fields that interest you can help. During his bachelor’s, Thijs Landman participated in the disciplinary honours programme. In the context of this programme, he performed some small-scale research at different institutes, such as the Donders Institute and the Radboud Institute for Molecular Life Sciences (RIMLS). Eventually, he performed research in the field of Physiology on ischemic conditioning for six months as part of his master’s research internship. Halfway through his master’s programme, a former mentor contacted him, asking whether he wanted to participate in the PhD-competition as his previous experience would make him a suitable candidate. Thijs took an interest in this and chose to further pioneer the field of ischemic conditioning, but this time combining it with the newer insights in its use in cerebrovascular accidents (CVAs). With the help of his current promotor, he produced a research proposal. In 2016 Thijs got selected and since December 2017 he has been receiving funding for his research. “Without this course of events, I would not be doing a PhD right now”.

He continues to explain the importance of engaging in research early on in your studies. “Preferably start in your bachelor’s, because of time management.” Also, early experience gives you an advantage in getting a PhD because the regular medical curriculum does not allow for obtaining much experience by itself.

Daan Viering’s previously performed research on the genetic causes of hypomagnesemia was in the context of the disciplinary honours programme he performed at the Department for Physiology and partially in London. At first, he doubted whether he wanted to continue within magnesium research or work on another subject. Now, he chose a subject within physiology which is more directly applicable to more patients than his previous research. Starting this year, Daan will study the role of mitochondrial biogenesis in the pathophysiology of hypertension. “This subject will definitely keep me interested for three to four years: we are still far from unravelling the cause of essential hypertension.” Daan is drawn to fundamental research because he feels like more boundaries can be pushed when you are still at the beginning of the research. This first part can be the base for many diagnostic or therapeutic strategies in the future. Next to a fundamental research aspect, it was important for him, being a future doctor, to incorporate a clinical aspect in his research proposal as well. “It is of great importance to me to eventually get to the relevance of the research for your patient.” Last but not least, the positive working atmosphere Daan experienced at the departments before were of great importance for choosing this field of research. “My supervisor was willing to check my work in the evening hours, this was a great help for me!”

Jeroen Slaats wanted to participate in the competition with the same lab he did his internship with but on a slightly different topic. “The research topic I am working on now is not the same as when I did my internship here. During my internship, I got to know the research topics of my colleagues and I quickly decided that one of those was the one I wanted to continue in. “To participate in the competition, you need a professor from a research group willing to supervise you during the competition and your PhD, which supports your project and ideas. “At a certain moment, I went to my professor and told him I wanted to participate and which research topic I wanted to explore. Fortunately, my professor was enthusiastic as well and together we participated in the competition. Participating is not something you do alone, you do it together with your supervisor who will help you with writing the proposal.”

Current limitations

Thijs was in doubt whether he wanted to do a PhD as he chose to study medicine to become a clinician, not a researcher. Four years of research seemed like a pretty long period. Looking back, he was largely motivated to complete a PhD to gain an advantage when applying for future jobs, which he admittedly says is not the most valid reason to start a PhD. Later, while writing the proposal, he found himself enjoying the process way more than he had previously expected. Reading the scientific literature on his topic, Thijs found himself becoming a lot more enthusiastic. Now he also realises that it is a path of personal development. Furthermore, he now acknowledges that you are still young when you finish your master's. Therefore, gradually becoming a clinician by first expanding your knowledge of research can be beneficial. Thijs humbly explains: "I do not think I will become a better doctor per se, but I can become the type of doctor I want to be: critical of the research underlying medical guidelines."

Daan's interest in research was raised early in his studies. In his second year of Medicine, he already performed his first research internship. "I have known that I wanted to do a PhD project for years." Daan really enjoys taking the time to dig and dive into a topic. Discovering new things and experimenting is something he wants to do besides his beloved patient communication. "I am curious by nature and want to find out the mechanism behind a disease. Within a PhD trajectory, I can really get to the bottom of this." Daan first heard of the PhD competition from an acquaintance when he was waiting to start his masters. In March 2017 he discussed the idea to apply for the competition with the supervisor of his previous internship, Jeroen de Baaij. The first deadline for a concept proposal was in September. When you get selected to further develop your proposal, you get approximately 1,5 months to write a full research proposal. "I started too late, which resulted in a race against the clock," Daan laughingly admits. At the time, Daan was also busy with his clinical internships, so he was designated to his weekends and evenings to meet the deadline. In the last week, there was a major setback, "The design for the clinical part of the study was considered unsuitable by an expert". Therefore, Daan and his supervisor had to think quickly for a new method and apply rigorous changes to the study design. "The end result was much better, therefore this was totally worth the hours of sleep I missed. These unforeseen scenarios are part of scientific research."

Jeroen's primary motivation to do research is not to help patients. "Of course, being able to help patients with your research is something you want to achieve, but curiosity and the ambition to investigate certain questions is my primary motivation. That you want to know how something works. It is important to be enthusiastic about problems and wanting to solve them. For me, that is what truly motivates me. I can become very enthusiastic by discovering new things and solving the puzzle." He already noticed this during his first internship in his bachelors, which is why he chose the research master Molecular Mechanisms of Disease, here at Radboud University. As part of his master's studies, Jeroen had already written several research proposals.

