

Knowse

An olfactory evaluation tool for preclinical
neurodegenerative diseases

Master thesis by
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**An olfactory evaluation tool for
preclinical neurodegenerative diseases**

Master thesis

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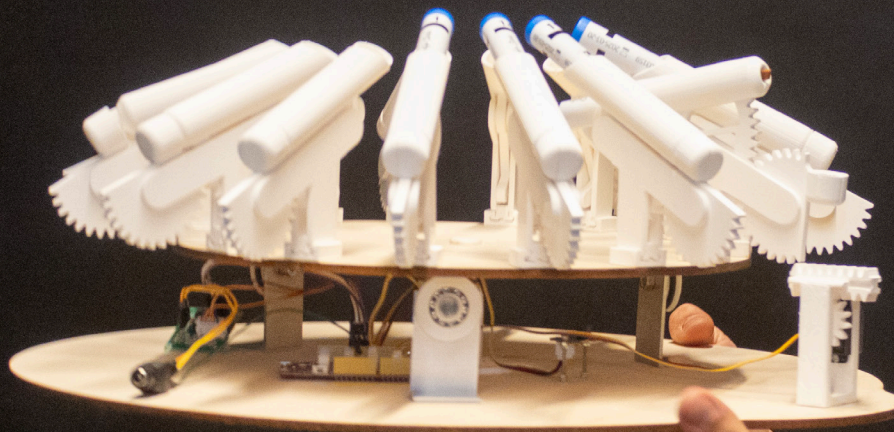
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Preface

Dear reader,

I am happy to share my graduation thesis with you. I truly hope you enjoy reading it, as much as I enjoyed writing it. This project marks the end of a wonderful time at Industrial Design Engineering, which shaped me as a designer and a person.

In the third year of my Bachelor's, I followed a minor at the Vrije Universiteit called *Psychology and the brain*. It was during this period, that I became interested in neuropsychology. Human behaviour and sensory perception have since then been a topic in many of my projects.

To me, the most intriguing sense is the sense of smell. Apart from primal instincts such as danger recognition and attraction, we appear to largely ignore our ability to smell. A shame, since it seems to hold much uncovered potential.

With this thesis, I aim to explore and utilise this potential in the medical context of neurodegenerative diseases and quality of life. The thesis is a personal mission, given life by curiosity and enthusiasm.

Although this was an individual thesis, it was far from an individual project. I would like to express my gratitude to a number of people that were of great value to me and this project.

To Sonja and Bas, who joined me on this journey as my supervisory team: your enthusiasm, positivity and open-mindedness made each coach meeting something I was looking forward to. I want to thank you for all your critical questions, which encouraged me to zoom out and reconsider assumptions. I also want to thank you for boosting my confidence and motivation. This project would not have been the same without you, especially not as joyful and relaxed.

A huge thank you to Wiebe and the others from the PMB. Your help as a sparring partner and material supplier for technical challenges and prototyping was invaluable. Your shared enthusiasm and comments starting with "So I was thinking about this at home yesterday evening..." brightened my days.

Many people shared their knowledge, experience and personal stories with me. They took time for me and allowed me to peek into their memories or tap into their expertise. These interviews brought this project to a new level and I am incredibly grateful for their

willingness to help. I hope these people recognise themselves in this paragraph.

To the friends that helped me along the way: Matthijs, Mick, Paulien, Sjoeke and Sterre, thank you for that inspiring creative session. Jeppe, thank you for your Arduino and prototyping help. Susanne, the pictures you took look incredible. Renzo, thank you for our sketch and sparring moments.

A final word of gratitude goes to my family and lovely girlfriend. Papa and mama, sometimes all I needed was to come home during the weekend, share all the things I did that week and have someone listen to it with interest and enthusiasm. You did that for me. I cannot begin to describe how much easier life is with such a loving and warm place to come home to. Papa, thank you for all the sparring and your help in prototyping. What a team we make! Emma, we were graduating together these last months. Thank you for your unconditional love and support. Your critical mind and caring actions were paramount in times I got stuck.

To you, dear reader, I hope this thesis brings across the passion and joy with which it was written.

Cheers,

A stylized, handwritten signature in black ink, appearing to be the letter 'B' with a loop and a long horizontal stroke extending to the left.

Abstract

Neurodegenerative diseases like Parkinson's and Alzheimer's have a huge impact on patients, their close ones and society as a whole. The negative consequences of these diseases are ever increasing due to our ageing society and growing shortage of healthcare personnel. Worldwide research efforts have thus far been unable to find effective treatment options.

Brain deterioration in neurodegenerative diseases sets in 15 to 20 years before clinical symptoms become noticeable. This means that even if better treatment options become available, much irreversible damage has been inflicted before we know to administer the treatment.

Early deterioration of smelling ability has been shown to provide a good risk indicator for future disease development. This thesis dives into the sense of smell as a means of recognising neurodegenerative diseases preclinically.

An olfactory evaluation tool, called Knowse, was developed. This concept product was designed to make the well-known ODOFIN Sniffin' Sticks test suitable for the context of

case-finding for neurodegenerative diseases. Knowse transforms the Sniffin' Sticks into an automatic self-test that people may use at a brain health clinic or optician. The product provides people with a relative trendline of their smelling ability, from which conclusions can be drawn over time.

The final design can be seen on the right-hand side. Knowse consists of 16 stick-holders on a rotating carousel. The Sniffin' Sticks are placed in the holders by medical personnel, like ink cartridges into a printer. Users place their head into a chin-head rest and provide input with a computer mouse as the different scent sticks are presented to them. They are guided through the test via a display.

This thesis report features a deep-dive into the neurodegenerative diseases Alzheimer's and Parkinson's, their impact and their current procedures. Possible future test locations, ethics of diagnostics and the current olfactory test market are explored through interviews and literature research.

Several design methods, prototypes and design iterations are described as they lead towards the final concept product of this thesis, Knowse. Design focused much on the technical, usability and error-proofing aspects of the concept product.



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1. Introduction

1.1 Problem definition

Neurodegenerative diseases like Alzheimer's disease (AD) and Parkinson's disease (PD) present a daily struggle for hundreds of thousands of Dutch citizens. With an ageing population and an increasing life-expectancy, this problem is expected to double in impact by 2040.

Researchers have not found a cure to either disease and treatment options are limited. Presently, many resources are spent on clinical research and trials, with the goal of developing more effective treatment alternatives.

However, brain deterioration in neurodegenerative diseases sets in 15 to 20 years before clinical symptoms become noticeable. Future treatments will only render useful when administered at an early stage, before severe brain damage occurs.

The potential added value of early diagnosis and treatment has a significant impact on prolonging and improving quality of life and reducing health costs.

Current methods that are suitable for early probability diagnosis are expensive and cumbersome. The medical field lacks cost-

effective, patient-friendly ways to detect preclinical neurodegenerative diseases.

Research shows that in both diseases, the sense of smell (olfaction) is affected in the earliest stages. This presents opportunities for disease detection. Numerous olfactory tests exist, but none of these were specifically designed for the situation at hand.

The challenge is not to create a clinical test from scratch, but rather to transform the existing clinical olfactory tests into a solution that suits the described problem in its present and future context.

The assignment is described as:

“Design a product to facilitate olfactory testing for preclinical self-screening for neurodegenerative diseases”

1.2 Methodology and approach

1.2.1 Project approach

The in Figure 1 displayed model is best used to describe this project from start to end. The addition of a third diamond is an adjustment to the original double diamond model by the British Design Council [63].

The first diamond was conducted before this thesis commenced. As the thesis is self-initiated, a research phase preceded this thesis. This is depicted by the Explore and Establish phases.

The Discuss phase was added to evaluate future implications and limitations of the final design.

In each phase, different questions were central. These are shown in Figure 1.

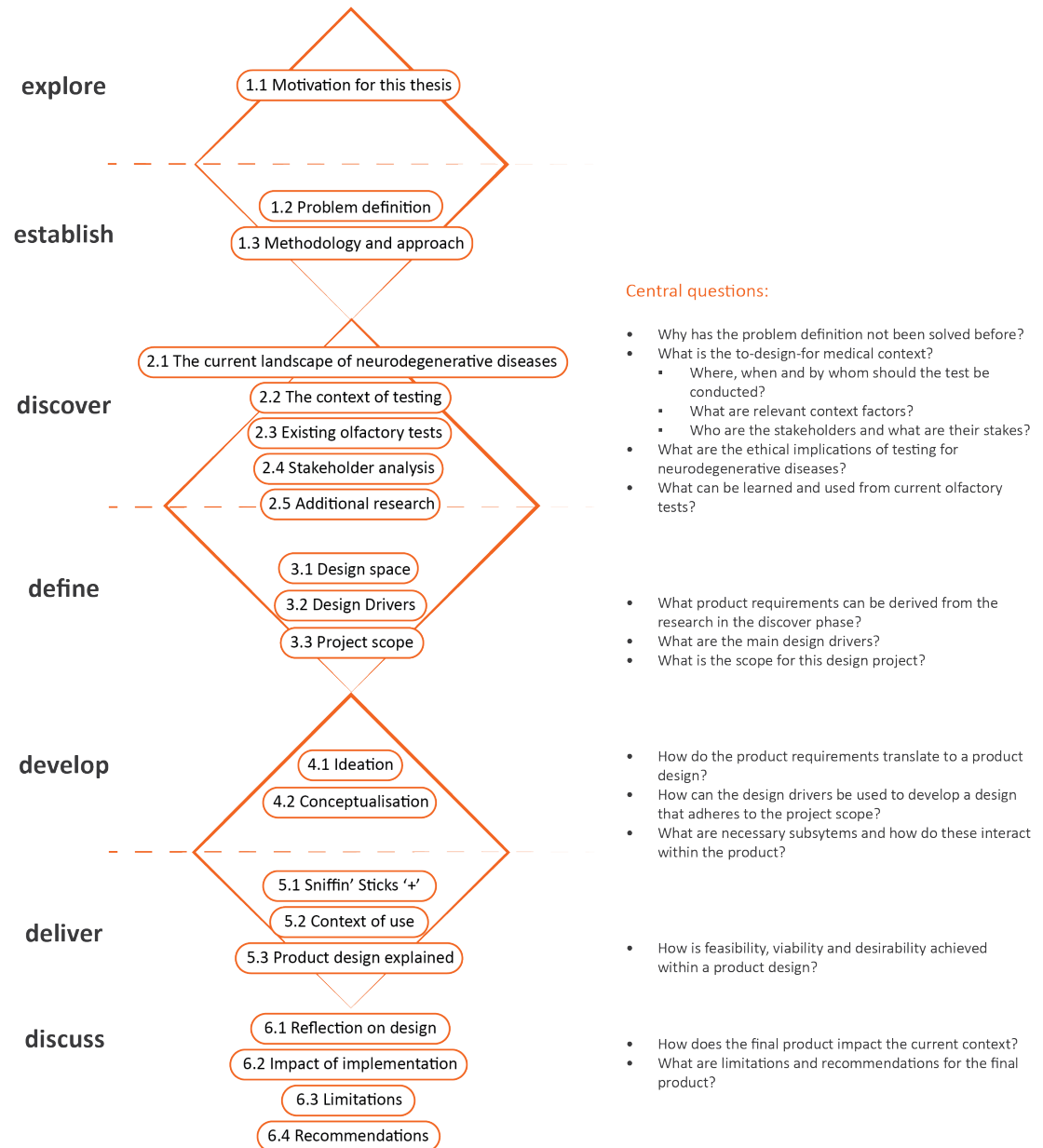


Figure 1, Design project build-up [63]

1.2.2 Report overview

Each of the project phases consists of mixture of research, design and validation activities, as shown in Figure 2. Within this project, criticism, contrasting thoughts and different opinions were actively sought after.

More about this can be found in Figure 3. These provided a broader understanding of the topic, its context and the different stakeholder perspectives. Figure 4 provides guidelines that help reading this report.

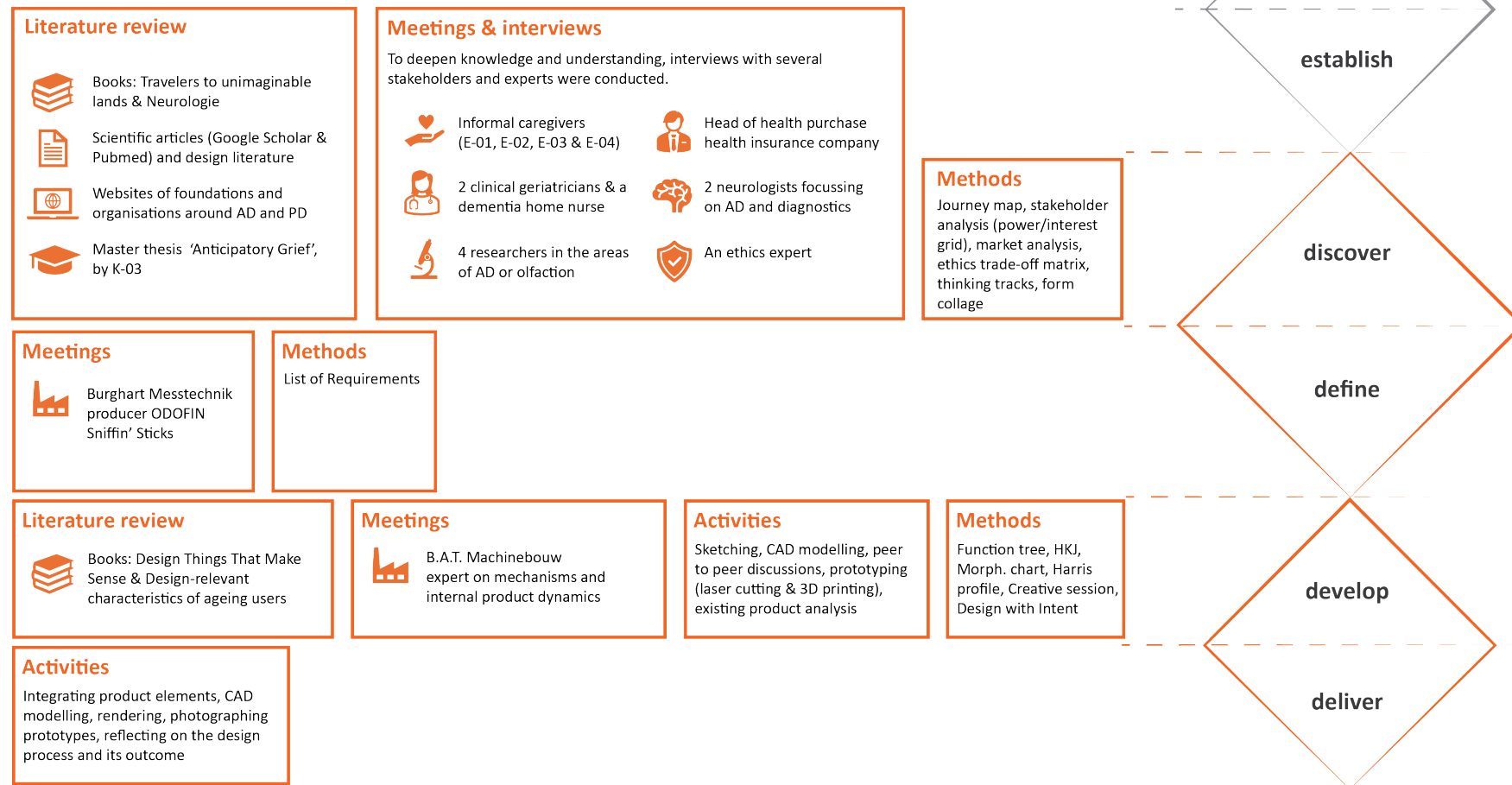


Figure 2, Project activities overview

Interviews & meetings

Several people were kind enough to boost this project by sharing their experiences and expertise during semi-structured interviews (Appendix A). Some of these people preferred anonymity. To respect their privacy, this report makes use of participant IDs. The overview below provides additional information. Experts were divided into two categories: *Experience experts (E-xx)* and *Knowledge experts (K-xx)*. Experience experts shared their personal stories about dementia with me. Knowledge experts shared their professional experience and knowledge.

Experience experts

ID:	Date:	Age:	Relation to patient:	Dementia type:	I.C.?
E-01	Feb/2024	60-65	Son (mother)	Alzheimer's	Yes
E-02	Feb/2024	20-25	Son (father)	Alzheimer's	No
E-03	Feb/2024	50-60	Daughter (mother)	Vascular dem.	Yes
E-04	Feb/2024	50-60	Stepson (stepfather)	Vascular dem.	Yes

Knowledge experts

Note: I.C. means informal caregiver.

ID:	Date:	Expertise:
K-01	Feb/2024	Neurology professor, Alzheimer's expert
K-02	Feb/2024	Clinical geriatrician & board member hospital
K-03	Feb/2024	MSc thesis on Dementia and its impact
K-04	Feb/2024	Dementia home nurse
K-05	Feb/2024	Geriatrician and Medisign professor (ageing)
K-06	Feb/2024	Head health purchase health insurance company
K-07	Feb/2024	PhD researcher Amyloid beta Alzheimer's
K-08	Feb/2024	Neurology researcher Alzheimer's & hearing loss
K-09	March/2024	Neurology researcher & olfaction expert Smell-RS
K-10	March/2024	Company: Burghart Messtechnik - Sniffin' Sticks
K-11	March/2024	Clinical geriatrician & diagnostics ethics expert
K-12	April/2024	Company: B.A.T Machinebouw (mechanisms)

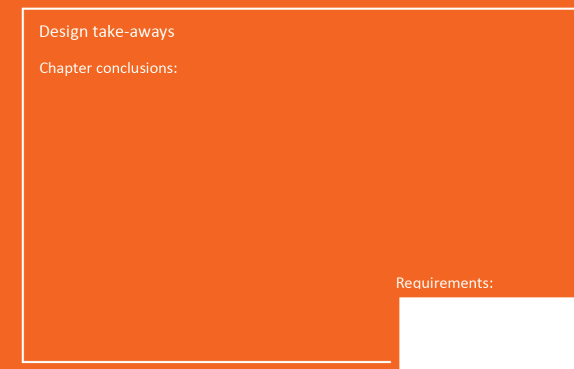
Figure 3, Private communication referencing

Report build-up

This thesis report is an overview of my design project. Research in this project was conducted in order to establish an understanding of the project's context and stakeholders.

The most important findings are marked throughout the report and summarized on the orange page after each chapter. The letters C (Case-finding), U (User ethics), T (Technical aspects), M (Maintenance) and P (Product use) are used. Requirements are later organised in these categories.

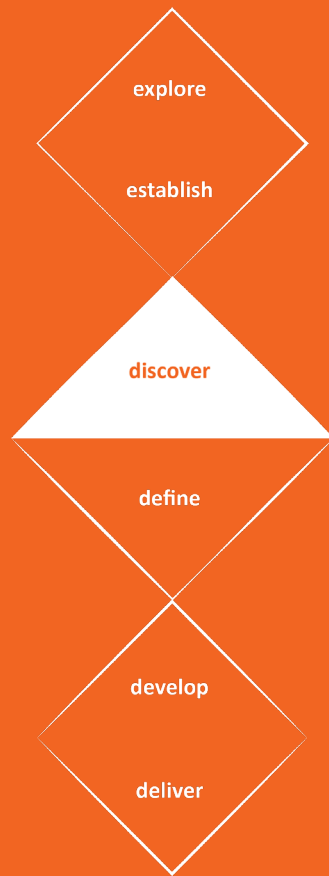
Each chapter finishes with a one-pager like this, titled 'Design take-aways'. On this page, the most important findings and requirements of the chapter are summarised.



The Institute of Electrical and Electronics Engineers (IEEE) referencing system was used in this report with slight adjustments. Private communication was added to the reference list at the end and are referred to as [*'number'] instead of the regular ['number'] in-text references.

Figure 4, Report reading guidelines

2. Discovering the design context



2.1 The current landscape of neurodegenerative diseases

2.1.1 Introduction

This chapter is about the neurodegenerative diseases Alzheimer's disease and Parkinson's disease. Initially, this project focused purely on Alzheimer's. As research revealed that Parkinson's may be an even better fit to the project, it was included for analysis. Both diseases have many similarities in procedures, stakeholders and impact on patients and their loved ones.

Focus on Alzheimer's helps finding relevant context factors that may remain hidden when researching both diseases equally, at a more general level. In the Chapter 2.1.3, focus lies on comparison and differences between Parkinson's and Alzheimer's in order to create a complete overview.

Further in this chapter, olfactory testing as a possible solution for early-stage case finding is explored. Lastly, a critical note is provided from an ethical point of view.

2.1.2 Alzheimer's and Parkinson's disease

Alzheimer's disease (AD) is the most frequently occurring type of dementia, constituting to 60-70% of all dementia cases [71]. Dementia is expected to triple its impact, affecting over 150 million people worldwide by 2050. It has been recognized by the World Health Organization as a global healthcare challenge [71]. In a study by Scheltens et al., Alzheimer's disease (AD) too, is displayed as a swiftly escalating problem, becoming one of the most expensive, lethal, and impactful diseases of this century [31]. Everyone can get AD, but it is most prevalent among elderly people.

As a neurodegenerative disease, AD features progressive brain deterioration over time. Symptoms appear 15 to 20 years after the onset of brain damage [9]. During this period, the disease progresses unnoticed.

No cure or effective treatment for AD has been discovered yet [40] and a definitive diagnosis can only be made post-mortem. However, researchers did discover several risk-factors and biomarkers, which indicate a high likelihood of the presence or chance of developing AD. Unfortunately, these markers are unsuitable for case-finding or screening at

a larger scale according to geriatric and neurological experts [*5] [*9].

