



THE
FOUNDATION
TO PREVENT ANTIBIOTIC RESISTANCE

Impact report 2021

Protecting modern healthcare for future generations





Evaluating impact is important to improve our work

Supporting research and other projects aiming at the prevention of the spread of antibiotic resistance is extremely important. However, it is equally important to see to it that the support is meaningful and effective. We therefore spend quite some time and resources evaluating the impact of the projects we are supporting. This will help us to direct our future funding in the most efficient way helping to reduce the risk of this very serious problem.

Peter Rothschild
Chairman
PAR Foundation

About PAR Foundation

PAR Foundation is a Swedish foundation formally registered in 2018 as *Stiftelsen för förebyggande av antibiotikaresistens* (The Foundation to Prevent Antibiotic Resistance). As a Swedish foundation, the organization is governed by an immutable section in its statutes which state that it shall fund research, education and information activities in Sweden and abroad with the purpose of reducing antibiotic resistance.

Board of directors



Lars Engstrand, Professor, Dept. of Microbiology, Tumour and Cell Biology (MTC), and Director of Centre for Translational Microbiome Research at Karolinska Institutet.



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Peter Rothschild, Chairman and founder of BioGaia, CEO of BioGaia 1996-2016.



Anna Nordlander, Assistant Senior Physician at the Department of Infectious Diseases at Karolinska University Hospital.



Marika Isberg, LL.M and BSc in Economics. Vice President and General Counsel for BioGaia.

BioGaia[®]
Probiotics grounded in evolution
Driven by science

PAR Foundation is funded by philanthropic donations from BioGaia, a Swedish healthcare company that has been a world-leader in probiotic dietary supplements for more than 30 years.

Our work

Gaps in knowledge...

PAR Foundation commissioned a study on knowledge gaps on prevention of antibiotic resistance that was published in Global Health Action in 2020. Among the 430 000 research papers on antibiotic resistance that were identified in an 18-year period, only 0.25% focus on preventive strategies, and the study concluded that more cross-disciplinary research and evidence-based interventions are needed for the prevention of antibiotic resistance.

Stig Wall (2019) *Prevention of antibiotic resistance – an epidemiological scoping review to identify research categories and knowledge gaps*, Global Health Action <https://doi.org/10.1080/16549716.2020.1756191>

0.25%

of the identified papers on antibiotic resistance focused on preventive strategies

