

Published: November 2024
Publisher: Stockholm Science City Foundation
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Introduction

Life science is all about revealing the mysteries of life. Life science research aims to understand and explain various processes and phenomena related to living organisms, with the ultimate goal of increasing human knowledge, allowing people and animals to lead healthier lives, and improving the well-being of our planet.

To explore how research and breakthroughs within life science affect society, healthcare systems and our lives, Stockholm Science City Foundation together with Nordstjernan hosts an annual symposium The Future of Life Science. At the symposium on May 23-24, 2024, the discussion revolved around global challenges related to health, including climate change, antimicrobial

"The symposium considered key questions that must be addressed to ensure that unfolding crises don't become acute disasters."

resistance (AMR), and an increase in age-related neurodegenerative diseases. The symposium considered key questions that must be addressed to ensure that unfolding crises don't become acute disasters: which advances within life science could mitigate these threats; could economic incentives promote more proactive activities and increase the rate of progress; and how should scientists and experts communicate their results more persuasively to engage political leaders and rally public support for change?

This report gives an overview of creeping global crises and their associated challenges. The intention of the report is not to cover all the topics discussed at the symposium, but rather to focus on key topics concerning escalating crises. It

highlights the status of specific threats, immediate challenges, and possible strategies to better handle future crises.



What are creeping crises?

Creeping crises is a relatively new term used to describe threats to widely shared societal values or life-sustaining systems. The development of these threats is gradual and of low intensity but often results in incremental societal disruption, culminating in a sudden major emergency. Creeping crises evolve, often quite slowly, over time and space and are foreshadowed by precursor events. Precursor events may be limited, acute crises such as several local outbreaks of a disease foreshadowing a pandemic. Similarly, increased frequency of thunderstorms or longer dry periods, which are geographically constrained, indicate acute crises we can expect from global warming.¹

Other examples of creeping crises are antimicrobial resistance (AMR), lifestyle-related diseases, climate change, declining biodiverity, migration streams, fake news and disinformation. Creeping crises are subject to various degrees of political and societal attention. **Magnus Ekengren**, Professor at Department of Political Science and Law at the Swedish Defence University, delivered a keynote speech at the symposium. Magnus is one of the researchers who coined the term and defined the concept of creeping crises. He contends that these crises are only partially recognized and dealt with by authorities - addressing them properly is challenging and, in most cases, we are unable to use evidence-based measures since knowledge from past crises may not be relevant.



Magnus Ekengren

The division between creeping and other types of crises may not be clear. It can be argued, for example, that AMR is an acute rather than a creeping crisis. However, even though 1.3 million people are dying worldwide every year due to AMR, the crisis is far from fully-fledged, and experts agree that measures taken globally and locally to address the issue are insufficient. It is still a crisis that mostly affects certain geographic areas (such as Russia and the African continent), and in other parts of the world the crisis is not yet exerting significant pressure on healthcare systems.

"These crises are only partially recognized and dealt with by authorities - addressing them is challenging and we are unable to use evidence-based measures."

Creeping crises that were highlighted during the symposium

Non-healthy habits driving the increase in lifestyle related diseases

It is estimated that around 40% of premature deaths worldwide are attributed to lifestyle factors, including too little physical activity and sleep, poor diet, and alcohol and tobacco use.² **Carl Johan Sundberg**, Professor at Department of Physiology and Pharmacology, Karolinska Institutet, ex-



Carl Johan Sundberg

plained that although calorie intake is lower today than 70 years ago, physical activity is much lower, leading to excess weight and weak muscles, including weak hearts. This trend is ongoing and in Sweden the proportion of citizens with health-threatening poor fitness has increased from 27% in 1995 to 46% in 2017.³ According to the World Health Organization (WHO) Europe, around 80% of all heart disease, stroke and type 2 diabetes, plus 30% of cancers are avoidable.⁴

All organs in our body are affected by lifestyle. Carl Johan Sundberg described the positive effects that physical exercise have on the brain, heart, skeletal muscles, endocrine glands and the immune system. Research has shown that even moderate exercise improves physical performance and mobility and contributes to the prevention of most

non-communicable diseases. Physical activity also improves mood and cognition. In addition, being physically fit provides better protection when the body is stressed and when responding to acute infections.

