Our scientific foundation - comprehensive version

Reviewing the market

In 2016, the two founders Chris Christiansen and Daniel Jensen were hired by the pharmaceutical company, LEO Pharma, in order to learn more about skin diseases and the existing solutions for them. The foundation of NØIE was originally initiated as a project within LEO Pharma's Innovation Lab, which still till this day reflects the high level of compliance and thoroughness NØIE operates under. LEO Innovation Lab was established to build and drive radical innovation and solutions for people living with skin conditions.

Initially the project began by visiting pharmacies in central Copenhagen. The founders asked for advice and recommendations for over-the-counter products for psoriasis and other skin conditions, which ended up in a lot of different products and recommendations. Today, there are still countless skincare products to choose from, and it can be difficult to find out which ingredients and products that suits a person's skin the best.

It became obvious that the experience of searching for products to alleviate not just psoriasis, but also other skin conditions like eczema, acne, sensitive skin or dry skin, could be optimised, and that the current approach of helping people with skin issues was outdated and a rather ineffective one-size-fit-all approach. This led to the idea to flip the mindset around and approach the issue of finding the right products from a reverseengineering perspective. By gathering over-the-counter solutions that were given to people with various skin conditions, researching them and asking the users about the effectiveness of them, the belief was that it could result in a better solution that could alleviate the problems of people living with skin conditions.

Screening existing products

In 2017 the founders teamed up with experts within dermatology, biology, toxicology and data science. They started a project of comprehensively screening 2,938 over-the-counter skincare products aimed at people suffering from psoriasis, eczema, acne, sensitive skin and dry skin.

The products were screened for clinical proof of effectiveness, as well as evidence on ingredients targeting the aforementioned skin conditions. Furthermore, the products were screened for ingredients with the potential to cause adverse events, such as perfumes, well known irritants and suspected endocrine disruptors, based on guidelines set up by a panel of external dermatologists, biologists, and toxicologists. The final result of the screening found that

of the 2,938 products, only a total of 566 products passed the screening, meaning that 81% of all the products were deemed to be without clinical evidence or potentially harmful for the patients. The products that fulfilled the strict criteria (i.e. the 566 products) were made available and sold through an online webshop named HelloSkin. The intention of the project was two-sided: Firstly, there was a wish to create a transparent and safe platform for people with psoriasis, eczema, acne, sensitive skin and dry skin to buy high standard products and get all necessary information about the products. Secondly, the aim was to examine the efficacy of the current products on the market, hence obtaining a collected and structured data overview on ingredient combinations and their effectiveness to help solve above skin issues. The users were categorised according to their skin issues, in order to provide them with a range of products that theoretically would be beneficial for the users in question. HelloSkin developed specific algorithms to take into consideration unwanted ingredients and beneficial ingredients. The algorithms were used to recommend products for people with specific combinations of skin conditions and their symptoms.

After purchase, a survey collecting indepth information was sent to each user. The users were asked about demographics, age, skin condition, symptoms, and affected area(s) of the body. Then after 30 days, the user was asked to evaluate the efficacy of the purchased products. A database was built by crowdsourcing data from the webshop. With the users' survey responses and evaluation of the products' effectiveness, and more than 750,000 actionable data points from the users were gathered.

In conclusion, this project obtained valuable knowledge on what ingredients worked for which skin conditions through feedback data and found that surprisingly many products on the market were deemed potentially harmful. Through precision and personalisation, the founders believed they could make a better solution, which formed the basis for NØIE.

Testing the learnings

In 2018 the research team initiated a pilot study with the aim of validating the findings from the data collection and testing the learnings on a smaller group of people in a more controlled setting.

Participants were recruited via HelloSkin's customer base. People that were eligible for the programme were the ones with either eczema or psoriasis, who had previously purchased two or more leaveon products. People wanting to participate were asked to fill out a detailed questionnaire on their disease, symptoms, allergies, needs and previous experiences with products. Further, people were asked to send photos of a target lesion. The participants were also selected for the study due to the severity of their skin disease, and leading up to the study, the majority of the participants were reliant on medical treatments such as topical steroids. A group of 10 people from the UK, who were diagnosed with either mild to moderate psoriasis (4) or eczema (6), completed the pilot study.

The aim of the pilot study was to test to what extent HelloSkin would be able to identify a combination of over-the-counter products, selected based on the data learnings, that participants would find suitable for their needs, and have the combination of products act as the first line of treatment.

Every week the participants were asked about their current state of skin condition.

At the start of the study, the products were selected to build and protect their skin barrier, before beginning treating underlying symptoms. Thus, the participants' product combinations were continuously adjusted, corresponding to the improvements they experienced, and the symptoms addressed. After 8 weeks, participants filled out a final questionnaire, and were asked to evaluate the programme and give general feedback. Data from baseline, week 1, 2, 3, 4, 6 and 8 were analysed to get an impression of overall trends and compare the different skin conditions (psoriasis or eczema) when relevant.

After just 8 weeks of testing, the study found that when providing hand-picked lines of products to each individual, the severity of the participants' disease decreased, and the requirement for topical steroids dropped on average by 40%. In other words, the conclusion was that the standard use of prescribed medication could be reduced, simply by providing the right first line of treatment, hand-picked for the individual.