Alzheimer's journey is like its symptoms, full of ambiguity and uncertainty. It consists of different phases, involving several stakeholders and procedures. These are described in the journey map in Figure 5. Notably, Alzheimer's is diagnosed after people visit the general practitioner on their own initiative. This means that Alzheimer's is never detected before clinical symptoms appear. Another conclusion that can be drawn from the journey map is that Alzheimer's journey is a social one. At each stage, several people are involved.

This project zooms in on the left half of the journey map, on the pre-clinical stage and diagnosis. Two main themes can be seen on this side of the figure: conflict and worry. Denial on both sides (patient and friends & family) may cause friction and grief. AD has substantial impact on patients, informal caregivers and society as a whole (see Figure 6). This is important to remember when designing for early recognition of the disease. A more elaborate analysis of Alzheimer's procedures, impact & biological features is presented in Appendix C.

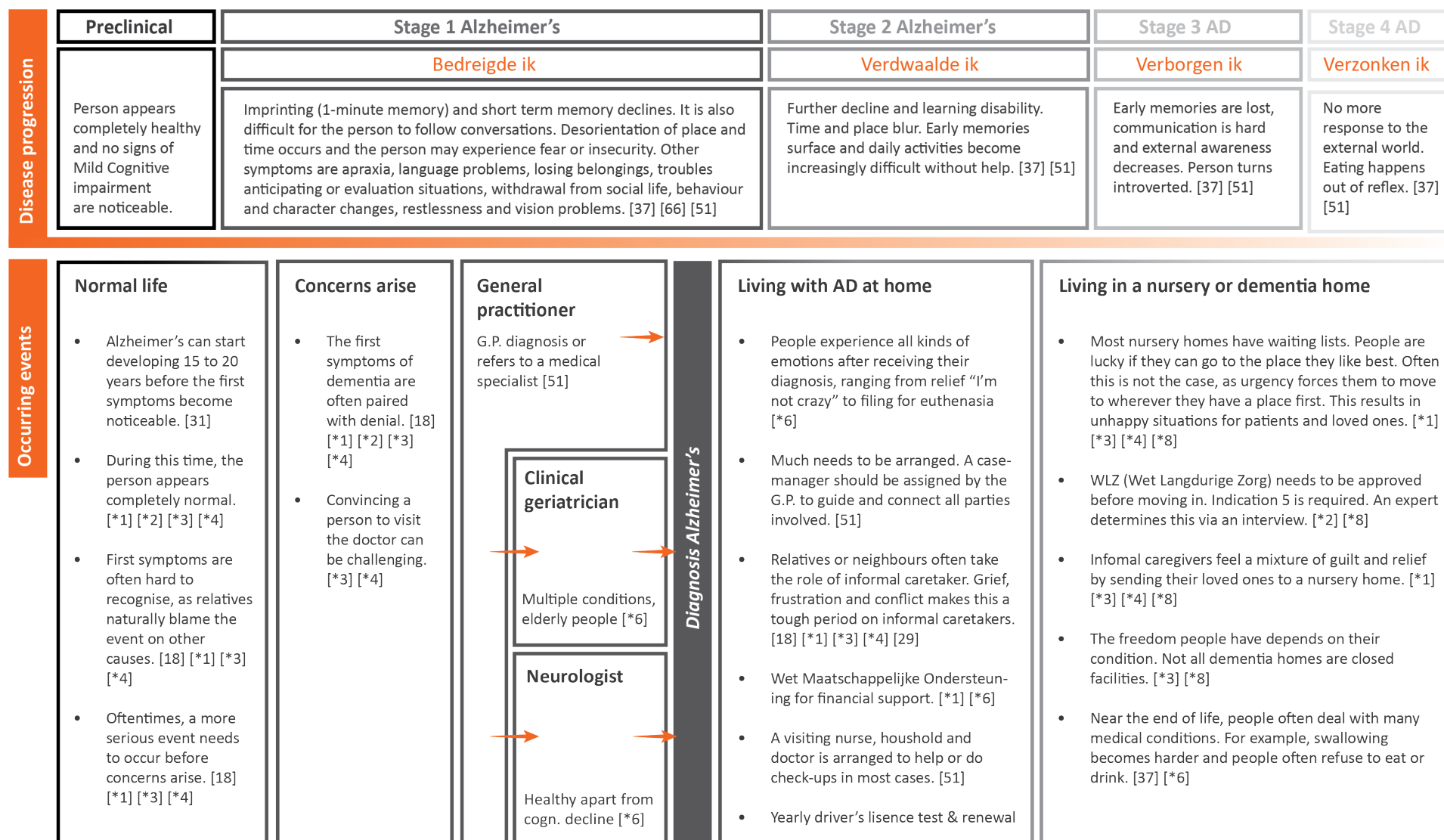


Figure 5, Journey map Alzheimer's disease

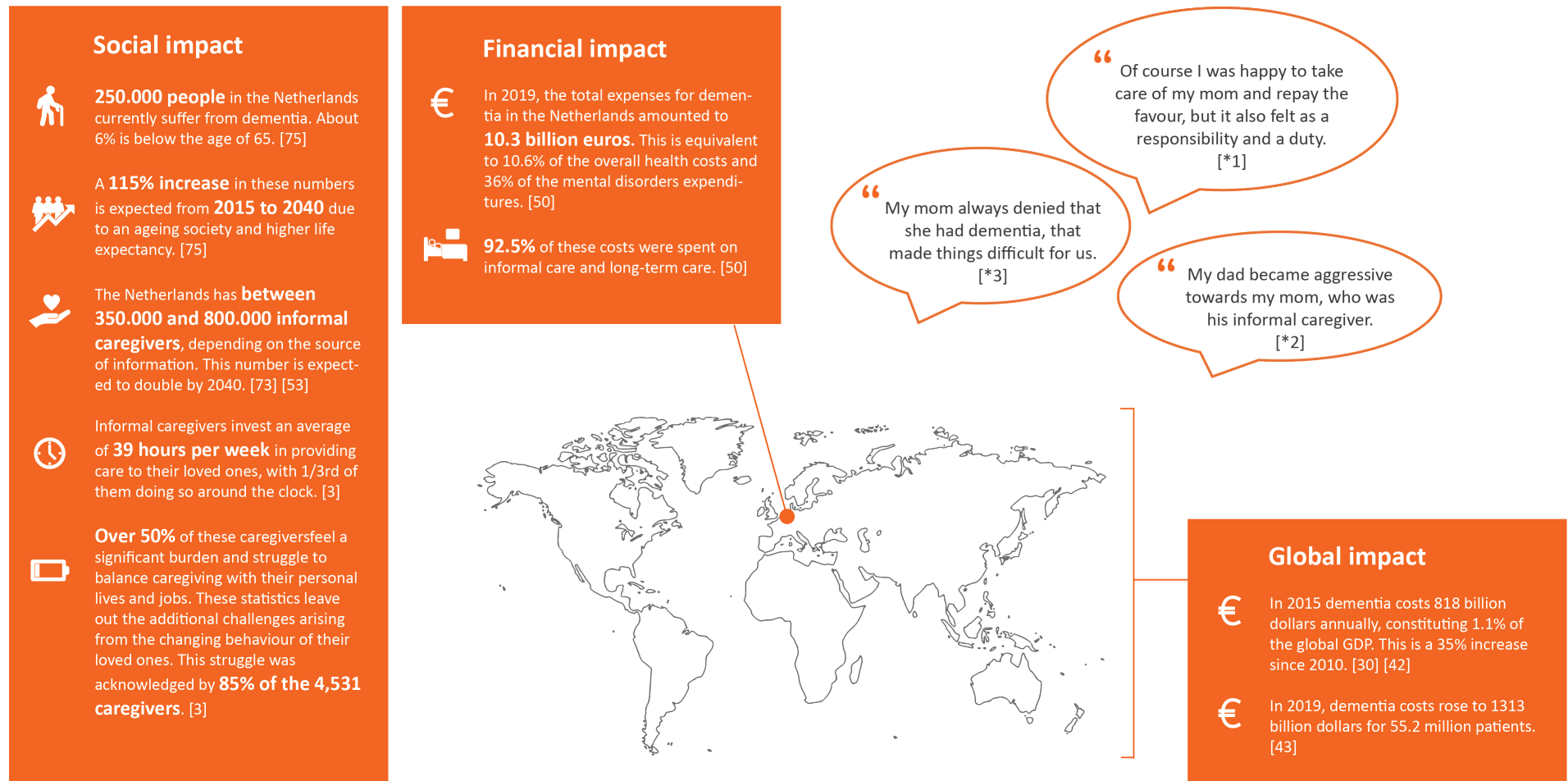


Figure 6, The impact of dementia and Alzheimer's

Like Alzheimer's, Parkinson's disease (PD) is a neurodegenerative disease. However symptoms and age of onset differ greatly. Symptoms of PD often set in between the age of 50 and 60 [74]. This is on average at least 10 to 20 years earlier than the symptoms of Alzheimer's.

Besides cognitive problems, people with PD also experience motor-symptoms, like tremors and movement difficulties.

Similar to AD, PD has no cure. However, a neurologist can prescribe medication that suppresses symptoms. This is an important difference between the two diseases.

A more elaborate overview of Parkinson's disease, its symptoms and its impact can be found in Appendix D.

2.1.3 Olfactory dysfunction; a window to cognitive health

Olfaction, the sense of smell, has long been associated with neurodegenerative diseases such as Alzheimer's and Parkinson's [39].

Deterioration of smelling abilities is present in both diseases at a very early stage, before clinical symptoms onset. Walker et al. explain

that in the context of neurodegenerative diseases, "...olfaction could be a common measure in a wide range of research and clinical settings." [39]. They furthermore highlight its suitability as a low-cost and low-effort detection method.



For Alzheimer's disease, amyloid beta plaques in the hippocampus and amygdala are important causes of this relation [33] [44]. Besides this, neurofibrillary tangles in the olfactory bulb are a typical early pathological sign of Alzheimer's. These neurofibrillary tangles are associated with olfactory identification deficits [6] [14] [41]. MRI research confirmed this by showing under activation of olfactory structures during various olfactory tasks including the primary olfactory cortex, hippocampus, and amygdala [39].

Over the years, several clinical studies have contributed to the growing pile of research that supports this claim. Recent studies pointed out the opportunity that olfactory identification diminishment presents as a cheap, accessible biomarker to detect Alzheimer's in its preclinical stage [15] [19] [44] [45] [46]. This was also confirmed by a longitudinal study, conducted over the timespan of 18 years, in which researchers looked at the predictive value of decline in

sense of smell (at least three measurements). Olfactory decline was proven to accurately predict future Mild Cognitive Impairment (MCI) and dementia [25].

The connection between olfactory diminishment and Parkinson's is even more prominent [*5]. Parkinson's is initiated by Lewy pathology, originating in the olfactory bulb. This is consistent with smell loss as an early sign of PD [39]. Ercoli et al. also conclude that especially in the initial stages of Parkinson's, a rapid deterioration of olfactory abilities can be found in PD patients [10].

People are generally unaware of their diminishing sense of smell. Therefore, objective testing is preferred over subjective assessment. An olfactory test is more reliable than self-reports from people [39]. This was also acknowledged by K-01, who shared an anecdote from experience:

"What I see with a large part of the patients when I ask:

'Before your Parkinson's clinical symptoms appeared, how were things with your smelling ability?'

They answer:

'Now you ask, well... coffee hasn't tasted well for years now. I also don't smell it when it is being prepared.'

[translated to English] [*5].

It appears to be hard for people to realise this and act upon this realisation in the moment, without formal testing.

Required olfactory test

There are different types of olfactory tests, as will be explained in detail in Chapter 2.3. The three types are identification, threshold and discrimination tests. For Alzheimer's, identification tests are preferred. Identification tests target elements of memory and recognition of scents, rather than pure smelling ability. This has been shown to provide a more reliable outcome than the two other tests as Alzheimer's starts in the hippocampus, rather than the olfactory bulb [19] [*5].

Parkinson's on the other hand, originates in the olfactory bulb. A threshold test is advised here, as this allows for accurate testing of the smelling organ. This is consistent with smell loss as an early sign of PD [39] [*5].

As described before, the goal is to detect diminishing olfactory function. For this, multiple tests need to be conducted over a period of time. Several lifestyle habits or contextual factors may influence singular, absolute test scores (e.g. smoking habits, COVID, respiratory infections and original smelling ability) according to Alzheimer's & senses expert K-08 [*12] Multiple, relative tests allow for a more accurate picture about the participant's olfaction status.

Further opportunities

Early detection of diseases may be a likely use case for olfactory tests, but it is not the only opportunity.

Research shows that olfactory testing may also aid in distinguishing diseases with otherwise similar symptoms. This is relevant for follow-up research and treatment. An example is Parkinsonism and PD. Like with dementia and Alzheimer's, Parkinson's disease is one condition within the Parkinson's spectre. It is often hard to distinguish between Parkinsonism and PD. The difference lies in dopamine: in PD the production of dopamine is disturbed, in Parkinsonism dopamine reception malfunctions. Symptoms are very similar, but treatments differ significantly.

Olfactory diminishment is an important feature of PD that allows for distinguishing the two [39].

Another major diagnostic challenge for cognitive neurologists is the discrimination between Alzheimer's and Lewy body dementia (LBD), the second most common type of dementia. Studies have shown patients with probable LBD perform even worse on odour identification testing than patients with clinical AD [39].

A second opportunity presents itself in predicting disease progression through olfactory disfunction. In PD, a steeper decline often means quicker disease regression [12].

2.1.4 Ethics of diagnostics

Disease diagnostics go hand in hand with ethical concerns. During interviews with experience- and medical experts ethical concerns were frequently raised. Being a designer puts one in a position of control and therefore responsibility over the ethical implications of products.

An ethics-focused interview was conducted with clinical geriatrician and diagnostics ethics expert K-11. According to K-11, ethics is about making decisions based on careful considerations of pros and cons. There is no absolute rule [*15]. This trade-off, shown in Figure 7, is a basis for discussion about whether or not this project should be implemented in this point in time. It also shows critical points to be aware of when implementing a diagnostic product.

A significant difference between PD and AD is that PD actually has treatment options, making the Sword of Damocles con much less prominent. Parkinson's is therefore easier to start with than Alzheimer's; the balance between pros and cons is different.



Receiving an earlier high-risk score for AD or PD

Pro(s)	Con(s)
• Preparations: Awareness of high risk may motivate people to write their living will before it is too late. Other preparations in and around the house, or moving towards a better community can be arranged. • Risk reduction: Awareness of high risk may motivate people to change their lifestyle and avoid activities or diets that heighten risk. • Acceptance: Awareness may reduce confusion, denial and conflict when symptoms become apparent at a later stage. • Bright side: Awareness of high risk may cause people to seize the day and enjoy more now.	• Sickness duration: Awareness of high risk may extend perceived sickness duration. People who would normally start showing symptoms in 15 years are suddenly already aware that they are sick and may feel worse because of it. • Sword of Damocles: There are no cures or promising treatments available, resulting in fear, paranoia and despair without benefit. This is mostly true for AD. For PD, dopamine treatment is available to suppress symptoms. However, this is not administered for prevention. • Hinder in life: People may face troubles with health insurance, loans and their driver's license

Conclusion

Ethics trade-offs have **no definitive answer**. Each individual will weigh the pros and cons differently. An option would be the present people with this trade-off upfront and allow them to decide. However, one might wonder if people are able to fully grasp the impact of a high risk diagnosis. As K-11 said from her experience: "People usually expect a negative outcome (positive news) and are oftentimes not prepared for a positive diagnosis." On a weekly basis, she says, the hospital deals with angry clients who willingly participate in a test, but did not expect or like the outcome [*15].

Figure 7, Ethics trade-off AD and PD testing [*1] [*2] [*3] [*4] [*5] [*6] [*9] [*15]



Expert K-11 noted that products can only be used for screening if they meet the Wilson & Jungner criteria [2]. These are shown in Figure 8. This was also indicated by Medical expert K-05 in an earlier interview [*9].

One could argue that screening for Alzheimer's could check rules 1, 4, 9 and 10. However, without treatment options, it becomes clear that a screening product for Alzheimer's will not be accepted.

This is different for Parkinson's. Although no cure has been found, medicines can be used to treat patients and suppress symptoms. For the same reason as mentioned in the trade-off, it seems that targeting **Parkinson's is a more viable first market strategy than Alzheimer's.**



Communication is a determining factor for both. Sharing of results by a professional is preferred in case of bad news, whereas a simple mail is preferred for good news.



Furthermore, it should be communicated upfront when and how people can expect to receive results [*3].

Wilson & Jungner criteria

- 1. The condition sought should be an important health problem.
- 2. There should be an accepted treatment for patients with recognized disease.
- 3. Facilities for diagnosis and treatment should be available.
- 4. There should be a recognizable latent or early symptomatic stage.
- 5. There should be a suitable test or examination.
- 6. The test should be acceptable to the population.
- 7. The natural history of the condition, including development from latent to declared disease, should be adequately understood.
- 8. There should be an agreed policy on whom to treat as patients.
- 9. The cost of case-finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole.
- 10. Case-finding should be a continuing process and not a "once and for all" project.

Figure 8, Wilson & Jungner criteria for screening [2]

Design take-aways I

Chapter conclusions:

Neurodegenerative diseases like Alzheimer's (AD) and Parkinson's (PD) have a significant impact on the lives of patients and their loved ones. For both diseases, no cure has been found. Treatment options are very limited, especially for Alzheimer's, where no treatment is available and the largest social and financial costs are related to (informal) caregiving.

Unfortunately, clinical symptoms in Alzheimer's and Parkinson's only appear after many years of neurodegeneration. When they appear, much irreversible brain damage has already been afflicted. The medical world lacks a cost-effective, quick and easy way to recognise neurodegeneration at an early stage. Early diagnosis is paramount once neurologists and researchers create more promising treatment options.

Olfactory loss is closely related to the early stages of Alzheimer's and Parkinson's disease. Recent research shows that olfactory identification (AD) and threshold (PD) tests may prove to be effective methods for early disease discovery, when combined with other tests. Repeated periodical testing is necessary.

However, it is important to consider the ethical aspects of preclinical diagnosis. Diagnosing people requires a treatment plan. There have to be benefits, that outweigh the longer sickness period and emotional impact of diagnosis. Research on PD is much further than that on AD. This can be seen in existing medication to suppress PD symptoms. From an ethical point of view it is therefore best to design for a threshold test that helps detecting PD, while keeping the door open for AD's identification test at a later moment.

Requirements:

- C1:** Testing for Alzheimer's should be based on the Olfactory Identification test.
- C2:** Testing for Parkinson's should be based on the Olfactory Threshold test.
- C3:** For reliable results about neurodegeneration, repeated relative tests over time should be conducted rather than one absolute test.
- U1:** Users must be well-informed upfront about possible implications and consequences of results.
- U2:** Testing must always be voluntary
- U3:** The product can only be used for screening if all 10 criteria of Wilson and Jungner apply.
- U4:** The sharing of good results can be automatic, bad results should be shared by a medical professional
- U5:** The product should communicate upfront how and when results will be shared.
- P1:** The test should be a quick, easy and low-cost way of testing.

2.2 The context of testing

2.2.1 Introduction

This chapter digs into the Dutch medical context and a suitable setting for implementation of an olfactory test product. It deals with the 'where', 'when', 'how' and 'by whom' of olfactory testing for neurodegenerative diseases, in order to find the most promising product-market fit.

2.2.2 The structure of the Dutch medical system

The medical world refers to different 'lines' within the customer journey. There are 4 professional lines in total. These are explained in Figure 9.

Neurodegenerative diseases are currently diagnosed in the 1st and 2nd medical lines, - according to a clinical geriatrician and board member of medical specialists in a hospital K-02 [*6]. She furthermore states that the increasing shortage of personnel is noticeable and problematic in hospitals. This is expected to become worse in the future [26]. The World Health Organization supports this claim and mentions that by 2030, there will be a world-wide shortfall of 10 million health workers,

mostly in low- and lower-middle income countries [52].

Olfactory testing for the purpose of discovering neurodegenerative diseases is currently non-existent. Implementing this should adhere to the present-day developments in the medical world. For this project this means that it is important that the product does not require additional medical workforce in the first and second line. A self-testing device with automatic processing of results is preferred. This could be used as a preventative measure in the 0-line or as time-saving aid in the first or second line. However, this leaves us with the questions 'where', 'when' and 'how'. These will be discussed in Chapter 2.2.3.



Structure medical system: The Netherlands

stage	description	parties involved
0 line	This concerns basic healthcare & prevention. People can choose to participate.	GGD (Gemeenschappelijke Gezondheidsdienst) and prevention workers. Campaigners or researchers.
1st line	Healthcare that is directly accessible on own initiative. General healthcare personnel.	General practitioner, dentist, physiotherapist, pharmacist, homenurse.
2nd line	Healthcare for which one needs to be referred by a first line professional. Specialist healthcare personnel.	Hospital staff and medical specialists like an orthodontist, neurologist or psychiatric doctor.
3rd line	Support second line professionals.	Academic hospitals and specialist centres. Blood research labs.
4th line	So-called 'top-care'. For very unique cases or high urgency complex surgeries.	Only a handful doctors are in the fourth line.

Figure 9, Structure Dutch medical system [49]

2.2.3 Case-finding for neurodegenerative diseases

The initial idea of using olfactory testing for population screening was dissuaded by neurology professor K-01, during an interview [*5]. Whether a test method is suitable for screening, according to K-01, depends on two variables: sensitivity and specificity. Both can never be 100%, but need to be as high as possible. The degree of certainty olfactory tests provide is not high enough for either of these.

Sensitivity means that the test never gives false negatives. The test should be sensitive enough to distinguish between all positive and negative cases.

Specificity refers to the degree of certainty, with which we can say that a positive test result points towards a single disease or condition.