In Sweden the healthcare law states that the most severe conditions should be given priority in healthcare. When the resources in the healthcare systems are limited and set by yearly budgets, it isn't easy to justify a large share of the money being invested in prevention. However, financial



Fredrik Söder

models may increase the incentives to work with prevention in healthcare. One example of such models is health impact bonds that was presented by **Fredrik Söder**, CEO and founder of Health Integrator, during the symposium. In a pilot study done together with Region Stockholm, 925 individuals with pre-diabetes (defined as long-term blood glucose levels, HbA1c, levels of 42-47 mmol/mol, indicating a high risk of developing type 2 diabetes) were identified and included in a program where they were offered different types of support for physical training, diet and other lifestyle-related factors. The cost of 30 million SEK for the support program was financed upfront by private money from an insurance company. Two years after study start, 54% of the participants had lowered their long-term blood glucose level to a value below the risk level, and 85% of the

participants felt that the health program had been a contributing factor to improved quality of life. Only 7.5% of participants developed type 2 diabetes over 2 years, compared to an average of 23% if

² Schroeder SA (2007). We Can Do Better — Improving the Health of the American People. N Engl J Med; 357(12) 1221-1228. https://www.nejm.org/doi/full/10.1056/NEJMsa073350

³ Ekblom-Bak E et al. Decline in cardiorespiratory fitness in the Swedish working force between 1995 and 2017. Scand J Med Sci Sports. 2019; 29: 232–239. https://doi.org/10.1111/sms.13328

⁴ World Health Organization (2014) Report: Prevention and control of noncommunicable diseases in the European Region: a progress report.

https://iris.who.int/bitstream/handle/10665/345525/WHO-EURO-2014-3441-43200-605190-eng.pdf

⁵ Health Integrator. (2023). Report: HEALTH INTEGRATOR - PREVENTION OF TYPE 2 DIABETES, 24-month report. Retrieved from:

no lifestyle intervention is used. Allocating private money to finance prevention upfront and letting the healthcare systems pay back once the cost savings are evident could solve the problem of limited yearly resources and diminish the risk of push aside other types of healthcare when introducing preventive interventions or new expensive treatments.

To work with preventive activities and promote healthy habits is however not only the responsibility of the healthcare system but also several other stakeholders. To achieve increased physical activity, city planning that supports active transportation such as cycling, walking and public transport is needed. Also, easy access to parks and other recreation areas is important. Schools play a crucial role in promoting physical activityfor people from a young age to adolescence.⁶

Some experts highlight that ways forward to promote healthy habits are stronger regulations for food producers and a taxation system that favors healthy food. The Swedish Cancer Society together with The Swedish Heart Lung Foundation has started an initiative to encourage politicians to develop a national strategy that promotes healthy lifestyles and sustainable diets for all. Their suggestions include banning advertising of unhealthy foods which targets children; removing VAT on fruit and vegetables; introducing a producer tax on sugar-sweetened beverages; and introducing mandatory labeling of healthy and unhealthy foods.⁷ As discussed at the symposium, such changes will certainly require brave politicians and strong opinion leaders.

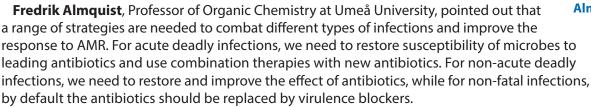
"To work with preventive activities and promote healthy habits is however not only the responsibility of the healthcare system but also several other stakeholders."

Antimicrobial resistance (AMR)

Each year 7.7 million deaths, equating to one in eight deaths globally, are caused by bacterial infections and many people around the world still do not have access to basic antimicrobials. However, almost 1.3 million of these deaths are due to AMR, which occurs when bacteria, viruses, fungi, or parasites no longer respond to medicines, resulting in infections that are difficult or impossible to treat.⁸

The causes of AMR are severalfold: over-prescribing of antibiotics or patients not taking antibiotics as prescribed, excessive use of antibiotics in farming, poor infection control in hospitals, poor hygiene and sanitation practices; and lack of rapid laboratory tests.