...and gaps in funding

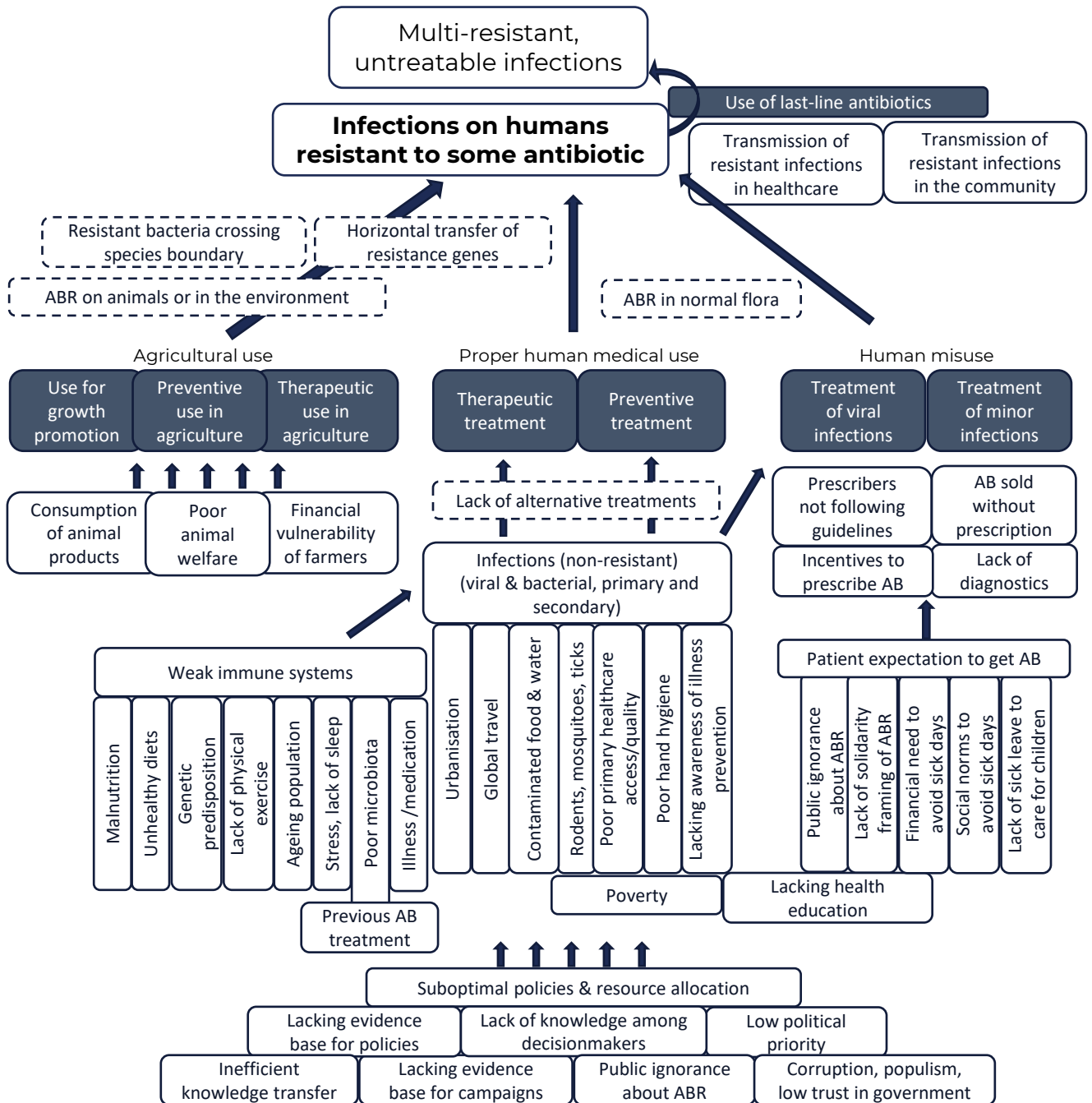
In February 2021 we announced a new collaboration with Global AMR R&D Hub. The Global AMR R&D Hub is an initiative that aims to enable evidence-based decision-making by providing a comprehensive and detailed mapping of ongoing research and funding sources.

One of the core criteria that PAR Foundation considers for which areas should be targeted for funding is the extent to which they have been neglected so far. This means that in addition to considering the potential impact of progress in a certain area, the extent to which progress is limited by funding is also assessed. The Global AMR Hub facilitates this by providing a searchable database of past and current funding, called the Dynamic Dashboard.

**GLOBAL
AMR R&D
HUB**



PAR Foundation problem mapping: Drivers of antibiotic resistance



The problem mapping above identifies drivers of antibiotic resistance and demonstrates how they directly or indirectly contribute to the occurrence of resistant infections. Each identified “driver” is a potential target area for interventions to prevent antibiotic resistance. To select which area that should be prioritized, our core guiding principles are used (next page).

Core guiding principles

As the problem mapping shows, antibiotic resistance is an incredibly complex issue and the work that can *prevent* antibiotic resistance involves virtually every aspect of how our society is organized. A challenge we have is that of distributing our limited resources in the way that will have the highest chance of generating impact, and we have therefore adopted the following core guiding principles for our work.

Importance

Perhaps the most obvious principle is that we should prioritize initiatives of high importance to prevention of antibiotic resistance. In practice, this can be understood as how much impact we could expect from addressing a certain problem: Would we potentially be preventing a hundred instances of antibiotic use annually, or a hundred thousand? Would we be addressing use that is especially prone to driving resistance development, or that is linked to what the WHO has identified as priority pathogens?