Besides this, as was mentioned in Chapter 2.1.4, Figure 8, olfactory testing does not adhere to the Wilson and Jungner criteria for screening for Alzheimer's. Here, Parkinson's is more likely to be accepted. Certain diagnosis for Alzheimer's and Parkinson's is impossible in the preclinical

stage with our current knowledge. As mentioned in Chapter 2.1.2, we can merely give a probability diagnosis, and only when people display multiple symptoms [*9].

Something different from diagnosis and screening is case-finding. There is much ambiguity about the definitions of each.

“ **Case-finding** will in this report be explained as testing people who worry about their health and visit a test facility on their own initiative to receive a personal risk profile for several diseases and conditions.

Screening on the other hand, is explained as actively approaching or inviting people to test with the goal to provide a positive or negative test result [*5].

Case-finding appears to be a better fit to olfactory testing in its current state. Case-finding moves the project away from diagnostics and the first and second line as explained in Figure 9. Instead, it focuses on the zero line, prevention.

2.2.4 Prevention: Brain Health Clinics

The medical world sees an increasing focus on prevention and early intervention.

Neurologists from several countries are collaborating towards the development and deployment of second-generation memory clinics, called Brain Health Clinics (BHCs) [*5]. The goal of BHCs is to allow people to take timely, preventative action like adjusting daily habits to limit the likeliness of disease development.

Current memory clinics focus on cognitively impaired individuals for diagnosis, staging and prognosis, but also treatment and support. BHCs on the other hand, target cognitively unimpaired individuals for risk profiling, risk communication, risk reduction, and cognitive enhancement [11]. Figure 10 explains more about the envisioned Brain Health Clinics.

The future Brain Health Clinics are a suitable setting for olfactory testing for multiple reasons. The first and foremost reason is its low-cost and low-threshold ability to screen for neurodegenerative diseases and other quality of life-reducing conditions. Besides this, as was mentioned in Chapter 2.1.3, olfactory testing cannot operate stand-alone. BHCs combine several different research

methods to provide a single risk indication. The sensitivity and specificity of olfactory testing are not high enough for screening, but very suitable for this use. They allow for a low/medium/high risk score, which is one of the aims of Brain Health Clinics.



Figure 10, Brain Health Clinics explained [11]

Design take-aways II

Chapter conclusions:

There is a need to relieve medical professionals in the first and second line of the Dutch healthcare system. A promising way of doing this, is to focus on prevention, which is in the zero line of care. Preventative actions may in time reduce the pressure on the first and second lines of care.

However, in order to prevent or slow down diseases and conditions, one needs to be aware of their presence. A new concept, called Brain Health Clinics, was developed by several European neurologists for this purpose.

Aiming at case-finding among healthy individuals who are worried about or curious to their brain health status. According to a personal risk profile based on a combination of tests, people

are advised preventative actions such as slight changes in their daily habits.

Olfactory testing is highly suitable for the context of Brain Health Clinics due to its ability to recognize neurodegenerative diseases at an early stage (see Chapter 2.1.4.). Besides this, olfaction serves better as a risk indicator, than as a screening or diagnostic test. This is due to its lower sensitivity and specificity.

Requirements:

- C4:** The product should enable users to self-administer the test without help of health care personnel, due to a shortage of personnel.
- T1:** Answers and results must be processed automatically, without additional administrative work.

2.3 Existing olfactory tests

2.3.1 Introduction

This chapter explores the current market of olfactory testing in order to learn the uses and the pros and cons of each available test. A comparative analysis was done to determine which test is most suitable to use as a basis for this thesis. Inspiration from other tests was drawn for further improvements. Tests for analysis were selected based on the number of references on Google Scholar and PubMed. Four additional interviews with researchers in the area of diagnostics and sensory testing completed the selection.

2.3.2 Current practice

Olfactory testing is no new phenomenon. Throughout the years, olfactory tests have been developed, proven and embraced in practice.

Currently, tests are mostly used in clinical context. For example before and after brain or nose surgery, tests are used to evaluate if the desired result was achieved and nothing else got damaged in the process. Olfactory testing also became popular during the COVID-19 pandemic, where diminishing scent was an

important indication of COVID. Yet another use is clinical research. For example on neurodegenerative diseases such as Alzheimer's or Parkinson's, but also on general ageing, cognition, quality of life and willingness to eat.

For Parkinson's, a verbal report of own smell diminishment is often asked to patients to serve as a check-the-box [*5]. However, as explained in Chapter 2.1.3, this is less reliable than real olfactory testing.

Olfactory test methods

Chapter 2.1.3 briefly introduced the different olfactory test methods: olfactory identification, olfactory threshold and olfactory discrimination tests. These tests have different purposes. The identification test is the most widely used method. The descriptions below are based on the ODOFIN Sniffin' Sticks [55].

[1] Olfactory identification provides the participant with 16 strong odours. After smelling an odorant, the participant is asked to choose out of four options what they just smelled. These options can be textual, visual or a combination of both. The number correct answers provides the result.

[2] Threshold testing aims at finding the minimum intensity required for participants to notice an odour. It requires 16 sets of 3 odours; 1 scented, 2 blanks. Starting at the lowest intensity (set 16), participants work their way down until they point out the one scented stick in a set correctly twice in a row. Then they move one set up to repeat the test with a lower intensity stick. When they fail the first or second try, they move one set down again. This process is repeated until 7 turning points are passed through. Results are then processed to find an average score.

[3] The discrimination test is only used in combination with one of the other tests. Again, 16 sets of 3 are used. Each set only has one scented stick. Participants must detect the scented stick from the two blanks. Out of 16 sets, the number of correct answers provide the score.

Ways to apply odours

The three test methods can be carried out with various testing tools. Different tools use different ways of applying odours.

- Scratch 'n' sniff strips:
Users use a pencil or pen to scratch off a thin protective layer from scented paper, freeing the odours.
- Glass vials or jars:
Small glass vials with liquid scents inside are used for testing and held close to the nose.
- Felt-tip pens:
Cylinders filled with liquid odour that comes free through the felt tip of the cylinder.
- Diffusion and masks:
Gas odours are diffused in the air or through a tube and face mask.

Relative scores from absolute tests

Research revealed that all olfactory tests are absolute tests in the basis. This means they measure the olfaction level at one moment. As was described in Chapter 2.1.3, there are many factors that weaken the reliability of an absolute test. Therefore, multiple tests should be conducted and results should be combined,

before meaningful conclusions can be drawn about neurodegeneration.

2.3.3 The olfactory test market

Between existing olfactory tests, many similarities can be found. Nearly all of them make use of the above mentioned methods and ways of application. Each test has their unique selling points and downsides. Figure 11 provides an overview of the most interesting olfactory tests.

The market of olfactory tests is small, especially outside of the research context. None of the described olfactory tests are entirely suitable for the envisioned context of Brain Health Clinics and only two of the tests mentioned are commercially available at this moment; the American University of Pennsylvania Smell Identification Test (UPSIT) and the German ODOFIN Sniffin' Sticks.

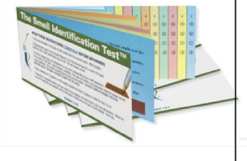
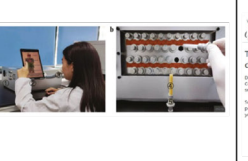
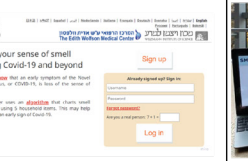
name	University of Pennsylvania Smell Identification Test (UPSIT)	ODOFIN Sniffin' Sticks	Odor ID Test (OIT)	Digital Olfactory Testing System (DOTS)	Smell Tracker (COVID)	SMELL-RS
supplier	Sensonics International [8]	Burghart Messtechnik [47]	NIH Toolbox (National Institute of Health, USA) [16]	None yet, being developed in China [20]	100+ researchers from different countries [32]	OW - Smell Digital [13]
method	Identification test	Identification, threshold and discrimination tests	Identification test	Identification test	Self-reported intensity + pleasantness test	Threshold and discrimination tests
tool	Scratch 'n Sniff	Felt-tip pens	Scratch 'n Sniff	Diffusion via face mask	Smelling self-selected household products	Diffusion via face mask
description	The test contains forty microencapsulated odorants. Users receive an absolute score (no loss - total loss) compared to a control population based on age and sex.	The test contains 16 odorant sticks or 16 sets of 3 odorant sticks, depending on the method. Users receive an absolute score (no loss - total loss) compared to a control population based on age and sex.	The test contains 9 folded paper sheets, that are send via the mail delivery service, and an online test where users fill in their answers. Single use for home use. Users again receive an absolute score.	The test contains a mask connected to the diffuser and a tablet to fill in answers. It is an automated alternative for UPSIT and the Sniffin' Sticks. Further intel was not published.	The test contains 5 self-selected household items. These must be rated on pleasantness & intensity via an online form. An Olfactory Perceptual Fingerprint (OPF) is created. Users receive a relative score.	The test contains a device that diffuses scents via a mask. Whereas most tests use monomolecular odorants, SMELL-RS makes use of newly created, unrecognisable odour mixtures to prevent bias.
pros	- Users can conduct this test and calculate results by themselves, at home. - Validated & accepted as a standard in the scientific community.	- Is the industry standard olfactory test in the Netherlands. [59] [58] [76] All three test methods, seperately offered. - Validated & accepted in the scient. community.	- Scores are calculated automatically. - The test is brief and inexpensive.	The modular system, allows for different scent containers to be added or removed, overcoming cultural bias.	- Inexpensive, widely available and no additional burden on delivery services or medical personnel. - Periodical testing reduces external infl.	Eliminates odor specific insensitivity and prior olfactory experience caused by as life style and living environment.
cons	- Data pool consists of American control subjects only, making the test susceptible to cultural bias. [8] - Memory of odours and verbal ability required. Not purely smell [7]	- The ODOFIN Sniffin' Sticks test requires a health care professional to present to sticks to the participant. - Similar to UPSIT, with a Northern European control group.	Like UPSIT, offers little control over external influences and prone to user errors.	- Like Sniffin' Sticks, has to be conducted on location. - Still in development, making it merely an inspiration.	- Uncontrolled context, lack of guidelines and user interpretation results in low reliability. - Test is no longer in use.	- No Identification test possible. - Still in development making it merel an inspiration. - Has to be conducted on location. - Relatively expensive.
image						

Figure 11, Market analysis olfactory tests

ODOFIN Sniffin' Sticks as underlying test

The Sniffin' Sticks appear to be the most promising test for this project. This has a few reasons.

Firstly, the ODOFIN Sniffin' Sticks are the current medical standard for Dutch hospitals. Using the Sniffin' Sticks as a basis for design might offer significant advantages for the acceptance of the final product in the medical field [*5] [*10].

Secondly, Sniffin' Sticks interprets results based on a Northern European control group, which suits the Dutch population.

Finally, as was mentioned in Chapter 2.1.4, Parkinson's appears the best disease to design for first. Chapter 2.1.3 describes that the threshold test is most suitable here. Most other tests are identification tests. The Sniffin' Sticks allow for all three test methods, enabling the user to also test for Parkinson's.

A significant downside of the Sniffin' Sticks is their reliability on medical professionals to conduct the test. This does not suit the healthcare perspective described in Chapter 2.2.2.

The other tests offer further inspiration for improvements. Examples are automatic processing of results, modularity and repeated

periodical testing to create a personal, relative score from several absolute scores.

Sniffin' Sticks threshold test procedure

The Sniffin' Sticks threshold test procedure is explained on the website of Burghart Mt. [60]. A summary is provided here:

The threshold test consists of 16 sets of 3 sticks, a red, a green and a blue one. All red sticks have the same scent. Green and blue sticks are blanks and have no scent. Red stick 16 has the lowest intensity, red stick 1 the highest. The user is blindfolded during the test.

The participant is presented the 3 sticks of a set at a distance of approximately 2 centimetres, for 3-4 seconds at 5 second intervals between sticks. The user then has to answer which stick is the red stick (with scent).

Starting at set 16, the participant works their way down towards the point where they answer a given set correctly twice in a row. When this happens, the participant gets the next set (lower intensity). If this fails the first or second try, a higher intensity set is presented. This process is marked with minuses and pluses on a sheet. When 7 turning points are passed through, a score is

calculated (see Figure 12). Figure 13 shows the repeating presentation sequence as prescribed by Burghart Mt. The smell threshold is the average value of the last 4 turning points. This score is compared to the graph with Normative data in Figure 14.

	Turning points						
Dilution	1	2	3	4	5	6	7
1							
2							
3							
4							
5							
6	x x		x x		x x		x x
7	x -	x x	-	-		x x	-
8	x -	x x	x -			x -	
9		x -					
10	-						
11							
12	-						
13							
14	-						
15							
16	-						

Figure 12, Scoring form Threshold test [60]

Presentation	sequence of the sticks
1	red – green – blue
2	blue – red – green
3	green – blue – red
4	red – green – blue
The sample repeats itself until the test is over!	

Figure 13, Presentation sequence [60]

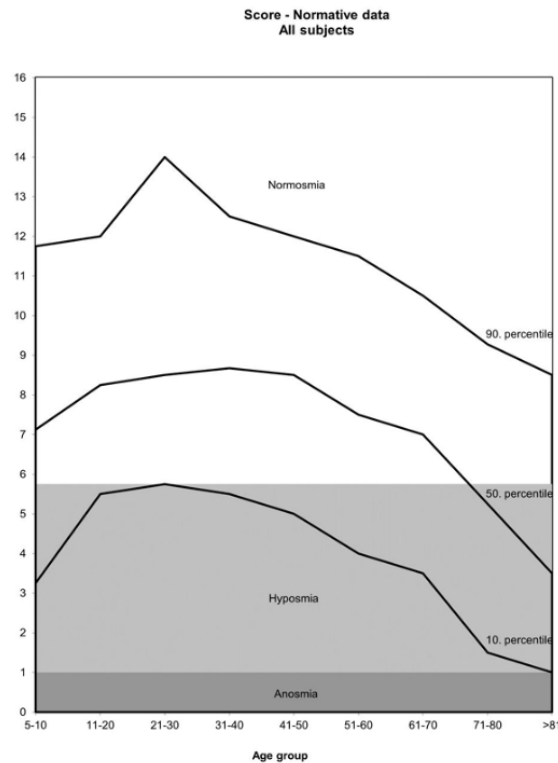


Figure 14, Comparative data test results [60]

Other tests

Other tests were researched but not mentioned in the table as they do not add to the analysis. They are either no longer being used or have too many similarities to other tests. This is the case for the glass jar Scandinavian Odor Identification Test (SOIT) [28], the European Test of Olfactory Capabilities (ETOC) [35] and the Digital Scent Device [23].

Professor Alan Chalmers is working on a smell and taste test at the University of Warwick in the United Kingdom [72]. Due to the addition of taste and its current development stadium, this test is not suitable for this thesis.

The computerized Olfactory Test for the Diagnosis of Alzheimer's Disease (TODA) had its first results from France and Canada published in 2022. However no further mention was found after that. The test is a combination of an identification and a threshold test, with 14 odorants diluted into 4 different concentrations [27].

Design take-aways III

Chapter conclusions:

Olfactory tests have thus far been used before and after brain or nose surgeries, for COVID testing and for clinical research on neuro-degenerative diseases, ageing, cognition, quality of life and willingness to eat.

Olfactory testing can be divided into three main categories: identification, threshold and discrimination tests. The method differs depending on the goal of testing. Odours are applied via scratch 'n sniff papers sheets, glass vials, felt-tip pens or diffusion.

Several olfactory tests were created, tested and used in practice. The American University of Pennsylvania Smell Identification Test (UPSIT) and the German ODOFIN Sniffin' Sticks are the most validated and used tests. For the Dutch context around case-finding, the Sniffin' Sticks appear the most suitable underlying test.

The Sniffin' Sticks is the standard test used in Dutch hospitals. It can also be used for all three categories mentioned before, whereas UPSIT only facilitates the identification test. This test is not suitable for detecting Parkinson's. Lastly, both absolute tests compare test results to a control group. The control group of UPSIT consists of American subjects. This may induce culture bias. The Sniffin' Sticks use a Northern European control group.

The Sniffin' Sticks rely on a healthcare professional to administer to test. This is a big disadvantage considering the growing personnel shortages in the medical setting.

Besides this, ways should be found to allow for modularity of different scents, repeated testing and automatic processing of results.

Requirements:

- C5:** The ODOFIN Sniffin' Sticks test must be used as underlying model, as this is the norm in the Netherlands and most of Europe.
- C6:** The official scoring method from Burghart Messtechnik must be used for a singular absolute score per test.
- T2:** Sticks must be presented at the distance and duration as prescribed by Burghart MessTechnik, producer. It must account for different user body sizes.

2.4 Stakeholder analysis

2.4.1 Introduction

This chapter provides an overview of the most relevant stakeholders and their stakes in the final product of this thesis. Despite this being a self-initiated thesis, there are several stakeholders to consider.

2.4.2 Stakeholder map

Different stakeholders were discovered when creating the stakeholder map (Figure 3) and researching the current olfactory test industry (Chapter 2.3). All stakeholders except the Nederlandse Zorgautoriteit (NZa) were contacted to discuss their stakes.

As can be seen in Figure 15, health insurances and the NZa possess much power but are only indirectly involved. Their stakes should be satisfied. This means that any design outcome should be in accordance with Dutch medical rules and regulations, including a clinical trial [*10].

Producer and seller of the Sniffin' Sticks, Burghart Messtechnik is an important stakeholder, as further development of this project may well depend on the company and

its resources. This too, goes for medical professionals. Whether they embrace or distance themselves from the design outcome is paramount for implementation. Their stakes should be considered carefully.

Lastly, as olfactory testing will be on voluntary basis, it should be desirable to future users. Keeping them up to date about developments may boost desirability and impact.

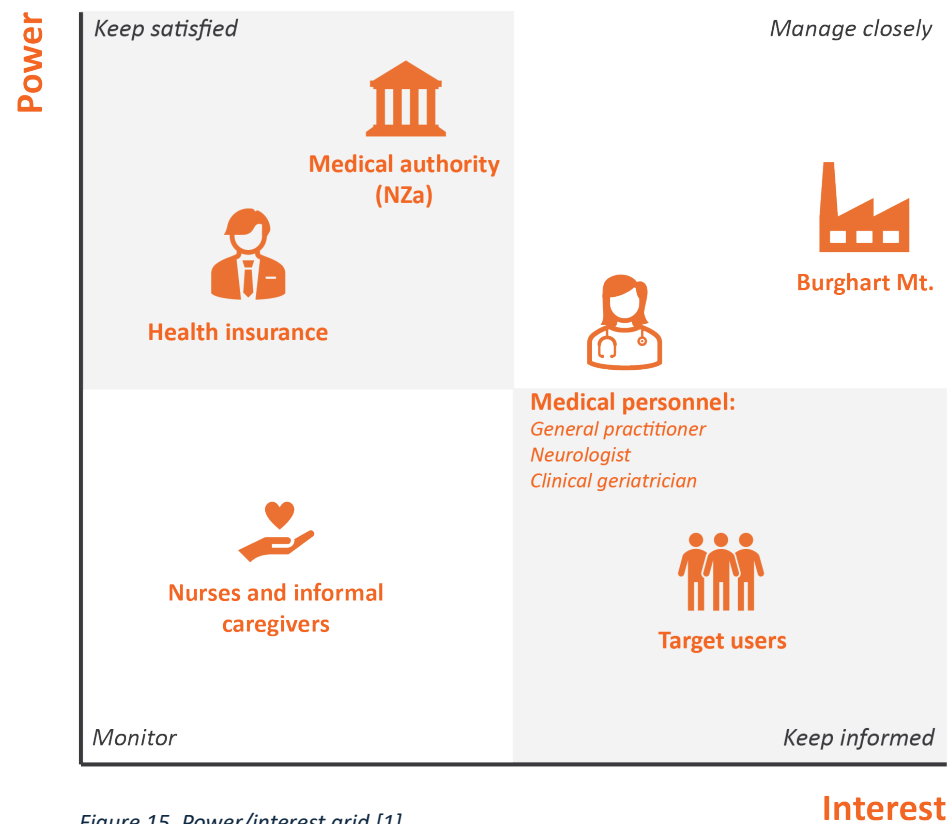


Figure 15, Power/interest grid [1]

Figure 16 shows the stakes per stakeholder. Notably, stakeholders that score higher on *interest* in Figure 15 have more to gain from the final design outcome. The gains for medical personnel, Burghart Mt. and the target users are much more specific than those of other stakeholders.

	Needs	Possible gains
 Health insurance	- Product must adhere to medical rules and regulations [*10] - Insurance policies differ in obstacles and benefits for coverage [*10]	A more attractive assortment for clients such as hospitals and clinics
 Medical authority (NZa)	Product must adhere to medical rules, regulations and procedures	A better and more efficient healthcare system
 Burghart Mt.	- An increase in product sales and profits - Defence of leading market position through innovation and value proposal - New markets and growth opportunities	- Increasing sales and profits - Future proofing of market position [*16]
 Medical personnel	- Relieving work-pressure for medical professionals in an ageing society [*6] - Reliable aids in practice	- Relieving work-pressure - Creating a bigger impact for patients
 Target users	- Reassurance [*1] - Knowledge about personal risks and recommended preventative actions [*1]	- Postponing/reducing inevitable symptoms and make timely arrangements - Prevent the burden of care-taking - Higher quality of life
 Nurses and informal caregivers	Relieving work-pressure for medical professionals and informal care-takers in an ageing society [*1] [*8]	Relieving pressure or burden

Figure 16, Needs and possible gains of stakeholders

Design take-aways IV

Chapter conclusions:

Stakeholders that are strongly related to the project were researched through personal interviews. A power/interest grid shows that especially Burghart Mt. and medical professionals should be kept in the loop while designing.

Health insurances and the Dutch medical authority hold much power, but little interest. They should be satisfied by following the rules and regulations for medical products. Clinical trials are also required here.

