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National Institute
for Public Health
and the Environment

Research with an impact

Annual Science Report 2006

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RIVM Annual Science Report 2006

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Text
Peter J. Vermij, Schuttelaar & Partners, The Hague

Published by
RIVM Publishers
Printed by
OBT, The Hague

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RIVM: Research with an impact

At an institute that is dedicated to public health and the environment, scientific research should also have a clear impact. To maximise our effect, we need to ask ourselves the right questions. What is our core message? To whom should it be addressed? And what do we need to make sure it reaches its target?

Marc Sprenger,
Director-General,
National Institute for Public Health and the Environment (RIVM)

At the National Institute for Public Health and the Environment (RIVM), researchers carry out a great deal of excellent research every day. Not a week goes by without one of them publishing a thorough report or an authoritative paper. To maximise the impact of that research, however, it is imperative that we start putting more effort into telling the world about our research and why it matters. And just as in some types of visual arts and in architecture, we have to learn that in communicating our science often 'less will be more'.

Jewels in the crown

In my latest New Year's speech, I alluded to an investigation by our colleagues at the Nutrition, Medicines and Consumer Safety Division (RIVM-VGC). They wondered what their clients had learned from the reports they had sent them. As it turned out, a great many details in those reports had not been picked up. In fact, the client did not fully understand some parts of the work.

From my days as a researcher, I remember all too well how a crucial part of our work can easily fall through the cracks. After completing an article or report filled with tables, figures and facts, we are often too close to the deadline to spend much time on the abstract. In those final few minutes, we end up producing a summary that is okay at best, forgetting that for the great majority of our audience members, that summary will be all they will ever see of our work.

What's more, after having done all that fascinating research and finding so many fine details, we think it is impossible to sum it up in just a few words. Yet in many respects, our abstracts and executive summaries should be the jewels in the crown of our research. If we take the time, capturing the essence in a few lines will prove to be possible after all. If we do it right, our impact will be much bigger. Policymakers will find it easier to incorporate our work into theirs; news media will more often pick up on our work. Our visibility will increase, and so will our ability to put issues on the agenda.

It is not just summaries we should care about more. At RIVM, when we design and budget our projects, we tend to push follow-up and communication to the bottom. But if we want to maximise the impact of RIVM's outstanding research — and that is indeed what I want — follow-up and communication need to be near the top. We should ask ourselves the right questions. What is our core message? To whom should it be addressed? And what do we need to make sure it reaches its target?

Last year, in a communications policy document, the board of directors said that communications expertise needs to be close to where the research takes place. All our divisions should have their own

communication specialists, we think, and we are working to implement that policy.
At the central RIVM level, we have also set up an editorial office that stands ready to assist our researchers in effectively phrasing their messages. As of 2006, one staff member at the office is available full time to make research summaries as effective as they can be.
But at the same time people should know that RIVM at its core remains a scientific institute. Our researchers work closely with colleagues across Europe and the rest of the globe. Everything we do meets rigorous scientific standards and our research, which covers the gamut from radiation and toxicology to influenza and obesity, is published in international, peer-reviewed journals.

For our own RIVM staff too, this report has a lot to offer. I hope all our scientists will take the opportunity to re-acquaint themselves with the breadth and depth of our common research effort. All too often, we are so focused on finishing our own projects that we forget to find out what colleagues just down the hall have been up to. What's more, given our research areas and the fact that we are mostly funded by tax-payers, it's only fair that society gets the chance to learn about our research.

Put to wider use

Of course, another way to increase our impact is not to follow a 'less is more' approach. By expanding international collaborations, for example, we can ensure that our research is used beyond national borders and helps not just to set Dutch priorities, but European priorities, as well.
Take for example our research into 'disease burden,' which is being used by the European Centre for Disease Prevention and Control (ECDC) in Stockholm to highlight problems in European health. Our collaboration with colleagues abroad has added weight to our work and has put it to far wider use than ever before.
Similar things have happened on other fronts. Severe health effects of particulate matter and the threat of drug-resistant tuberculosis, for example, have moved up the European priority ladder thanks, in part, to research carried out by RIVM.
In the next few years, working with the ECDC, the European Medicines Agency (EMEA) in London, the European Food Safety Authority (EFSA) in Parma and the European Environment Agency (EEA) in Copenhagen should continue to be at the top of our agenda.