Neglectedness

The second principle is to prioritize work that, despite being important for prevention of antibiotic resistance, receives little funding from other sources. For a field of research that already receives a lot of resources from major funding agencies, a few additional grants a year would not matter much: the most valuable projects would be funded regardless of our contribution. Meanwhile, there are initiatives with great potential that struggle for funding because seem less academically prestigious or because they are carried out in a region of the world where funding is scarce: for such work, our funding can make a great difference.

Catalyst role potential

As we are a relatively small funder we also aim to prioritize projects where there is a potential that our contribution could have a catalyst role. This could mean that we pitch in the first funding for a bold project that helps it to attract additional funding from other sources, or that we might fund pilot studies to generate preliminary results that could support an application to a major grant agency.

Transparency and accessibility

Finally, we require grantees to provide transparent and accessible reporting of results and methods. Preregistration is encouraged for hypothesis-testing research, as well as open data sharing. Protection of IP should however always be considered since this can be of importance to the potential for results being used.

Feasibility

Feasibility is an important criteria, but it should not be confused with risk aversion. What we aim for with the principle of feasibility is to assess that there is a plausible theory of change, that is, a plausible way that an initiative can lead to significant impact, and that the team is competent and have reasonable resources.

Member of *Effektfullt* network



Since 2020 PAR Foundation is a member organization of the Swedish impact measurement network *Effektfullt*.

We have participated in training sessions on monitoring progress toward system change and impact reporting, and we are a part of a collaborative cluster of funding organisations. The aim is to continuously improve how we measure, evaluate and report the impact of our work. By doing so, we can share what we learn with other stakeholders as well as refine our strategies to prevent antibiotic resistance.

Training programme on AMR with Students for Global Health Cambridge

In the beginning of 2021 PAR Foundation supported the organization of an extra-curricular initiative by Students for Global Health (SfGH) Cambridge called “Become an Antibiotic Ally Against AMR”. A total of 75 participants joined the six-week programme from a wide range of subject backgrounds to learn about antimicrobial resistance (AMR). After some initial training on AMR and project management, participants were split into teams to work on specific projects.

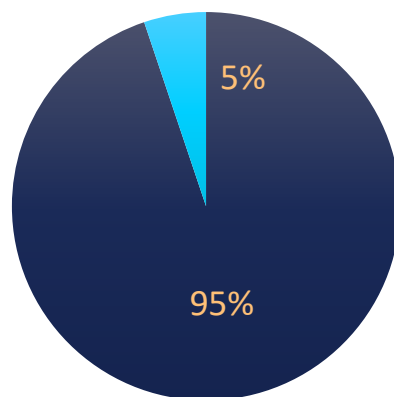
– We are really excited to see how much engagement there has been from students about this programme, says Christine Agbenu, the president of SfGH-Cambridge.

Following the training programme, a National Working Group on AMR was formed within Students for Global Health UK and a new round of the training programme with participants from all of UK is planned for 2022.