The future target group has a vested interest in the product, as it will benefit them most in the end. However, they have little power in the medical system and just follow what is being decided for them. It is wise to consider the desirability aspect from their perspective. As testing in the envisioned is voluntary,

users largely determine the success of implementation.

Main gains for stakeholders focus on relief of medical personal, financial gain and personal risk reduction.

Requirements:

-

2.5 Additional research

2.5.1 Introduction

This chapter explores new perspectives on the design challenge at hand.

2.5.2 A broader perspective on the challenge

In order to gain a broader perspective on the topic, six Thinking Tracks were used [4]. Different perspectives on the product aided in asking relevant questions. These questions result in new product requirements (see Figures 17 & 18).

The completely orange bubbles are described by Bonnema et al. in the book Systems Design and Engineering. Error-proofing, Product functionality and User experience were added to target important themes. This is emphasised by the relevant questions they give rise to.



Figure 17, Thinking Tracks part 1 [4]

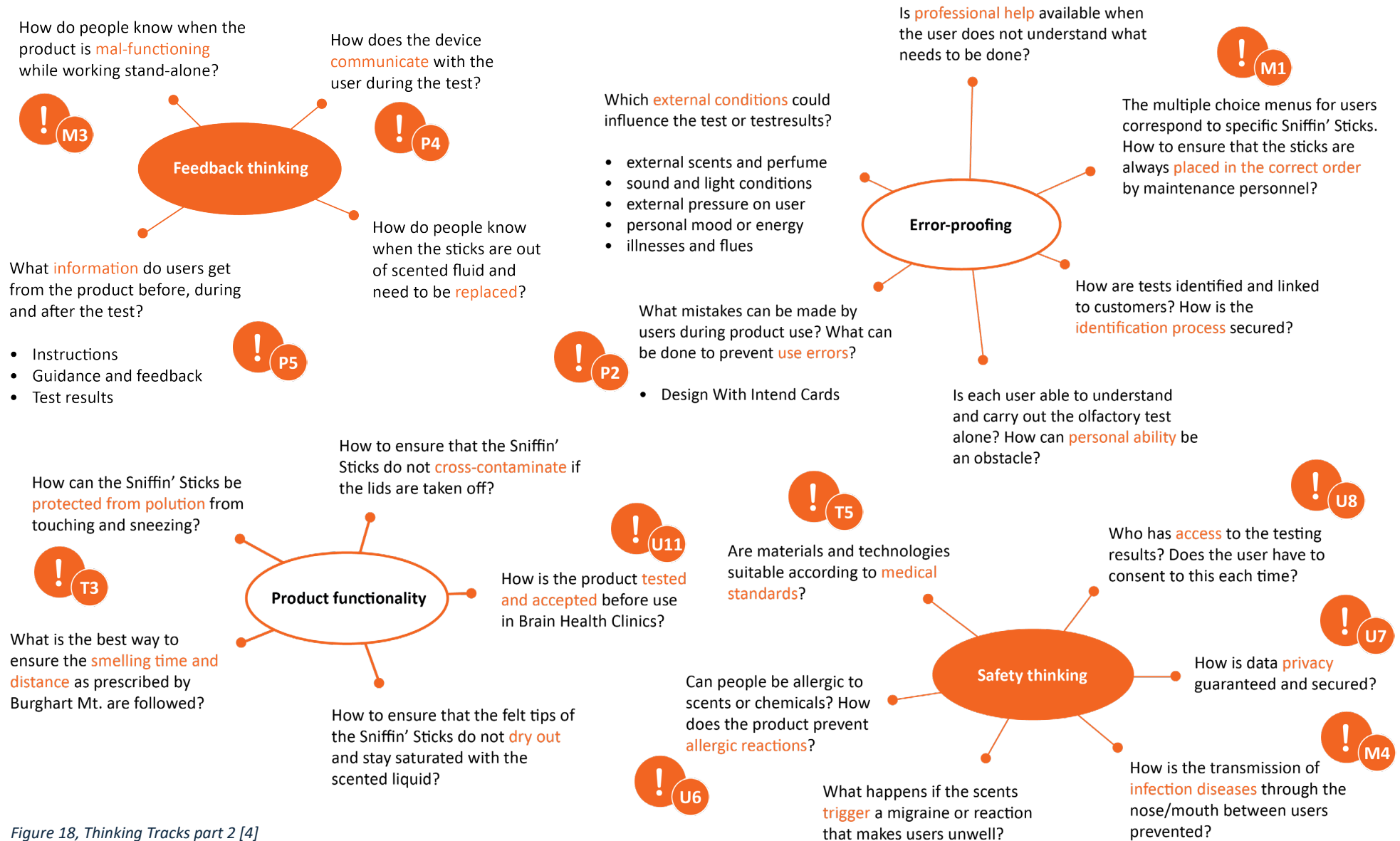


Figure 18, Thinking Tracks part 2 [4]

The questions in Figures 17 and 18 result in new product requirements. These are listed in Design take-aways 5.

The technical questions about the Sniffin' Sticks were answered in an interview with Burghart Messtechnik [*14]:

-  Sticks will cross contaminate if they are close together without a lid for a longer period. They need to be encapsulated separately.
- Sticks need to be stored at room temperature between 20 and 35 degrees Celsius. Direct sunlight should be avoided.
-  Sticks need to be stored in a vertical position with the felt tip pointing downwards.
-  Sticks have an expiration date. It does not matter how often they are used until this date.

Questions about look and feel of the product will be answered in Chapter 2.5.3.

Other questions are kept in mind for not require direct answering. The answers will follow in the develop and deliver phase through product design and additional research.

2.5.3 Appearance of medical devices

Much can be learned from existing medical devices in terms of aesthetics and form language. For this project, an aesthetic appearance that is professional and trustworthy, yet not overly medical, is preferred. The product should convey its expertise and reliability, without pressuring people to perform or worry people unnecessarily.

Figure 19 shows a collage of medical products gathered from the Spark Design & Innovation website and the iF rewards website. Learnings are shown on the left of the figure.



- Most angles are rounded
- Products have white, black and grey tones, sometimes supplemented by a single colour
- Form language is mostly geometric, apart from curvature of fillets and chamfers
- Slot shapes are frequently used
- Products are matt, not shiny
- 'Sleeves' are frequently used, for example in the upper left corner
- Shape changes are gradual and filleted
- Form and colour communicate functionality
- Products have large white surfaces, without unnecessary details



Figure 19, Medisign aesthetics form collage

Design take-aways V

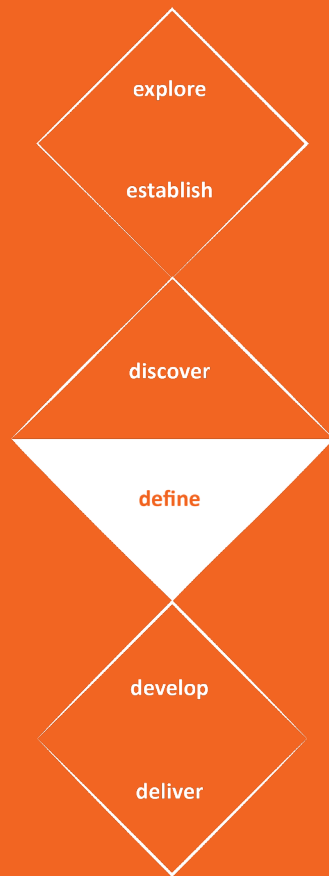
Chapter conclusions:

Different perspectives yield new insights and product requirements. Product functioning, error-proofing and user experience are shown to be major aspects of the design challenge, resulting in many relevant questions.

Requirements:

- T3:** The Sniffin' Sticks should be protected from pollution though sneezing and touching.
- T4:** The Sniffin' Sticks must not cross-contaminate.
- T5:** Materials and technology used must adhere to medtech standards and regulations.
- T6:** ODOFIN Sniffin' Sticks must be stored in vertical position with the felt tip pointing downwards.
- T7:** The product aesthetics should adhere to the Medisign form and colour findings in Chapter 2.5.3.
- U6:** Allergies must be ruled out upfront.
- U7:** User privacy must be considered to protect data and results [logging in with personal ID/DigiD].
- U8:** Permission to share data with the general practitioner and other parties must be given.
- U9:** The user must be able to stop at any given moment if feeling unwell. Uncompleted tests must be discarded.
- U10:** The test should be as inclusive as is realistic.
- U11:** The product must go through clinical trials.
- M1:** Sniffin' Stick placement must be error-proof to prevent misalignment between hard- and software.
- M2:** Sniffin' Sticks must be replaced before they start giving off less scent. This must be monitored.
- M3:** Malfunction must be recognizable and communicated to medical staff.
- M4:** The product must be easy to clean according to medical standards [the nose and mouth areas are prone to transmission of diseases, making cleaning and hygiene extra important].
- P2:** The test must be user error-proof. The user should be able to complete the test, regardless of ability, without help from personnel. Exceptions can be made and need to be listed.
- P3:** Pressure to perform well should be prevented.
- P4:** The product must be able to communicate with the user, and receive communication back.
- P5:** The user must be guided through the test procedure by the product.

3. Defining the design direction



3.1 Design space

3.1.1 Introduction

This chapter sets out the prerequisites and requirements that were obtained during the discovery phase (Chapter 2). A design space is sketched, which sets the premise for ideation and conceptualisation. Combined with the design drivers described in Chapter 3.2, this results in a project scope, as will be described in Chapter 3.3.

3.1.2 Compilation of design take-aways

All needs and wants discovered and described in Chapter 2 are listed in Figures 20 and 21. The Roman numbers (e.g. DT III) correspond to the Design Take-away chapters in which the needs and wants were mentioned.

case-finding

NEEDS:

- | | |
|---|--------|
| C1: Testing for Alzheimer's must be based on the Olfactory Identification test. | DT I |
| C2: Testing for Parkinson's must be based on the Olfactory Threshold test. | DT I |
| C3: For reliable results about neurodegeneration, repeated relative tests over time must be conducted rather than one absolute test. | DT I |
| C4: The product must enable users to self-administer the test without help of health care personnel, due to a shortage of personnel. | DT II |
| C5: The ODOFIN Sniffin' Sticks test must be used as underlying model, as this is the norm in the Netherlands and most of Europe. | DT III |
| C6: The official scoring method from Burghart Messtechnik must be used for a single absolute score per test. | DT III |

technical aspects

NEEDS:

- | | |
|--|--------|
| T1: Answers and results must be processed automatically, without additional administrative work. | DT II |
| T2: Sticks must be presented at the distance and duration as prescribed by Burghart Messtechnik, producer. It must account for different user body sizes. | DT III |
| T3: The Sniffin' Sticks must be protected from pollution though sneezing and touching. | DT V |
| T4: The Sniffin' Sticks must not cross-contaminate. | DT V |
| T5: Materials and technology used must adhere to medtech standards and regulations. | DT V |
| T6: ODOFIN Sniffin' Sticks must be stored in vertical position with the felt tip pointing downwards. | DT V |
| T7: The product aesthetics should adhere to the Medisign form and colour findings in Chapter 2.5.3. | DT V |

Figure 20, Needs and wants 'case-finding' and 'technical aspects'

user ethics

NEEDS:		
U1:	Users must be well-informed upfront about possible implications and consequences of results.	DT I
U2:	Testing must always be voluntary.	DT I
U3:	The product can only be used for screening if all 10 criteria of Wilson and Jungner apply.	DT I
U4:	The sharing of good results can be automatic, bad results should be shared by a medical professional.	DT I
U5:	The product must communicate upfront how and when results will be shared.	DT I
U6:	Allergies must be ruled out upfront.	DT V
U7:	User privacy must be considered to protect data and results [logging in with personal ID/DigiD].	DT V
U8:	Permission to share data with the general practitioner and other parties must be given.	DT V
U9:	The user must be able to stop at any given moment if feeling unwell. Uncompleted tests must be discarded.	DT V
U11:	The product must go through clinical trials.	DT V
WANTS:		
U10:	The test should be as inclusive as possible.	DT V

maintenance

NEEDS:		
M1:	Sniffin' Stick placement must be error-proof to prevent misalignment between hardware and software.	DT V
M2:	Sniffin' Sticks must be replaced before they start giving off less scent. This must be monitored.	DT V
M3:	Malfunction must be recognizable and communicated to medical staff.	DT V
M4:	The product must be easy to clean according to medical standards. The nose and mouth areas are prone to transmission of diseases, making cleaning and hygiene extra important.	DT V

product use

NEEDS:		
P2:	The test must be user error-proof. The user should be able to complete the test without help from personnel.	DT V
P4:	The product must be able to communicate with the user, and receive communication back.	DT V
P5:	The user must be guided through the test procedure by the product.	DT V
WANTS:		
P1:	The test should be a quick, easy and low-cost way of testing.	DT I
P3:	Pressure to perform well should be prevented.	DT V

Figure 21, Needs and wants 'user ethics', 'maintenance' and 'product use'

3.1.3 Prerequisites & list of requirements

The needs and wants described in Chapter 3.1.2 were analysed and categorised as either prerequisites or requirements.

Prerequisites are used as a project basis. They describe the contours of the project. Requirements on the other hand, are used to validate or discard ideas and concepts.

The compiled list of requirements [36] is shown in Figure 22. The needs and wants from Figures 20 and 21 that are not mentioned here are considered prerequisites. This is for example true for all 'case-finding' needs.

Keeping the number of requirements low allows for a more streamlined design process. Different needs and wants were combined to ensure a comprehensible and operable list. The result is four main items, focusing on independence, error-proofing, accessibility and reliability.

List of requirements

Needs/wants

A:	The product must enable the user to complete the olfactory test independently , without help from a healthcare professional.	P2
B:	The product must prevent human error during use or maintenance of the product. This includes: - during olfactory testing - in the evaluation of results - during (re)placement of sticks - during cleaning - during maintenance	M1, M2, M3, P2, P3, P5
C:	The product should allow for wide accessibility . This includes: affordability: as low as possible implementation and operation costs inclusivity: enable people with different physical and mental abilities to self-test without excessive physical or mental strain simplicity: reduce the threshold for maintenance, stick replacement and repair and make the product easy to operate and understand	P1, U10, M4, P3
D:	The product must be reliable in operation. This includes: - The Sniffin' Sticks must be protected from pollution through sneezing and touching. - The Sniffin' Sticks must not cross-contaminate. - The product must communicate errors and maintenance necessity. - The product must ensure correct procedures and scoring as described by Burghart Messtechnik. - Materials and technology used must adhere to medtech standards and regulations.	C6, T2, T3, T4, T5, T6, P4

Figure 22, List of requirements [36]

3.2 Design drivers

3.2.1 Introduction

Design drivers are determining factors that shape a design project and its final outcome. They are created during the Discover phase and the resulting requirements, discussed in Chapter 3.1.3.

3.2.2 Focus fields

The 3 design driver's for the coming Develop phase are *Product performance*, *Error-proofing* and *User experience*. The relevance and impact of each design driver is explained here.

1. Product performance:

Product performance aims at creating a functional model as prototype to validate the working principle. The functionality of the product is paramount. Within product performance, the aim is to create a working product in terms of internal dynamics. This means that the final product should enable independent olfactory testing.

2. Error-proofing:

In the medical context, error-proofing and safety are of the second highest concern.

Especially in self-test products, error-proofing plays a large role. Wrongly conducting a test could result in false results and false risk profiles.

3. User experience:

In order for the product to be accepted and embraced, user should want to use it. User experience is important both from a viability and a desirability point of view. This also deals with ethical considerations and user comfort.

3.2.3 Order of focus

Even though each of the three design drivers will contribute to the feasibility, viability and desirability of the product, an order of focus is required.

The intended final outcome of this thesis is a functional model of a product. As such, Product performance has the highest priority. This is followed by Error-proofing and lastly user experience.

3.3 Project scope

3.3.1 Introduction

The project scope describes the focus of this project, as influenced by the research findings. This includes the project goal and the primary design challenges. The scope is used as a lifeline throughout the design process.

3.3.2 Scope

“

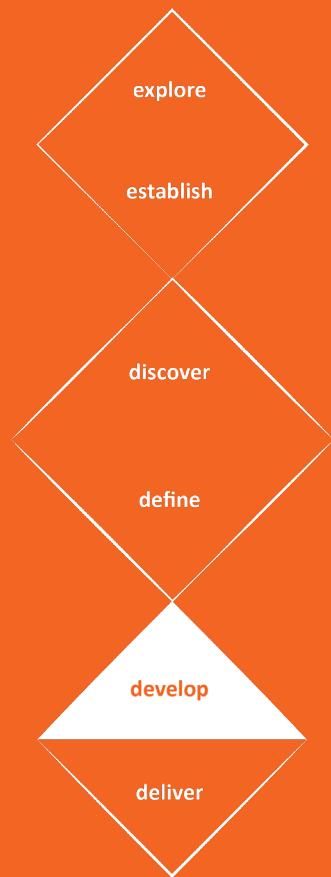
The challenge is to transform the original Sniffin' Sticks test from Burghart Messtechnik into an olfactory selftest that requires no professional assistance, while upholding or improving its reliability and error-proofness.

The product should be easy to use*, widely accessible** and suitable for the early-stage risk identification of Parkinson's Disease.

* easy to use = not causing people physical or mental strain

** widely accessible = affordable and obtainable for Dutch healthcare facilities, to ensure access in cities all over the Netherlands

4. Developing a concept product



4.1 Ideation

4.1.1 Introduction

This chapter attempts to illustrate how research insights resulted in product ideas through Design Thinking.

Design Thinking is the iterative process of generating ideas, testing them and evaluating results in order to obtain a satisfactory solution that adheres to the scope and requirements of the project.

A combination of sketching, peer-to-peer discussions and the use of creative methods was used. The outlines of this process and relevant findings are discussed here.

Valuable discoveries and conclusions along the way are indicated with orange markings and explained in the orange Mini Design Take-aways box on that page.

4.1.2 Basis for ideation

An adjusted version of the function tree, as described by the Delft Design Guide [36], was used to create an overview of the product's tasks and activities.

The thinking track *Dynamic thinking*, by Bonnema et al., was applied to ensure completeness of the function tree [4]. The function tree is shown in Figure 23. The list of tasks was used as design input.

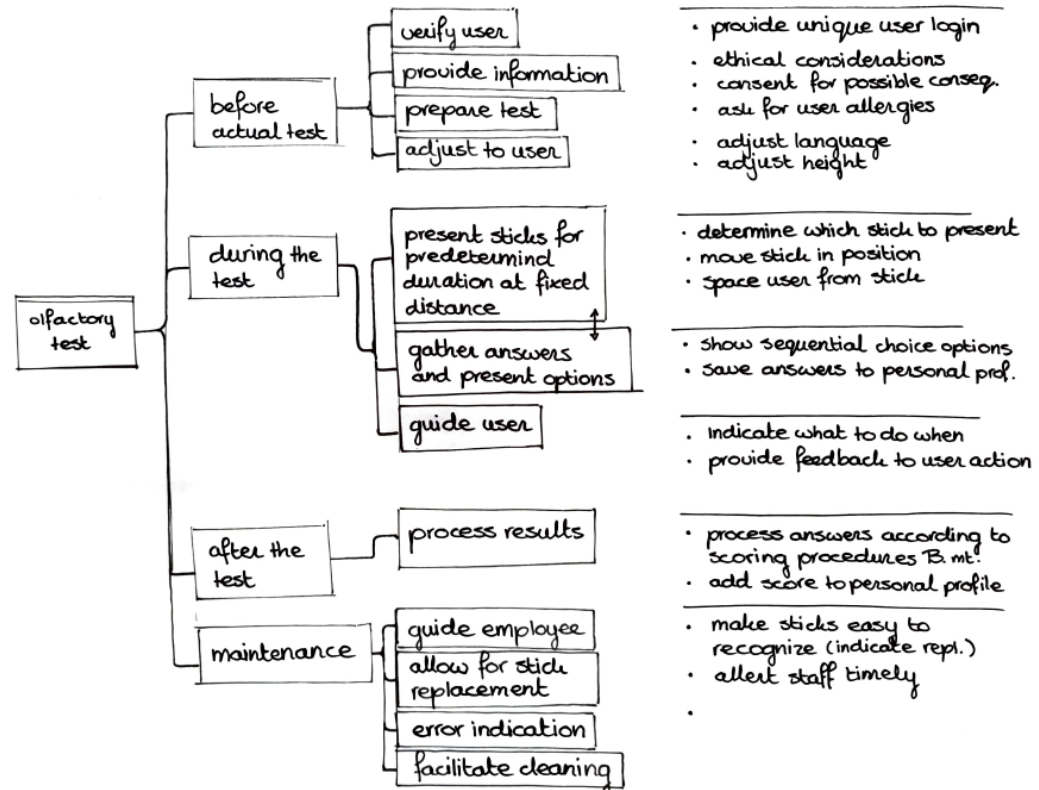


Figure 23, Function tree [36]

4.1.3 Overview of activities

Design activities

Note:

This report is structured to boost readability and does not reflect all under-the-shower ideas, back of the envelope sketches, unplanned activities and casual conversations over dinner that were part of this project.

1

ideation

- initial ideation sketches
- morphological chart: 3 idea directions
- Harris profile: choice automatic self-test
- creative session with peers: HKJs, morphological chart, brainstorm
- Design with Intent: creating a strategy for error-proofing
- shape and mechanism sketches

2

conceptualisation

- consult with B.A.T. Machinebouw: a single carousel as product base
- ideation & discussions stick-holder options on carousel
- identification of challenge areas

Further activities are described per identified challenge area (chronological within categories) | explained in Chapter 4.2.3

2A stick-holder mechanism	2B product base	2C positioning & adjustment	2D user interaction	2E programming & electronics	2F experience & communication
• prototype A0 • prototype A1 • prototype A2 • prototype A3 • prototype A4 • prototype A5 • prototype A6 • prototype A7 • prototype A8	• prototype B1 • prototype B2 • prototype B3 • prototype Open-close 1 • prototype Open-close 2	• head & chin rest concept • stand-alone vs table top research & peer discussion	• ideation & peer sparring sessions • prototype D1 • prototype D2 • prototype D3 • user interaction experiment	• prototype E1 • prototype E2 • prototype E3 • prototype E4	• literature study [2]: finding a strategy • clustering • ideation & peer sparring session
3 integration	• The integration of prototypes A8 (16x), B3, Open-close 2 and E4 is the final functional model shown in Chapter 5.				