There is a pressing need for new, innovative antibacterials, to replace those which are becoming ineffective or less effective due to widespread use. According to WHO, there were 97 antibacterial agents in the clinical pipeline as of 2023. This can be compared to about 10,000 new oncology drugs in clinical trials.⁹





⁶ International Society for Physical Activity and Health (ISPAH). Report: ISPAH's Eight Investments That Work for Physical Activity. November 2020. Available from: www.ISPAH.org/Resources

⁷ Cancerfonden & Hjärt-Lungfonden. Folkhälsa för alla. (2024) Rapport: Handlingsplan för hälsosamma matvanor. https://www.folkhalsaforalla.se/#reports

⁸ Murray, Christopher J L et al. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. The Lancet, 399(10325), 629 – 655 DOI: 10.1016/S0140-6736(21)02724-0

⁹ Butler, M.S., Henderson, I.R., Capon, R.J. et al. (2023). Antibiotics in the clinical pipeline as of December 2022. J Antibiot 76, 431–473. https://doi.org/10.1038/s41429-023-00629-8



Olivier Rubin

Experts in the antibiotics and AMR field agree that too little is being done at all levels to address the AMR crisis. According to **Olivier Rubin**, Professor at the Department of Social Sciences and Business Globalization and Europeanization, Roskilde University, there are many reasons for this. One is that it is a silent crisis that is difficult to visualize, and the crisis is very fragmented across time, space, different types of diseases and health-care processes. Another is that there is insufficient backing from the public to implement the measures needed to combat AMR. There are experts and advocates in the field, but more activists are needed.

Since the agreement of a global action plan in 2015, 170 countries have created national AMR action plans. ¹⁰ However, Olivier claims that we are now losing momentum due to declining political commitment to the processes. This is observed as limited implementation of policies, limited budget allocations in national action plans, and limited commitment to international collaboration.

"Handling creeping crises, such as AMR, requires both momentum and endurance." Politics is about how power and resources are distributed and allocated in society, and prioritizing the implementation of policies, laws and regulations. In democracies, policies should align with broad public opinions. Olivier highlighted that handling creeping crises, such as AMR, requires both momentum and endurance. The issues need to be kept on the political agenda for many years, and they need to have a public anchoring. He suggested a few points to improve global AMR governance: 1) to focus more broadly on antimicrobial usage, 2) to agree upon and measure national contributions (compare to the Paris agreement for reduction of

CO2-emissions), and **3)** to form an international expert organization to follow the development of AMR and suggest mitigation measures.

Most modern cancer therapies rely on effective antibiotics. This suggests that pharmaceutical companies which have developed cancer drugs or have a strong pipeline of drugs in the cancer field, should be interested in the antibiotics field. Some pharmaceutical companies, for example Roche and GSK, do have novel antibiotics in their pipeline, but major investment in the field is still lacking. Most of the pre-clinical and clinical development is instead being carried out by smaller companies.

A key reason why so few new antibiotics are developed that was discussed at the symposium is the weak business case for antibiotics. Once new powerful antibiotics are developed, they should not be used until it is absolutely necessary. With current models of pharmaceutical development and reimbursement of drugs it is difficult to justify investments in the field. As monetary incentives



Nina Rawal

for developing new antibiotics are insufficient, new initiatives are attempting to address this issue. There are ideas on subscription models whereby states pay an annual fee to access new antibiotics once they are needed. However, political enthusiasm for these models has been lukewarm so far. According to **Nina Rawal**, partner and co-Head of Impact Ventures at Trill Impact, Sweden and the UK are trying to champion subscription models, but a larger group of countries is needed to make such models feasible. At the symposium, it was mentioned that there may also be a challenge with trust between countries. Models to restrict the use of new antibiotics require that no country overuses them once they are developed and released.

Age-related neurodegenerative diseases

With aging populations globally, the incidence of age-related neurodegenerative conditions such as Alzheimer's disease is increasing. This brings suffering among those affected, both patients and their families, and pressure on society. The global cost of dementia is estimated to be 1.3 trillion USD per year, implying that a cure for dementia would have a value approximately equal to the global GDP. Only a small proportion of the costs associated with dementia today are healthcare costs, and an even smaller part of this is expenditure on drugs.¹¹

"Only a small proportion of the costs associated with dementia today are healthcare costs."

Promising new anti-amyloid drugs that slow disease progression are being developed. The first of these drugs (Lecanemab, co-developed by the Swedish company BioArctic) has been approved for use in large parts of the world, including US, Japan and China. Also, simpler and more accurate diagnostics methods consisting of blood tests for Alzheimer's disease are making it much easier to detect the disease and identify patients who would benefit from drug treatment.¹²

The new anti-amyloid drug is based on antibody technology and therefore expensive. In the US the cost of treating one patient is 56,000 USD/year.¹³ The drug is not yet approved in EU, but with a similar pricing, if it were to be provided to all eligible patients it would account for 80% of our total national drug budget in Sweden.