Grants

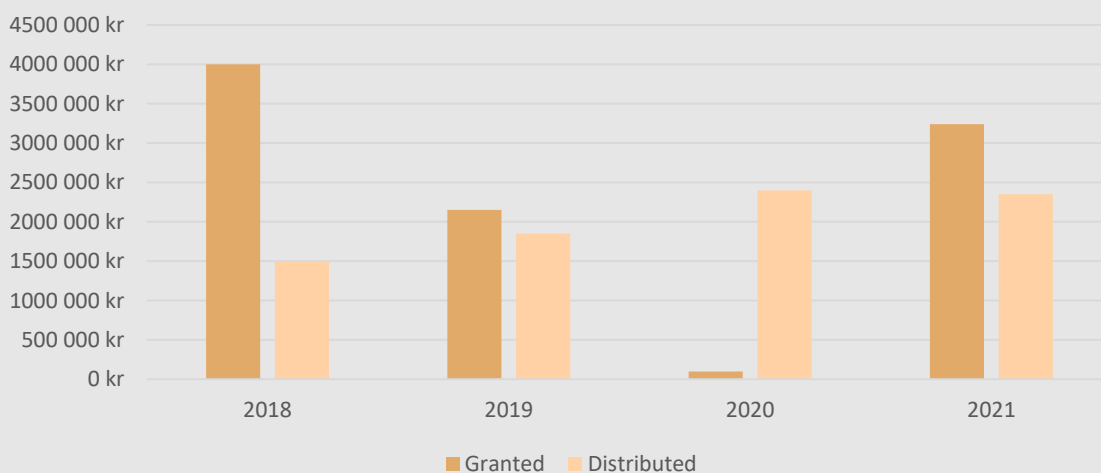
Grantmaking in 2018-2021

Since PAR Foundation was founded, a total of SEK 9,490,000 (approx. EUR 950 000) has been granted to research, education and information projects aiming to prevent antibiotic resistance. The covid-19 pandemic has affected many of the projects funded by us, mainly in the form of delays. Most of the projects are therefore still in progress, but one that was concluded in 2020 by Dr Peter Bergman is presented in detail on the following pages.



■ Research ■ Education and information

Grant decisions and distribution



Projects typically range between 1-3 years in duration, and receive their grants in annual pay-outs. The darker columns indicate the amount that was granted in a given year, while the brighter columns indicate the transactions.

The low amount granted in 2020 was caused by a decision to pause the grant making in favour of more extensive preparation of the 2021 call.

Grant overview

The table below lists all funding granted by PAR Foundation since the organization was founded. The first two calls, 2018 and 2019, were exclusively for Swedish applicants and had a focus on projects that related resistance prevention to the immune system. Following internal assessments of how to achieve the highest impact with our funds, the grant call in 2021 opened for international applications and targeted infection prevention among elderly. Almost every project has experienced delays caused by the covid-19 pandemic.

Grant year	Recipient	Project	MSEK
2018	Bergman, Karolinska Institutet	Activation of innate immunity as a novel treatment against multidrug resistant bacteria (Completed)	0.5
	Brighenti, Karolinska Insitutet	Studies on immune modulation and host-directed therapies with the aim to prevent antibiotic resistance in tuberculosis (-2022)	1.6
	Koskiniemi, Uppsala University	The use of armed probiotics to prevent bacterial infections and to eradicate multi-drug resistant normal flora (-2022)	1.4
	Giske, Karolinska Institutet	Engineering the intestinal microbiome in patients with gut carriage of resistant bacteria (-2022)	0.5
2019	Hildebrand	Documentary film project (-2022)	0.15
	Sjöling, Karolinska Insitutet	Inhibition of attachment of pathogenic bacteria can prevent an inflammation-induced overgrowth of pathogens, inhibit disease, and minimize preventive and therapeutic antibiotic use (-2022)	1.0
	Lindén, Gothenburg University	Induction of the mucosal defence mechanisms against infection (-2022)	1.0
2020	Uppsala Health Summit	Managing Antimicrobial Resistance through Behaviour Change: Conference support (Completed)	0.1
2021	Bergman, Karolinska Institutet	Investigating higher doses of Vitamin D for prevention of respiratory tract infections among elderly (-2024)	1.0
	Frimpong, University of Ghana	Exploration of genomics of host-pathogen interactions underlying Streptococcus pneumoniae infection in the Ghanaian elderly population (-2023)	1.0
	PPCIRA, Portugal	Reducing urinary tract infections in Portuguese elderly care through training and behaviour change interventions for caregivers (-2023)	1.0
	Govett	International fellowship program for future leaders in AMR (-2022)	0.24

Concluded grantee project: A new approach to prevent infections in vulnerable people

Peter Bergman, researcher and senior physician at Karolinska Institutet, received funding from PAR Foundation for a project investigating how a novel compound could trigger the immune response to treat or even prevent infections. The compound, named HO53, triggers the body's production of *antimicrobial peptides* (AMPs), which are a part of the innate immune response and function as a natural, broad-spectrum antimicrobial that can kill or destroy bacteria, viruses, and fungi.