4.1.4 Different idea directions

With the function tree in mind, numerous ideas were generated. A selection is shown in Figure 24. Methods like SCAMPER and Hoe Kun Je (HKJ) from the Delft Design Guide were used to fuel creativity [36]. Inspiration was taken from existing products as well. New things were discovered during sketching. These are written in the Mini Design Take-aways.

Mini Design Take-aways

- A** Existing tests (e.g. eye-tests) use a chin- and headrest to fixate the head in a right position. It seems to be generally regarded as the optimal method and can be used in the product as well.
- B** The Sniffin' Sticks have lids, which could be removed manually by the user. If not, they need to be removed before the sniff goes into the machine. A cover could replace the original lid.
- C** For scented fluid to reach the felt tips under the force of gravity, sticks need to be stored in a vertical or angled position.

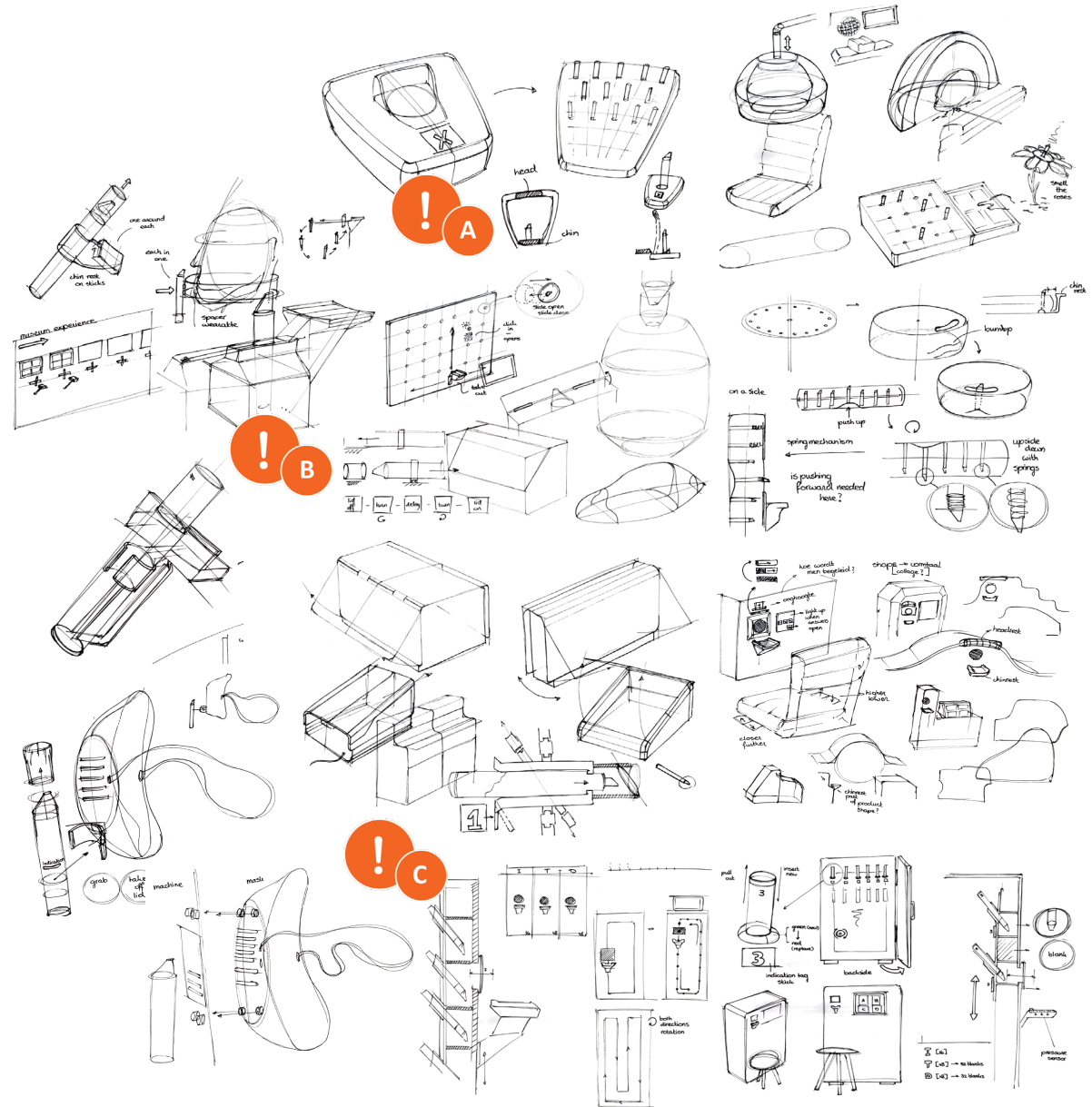


Figure 24, idea generation sketches (diverging)

The initial ideation phase resulted in several product ideas, which were analysed with the help of a morphological chart (See Figure 25) [36]. This analysis resulted in three possible product directions:

A. Guiding self test: Add-on

Allow users to conduct the test on their own by creating a product that can be attached to individual sticks and helps determining distance and duration.

B. Duo-test: Pick 'n Place

Allow users to conduct a test in duos, where the second person takes the current position of the medical expert. Create a product that allows the second person to lead and conduct the test properly without expertise.

C. Automatic self test: Sit 'n sniff

Allow users to conduct the test on their own by creating a completely automatic setup, where users only need to smell and answer.



A. Guiding self-test: Add-on

B. Duo-test: Pick 'n Place

C. Automatic self test: Sit 'n sniff

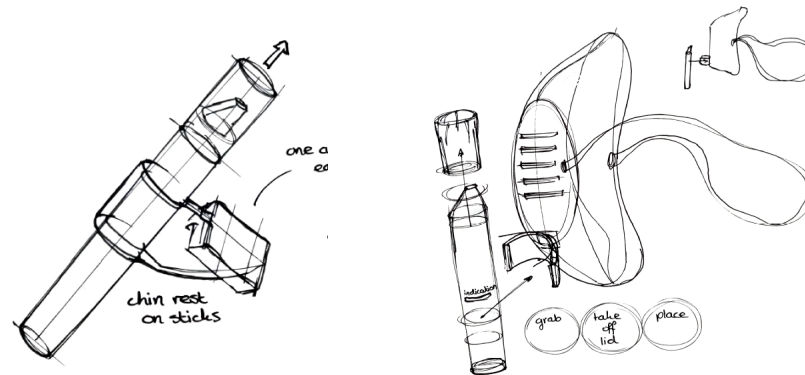


Figure 25, Morphological chart [36] and idea directions

The directions were compared with a Harris profile [36] based on:

- most reliable (**R**)
- lowest development costs (**C**)
- easiest to use (**E**)
- least distracting, most focus on smelling task (**F**)

These four cover the most important aspects of the scope and requirements, and are therefore suitable for quick, interim evaluation. They are listed in order of importance (see Figure 26).

The automatic self-test appeared to score best and is selected for further development.

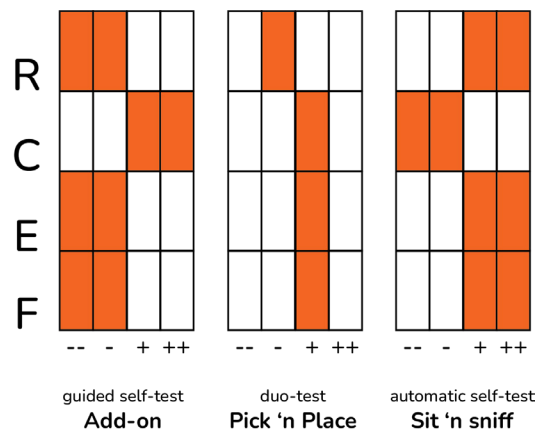


Figure 26, Harris profile [36] for idea comparison

4.1.5 Creative session

A one and a half hour creative session was organised to gain the fresh perspectives from five peers. They were given only selective information to prevent limitations. Notably, ideas were mainly experience-focused and included sensory and room design. These are shown in Appendix B.

This poses interesting questions about the atmosphere around testing and the product.

An interesting comparison was mentioned between the smell test and taking passport pictures in a self-service cubicle at the city hall.

These cubicles may serve as inspiration in user guidance.

4.1.6 Error-proofing in design

The product should minimise the risk of an erroneous test result. Unexperienced users with different mental and physical abilities should be able to conduct the test and receive valid results. Use stages were identified and the Design with Intent (Dwl) method [21] was used to devise an error-proofing strategy per use stage. This results in guidelines to follow

while designing different aspects of the product. This is shown in Figures 27 and 28.

Use stage:	Strategy (Dwl):	Lens Dwl:
0. marketing	Worry resolution	Machiavellian lens
1. user arrives at test location		
2. user logs in or is signed in	What you know	Security lens
3. user gets into the right position	- Matched affordances - Angles - Colour association	Errorproofing lens Architectural lens Perceptual lens
4. user gets test instructions and try-out	- Defaults - Anchoring - Do as you're told - Serving suggestion	Errorproofing lens Machiavellian lens Cognitive lens Machiavellian lens
5. user conducts test	- Prominence - Habits - Kairos - Proximity & grouping - Are you sure? - Progress bar - Interlock - Implied sequence	Perceptual lens Cognitive lens Interaction lens Perceptual lens Errorproofing lens Interaction lens Errorproofing lens Perceptual lens
6. user finishes test and leaves	- Conditional warnings - Rewards - Partial completion - Summary feedback	Errorproofing lens Ludic lens Interaction lens Interaction lens
7. maintenance and cleaning	Perceived affordances	Perceptual lens
overall safety	- Hiding things - Coercive atmospherics - Simplicity	Architectural lens Security lens Architectural lens

Figure 27, Error-proofing strategies per use stage



Figure 28, Selected Design with Intent cards [21]

4.1.7 Shape and mechanism

Different sketches and discoveries lead to a pulleys-timing belt mechanism, which is powered by a motor to transfer the sticks via the belt (see Figure 29).

Mini Design Take-aways

- D** The threshold test consists of 16 scented sticks and 32 blanks (no scent). A machine allows the sticks to be hidden from sight. Blank sticks can be 'faked' by not presenting anything. Leaving blanks out allows for a size reduction of 2/3rd.
- E** It is uncomfortable to look at the product up close while doing the test. Users should be able to look over the product while smelling.
- F** The largest surface area of the product should be horizontal, not vertical, for steadiness, adjustability of smell height and ease of maintenance.
- G** A screen in the same plane as the scent outlet forces users to move their head continuously. This disrupts flow. A screen should be placed at comfortable distance without need to move the head.
- H** Sniffing a flat surface or edge is uncomfortable. An ergonomic indent is preferred for comfort and guidance.
- I** Pulleys combined with a timing belt or chain allow for precise stick presentation.

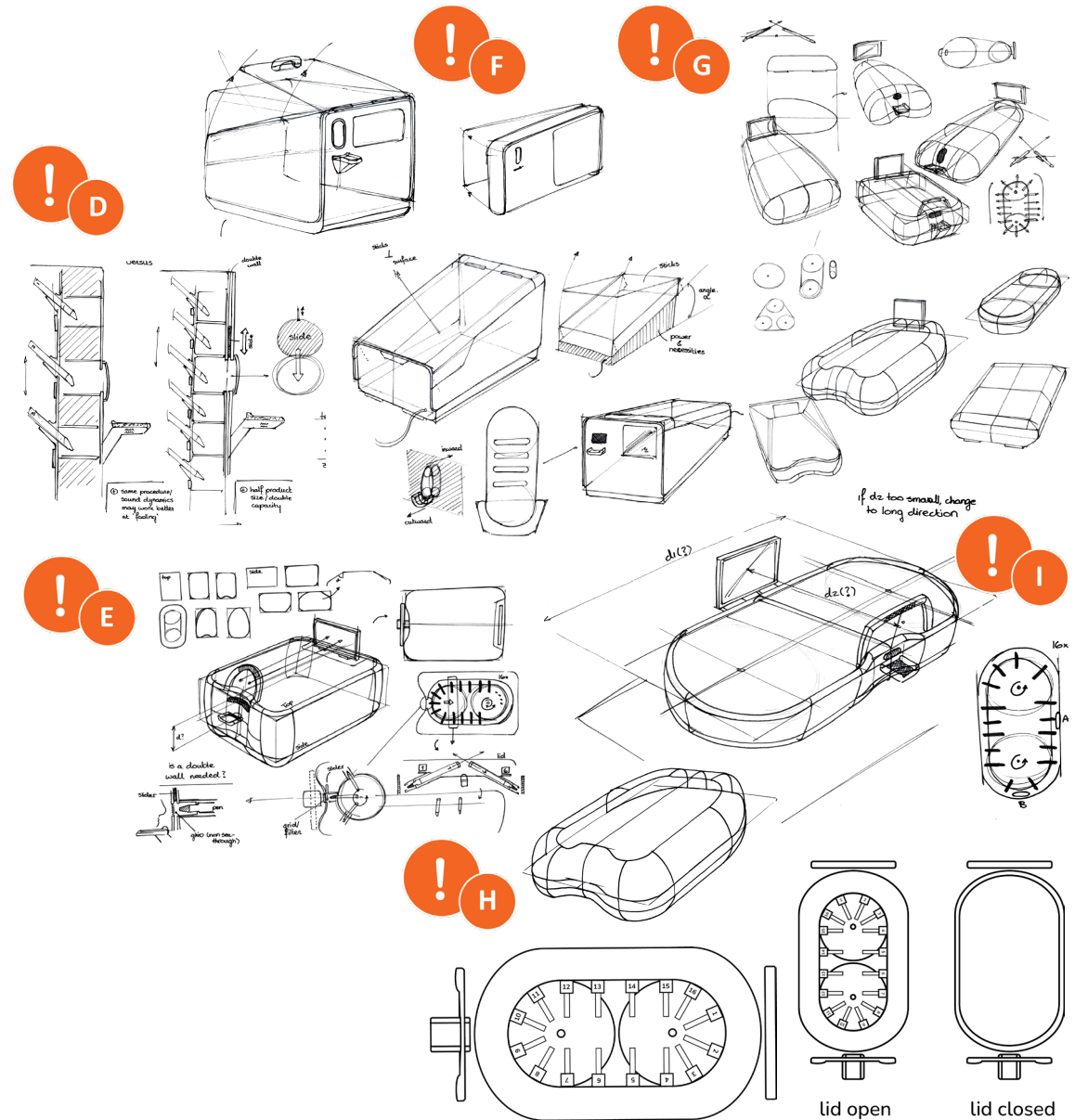


Figure 29, Shape and mechanism ideation

Design take-aways VI

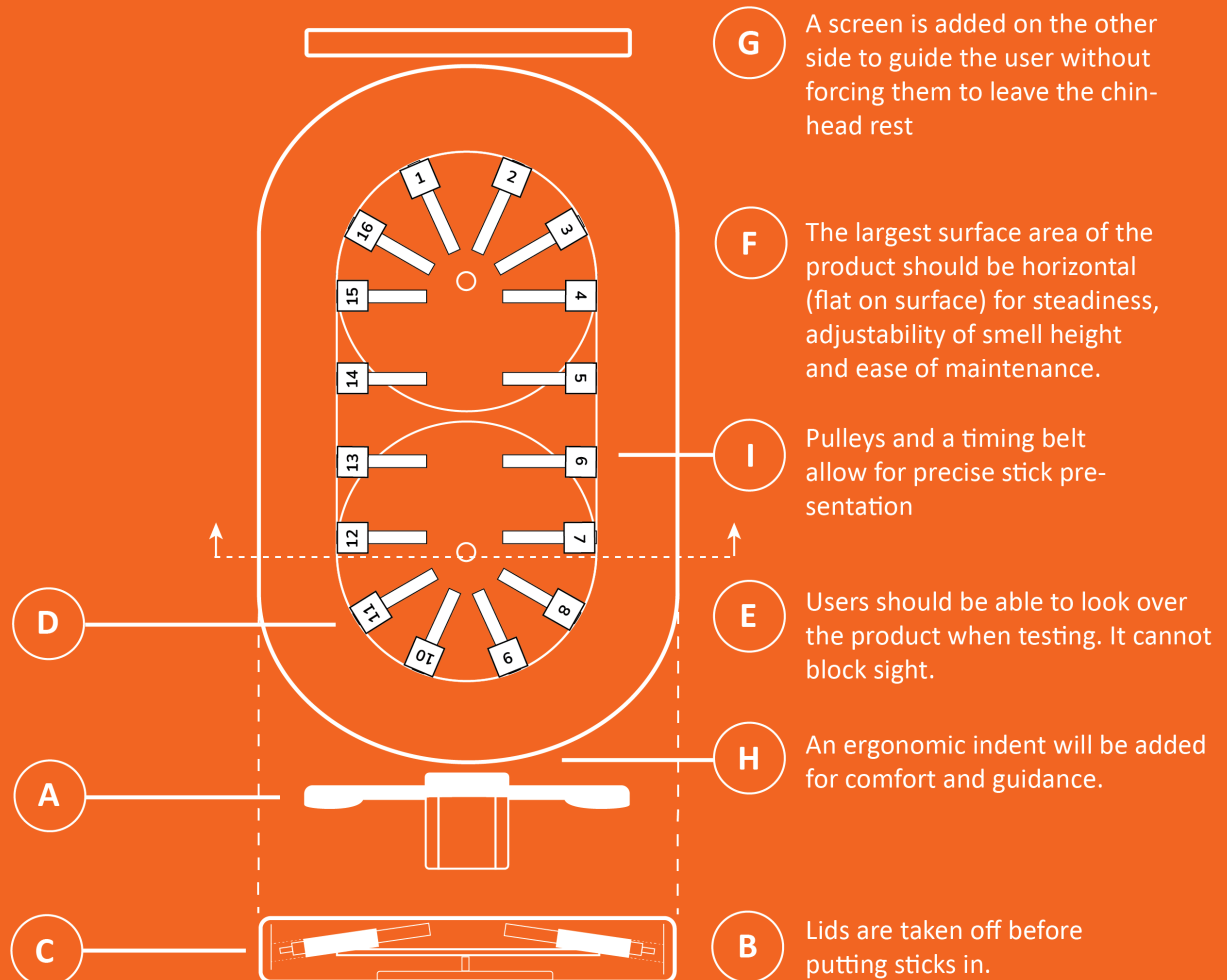
Chapter conclusions:

The ideation phase led to the design idea that is shown here. It entails an automatic olfactory self-test that allows users to conduct tests without professional assistance, as prescribed by the project scope. Sketches and peer discussions have resulted in new discoveries and requirements. These are integrated in the product idea and listed around the graphic. The internal mechanism is based on pulleys and a timing belt.

By hiding sticks from users, all 32 blanks can be left out, reducing the number of sticks needed for a test from 48 to 16.

Chin- & head rest for secure positioning

Sniffin' Sticks are stored under an angle so that fluid flows to the tip



4.2 Conceptualisation

4.2.1 Introduction

This chapter describes how the results and findings from the ideation phase further develop into a concept following an iterative process of sketching, prototyping, peer discussions and expert feedback.

Mini Design Take-aways

J V2 allows for removal of multiple components, such as a timing belt or chain and the pulleys. Merely a disc is required. This drastically reduces the costs of V2 compared to V1, according to B.A.T. Machinebouw.

K A round shape is in general more space efficient, resulting in smaller product size and less materials.

L A round shape is more errorproof as there is no mechanical transition or non-fixated components.

4.2.2 General concept: a single carousel

The final idea described in Design take-aways VI was discussed and improved during a consult with B.A.T. Machinebouw [*16]. B.A.T. is expert in mechanisms, related costs and

feasibility. The aim was to explore and discuss new possibilities for optimizing the internal mechanism. The meeting transformed product idea V1 into V2 (Figure 30), reducing product costs, size and proneness to failure.

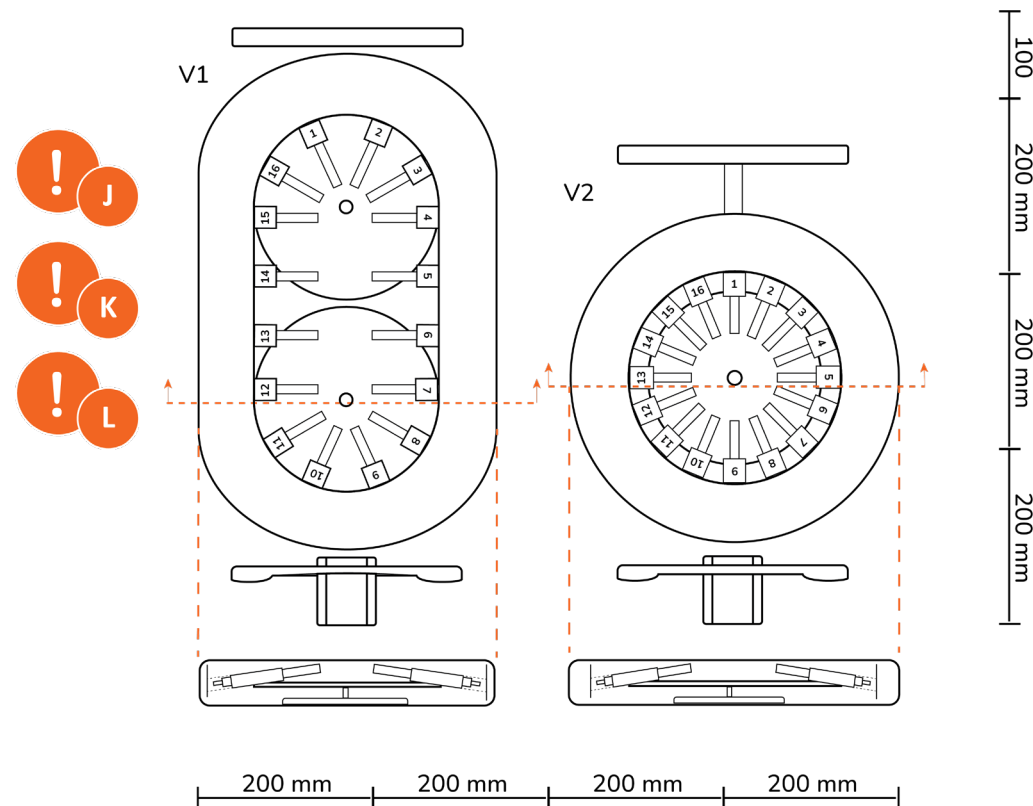


Figure 30, Concept improvement size comparison V1 and V2

4.2.3 Six challenge areas

Six different challenge areas were identified within the chosen single-carousel concept direction: Product base, stick-holder mechanism, user interaction, positioning & adjustment, programming & electronics and experience & communication. These are listed and explained in Figure 31.