The new drugs are delaying disease progression, but it was suggested that in the future, the greatest impact would probably be achieved by using two or three different drugs in combination. To achieve the full potential of new products, the experts at the symposium thought that health-care systems first need to set up processes where people at risk are identified, preferably through digital cognitive screening, followed by blood plasma tests. There has to be preventative programs and for those who may benefit from drug treatments, combination therapies would probably be needed. Currently, healthcare systems and budgets are not set up for handling such approaches.

Recent research has shown that preventive actions and lifestyle choices may delay the onset of Alzheimer's disease and slow its progression. In 2020, the Lancet Commission presented a list of twelve risk factors for dementia: diabetes, high blood pressure in midlife, obesity in midlife, physical inactivity, depression, smoking, low education, hearing loss, traumatic brain injury, high alcohol consumption, social isolation, and air pollution.¹⁴

¹¹ Frisell O et al.(2023). https://www.demenscentrum.se/sites/default/files//dokument/FORSKNING/demenssjukd_samhallskostn_2019.pdf

 $^{^{12}}$ Brum, W.S. et al. A two-step workflow based on plasma p-tau217 to screen for amyloid β positivity with further confirmatory testing only in uncertain cases. (2023). Nat Aging 3, 1079–1090. https://doi.org/10.1038/s43587-023-00471-5

¹³ Jönsson, Linus et al. The affordability of lecanemab, an amyloid-targeting therapy for Alzheimer's disease: an EADC-EC viewpoint. (2023). The Lancet Regional Health – Europe, Volume 29, 100657

¹⁴ Livingston, Gill et al. Dementia prevention, intervention, and care: 2020 report of the Lancet Commission. (2020). The Lancet, 396(10248), 413 - 446



Francesca Mangialasche

Francesca Mangialasche, assistant professor at Department of neurobiology, care sciences and society, Karolinska Institutet, described results from clinical studies where the so-called FINGER-model has been applied. This model focuses on five lifestyle interventions: healthy and balanced food, physical exercise, cognitive training, social activities, and management of vascular and metabolic risk factors. Today, 5-, 7- and 11-year follow-ups have been completed and the results show: cognitive benefits, 20% lower risk cardiovascular events, 30% lower risk for functional decline, 60% lower risk of chronic diseases, better health related to quality of life, reduced costs for healthcare and health-economic benefits.¹⁵



Linus Jönsson

Can we also expect that such preventive interventions will save money? **Linus Jönsson**, professor in health economics at Karolinska Institutet, pointed out that it depends on how the interventions affect the progression of the disease. With compressed morbidity, i.e. when the period of illness and disability preceding death is shortened, expenditure is likely to be lower. On the other hand, if the progression is slower and the time the patient spend in severe states before death is prolonged, the costs may instead increase. Current modelling shows that preventive interventions give some some cost savings, but the biggest benefit would be in Qalys (Quality Adjusted Life Years), i.e. more time would be spent in less severe states of ill health. The experts at the symposium all agreed that when discussing dementia interventions, we need to shift the focus from cost savings to increased health and wellbeing. However, the cost issue is impor-

tant when deciding upon which interventions to use. Health economics programs must compare outcomes to help decide which healthcare programs should be funded to maximize health gains under given budget constraints.

Why are creeping crises difficult to handle?

Why is it difficult to address and implement measures to manage creeping crises? There are several contributing factors and some of the challenges discussed at the symposium are summarized here.

It is difficult to imagine and visualize the consequences of a fully developed crisis

Creeping crises concern intangibles of the future, and often we can't directly see or imagine the likely consequences here and now. Even though precursor events hint at what to expect from a developed crisis, these events may be limited in time and geographical distribution. Events that occur far away are harder to grasp, and it is only when the crisis is knocking on our door that we understand its power. Researchers are usually very good at providing figures and charts but a call to action requires a combination of facts, figures, compelling storytelling and images.

Uncertainties

It is difficult to forecast the outcomes and effects of creeping crises as they evolve over time, and dealing with uncertainties is always difficult.

The handling of creeping crises often requires global collaboration

Handling creeping crises requires collaboration between many stakeholders, often at a global level. Different countries may have conflicting interests and the resources for managing specific emergencies are not equally distributed. Global creeping crises require global agreements, strategies and action plans that should be feasible at both national and local levels. Keeping pace and synchronizing responses, all the way from the global agreements to municipal action plans, is difficult and may require farsighted politicians.