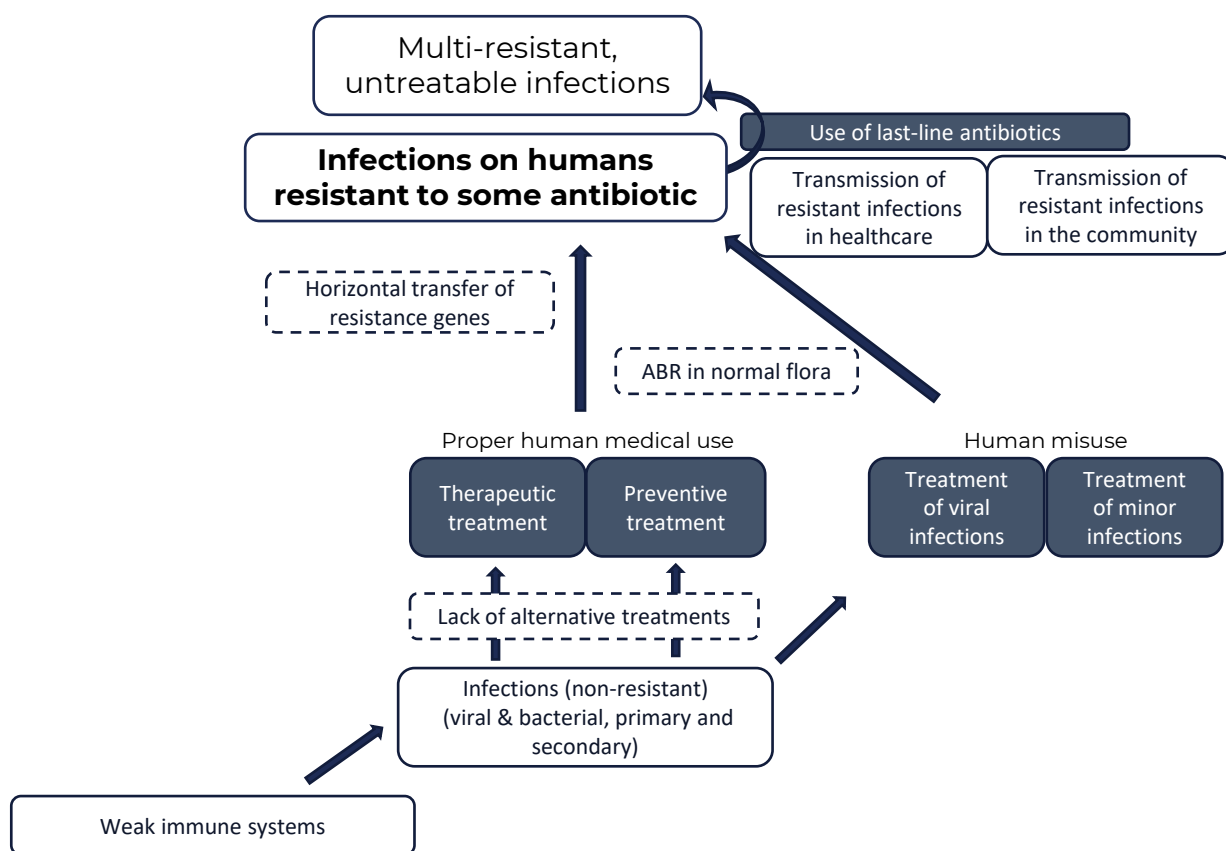


An important feature of this kind of treatment is that the risk of driving resistance is particularly low. Studies have indicated a low risk for resistance development for AMP treatments, and triggering the body's own AMP production rather than inserting a specific AMP reduces this risk even further. This way, it is not one but a multitude of different AMPs that are produced simultaneously, and the likelihood that the bacteria could develop resistance to all of them simultaneously is extremely low.

HO53 could be used in combination with first-line antibiotics to treat resistant infections as well as a stand-alone treatment for infections, reducing the need for antibiotics, and ultimately it could even be used to prevent infections before they occur. Preventive treatment could be particularly interesting for vulnerable groups such as elderly, immunosuppressed or cancer patients that are particularly susceptible to infections. Preventive use could also be valuable for healthy individuals that temporarily experience a higher infection risk – at the beginning of the school-year, say, or when taking an intercontinental flight.