The obstacles to doing a PhD

"At some moments it might be a little dull," Thijs admits. It will take some time before the trial starts and most of the preparations are already done. Meanwhile, he is expanding his knowledge by studying more literature, but he would rather start putting it into practice. "It is also about keeping a daily routine to stay mentally fit, so that I will be ready when the trial starts." Besides studying literature, there are still some e-mails to be sent concerning preparations and sending those can be a bit frustrating. "It can take days before I get a reply to my e-mails. Luckily, the professor forwards important e-mails and not surprisingly he gets a reply the next day!" Most importantly, Thijs mentions that it is important to be very critical about

whether your research topic is interesting to you. "Otherwise, four years can be a very long time."

"I like living in Nijmegen, so I do not mind being bound to the Radboud university medical center. However, when you do not want to stay in Nijmegen this could be an obstacle for entering the PhD competition," Daan says. However, the PhD competition is obviously not the only way to obtain a PhD position. You can find a PhD programme that fits you when you are willing to spend enough time and energy in it. Secondly, Daan mentions that by doing a PhD within the format of the PhD competition, you have to start with your PhD traject within a certain period of time. The downside to this is that you postpone your development towards becoming a medical doctor.

When asked which parts of his PhD he enjoys less, Jeroen answered kiddingly: "There are only enjoyable things about doing a PhD." After a few seconds of silence, he concedes. "Doing research can be very frustrating." He explained that often expectations will not be realised, results are disappointing, and many experiments do not work out. "As a researcher, you need unjustified optimism. Even if twenty things go wrong or you are behind schedule, you still need to think: "If I try it this way, it will work". He reveals that currently, after his first year of his PhD, he is already behind schedule. However, Jeroen did not seem distraught or anxious about this. "That is PhD-life," he shrugged. "Eventually it will work out." These negative aspects disappear once a discovery is made. "When you finally discover great or unexpected findings, it boosts your motivation enormously," he said enthusiastically. "Champagne will be flowing and none of the disappointments and frustrations will matter anymore."

The perks of doing a PhD

"It all takes a lot of work, but you are the one putting your knowledge and literature searches into practice, that makes it a lot of fun!" Thijs also believes that, after a study in medicine, there is still a lot more to learn about statistics and methodology. Additionally, Thijs looks forward to attending interesting conferences or to link a business trip to his research. "It is not only about the PhD itself, having a PhD creates new possibilities and further develops your personality." Moreover, after receiving the title, it could be easier to combine his job as a clinician with research, working in an academic hospital and to teach at a university.

The PhD competition is a wonderful opportunity to fund your PhD-trajectory. Daan thinks the advantage of bringing in the money yourself is the freedom you get in coming up with your own research question and design. Because of his research experience, Daan is already noticing that it is easier for him to critically read scientific articles than for students without this experience. His former position in RAMS also contributed to the improvement of this skill. As mentioned earlier, Daan stresses that performing a PhD gives you the opportunity to delve into a topic.

Doing a PhD most likely means that now and then you will spend evenings and weekends working. However, despite the irregular working hours, Jeroen considers his work as a hobby and regards the irregularity as an advantage. "You can decide for yourself how you want to spend your time, it is very flexible," he said cheerfully. "As long as you finish your work and show progress, nobody cares what time you start or finish the day, or if you work from home. Admittedly, not everyone works as much outside the regular working hours, but I do not mind working during weekends." Jeroen's impatience to get the results of his experiments are often the reason he spends evenings or weekends working. Aside from the flexibility, Jeroen enjoys other activities that accompany doing a PhD, like attending workshops to improve, for instance, his writing skills. "During a PhD, you do not just learn to do research. You learn to communicate and to present. What I also enjoy is being critical towards research of yourself

and others." Besides acquiring experience in writing research proposals, at the start of the PhD-trajectory, you are up-to-date with the literature in the field and familiar with the project.

The road ahead

Thijs anticipated his PhD to be a lot of work right away but for now, life is pretty laid back as he is waiting for the trial to start; the calm before the storm so to say. "At the beginning, the trial will be a lot of "hands-on" work for everything to go as planned, such as the inclusion of patients and pressuring the cuffs". Later on, Thijs can use the electronic health records to gather the information needed from roughly 200 patients. He can then focus on smaller scale research projects, such as the autoregulation of perfusion in the brain. Eventually, he would like to work at the Emergency Department as a dedicated doctor and boost research in this field of work because in the Netherlands it is relatively new specialisation.

Halfway November 2018, Daan will officially start with his PhD. However, preparations such as applying for the ethics committee to be allowed to work with animals and obtain patient samples will keep him tied up for a while. "What does my future look like careerwise?" Daan wonders. "Well, in the short term I hope that part of my PhD-trajectory will take place abroad and in the long term I am hoping to become a physician in Internal Medicine."