The different challenge areas were created through brainstorming and peer discussions. ChatGPT helped completing the list.

Each of the directions can be regarded as a subassembly, that will be integrated into the main assembly once it is fully designed and tested. It goes without saying that these areas may overlap or influence each other. Cross-links are explained in the Integration Chapter.

An overview of activities per area is provided in Chapter 4.1.3. These activities are explained in more detail on the following pages.

A. stick-holder mechanism

Stick-holder mechanism entails the challenge of finding a suitable manner of storing, presenting and replacing sticks after the lid of the sticks is taken off.

Main challenges are:

- Sticks must be stored under an angle, tip down
- Users must be able to look over the device while testing
- Felt tips must not dry out
- Scent must not spread through the product to prevent cross-contamination of sticks

B. product base

Product base includes the rotating disc to which stick- holders are attached and the housing of the product.

Main challenges are:

- Carousel mechanism
- Minimizing the size and weight of the product
- Product appearance
- Atmosphere inside the product (scents, heat etc.)

C. positioning & adjustment

Positioning & adjustment focuses on physical ergonomics.

Main challenges are:

- Users should have their head in a predetermined position during the test
- The product should be adjustable in height to accommodate for different people

D. user interaction

User interaction is about finding a suitable way to receive feedback and answers from users, while their head remains in the chin- head rest. The latter is important for keeping focused, reducing test-duration, minimizing physical effort and preventing variation in position.

Main challenges are:

- Inclusivity: the device should ensure that users are mentally and physically able to provide their answers
- Optimising usability: there should be no difference between intended answer and registered answer

E. programming & electronics

Programming & electronics is about finding suitable hardware and creating an Arduino code that supports this hardware.

Main challenges are:

- Rotating, positioning and timing the carousel
- Supporting prototyping and user testing for area D.

F. experience & communication

Experience & communication is all about how to present the product to users for desirability and retention.

Main challenges are:

- Positioning the product in a manner that is appealing to people, without undermining the possible serious outcomes

Figure 31, Identified challenge areas

4.2.4 A. Stick-holder mechanism

The stick-holder mechanism encompasses a combination of different challenges:

- Sniffin' Sticks should be easy to place and remove after they expire by maintenance workers.
- Sniffin' Sticks must be stored in a vertical or angled position with the tip down, to ensure fluid flowing towards the tip under the force of gravity.
- Sniffin' Sticks are placed without lid, since automatic lid removal is costly and requires a lot of space.
- The felt tip of Sniffin' Sticks must be enclosed, to prevent them from drying out and cross-contaminating.
- Users must be able to look over the product when smelling the sticks. It is uncomfortable to be at a close distance from a vertical surface with your eyes.

1. Finding a suitable mechanism

From several options generated through ideation and sparring sessions prototype A0 prototype A1 were selected. Prototype A0 is an elastic band, wrapped around the carousel to cover all holes, except for one. The band is

pulled away by three pulleys at front. When the disc rotates, holes open and close.

Prototype A1 is a stick-lid mechanism that is opened and closed by a rack and pinion mechanism acting on the lid-gear (Figure 32). It was found that prototype A0 is prone to

cross-contamination. Due to a difference in circumference between band and carousel, the band does not align with the same hole each rotation. Prototype A1 was selected for further development. The modular aspect of the elastic band prototype was integrated.

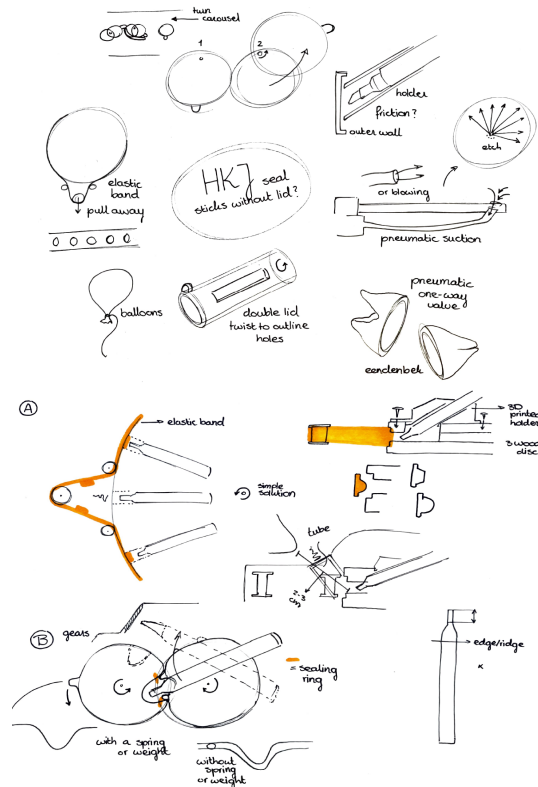
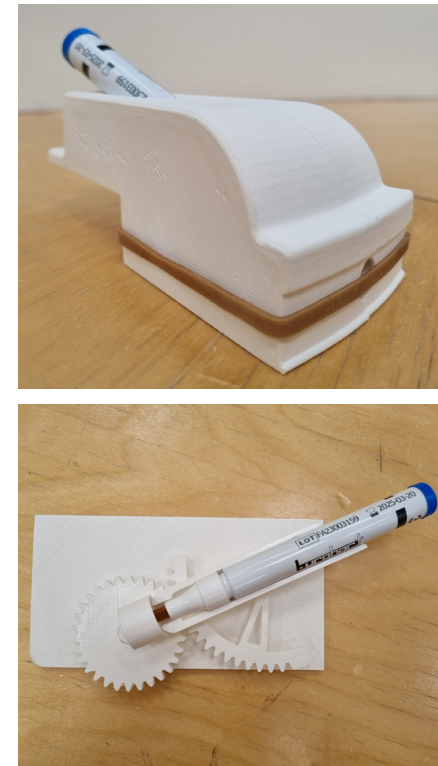


Figure 32, The development of prototypes A0 and A1



2. Developing the gearing mechanism

Selected prototype A1 was developed over a series of prototypes. The specific

improvements in prototypes A2 to A8 are shown in Figures 33 and 34.

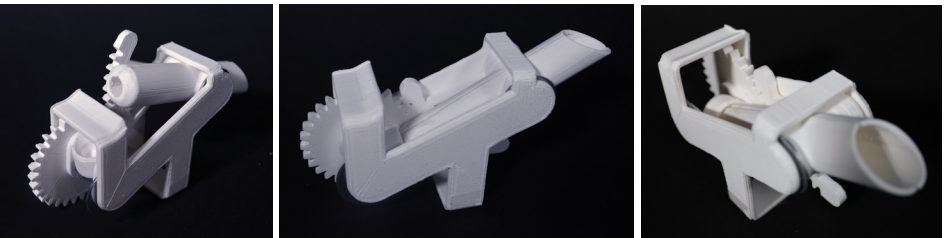
Prototype iteration	Information	Images
Prototype A1	Prototype A1 features a gearing mechanism with a stick-holder and a lid gear. An anti-clockwise rotation of the lid-gear forces a clockwise rotation of the stick gear. Both turn upwards, pushing the Sniffin' Stick out of the lid. Rotations are initiated by a rack and pinion mechanism acting on the lid-gear.	
Prototype A2	A1 was selected over A0 (Figure 32). However, the modular character of A0 was integrated. A module (or sub-assembly) is easier to (re)place, clean and repair.	
Prototype A3	Several inner diameters were tested in a shape experiment to find a diameter that allows for easy (re)placement, clamps the stick to prevent it from sliding out & uses the O-ring on the stick for sealing to prevent scent leaks.	
Prototype A4	Prototype A4 is a leaner version of A2. The rear width of the stick-holders determines product size. The smaller this width, the smaller the required carousel diameter. This finally results in a smaller and lighter product.	

Figure 33, Design iterations stick holder mechanism

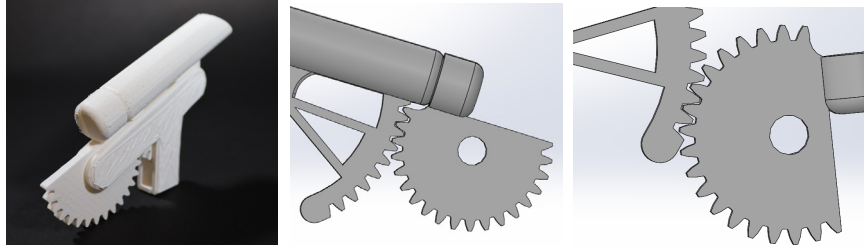
Prototype iteration	Information	Images
Prototype A5	Prototype A5 significantly decreases rear width by outlining the stick-holder and lid with the gears. This can be seen in the three images for comparison. Required carousel diameter was reduced from 45 cm to 30 cm.	
Prototype A6	Prototype A6 has a module housing, which keeps all parts together. The gears were adjusted to set more accurate limits to the possible rotation angle.	
Prototype A7	Prototype A7 adds a fastening mechanism to the bottom of the stick-holder, allowing maintenance workers to attach and remove the stick-holders from the carousel. This is a first version and will require further development.	
Prototype A8	Prototype A8 gives a finishing touch to the stick-holder mechanism by adding a rubber O-ring to the lid, that functions to seal off any openings and prevent the stick from drying out or cross-contaminating.	

Figure 34, Design iterations stick holder mechanism

4.2.5 B. Product base

This chapter explains the design process of the carousel, the open-closing mechanism and the product housing.

1. Carousel design

Figure 35 shows how the carousel developed over time, highlighting the most important learnings and developments.

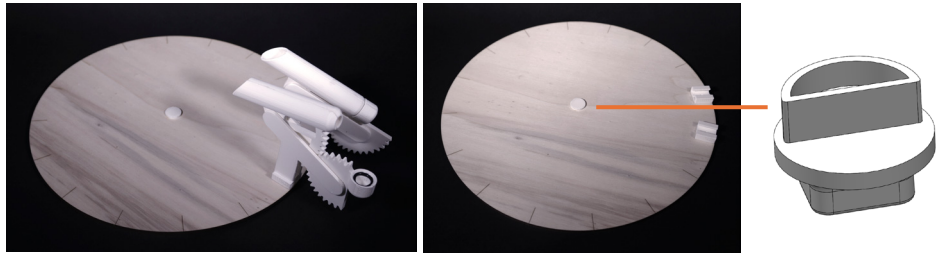
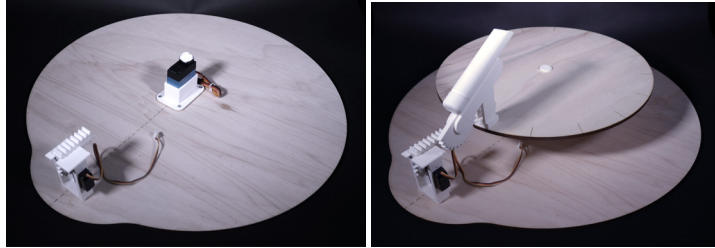
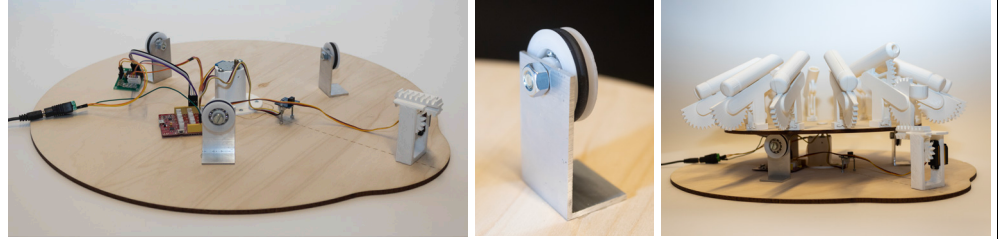
Prototype iteration	Information	Images
Prototype B1	Prototype B1 was created after the minimal required diameter was determined with prototype A5 (stick-holder design).. A half circle was removed the middle of the disc. The white centre piece of the disc has a form fit for both carousel and motor to control rotation.	
Prototype B2	Prototype B2 added the lower product part, on which drivers 1 and 2 are placed; the motor that rotates the carousel and the rack and pinion mechanism that opens and closes stick-holders.	
Prototype B3	Prototype B3 has 3 lagers on the baseplate. These carry the carousel, so that no additional weight is put on the motor. They also ensure steady and smooth rotation of the carousel, despite the additional weight of the stick-holder mechanisms.	

Figure 35, Design iterations carousel

2. Open-closing mechanism

Figure 36 shows how the open-closing mechanism developed over time, highlighting the most important learnings and developments.

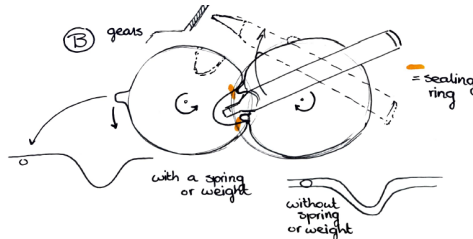
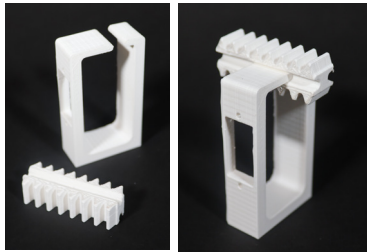
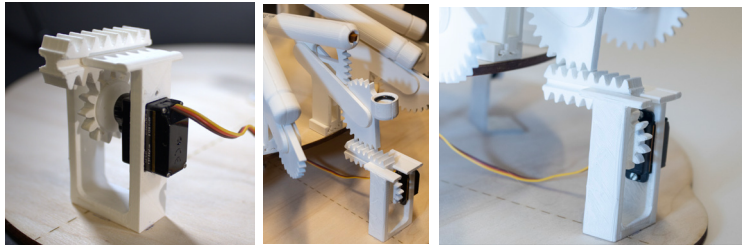
Prototype iteration	Information	Images
Ideation	The initial idea was to let the lid-gear slide along a guiding ridge or slot in the product housing. However, due to the resistance from 16 stick-holder mechanisms and the sounds it would make, this idea was dismissed and replaced by a rack and pinion concept.	
Prototype Open-close 1	Prototype Open-close 1 features a rack and pinion mechanism powered by a servo motor. The rack slides on the guiding ridges of the frame.	
Prototype Open-close 2	Prototype Open-close 2 has a longer guiding ridge than version 1. This was necessary to ensure stable rack and pinion movements at both ends.	

Figure 36, Design iterations Open-closing mechanism

3. Product housing

The design of the product housing is based on the form collage and findings from Chapter 2.5.3. Figure 37 follows on previous form sketches from Chapter 4.1.7. Apart from Medisign aesthetics, focus lies on usability and user guidance. A design with foldable display, headrest and lower frame was chosen for transportation and storage. It also helps creating an integrated look; a single product instead of a multiple component test setup (see Figure 38).

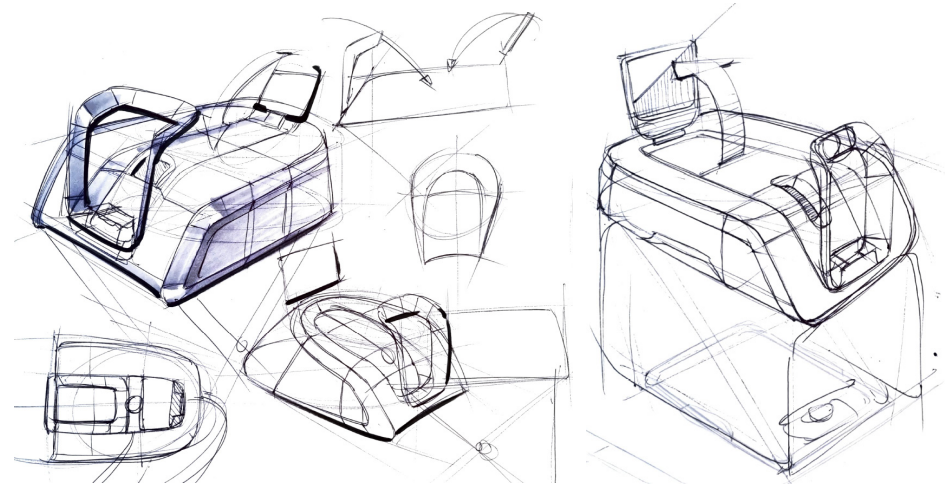
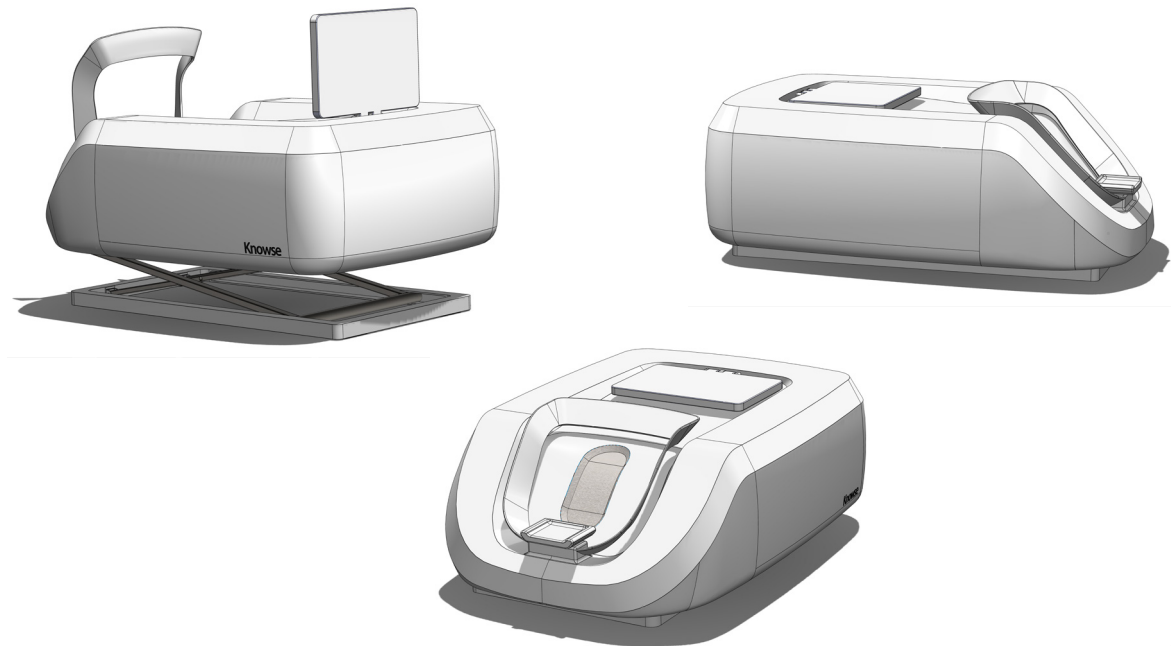


Figure 37, Final sketches product housing (by Renzo Vonk in a collaborative session)



Figure 38, SolidWorks model of the final sketches



4.2.6 C. Positioning and adjustment

Positioning and adjustment covers the physical ergonomics challenges. Inclusivity of the concept product is largely determined by this.

1. A sitting position

People conduct the test in a **sitting position**. This is in line with other sensory tests, like hearing and vision examinations. An important reason for this is that not everyone is able to stand (for the full test duration). Similar tests are always conducted in sitting position for standardization and test comparability reasons.

2. Tabletop over stand-alone

The product can be presented to the user in different ways. It can be put on a table, stand-alone or hanging from the ceiling or a wall. The latter was discarded, as this is expensive and adds unnecessary complexity for installation. The tabletop and stand-alone options are provided in Figure 39. Stand-alone devices are often used in the medical context for their manoeuvrability. This advantage lies in the possibility of adding wheels, like is done in mobile medical workstations. Additionally, no table is needed.

However, a stand-alone device brings complications like product size, weight and construction challenges. This has an effect on costs, storage options and transport.

As no manoeuvrability is required in this context, the costs outweigh the benefits of a stand-alone device. The product will therefore be placed on a table.