The project was run in collaboration with a group of Icelandic researchers, and there is an associated start-up company, Akthelia, that is now aiming to turn the results into novel drugs. Akthelia secured 42 MISK in equity funding in 2020, and received a grant of 45 MISK in 2021.

The impact assessment of this project will be done over several years by tracking the development of Akthelia as well as the indicators of impact listed in the table on the next page: patent maintenance and use, and citations linked to similar novel treatments. The potential impact of a treatment that would make people less susceptible to infections is in principle enormous, but actual impact will depend on if such treatments are successfully developed and if so, how widely used they would be, by whom they would be used and how effectively such treatments would decrease the need for antibiotic treatments among users.



The figure displays a section of the problem three from page 7 relevant to this particular project. A treatment that could prevent infections, particularly in people with weak immune systems, has potential to offset a large share of all human antibiotic use and thereby slow down resistance development.

Funding	SEK 0.5 M (EUR 50 000) corresponding to 10-20% of the funding for early work on HO53
Project period	2018-2020
Publications	Rekha RS, Karadottir H, Ahmed S, Gudmundsson GH, Agerberth B, Bergman P. Innate Effector Systems in Primary Human Macrophages Sensitize Multidrug-Resistant <i>Klebsiella pneumoniae</i> to Antibiotics. <i>Infect Immun</i> . 2020 Jul 21;88(8):e00186-20. doi: 10.1128/IAI.00186-20. PMID: 32513857; PMCID: PMC7375773.
Indicators of impact	Status of patent owner Akthelia: Additional grant funding in 2021 of 45 MISK Patent activity and use: Granted in the USA 2018, China and EU 2020 Citations linked to similar novel treatments: 0

Looking forward: Grants in 2022

In the upcoming year of 2022, we plan to reiterate the grant call from 2021 with some minor adjustments, targeting infection prevention among elderly. Since we received many high-quality applications where the alternative funding sources seemed scarce, our assessment is that it is well justified to keep focusing on this area. We also plan to establish smaller early-career grants, building on previous successful student collaborations. All grants will be open for applicants from any country in the world.

Infection prevention among elderly

The number and proportion of elderly in the global population is increasing, and for several reasons this is a driver for antibiotic use and antibiotic resistance.

Elderly are generally more susceptible to infections, and diagnosis is more difficult since typical symptoms are often absent or blunted. Knowledge and guidelines for optimal drug use for elderly are also lacking.

Antibiotics are among the most frequently newly-prescribed drugs in elderly patients. Between 25% and 75% of antibiotic prescriptions in long-term care facilities for the elderly are thought to be inappropriate. Meanwhile, little research on preventable inappropriate medication use has been carried out in residential elderly care. Most research on antibiotic resistance prevention is done in hospital settings, while most elderly either receive care at home or live in residential care facilities.

Early-career grants

The drivers of antibiotic resistance need to be addressed with competence from diverse fields. Meanwhile, our assessment is that the potential career paths in AMR for early-career individuals outside the mainstream AMR sciences (medicine, biotechnology and biology) are often unclear, making it harder to attract such talent to work in the field.

We therefore plan to create a grant programme targeted to improve the ability and interest of promising early-career individuals to contribute through their professional careers to effective AMR work. Funding could be granted for example to early-career individuals running independent projects, to finance internships at established organizations or to enable junior researchers from different fields to work on projects related to prevention of antibiotic resistance.

Details regarding the early-career grant will be announced early in 2022 at parfoundation.org

Grant call activities in 2020-2021

During 2020 potential focus areas from the problem mapping (page 7) were investigated, and infection prevention among elderly was selected as the driver that best corresponded to the core guiding principles. Potential applicants were reached through newsletters, social media and by contacting corresponding authors of relevant research articles, resulting in 31 applications. After initial screening, seven applicants were invited to interviews out of which three were awarded grants. We always appreciate feedback on our strategy and process, as well as support with spreading information to potential applicants – please find our contact details at www.parfoundation.org