Raise awareness

RIVM is not a political action group. However, it is a good thing when our research raises awareness about difficult problems in our society, either by alerting governments or by attracting attention from the mass media. That is why, besides doing great research, it is important that we also make sure it is having an impact.
As a scientist, I will not let pass any opportunity to emphasise how important it is for people to quit smoking, have healthy diets and exercise frequently. As an institute, too, we have a duty to get such messages out as effectively as possible — even if that means that, often, 'less will be more'.

Marc J.W. Sprenger, Ph.D. M.D.
Director-General, National Institute for
Public Health and the Environment (RIVM),

April 2007, Bilthoven, The Netherlands

Frits Mooi,
Centre for Infectious
Diseases Control
(RIVM-CIb)

Chasing after a highly successful bug

The recent flare-up of serious whooping cough could be a side effect of successful childhood immunisations introduced in the 1950s. The causative agent, the Bordetella pertussis bacterium, has evolved into a form that is better able to withstand the vaccines. More effective vaccines could stem the resurgence.

For much of his scientific career, Frits Mooi has been tracing the path of a microbe that many once thought was a thing of the past.
Bordetella pertussis, whooping cough's causative agent, is a bacterium that as far as we know infects only humans. Spread by infected droplets from patients, the microbe first causes symptoms similar to a cold before becoming more serious or even deadly. In The Netherlands, in the first half of the 20th century, whooping cough killed hundreds of infants each year. After vaccines became available in the 1950s, numbers dropped dramatically — Bordetella seemed on its way out.
Since then, it has become clear that Bordetella is "a highly successful pathogen," says Mooi.
"In The Netherlands, an estimated one million infections occur each year. Although a large fraction of these infections are subclinical or mild, there probably is no other infectious disease in this country with that much transmission."
Bordetella's staying power became apparent when in the 1990s, after decades of child immunisation, the number of registered whooping cough cases began to rise suddenly. Even the number of deaths among infants is climbing. However, most of the increase in the disease is found in adolescents and adults.

Controversial

Frits Mooi has been studying Bordetella's return, and he developed a theory that became widely known but controversial: According to Mooi, the bacteria has been evolving, subtly changing its mantle and rendering the vaccine less effective. What's more, a new type of bacteria recently appeared that is more virulent than previous ones and better able to strike adults in whom the effects of childhood immunisation has waned.
"As a microbiologist, I was used to the idea that 'nothing in biology makes sense except in the light of evolution,' as Theodosius Dobzhansky once said," Mooi says, explaining why he, more than some

How Bordetella pertussis got away

For his Ph.D., Marcel Hijnen studied how evolutionary changes in a gene coding for the pertactin toxin by Bordetella pertussis may have helped the bacterium to evade whooping cough vaccines targeted at the original molecule. All current vaccines trigger immune responses by confronting immune cells with three to five bacterial proteins, and pertactin is one of them.
By closely watching the pertactin protein, and using molecular tools to tinker with its various regions, Hijnen discovered how variations in the protein can significantly influence the immunogenicity of the protein. Variable parts of the toxin are able to hide other parts, effectively preventing the immune system from responding.
Some pertactin variants turned out to be more effective than others in doing just that. Removing these variable regions resulted in pertactin proteins that were more effective than conventional vaccines.
Hijnen used the data to build a synthetic peptide vaccine and tested its efficacy in a mouse model. The new vaccine provided stronger protection than the wild-type vaccine, offering new routes to potentially more effective vaccines against whooping cough. The study was carried out in co-operation with the Department of Medicinal Chemistry at Utrecht University.