This pilot study demonstrated how finding the right product(s) is important to reach the true potential of using moisturisers among people living with a chronic skin condition.

These findings emphasise the importance of considering people with eczema or psoriasis as unique individuals. Every condition is unique in response to symptoms, acceptability, and ingredient tolerance.

However, in order to provide the handpicked routines for the participants in the study, it required 3-4 different products and brands to be used on a daily basis, risking a lack of adherence and exposing the user to ingredients that weren't actually necessary. This was the beginning of a desire to create a recommendation system that would be able to put together products that only contain what the user needs, nothing else, and recommend the products with the highest likelihood of helping the user.

Building the NØIE algorithm

In 2019, Jensen and Christiansen founded NØIE. NØIE started to develop and manufacture its own formulations and offer its own customised solutions to people with skin concerns. NØIE is building on the structured and solid data foundation and extensive knowledge of real-life people using products and ingredient combinations. The data collected was used to reverse-engineer, develop and manufacture the very first NØIE products, that could help improve the quality of life for people dealing with skin concerns.

NØIE's mission is to provide personalised skincare solutions to people suffering from skin conditions by leveraging direct user feedback, crowdsourced data, science, and machine learning.

NØIE is driven by data and collects both user surveys, image data and follow-up evaluations about the products' effectiveness for every individual user. In order to receive a product recommendation, the user fills out a detailed online survey, taking all relevant clinical aspects of the skin into account. On a general level, every user submits on average 31.7 data points on their skin, treatment, and lifestyle before receiving their first recommendation from NØIE. This in-depth information enables NØIE to produce tailored formulations for the individual user's needs. NØIE utilises this information in Bayesian statistical machine learning models that allow for combining both evidence-based knowledge and user feedback. The data model is guided based on which ingredients that are scientifically and theoretically working for the specific skin condition. Then the data model makes an assessment based on what the data shows is working for the user based on what has worked for other users with similar traits. So when a user submits the survey, the data is being fed into predefined stratification clusters, supporting each Bayesian model, as each product type has its own underlying model and well-defined clusters. This data is being processed through machine learning algorithms that are defining the most optimal routine for alleviating the real-time clinical state from a phenotype perspective.

After 30 days the user is requested to provide feedback on the recommended products' ability to improve the skin concern. As part of NØIE's service, all users are requested to provide explicit feedback after 30 days of using their products, with the possibility to postpone giving the feedback up until 100 days of use.

Feedback, both the positive and negative, is highly valuable since it is not only training the algorithms - it is also feeding the research and development, clarifying where NØIE has unmet user needs. This means that the feedback, which the users provide, not only improves the knowledge about their individual skin and ingredient combinations, but also all others. Hence, every single piece of user feedback contributes to making NØIE a better product for all current and future users too.

The unique feature of NØIE's approach is closely tied to the fundamental principle of Bayesian Modelling, as it requires closed feedback loops to investigate the hypotheses; in this case, the hypotheses are set up in the form of specific products with unique ingredient combinations. The latter is where NØIE truly stands out from other skincare companies that might also be built from vast amounts of research and take an individualised approach, since NØIE has a user-driven data model that improves with every single feedback input, every single day. While initially guided by expert knowledge and prior information, the models get smarter over time and as data amasses, they're becoming more and more precise in assigning products to the individual users.

Improving the results

When first launched, NØIE only supported eczema, psoriasis and dry skin. In April 2020, NØIE expanded the solutions to acne and other skin conditions. To begin with, the first success rate (the ratio between positive evaluations and the sum of evaluations) of NØIE's solution was 30%. The success rate increased from 30% (2020) to 72% (2021) over the course of a year. Today, the success rate of NØIE's approach, using nothing but the right and unique combination of ingredients, is 86% (Figure 1).



Figure 1: Success rate is being calculated as a ratio between the total number of positive evaluations out of the total number of evaluations. The open timeframe of providing feedback is between 30-100 days after receiving and taking the NØIE products into use.

Regardless of the expansion into new skin conditions, the success rates grew as a result of two different factors. First and perhaps foremost, the continuously collected feedback developed the algorithms which led to more precise user clusterfication - something that clearly increased the precision of the recommendations. At the same time the strengthened user clusterfication gave rise to the development of new and superior formulations for specific segments based on closed-loop feedback, as the Bayesian algorithms obtained a critical mass of data that validated these needs. To sum up it's in the interplay between machine learning, science, data, user care and feedback that creates the product success rate. This is how NØIE predicts what's going to work for the individual based on the characteristics and the learnings from the many (see Appendix 1).

Today, NØIE's algorithm works with over 3.5 mil. (still counting) feedback points from over 80,000 people living with skin problems, and from that it picks the formulation(s) where the user has the highest statistical chance of seeing results.

Appendix 1



Rachel (27) lives in the Netherlands. She is a teacher and has struggled with acne due to a hormone implant. The images above are before and after using NØIE.

Earlier this year, we had a conversation with Rachel, which we cut down to a 5 min. user story video that you can watch <u>here</u>.

It's due to stories like Rachel's that we go to work every day.

We have <u>hundreds of stories</u> like these, as proof that NØIE is making a true difference for people out there.