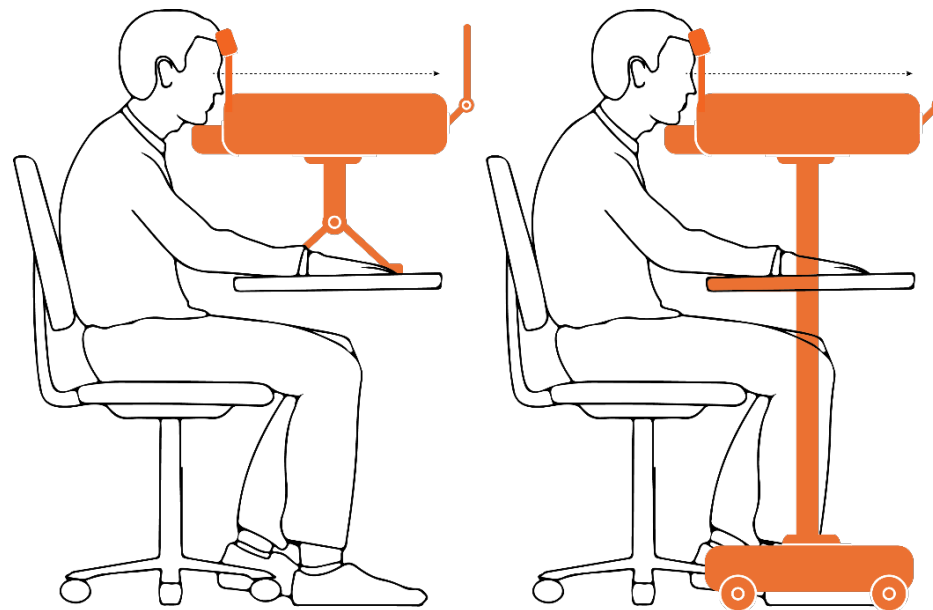


Figure 39, Tabletop versus stand-alone product

3. Height adjustability

The device must be adjustable in height to accommodate for a large variety of people. People have different upper-body lengths. As can be seen in Figure 39, the product needs to bridge the distance between tabletop and the user's head. Two things are important for the lower structure:

- The **stability** of the product. Users will put their head in a chin-head rest, which will cause additional load on the front edge of the product.
- The **ease of adjusting** product height. New user may require another product height.

Ideation through sketching and peer discussions resulted in 4 possible solutions inspired by existing products (see Figure 40).

Option 3 was selected for its stability, height adjustability and space-efficiency for storage. The part was purchased from Ivono to be added to the product. The Ivono laptop stand is not perfect for this specific application however, and should be redesigned before integration.

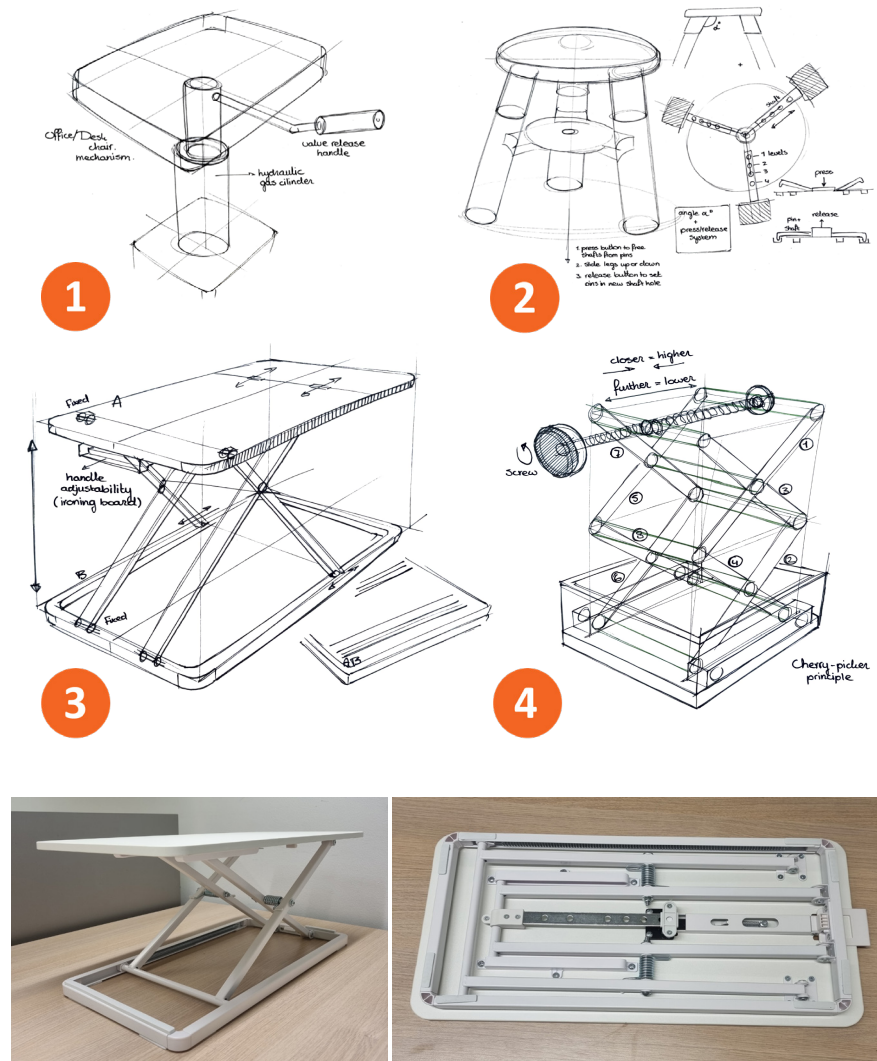


Figure 40, 4 possible solutions for height adjustment and prototype C1

4. Chin-head rest

The Sniffin' Sticks threshold test by Burghart Messtechnik has a strict procedure, which the product needs to adhere to. This procedure is described in Chapter 2.3.2. This also includes a prescribed distance between the stick and the nose of 2-3 centimetres.

A chin-head rest is used to support the user's head and space it from the sticks. A chin-head rest also minimizes required body movement, test-duration and distraction, while improving consistency. Chin-head rests are the norm in the vision testing industry.

5. Arms position for input

The most comfortable position for the hands, in upright sitting position, is at table height [34]. Consequently, people should be able to place their hands on each side below the product (see Figure 41). This is outside the user's range of vision, forcing users to **provide answers with their hands in a blindly manner**.

An alternative is to place the feedback input mechanism on the device itself. However, this idea was dismissed as rising and upholding the arms for a longer period of time requires flexibility and strength that is uncomfortable or even impossible for most users.

4.2.7 D. User interaction

An important function of the concept product is to guide users through the test and to enable them to provide their answers to the questions.

In the before described sitting position, with eyes on the guiding screen, the user is unable to see their hands. A blind feedback mechanism is required. This mechanism should be foolproof; **the given answer should always be the intended answer**.

The book Design-relevant characteristics of ageing users [34] was used to determine the following guidelines for the design of a blind feedback mechanism:

- Subtle hand movements and high sensitivity should be avoided. The mechanism should be robust and 'clumsy'. Arm movements > hand movements > finger movements.
- Buttons on new products should be avoided if people cannot see their hands.
- Wrist twisting range is limited and should be avoided if possible.
- The mechanism should be suitable for left- and right-handed users.

- The arm should be able to rest on the table while giving input.
- Haptic feedback should be combined with visual feedback from the screen. Confirmation for answers should always be asked.
- Familiar mechanisms are intuitive.

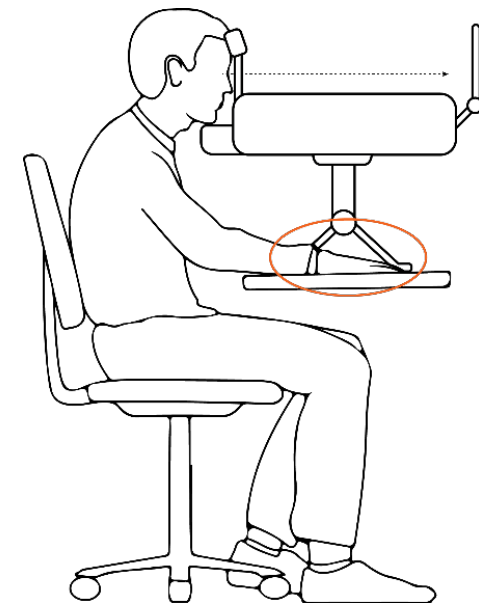


Figure 41, Arms in sitting position

From a brainstorm session, two viable options were selected for prototyping and user testing; a standard HP computer mouse and a slider prototype (D3) that was designed according to the guidelines (see Figure 42).

A qualitative user experiment (n=7) revealed that people preferred the computer mouse in terms of usability. The full research report is added in Appendix F.

The device will be connected to a computer mouse, through which people provide their answers. Users are guided by a screen on the product. A computer mouse can be used on either side of the product for left- and righthanded users.

4.2.8 E. Programming & Electronics

Programming and electronics covers the electronic design of the product and input device prototype D3. Consults with PMB staff and Applied Labs helped in finding the right hardware. Programming was done with the help of ChatGPT and peers. Arduino codes are added to the data package.

Carrousel driver

Figure 43 show the different steps in the design process from a servo motor to the final stepper motor design. This final design does not yet work properly and further iterations are required.

Open-closing mechanism driver

A small servo motor powers the gear in the rack and pinion mechanism that opens and closes stick-holders for stick presentation.

Prototype D3

Prototype D3 has two main electronic functions:

- Upon moving the slider, as indicated in Figure 42, the device has to update the user on the real-time location of the slider. In the prototype this is achieved with 3 Infrared reflective sensors as input and blue LEDs as output.

- When the user presses the slider knob, the device sees this as a 'submit answer'. 3 buttons allow for pressing the knob at the 3 locations. Again, this is communicated to the LED, which will emit green light.

Details on this design can be found in Appendix E.

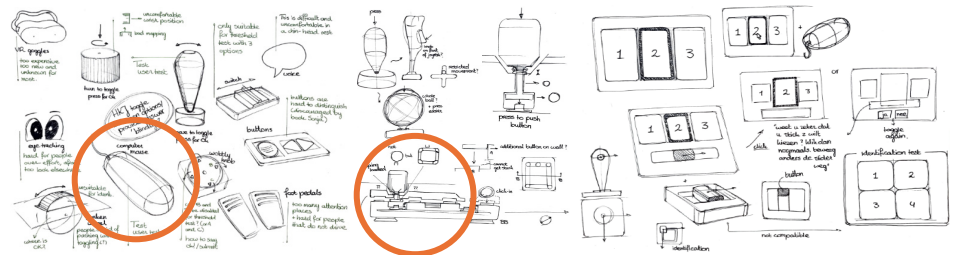
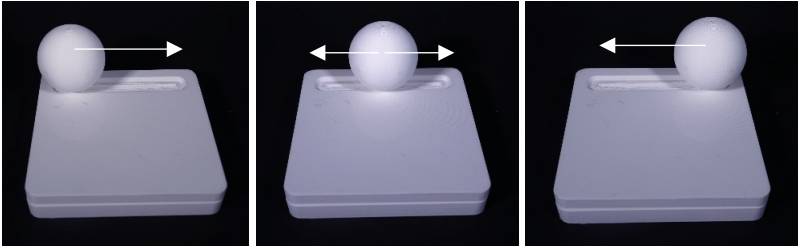
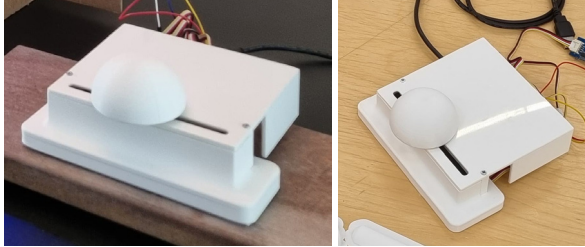
Prototype iteration	Information	Images
Ideation	A brainstorm session resulted in different blind input mechanism options. A computer mouse and a self-designed joystick-slider mechanism were deemed most promising when judged on the before described guidelines.	
Prototype D1	Prototype D1 features the first version of the slider input device. Users grab the spherical handle and slide it along the slot to select one out of three options (left, middle, right). Location feedback is given by 3 buttons via a screen. Users can press the sphere to submit answers through another 3 buttons.	
Prototype D2	Prototype D2 is more refined than D1. Location tracking is now done by infrared reflective sensors instead of buttons. This, combined with several 3D printing improvements makes sliding much smoother.	
Prototype D3	Prototype D3 only has another upper part than D2, in order to hide and protect the electronic components during user testing.. The details of the prototype are given in Appendix E.	

Figure 42, Design iterations input mechanism

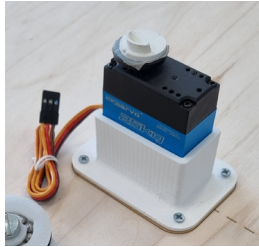
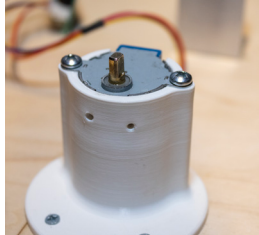
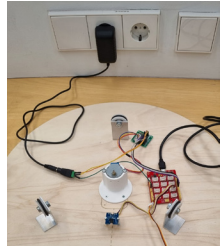
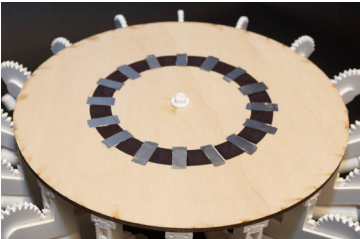
Prototype iteration	Information	Images
Prototype E1	Initially, a 360 degrees high torque servo motor was selected to rotate the carrousel. Servo motors have an built-in potentiometer that allows it to always know its position. This worked, but lacked accuracy and only rotated 180 degrees due to a delivery mistake.	 
Prototype E2	As full rotation and better precision is required, a 5V stepper motor was used. Stepper motors offer more precise rotation control than servos, but do not know their location.	 
Prototype E3	The 5V stepper motor did not have enough power to initiate rotation of the carrousel with stick holders. A 12V stepper motor is used instead. This motor is connected to a power outlet with a power plug. The 12V motor has sufficient rotation power, but still lags from the carrousel's inertia.	 
Prototype E4	As the stepper motor does not automatically register its location, an additional infrared reflective sensor was added. This sensor registers black and reflective surfaces on the carrousel above it to determine position.	 

Figure 43, Design iterations carrousel driver

4.2.9 F. Experience & communication

This challenge area covers how the product should be positioned in order to be adopted by users. This is important for marketing as well as user experience. The message “*An olfactory test that might tell you that you have a high risk for life-threatening neurodegenerative diseases*” may not be the most successful means of communication. It could even have a negative effect on the testing experience and the results.

The book *Design Things That Make Sense* by Deborah Nas was used to design a positioning strategy that strengthens benefits (B...) and mitigates resistance (R...) [24]. It is based on the Typology of needs for human centred design [5]. A selection of the proposed strategies was used to create a strategy, product name and positioning statements (see Figure 44).

The industry of case-finding for neurodegenerative diseases is currently non-existent and will appear only once more reliable treatment options have been found. A two-phases strategy is proposed, with two different goals in mind.

Phase 1, finding acceptance

The first phase is about normalising olfactory testing, without risk-profiling, so that the product finds more recognition and embrace when treatment options become available.

The positioning, according to strategies B13 ‘evoke joy’, B15 ‘stimulate learning’, B16 ‘provide insight’, B17 ‘fuel motivation’ and R3 ‘offer transparency’ [24], lies on the curiosity and learning aspect that the product could offer. This is described in positioning statement 1.

The product is called **knowse**. knowse is a portmanteau (combination of two words): nose + knows. It aims to emphasise the curiosity and learning aspects of the interaction.

Phase 2, creating impact

Phase 2 is about case-finding for neurodegenerative diseases like Parkinson’s and at a later stage, Alzheimer’s. A link could be made to official healthcare institutes and risk profiling may be done based on test results, in combination with other tests.

Positioning statement phase 1:

“For individuals curious about their health status and interested in enhancing their personal wellbeing, knowse is an olfactory test that provides insights into one’s sense of smell and its impact on daily life. Unlike other sensory examinations, knowse enables users to self-test and track their olfactory health over time.”

Positioning statement phase 2:

“For individuals worried about their health status and looking for answers, knowse is an olfactory test that provides insight into one’s risk for neurodegenerative diseases based on sense of smell. Unlike other tests, knowse is comfortable, non-invasive and accessible.”

Figure 44, Positioning statement 1 and 2 knowse

Design take-aways VII

Chapter conclusions:

The basic product idea that was created during ideation, was divided into 6 challenge areas for the conceptualisation phase. Each area represents a different aspect of the overall conceptualisation challenge. This sub-division helped simplifying and structuring the complex design project:

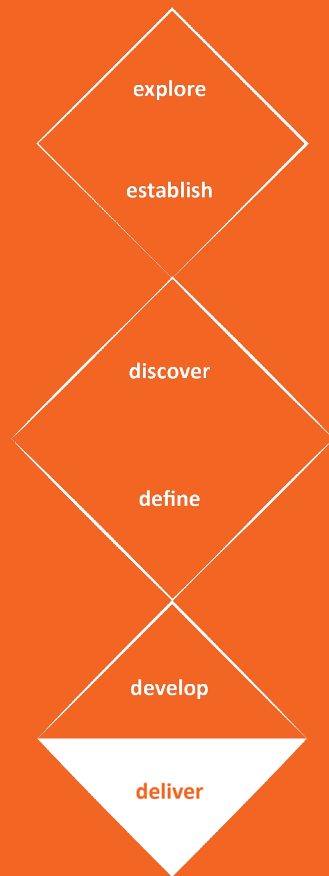
- A. Stick-holder mechanism
- B. Product base
- C. Positioning & adjustment
- D. User interaction
- E. Programming & electronics
- F. Experience and communication

The areas are given in global order of importance, although one could argue that in this project areas C and D were given equally much attention.

The specific solutions to each challenge are combined in the Deliver phase, which is the next chapter of this report.

Besides the 6 challenge areas, this conceptualisation phase also considered overarching challenges, like error-proofing, ergonomics and product size and costs. These can be seen as a blanket over each challenge area. Although not always mentioned, they were considered every step of the process.

5. Delivering Knowse



Knowse is an **olfactory evaluation tool**, that allows users to conduct the **ODOFIN Sniffin' Sticks** test without the assistance of a medical professional.

By automating stick presentation, answer processing and score calculation Knowse offers **better reliability on a bigger scale**.

The error-proof design, based on simplicity and active user guidance, accommodates for both the threshold and identification test, allowing the product's use for early stage **risk-profiling** of neurodegenerative diseases.



5.1 Sniffin' Sticks '+'

Knowse is an addition to the existing Sniffin' Sticks test (see Figure 45) from Burghart Messtechnik. In its current context, the Sniffin' Sticks test is manually conducted by medical professionals. For example, to detect brain damage and to understand olfactory function of patients.

For the context of case-finding of neurodegenerative diseases, the current test is unsuitable. Knowse enables automated self-testing, scoring and processing of results.

Knowse removes the human facilitator from the test. This makes the Sniffin' Sticks more future-proof, increases accessibility and decreases costs per test. Automatization combined with error-proofing strategies also reduces its proneness to human mistakes, making the test more reliable, if designed well.

Figure 46 provides a first glimpse of Knowse. The product housing was made transparent in the visualisation below to show the internal mechanism inside the product. The Sniffin' Sticks are inserted to the product via the top side. Medical personnel remove the lids and slide the 16 Sniffin' Sticks

into the stick-holders, tip down. After loading Knowse, users can conduct self-tests at location. The carousel rotates and presents the different stick-holders with sticks in order. More about the internal mechanism is explained in Chapter 5.3.

Knowse facilitates for both the Sniffin' Sticks threshold test and identification test. As was explained in Chapter 2.3.2, the threshold test requires the product to be able to present the previous and next set of sticks. The carousel therefore turns both ways, depending on user input.



Figure 45, Sniffin' Sticks test, by Burghart Messtechnik



Figure 46, Housing and internal mechanism Knowse

5.2 Context of use

Knowse can be used to track improvements or decline in olfactory function. The product is placed on a table (see Figure 47) and could in the future be found in Brain Health Clinics or at the optician.

Users take a seat (see Figure 48), place their head in the chin-headrest and adjust its height if necessary. They then log in to the program. A full threshold or identification test is estimated to take about 20 minutes.



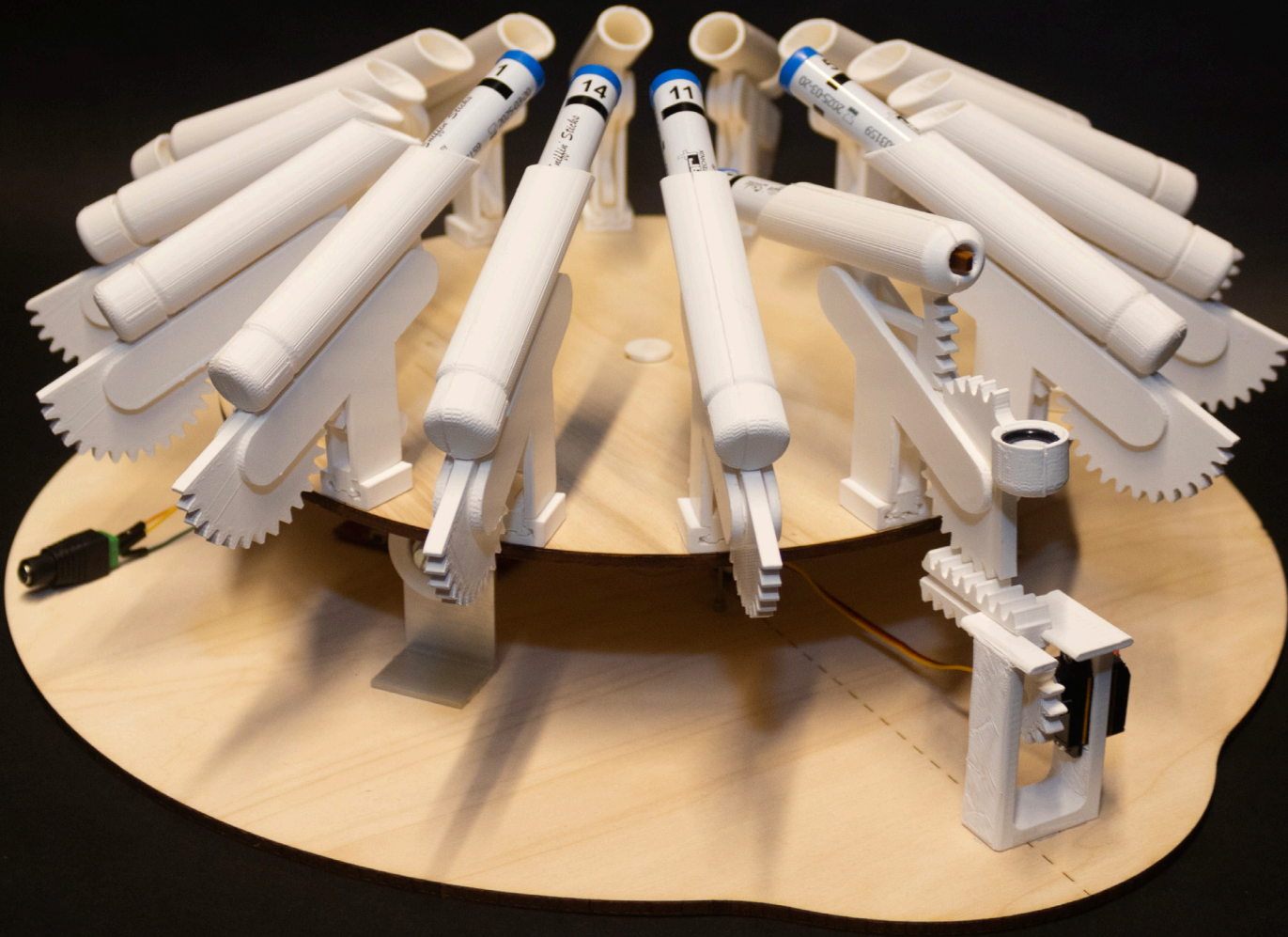
Figure 47, Setup Knowse



Figure 48, Person using Knowse

After the test, results are saved to a personal profile. After multiple tests at time intervals of half a year to a year, a trendline becomes visible. This personal, relative profile provides insight into one's olfactory development over time.

