Tight interactions

Professor Dr med Henry Völzke of the University of Greifswald, Principal Investigator of the Study of Health in Pomerania (SHIP) project, details some of its current research findings and methodologies

What makes your approach and methodology unique from other population-based studies?

The unique selling point is the wide focus of the project. It is based on the general hypotheses that common diseases share common risk factors, i.e. that there are tight interactions among common disorders and factors which predispose humans toward developing certain diseases. These hypotheses require comprehensive examination. Indeed, the current data collection for the 15-year follow-up of the original cohort (SHIP-2) and for the baseline examinations of SHIP-TREND include the most comprehensive analysis programme ever performed in population-based research.

Has the project yielded any significant findings to date?

The comprehensive examinations allow us to investigate associations between disorders that might be regarded as being separate from each other. SHIP data suggests that dental diseases and thyroid disorders contribute to metabolic and cardiovascular diseases. We have demonstrated that fatty liver disease is a classical multifactorial disorder and tightly related to endocrine disorders, cardiovascular diseases and mortality. SHIP has also contributed to genome-wide analyses that uncovered the genetic basis of common diseases including gout, hepatic steatosis and goiter to name but a few. Currently, about one paper a week based on SHIP data is published in peer-reviewed scientific journals such as Science, Nature or Nature Genetics and others.

How did you ensure the accuracy of your sample data and its overall representation of the population?

SHIP-0, the baseline study has started as a classical prevalence study with significant recruitment efforts undertaken, mirrored by a relatively high baseline response. Consequently, large efforts were also made in the recruitment for the first follow-up. The response of 83.6 per cent achieved for the five-year follow-up SHIP-1 is lower than follow-up responses in studies that have been a priori designed as cohort studies with less recruitment effort at baseline, but our follow-up response has also been adjusted for the comprehensive examination programme of the SHIP project. The advantage of our approach with high baseline response over the approach of ‘classical’ cohort studies with low baseline response is that bias in both incidence estimates and association analyses can be evaluated.

SHIP study populations comprise inhabitants of West Pomerania selected from local population registries – the only inclusion criterion is German citizenship. The high baseline and follow-up responses are achieved with a multi-step invitation procedure. Firstly, we approach selected persons with up to three invitational letters. Secondly, we attempt to make an appointment with telephone calls. Thirdly, for persons who are not reachable after several attempts, we undertake in-person contacts at home. And finally, those unwilling to participate for reasons such as illness or lack of time or interest are offered examinations at their home (SHIP-Home) or in temporary examination centres, which we currently have in the larger cities of the rural study region to shorten the distance between the participant’s home and the SHIP examination site. Initial experiences indicate that this is a very effective way of recruitment, as over 20 per cent of initial non-respondents, subsequently decide to participate.

Moving forward, will you recommend actions to improve the health of individuals residing in Pomerania and put it on a par with other regions?

Given the huge burden of modifiable risk factors in the community, political action is required. Indeed and as an example, the Federal State of Mecklenburg-West Pomerania has recently established one the strictest non-smoker protection laws in Germany. Some preventative programmes targeting overweight and obesity have also been introduced, but there is a need to do more.

Poverty Risk Rate 2007

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The University Medicine Greifswald contributes to the German Centre of Cardiovascular Research with the large CARDIO-PREVENT project, which investigates new ways of primary and secondary prevention in West Pomerania. This project has just started, but may provide knowledge on how to make prevention effective.

What are the next steps in this project and what remains to be done?

The GANI_MED consortium is an important extension of SHIP to clinical practice. Within GANI_MED, SHIP standards are transferred to clinical routine. Applying these standards, large patient cohorts are recruited from the University Hospital Greifswald. The common approach to standardisation ensures the best possible comparability between SHIP and GANI_MED cohorts, and not only allows case-control studies but will also serve as infrastructure to help select patients for clinical studies.
AFTER THE REUNIFICATION of Germany in 1990, it became clear that there were substantial disparities in life expectancy not only between West and East, but also between Southeast and Northeast Germany. The population of West Pomerania – the most Northeastern region – had the lowest life expectancy, but the reasons behind this were unclear. There was no available scientific data from East Germany which would enable a comparison of the health status of its communities with Western counterparts. This necessitated population-based research to try to answer the question of what risk factors and diseases were at play, and to create the basis for interdisciplinary research.

In the second half of the 20th Century, population-based studies were mainly designed with a focus on specific questions or diseases. Besides a growing number of population studies specifically addressing the heart, other studies exist which focus on, for example, thyroid, liver or dental diseases, but very few provide comprehensive information on the complex associations between risk factors, subclinical disorders and diseases of different organ systems. Historically, the University of Greifswald, like many other East German universities, had a good reputation for student training but lacked a scientific one, leading the Federal Ministry of Education and Research in the 1990s to invest in research infrastructure in East Germany, creating the Community Medicine Research Network, which subsequently initiated the Study of Health in Pomerania (SHIP) project.