Often, there may be conflicting interests, such as those between oil-producing countries and the flooded Pacific islands. The same is seen in AMR where there are different levels of ambition in different countries regarding restriction of antibiotics use for humans and animals. There are also conflicting interests on personal and societal levels, as people may want antibiotics when they are ill, even though it is unnecessary and unsound at societal level.

It may be costly to handle creeping crises

At least in the short term, it may be expensive to manage creeping crises. Money needs to be invested early on to prevent something (uncertain) from happening in the future. With restricted budgets, such expenditure on preventive actions is difficult to justify, even though the consequences of doing nothing may be much more costly in the long run.

It is difficult to determine which measures will be most effective

Evidence-based measures cannot be used since they are relate to past crises and knowledge.

Ambiguous political incentives

Political decisions needed to handle creeping crises may interfere with personal freedoms, and therefore carry a risk of making politicians less popular.

Conflicting business and societal interests

Businesses like the oil industry and parts of the food industry depend on products that are driving evolving creeping crises, such as global warming and lifestyle-related diseases, respectively. In areas with strong business interests, powerful lobby organizations try to hinder regulations, which negatively affect their businesses.

What can be done to better handle creeping crises and avoid them from escalating into acute ones?

Use methods for visualizing and experiencing the consequences

As mentioned, creeping crises are often intangible, and the future consequences of developed crises are difficult to visualize and imagine. Modeling of future scenarios and the use of new technology such as virtual and augmented reality may provide effective means to make threats less abstract and to understand the consequences, increasing the willingness to act.

Learn from countries where the creeping crises have progressed the furthest

Visiting and learning from countries where creeping crises have progressed and precursor events have occurred may help us both to understand their consequences and to find methods to reduce their impact. Visits and/or taking part in stories may also increase engagement in questions related to the crises and the will to invest in solutions.

Experiment with new interventions

The standard working method in healthcare, as well as crisis management, is to use evidence-based interventions. During the symposium, it was agreed that when handling novel challenges and crises, the trusted methods may not work. Hence, there should be space for experimentation, innovation and testing of new methods. It was also highlighted that even in governmental work, experimentation and innovation are needed to tackle new challenges.

Inspire public engagement

Several of the experts at the symposium stressed that public engagement is required to drive the changes needed to address creeping crises. Real-world stories from those caught up in disasters are most effective at achieving engagement and shifting public opinion. Scientists, advocates, activists and media are all essential to achieve this change. Behavioral science has demonstrated that if you want people to have an appropriate level of concern you should offer a solution which gives them an opportunity to take steps to reduce the threat. Concern is different from fear, which may be paralyzing and counterproductive.

Raise political awareness and enable political actions

It is important to note that the actions of politicians and policymakers are driven by both economic and political rationales. Politicians want to make the most effective use of the available budget within the framework of their respective ideologies, but they also want to take actions that are in the interests of their current and potential new voters. Hence, public engagement in questions relating to creeping crises is crucial.

The basics of communication strategies that can be used to engage the public mentioned above are relevant when communicating with politicians. Effective communication from experts in the field should include:

- · facts and figures on the creeping crisis and its development
- · facts and figures on the costs of the crisis today and different future scenarios
- · engaging stories
- descriptions of public opinion, providing political incentives
- suggestions on solutions to handle the crisis. These could be new regulations, economic incentives (taxes and investments) or expanded international collaborations.

Implement regulations and measures to understand the development of creeping crises and increase international collaborations

Since handling creeping crises requires synchronized actions on a global scale, international collaboration is needed. At the symposium it was highlighted that structures similar to those used to deal with the climate crisis would help to address other creeping crises. This means having an expert group like The Intergovernmental Panel on Climate Change (IPCC) that regularly assesses the current science of the respective crises, combined with global conferences that determine global strategies, which are then translated to national commitments. When national actions such as regulations or taxes encounter opposition from the public, they may be easier to justify on the basis of relevant international agreements.