Once treatment to neurodegenerative diseases like Parkinson's and Alzheimer's becomes available, the product can be used for preclinical case-finding.



5.3 Product design explained

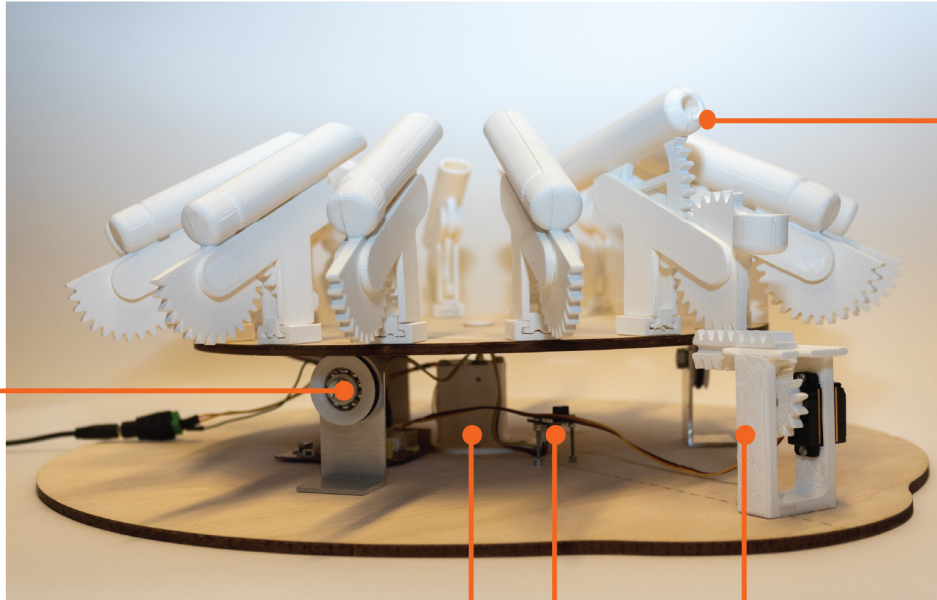
5.3.1 Internal product features

Knowse features a carousel on which stick-holders are mounted. Sniffin' Sticks are put into the stick-holders without their lid. As the carousel rotates, different sticks come forward. A rack and pinion mechanism opens the stick-holders to present the Sniffin' Stick to the user.



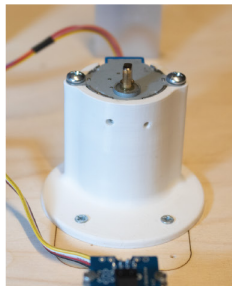
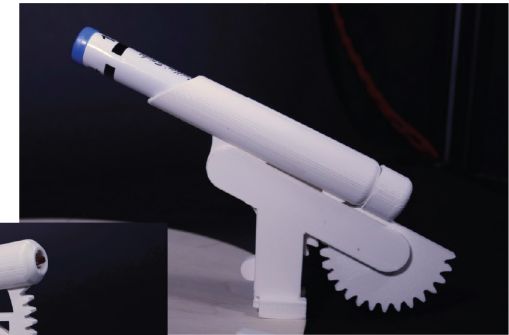
Carousel stability

Three bearings carry the carousel weight and ensure smooth rotation.



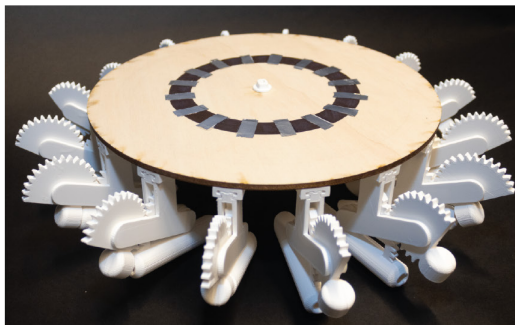
Stick-holder mechanism

Sniffin' Sticks are inserted into the stick-holder mechanism without lid. The mechanism prevents drying out of sticks and cross-contamination. Its mechanics allow for stick presentation at a precise, pre-determined location when opened by the open-closing mechanism.



Stepper motor

The carousel is rotated by a stepper motor, connected to a 12V power plug.

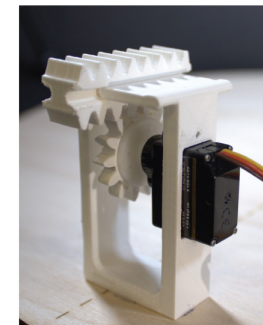


Infrared reflective sensor

Location information is provided by an IRF that registers differences between reflective and non-reflective boxes. This allows the stepper motor to rotate accurately.

Open-closing mechanism

A rack and pinion mechanism pushes and pulls on the front stick-holder to present or remove Sniffin' Sticks.



5.3.2 External product features

Knowse was designed with a focus on user guidance and error-proofing. Its aesthetical appearance is inspired by existing medical product designs.

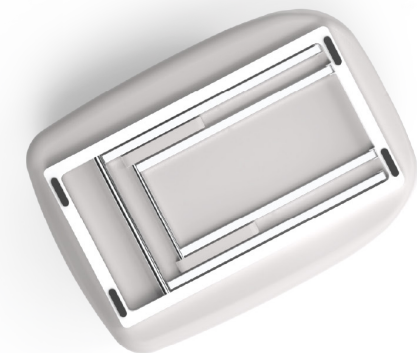
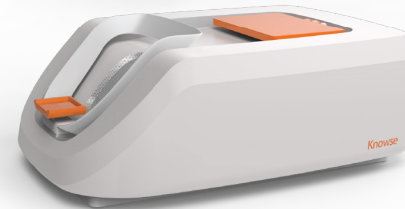




Guiding display
Users are guided through the test via a display. It provides information and real-time feedback.



Foldable design
The display, headrest and the height-adjustable standard can be folded in to facilitate transport and storage.



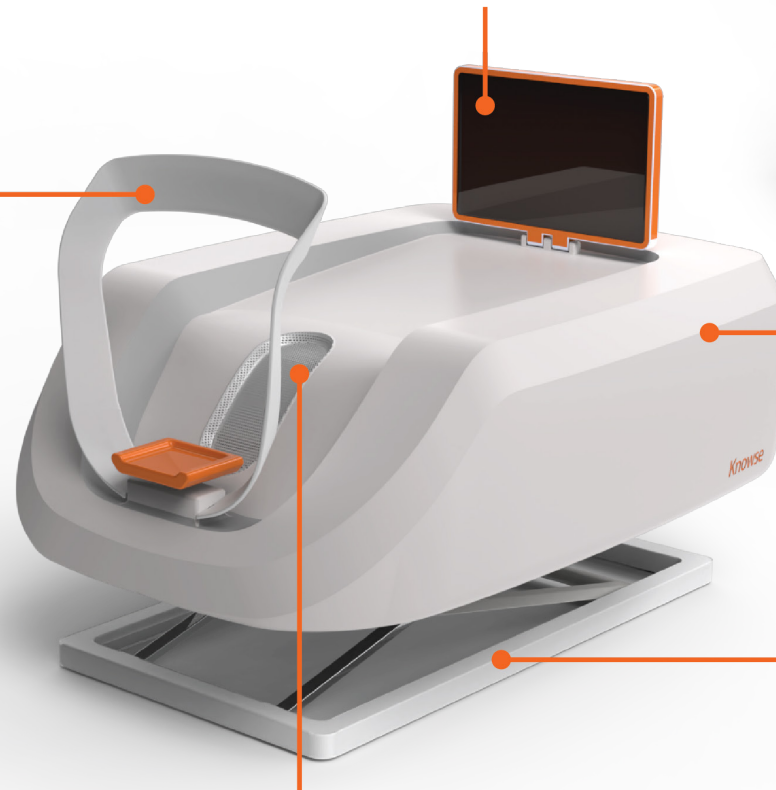
Chin-head rest

An in height adjustable chin-head rest is used to support and position users to ensure the right nose-to-stick distance.



Computer mouse

Users use this blind input device to provide their answers to the product.



Scent outlet

Users smell the sticks through this non-see through raster, which can be replaced and cleaned.

Guiding through shape

The lines and surfaces in the product guide user attention towards the screen.

Height-adjustable standard

The underframe bridges the gap between the table and the user's head, while giving the product a floating appearance that reduces its bulkiness.

5.3.3 Error-proofing by design

For designing a medical self-test, error-proofing is paramount. Mistakes by the product or unintended user actions could lead to false test results, which could lead to faulty risk profiles. Knowse was designed to be error-proof in use.

Error-proofing is mainly focused on simplicity and human intuition. Users are presented with only 1 action at a time and are guided at every step. A computer mouse is used as blind input mechanism because it was proven to be the most familiar and intuitive option.

The display guides users through the test. For the threshold test, users are asked to select one out of three answers each time. Figure 49 illustrates how the display provides real-time feedback and asks for extra confirmation after submitting an answer.

As will be further explained in the recommendations, users should be able to 'practise' first, after watching an explanation video about the test they are about to start. The Sniffin' Sticks test also has a built-in error-proofing mechanism; only the second half of the test counts for the results.

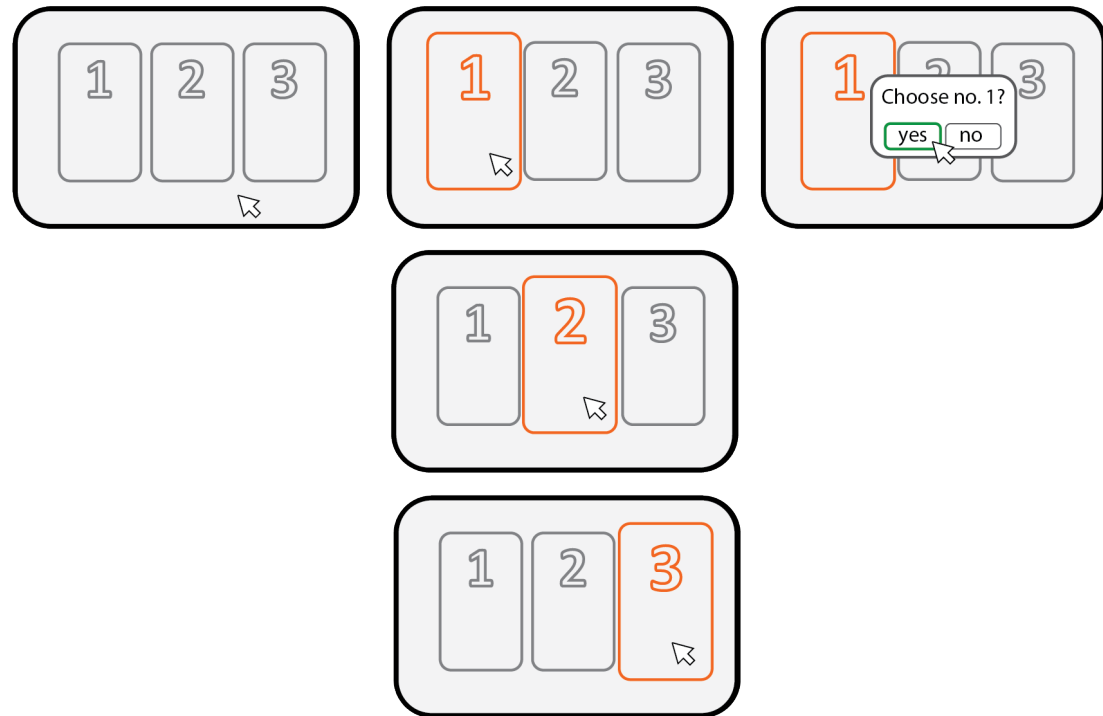


Figure 49, Display interface threshold test

6. Discussion

6.1 Reflection on design

6.1.1 Introduction

This master's thesis started with a design brief, in which intentions, learning objectives and goals were described. Now, almost 100 days later, it is time to reflect on the design project and how the chosen approach benefited or hindered the design outcome. Please note that this is based on personal experience.

6.1.2 Methodology take-aways

As graduation too, is a learning opportunity, I will take this chance to reflect on my project approach. Instead of discussing the several design methods that were used throughout this project, I will take a more holistic approach with a focus on key learnings. These may also be of use to others within the field of design or engineering.

1. Talking to people

My research phase consisted of both literature research and expert interviews. Especially the latter has helped this project a lot. Talking to stakeholders and experts allowed me to gain valuable insights about different stakeholders

and perspectives within the scene of neurodegenerative diseases and diagnostics. It provided the insights you will not find online.

An interesting example is the contradicting perspectives between neurologists and clinical geriatricians. Whereas the first spoke about future treatments in a more theoretical and optimistic way, the latter had a more reserved and practical view on developments. It made me realise that one should never rely on the opinion or Weltanschauung of one expert, however reputable they may be. Each story seems to have multiple narratives, depending on who is asked to tell it.

2. Dealing with uncertainty

As a design student I have always seen great value in prerequisites and requirements. They draw the framework, within which solutions can be found. However, testing ideas on the list of requirements becomes challenging when requirements are harder to define. The absence of a client, an existing market or specific target group caused much 'wiggle' room in this project. I learned that requirements do not always need to be SMART before ideation. Design activities themselves are a good way to specify requirements.

3. Broadening my perspective

I discovered that motivation matters. I started this project with the intention of continuing as a startup after graduation. This made me want to become an absolute expert on the subject and design a realistic solution. Throughout the last 100 days I have used multiple methods that helped me broaden my perspective. I found this very helpful.

Expert interviews, the Design with Intent method and the Thinking tracks method forced me to consider other perspectives and helped preventing tunnel vision.

They also allowed me to look at the project from a distance and remain neutral. "Criticism on the project is not criticism on me if I actively look for it. Then it is just obtaining new insights", was my (rather long) mantra during this project.

Instead of asking experts if they had any more tips, I asked them "Why is this project going to fail?" or "What is needed for you to endorse this project with your name?". Answers sometimes required me to repeat my mantra, but did bring this project to a higher level.

4. Sprinting in design

This thesis showed me the effectiveness of design sprints. For each challenge area focus on ‘failing fast, failing early’ appeared a very time-efficient way of working. Sketching an idea on paper, putting it in SolidWorks, printing it the same day and repeating this process the next day for a new iteration worked very well for me. The stick-holder mechanism for instance, went through 8 iterations within two weeks.

As a person that is prone to think things through before doing, this new way of doing was an eye-opener for me. This is one of my main take-aways. It aligns with the startup attitude that I wished to develop during graduation: “If you ask for feedback on a prototype that you feel confident showing, you are asking for feedback too late”.

5. Weekly reflection

Weekly STARR reflections were useful in the beginning of this project. They provided overview and served as incentive to keep track of my project risk management. I found that it is a useful motivation tool as well. Adding a check box with the text “I am doing a great job” allowed me to realise and appreciate what I was doing.

6.1.3 Design achievements

My design brief contained several learning goals and intended project deliverables. The intended project deliverables were:

- A functional model that shows the working principle of the project. This is a proof of concept.
- A digital aesthetic model that conveys product appearance.
- An operational model, for the purpose of testing and showing the intended user interaction.

Each of these targets were, at least to some extend, achieved within the project. Functional proof of concept is there for each part, but was not achieved for the integrated whole. An operational model was created for the user interaction test. However, sticks were presented to the user by hand. As such, the full product interaction could not be tested.

Overall, this project followed the initial planning, five out of six personal learning goals were addressed and the deliverables were completed. Even though this is great, it also begs the question if foresight was very accurate or if this process and its outcome are subjected to personal preference and bias. The

latter is likely true to some extend. This may be explained as designer identity or gut feeling and does not necessarily have a negative impact on the design outcomes. However, I find it useful to consider this before further developing the product.

6.2 Impact of implementation

6.2.1 Introduction

As a designer, one should reflect on the final design and the positive and negative aspects of its implementation. The central question in this section is:

Why should or shouldn't Knowse be further developed and implemented?

6.2.2 Impact on healthcare

Knowse will automate the Sniffin' Sticks olfactory test. This suits the growing shortage of medical personnel and increasing pressure on healthcare.

However, automation also de-humanizes industries. Although Knowse allows medical professionals to spend their time on other tasks, it may not be the preferred option for all

scent tests. Current use before and after surgeries appear to benefit from a human touch. Implementation should be carefully considered per application.

I believe the product to be a welcome solution for the future application of case-finding for neurodegenerative diseases. This is due to its accessibility and cost-efficiency. The missing human touch appears unnecessary and perhaps even undesired in most cases. Knowse is meant to lower the threshold and emotional weight of conducting a test.

6.2.3 Ethical considerations

Knowse should only be used for its intended purpose of case-finding when a solution is available in case of a high-risk profile. For less serious use-cases this restriction does not apply. For example testing for the purpose of increasing smelling ability or quality of life.

6.3 Limitations

6.3.1 Introduction

Like any other project, this project too has its limitations. Understanding the limitations is

important as they add to a realistic understanding of the project.

6.3.2 Unfinished design work

This master thesis was written in 100 days. Due to time restrictions, the number of iterations that could be managed for each challenge area was limited. None of the areas is completed, although the amount of work still needed differs per area.

Besides the areas mentioned, there are other important challenges that need to be tackled as well. An example is air purification inside the product and at the user smelling point.

Lastly, it is important to note that limited work was conducted on the integration of components. Integration will likely lead to new, unforeseen challenges.

6.3.3 Limited validation

Thus far, the product has gone through limited user testing and feedback sessions with future users and professionals. Its potential, market and embrace will remain uncertain until more validation experiments are completed.

6.3.4 Dependency on others

Knowse is designed for the ODOFIN Sniffin' Sticks from Burghart Messtechnik. This is a unique and patented product. The success of Knowse depends on the reputation and cooperativeness of this company.

Furthermore, it is designed for a use-case that will only exist when researchers are successful in developing treatment options for neurodegenerative diseases. Without these scientific breakthroughs, Knowse will not be able to make its intended impact.

6.4 Recommendations

6.4.1 Introduction

Knowse is far from a finished product. As mentioned in the Limitations of this project, the project was bound by time, budget and available knowledge. The recommendations serve as a basis for further development of this project.

6.4.2 Further development Knowse

As was also mentioned in Chapter 6.3.2, Knowse is a concept-product with much unfinished design work.

Each of the challenge areas discussed in this thesis requires further iterations. Besides currently existing challenges, new challenges will be added when integrating different product elements. Examples are:

- Air purification for the user and inside the product to prevent cross-contamination and lingering scents.
- The placement and removal of sticks and stick-holders requires more attention, as the current solution does not fixate in all directions.
- The mechanical interplay between the carousel, stick-holders and the Open-close mechanism needs to be finetuned and automated.
- Positioning and adjustment requires ergonomic evaluation through user testing. Databases like DINED could be useful for a more accurate design.
- Materials, manufacturing, product weight and costs and a sustainability analysis must still be considered.

- Once a fully working prototype is developed, user testing needs to be done. Eventually, the medical product needs to pass clinical trials.

Multiple pages could be filled with further development steps. The main take-away here is that Knowse is a concept product. It is unfinished and requires further development if it is to be implemented.

6.4.3 Alternative use-cases

Besides the use of Knowse for the early-stage risk-profiling of neurodegenerative diseases, alternative use-cases are also imaginable:

- **Improving sense of smell and quality of life**

As mentioned in Chapter 4.2.9, the concept product could be positioned to targets people's curiosity and eagerness to learn about their health status.

Sense of smell was proven to have significant effects on quality of life. Examples are enjoying food and drinks or smelling the forest in spring time. A good sense of smell also functions better as danger recognition

mechanism in case of fire, chemicals or spoiled food and drinks.

Sense of smell can be trained through focus and simple exercises. Knowledge about one's sense of smell can lead to an enriched life.

- **Scent-sensitive industries**

The product could be used for the blind comparison and evaluation of different fragrances in the perfume industry, different coffee or bean types in the coffee industry and training purposes in fine food and beverage industries like wine, herbs and liquors.

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