MAPPING DISPARITIES

SHIP has three major objectives: (1) to describe the health status of the Northeast German population and find answers as to why Northeast German people die earlier than Germans from other regions; (2) to investigate the complex associations among risk factors, subclinical disorders and diseases without focusing on one specific disease or disease group; and (3) to provide the Community Medicine Research Network with high-quality data for research questions.

Professor Dr med Henry Völzke is Chair of Clinical Epidemiology at the Institute for Community Medicine in Greifswald and Principal Investigator of the SHIP project, and he confirms that analyses of baseline SHIP data supports the hypothesis of an accumulation of common risk factors and disease in the West Pomeranian population. "In comparison to Southern Germany and the Ruhr area, West Pomerania has a higher prevalence of overweight and obesity. This results, for example, in an exceptionally high prevalence of gallstone disease in the region," he reveals. "Every second woman and third man aged 60 to 79 years has either a history of cholecystectomy or sonographic evidence of current gallstones."

This prevalence is one of the highest ever reported; only Native Americans exhibit higher figures. Obesity is also a risk factor for hepatic steatosis, and a fatty liver affects approximately 30 per cent of all adults in West Pomerania. The prevalence of hypertension is also high, with 50 per cent affected; among men living in Northern Germany as a whole it is 61 per cent, whereas it is just 40 per cent among men living in Southern Germany. Similarly, the prevalence of left ventricular hypertrophy in West Pomerania is 50 per cent higher than in Southern Germany. These disparities cannot be explained by regional differences of the German healthcare system.

RAISING THE STANDARD

There are at least three significant challenges for large-scale longitudinal studies with population representativeness. Firstly, both high baseline and follow-up responses are needed, and SHIP has developed innovative examination methods and logistics in order to recruit as many participants as possible. Secondly, very high levels of standardisation are required to enable the best possible internal and external validity of data collection. Standard operation procedures
are in place for all examinations, and the flow of the examinations is tested in pilot studies.

“AlI examiners are trained over several months before being certified,” explains Völzke, “with at least one observer taking part who is already certified as a SHIP examiner. Statistical analyses are conducted using Bland & Altman Plots for continuously distributed variables. Certifications are repeated semi-annually with six to 10 volunteers; indeed, SHIP is continuously monitored by an external board of independent scientists, and descriptive statistics and controls for plausibility are performed every three months and reported to the data safety and monitoring committee.”

Völzke is confident that the effort to safeguard the highest quality standards results in low method and observer variabilities, which is important considering the long duration of the project. And in that duration lies the third challenge, and perhaps one of the greatest: obtaining funding commitments for long-term studies such as SHIP can be hard work. For many agencies, a funding period of five years might already seem long, but 10 years or more could seem like an eternity. However, large cohort studies can require funding of 30 years or more in order to collect information on future events that is as extensive as possible.

“We are working on making the SHIP unsinkable,” smiles Völzke. “Up until now, our basic funding has made morbidity and mortality follow-ups of our cohorts possible. However, we are strongly interested in continuing the comprehensive examinations and in drawing further TREND samples over the coming decades, and are engaged in ongoing talks with potential funding sources which we hope will enable us to achieve this goal.”

MANY PORTS IN A STORM

SHIP is based on a fruitful collaboration between various medical disciplines, and it is this tight cooperation between epidemiologists and local and external medical specialists which ensures the high quality, comprehensive nature of the SHIP project, as Völzke is keen to point out: “SHIP is not a one-man-show. The local collaborators are organised within the Research Network of Community Medicine. The network was founded in 1995 and comprises scientists and clinicians from numerous disciplines including epidemiologists, biometricians, statisticians, internists, cardiologists, neurologists, psychiatrists, psychologists, social scientists, dentists – including several subspecialties such as periodontology and prosthetics – molecular biologists and paediatricians.”

Collaboration occurs not only between different specialities within the medical faculty, but also between scientists belonging to different faculties. Beyond local collaborations, many national and international partners utilise SHIP data in common data analyses, and their investigators are tightly involved in international consortia to explore genetic factors of diseases. Within these consortia, SHIP collaborates internationally on major population studies such as the Framingham Heart Study in the U.S., the Rotterdam Study in the Netherlands or Denmark’s INTER99. Moreover, there are various collaborations in place which compare the prevalence and incidence of diseases and replicate non-genetic associations. SHIP is tightly linked with large-scale German studies including KORA, CARLA and the Heinz Nixdorf Recall study.

BRIGHT HORIZONS

SHIP is sailing toward a promising future, with the team’s expertise proving invaluable in population-based studies which will contribute toward the establishment of the German National Cohort, a nationwide study some 200,000 subjects strong.

An indicator of the project’s future success lies in the fact that the team understands that population-based research entails working not only with, but also for the population. “In West Pomeranian people, there are high levels of awareness that SHIP provides important contributions for them and their community,” reveals Völzke. “Last week, one of our collaborators took a taxi from the railway station to our examination centre, and the taxi driver was keen to give him lots of details about SHIP! He clearly appreciated the regional value of the study. We are deeply thankful for the support of our population, and grateful that so many participants are willing to provide data to our research project.”