Jeroen is not sure yet what he wants to do after his PhD. "Maybe you can tell me?" he said jokingly. We suggest a postdoc. "Perhaps I will be a permadoc, a permanent postdoc." In the academic world, it is not common to be a permanent postdoc. However, apart from becoming a postdoc after a PhD, there are numerous alternatives. "The advantage of doing a PhD is that you learn so much that it does not limit you to a future career in the academic world. It is possible to do research as part of a company, or apply for a job in marketing." As Jeroen still – or only – has three years to go before he finishes his PhD, he has plenty of time to trouble his head about it.



Jeroen Slaats

More than two years ago, Jeroen, former student Molecular Mechanisms of Disease, decided to compete in the PhD proposal competition and subsequently was one of the winners. Now, Jeroen is a PhD student at the Department of Cell Biology at the Radboud Institute for Molecular Life Sciences. He investigates how cancer cells mislead the immune system in different parts of a tumour in order to prevent immune recognition

and killing of these cancer cells. Jeroen uses various microscopy techniques to visualize these processes. Even though he started approximately a year ago with his PhD and receives a salary each month, he admits he still feels like a student, saying: "It is called being a PhD student for a reason."



Thijs Landman

Being fresh out of medical school, Thijs Landman is about to start his clinical trial on remote ischemic postconditioning in patients with an ischemic cerebrovascular accident (CVA) at the Department of Physiology. The technique of ischemic conditioning, first described in 1986, boils down to exposing tissue to short periods of hypoxia,

which results in a smaller sized infarction when an actual ischemic event takes place. This can be pre-conditioning when it is performed before the ischemic event, or post-conditioning when done afterwards. Right now, "remote" ischemic conditioning is being tested in a major trial in Cardiology. "Remote" means that hypoxia will not be induced locally, but in a distant tissue, usually by inflating a cuff around the upper arm (just like when you are taking someone's blood pressure). Small-scale research suggests that it might also reduce ischemia after a CVA. Thijs is going to test this in a clinical trial. The hypothesis is that the remote postconditioning produces a systemic anti-inflammatory response. This in turn, reduces the penumbra, an area of ischemic but still viable brain tissue, around the actual infarction. Hopefully, this very patient-friendly intervention will reduce the size of the definite infarction size.



Daan Viering

Daan will start his research on hypertension at the Department of Physiology half November 2018, after finishing his clinical internships. Hypertension has a high prevalence within the population. For most of the people with hypertension there is no identifiable cause found for their high blood pressure, which is labelled as essential hypertension. There is

evidence pointing towards a role for the mitochondria in causing essential hypertension. In his PhD project, Daan hopes to clarify the role of mitochondrial biogenesis in the pathophysiology of hypertension. This may lead towards innovative prevention and treatment strategies. Daan's research includes *in vitro* studies, *in vivo* experiments in mice and clinical experiments on humans.

Small overview of the competition

1. The first step in participating in this competition is finding a topic you would like to do research on for four years. Once you have found a research group and professor willing to guide you during the process, you start writing a pre-proposal. This pre-proposal comprises of your CV and a summary of your project proposal. The emphasis is laid on your CV, which should convince the jury of your abilities and motivation and show that you are a suitable candidate.

2. From all students that submitted a pre-proposal, approximately 10 will be allowed to proceed to the next round, in which you have to write the full research proposal. The time to write the full research proposal is limited and involves frequent meetings with your supervisor.

3. All students that write a full proposal will need to defend it in front of a jury. In 5 minutes, you need to explain the content and relevance of your proposal, after which questions will be asked. Hereafter, five to six winners will be announced that will receive a grant.

Checklist

- Perform research earlier in your studies, for example as part of the honours programme.
- Write an article, for example a short review, for RAMS to get familiar with the reviewing process.
- Contact a department and brainstorm together.
- Start writing your research proposal early enough.
- Identify your field of interest and make sure to choose a subject of research that will keep you interested for several years.
- Your topic should provide for at least 4 publications.

EXAM QUESTIONS

As RAMS aims to enlighten both students and professionals, we would like to present you two exam questions. Find out if you can remember what you have learned during your bachelors!

We challenge you!

Question 1

An alpinist resides at high altitude for several weeks and is, therefore, able to deliver better sports performances. This difference can be attributed to a change in his erythroid progenitor cells. What is this change?

- A. Dysplasia
- B. Hyperplasia
- C. Hypertrophy
- D. Metaplasia

(Topic: Farmatocology, Module Q6 Movement and Flow 2017)

Question 2

A 70-year-old patient has a slow ventricular rhythm. The ECG exhibits normal QRS-complexes but with no connection to the P-wave. Apparently, there is a total AV block with a narrow ventricular escape rhythm. Where does this escape rhythm originate from in this case?

- A. Bundle of His
- B. Left bundle
- C. Purkinje fibres
- D. Right bundle

(Topic: Heart, Blood and Gas Exchange, Module Q6 Movement and Flow 2017)

The answers to these questions can be found on page 25 in this journal.