Find functioning economic models for prevention

The handling of creeping crises is all about using early, preventive measures to avoid these low intensity, developing crises from reaching a state where they are acute crises leading to significant pressure on states, large amounts of suffering and high monetary costs. To allocate resources for preventive actions when resources are restricted, we must develop economic models that are supportive. One example is impact bonds; these include financing mechanisms whereby private investors fund social or environmental projects upfront, and the government or other public payers repay them only if the project meets pre-agreed targets. These bonds are designed to address social issues like education, healthcare, and poverty reduction by aligning financial returns with measurable positive impacts. It is pleasing to see that the Swedish government is now allocating (albeit a small amount of) money to expand the use of impact bonds.

Appendix: Program for symposium

The Future of Life Science: Creeping Crises May 23-24, 2024

Session 1: Introduction to creeping crises and different perspectives on handling global health challenges.

- Magnus Ekengren. Professor, Department of Political Science and Law, Swedish Defence University.
- Carl Johan Sundberg. Professor, Department of Physiology and Pharmacology, Karolinska Institutet.
- Susan Michie. Professor of Health Psychology, University College London.

Session 2. Antimicrobial resistance – the science, the business, and the governance.

- Olivier Rubin. Professor, Department of Social Sciences and Business Globalization and Europeanization, Roskilde University. Editor of the book: Steering Against Superbugs: The Global Governance of Antimicrobial Resistance.
- Fredrik Almqvist. Professor of Organic Chemistry, Umeå University.
- Eva Garmendia. Project Coordinator, Uppsala Antibiotic Center, Uppsala University.
- Nina Rawal. Partner and Co-Head of Impact Ventures, Trill Impact.

Fireside chat: Experiences from national crisis management and what we learned from the COVID-19 pandemic.

 Maja Fjaestad. Expert coordinator for policy and preparedness at the Centre for Health Crises, Karolinska Institutet. Associate professor from KTH. Senior adviser to the European Policy Center in Brussels. Former State Secretary for the Swedish Minister for Health and Social Affairs, Lena Hallengren.

Session 3. The challenges and opportunities of handling Alzheimer's disease and other types on dementia – new treatments, prevention, and socioeconomic considerations.

- Stina Syvänen. Professor at Department of Public Health and Caring Sciences, Uppsala University.
- Francesca Mangialasche. Assistant Professor at Department of Neurobiology, Care Sciences and Society, Karolinska Institutet.
- Linus Jönsson. Professor at Department of Neurobiology, Care Sciences and Society, Karolinska Institutet.
- Cecilia Lundberg. Professor, CNS Gene Therapy, Lund University. Chairperson of the scientific board at The Swedish Brain Foundation (Hjärnfonden).

Session 4. How to act upon creeping crises.

- Staffan Svärd. Deputy Vice-Rector, Faculty of Science and Technology, Uppsala University. Director of the Pandemic Laboratory Preparedness program, SciLifeLab.
- Fredrik Söder. CEO and founder, Health Integrator.
- Magnus Björsne. Head of AstraZeneca BioVenture Innovation Unit.
- Petra Noreback. State Secretary to Jakob Forssmed, the Ministry of Health and Social Affairs, Swedish Government.

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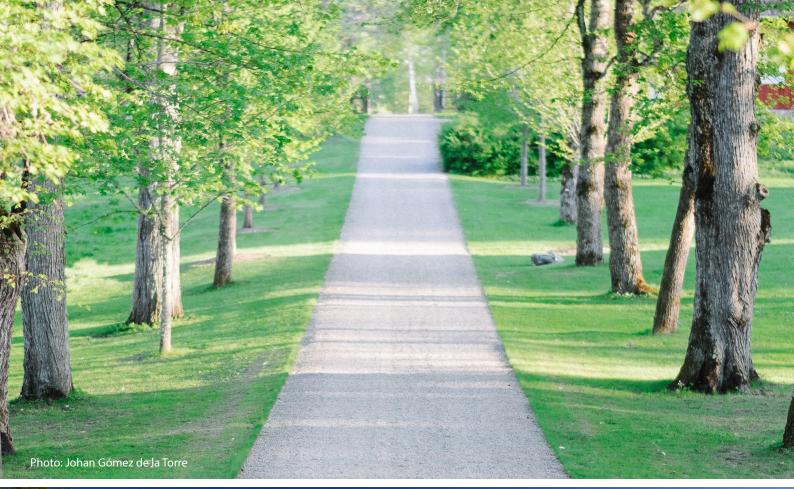














A report from the symposium *Creeping Crises*

Published: November 2024

Publisher: Stockholm Science City Foundation Analysis and author: Andreas Namslauer