Hijnen M
The Bordetella pertussis protein Pertactin: role in immunity and immune Evasion. Doctoral thesis, Utrecht University, Utrecht

medically trained colleagues, tended to blame evolution. Because to his initial surprise, his hypothesis has at times been unpopular.
According to Mooi, the evidence gathered over the years suggests that vaccines should have been kept up to date better and that new vaccines should be designed to elicit a longer-lasting immune response. The trouble is that in the difficult world of vaccine development, such advice is easier given than followed, explaining in part why his ideas have not been met with applause. “People do not deny that there have been changes to the bacterium,” Mooi says, “but most of them doubt whether it was relevant for the effectiveness of the vaccine.” Not unsurprisingly, much of the scepticism comes from vaccine manufacturers or researchers he considers close to that industry.
If Mooi is correct, vaccine producers skipped their homework when they developed a new generation of safer vaccines in the 1980s. Instead of checking whether new strains had appeared, a half-dozen companies raced to market using the old strains.
After studying the recent upswing in whooping cough cases, however, Mooi believes that he found even more important mutations in the bacterium. His group found that the old Bordetella strain has been replaced by a new strain with a mutation in a regulatory gene that probably results in the production of more toxin. By making more toxin, Mooi suspects, the bacterium is able to ward off the low level of immunity in adults vaccinated decades ago. As a by-product, the higher production of toxin has made the bacterium more virulent.
“After childhood vaccination wiped away the main transmission vehicle of Bordetella, that is non-immune children, evolution selected for more aggressive strains able to survive in adults with waning immunity,” he says. The solution could be to develop DNA-based vaccines, Mooi says, which would not require chemical detoxification, a step that makes the vaccine less immunogenic. A DNA vaccine, Mooi suggests, could induce antibodies to the toxin that would last longer.

Investment

According to Mooi, many of his colleagues have warmed to the idea that current vaccines are not optimal. The problem is that it will be hard to replace the vaccines because registration authorities do not accept changes in vaccines without repeating many years of research, costing many millions of euros — an investment that probably no vaccine maker is willing or able to make. However, Mooi says, some modifications probably can be implemented without extensive field trials, such as adapting the vaccine to the current circulating strains and increasing the immunogenicity of the toxin. Immunity could also be prolonged by additional (booster) vaccinations, especially with toxin-containing vaccines. In the long run, Mooi says, vaccine companies and regulatory authorities should realise that pathogens are “moving targets” and that vaccines will have to be updated regularly.

Pieter van Baal
Public Health and Health Services Division
(RIVM-V&Z)

Counting the costs of healthy living

Compared to many curative treatments, disease prevention programmes are really a great deal even if you account for the extra healthcare costs caused by people living longer lives. In terms of healthy life years, prevention gives you more bang for the buck.

Some people working in disease prevention don't really like what he does, says Pieter van Baal. As an economist, he adds income, subtracts expenditures and comes up with the price of intervention. "Cold numbers," people will say, and counterproductive because they show that prevention comes at a cost.
"It's true that economists focus on numbers," Van Baal says. "It's also true that some people will write off prevention programs if they do not save money." "However, as an economist, I think people are prepared to pay for their health. Even if prevention turns out to be more expensive when you include all the numbers, it still is a lot cheaper than many curative treatments. Prevention programs should be seen as investments in years spent in good health, and as such they can yield great results.
A government that would spend more on prevention would get lots of health in return."

Investment

For much of 2006, Van Baal worked on calculating the real costs of helping people to quit smoking. He used to smoke, he says, when as a Ph.D student he was crunching numbers about crime, not healthcare. "I liked smoking," he now says, "but when I had to go out for every cigarette, being an addict felt rather pathetic."
In pharmaco-economics, it is unusual to put the life years gained by successful treatments on the balance sheet as expenditures. However, according to some researchers, when dealing with prevention it does make sense to include indirect healthcare costs when more people will reach old age, if only because ignoring such costs makes the case for large-scale interventions less convincing.
Van Baal got to work comparing separate approaches. First, using the traditional approach, he only

Why unrelated medical care should be related

In this paper, accepted in 2006 but published in 2007, the authors explore whether costs of unrelated medical care in life years gained should be included in cost-utility analyses of health care programmes, especially in the case of primary prevention. This paper presents different ways to include costs and health effects of unrelated medical care in economic evaluations. Four cost-utility ratios are evaluated. As an example, they were applied to smoking-cessation interventions in two age groups. Depending on the ratio that was used, intervention costs varied between 900 EUR and 6,600 EUR per QALY gained. Ignoring costs of unrelated medical care in life years gained would unduly favour interventions that increase length of life (such as smoking cessation) over interventions that primarily increase quality of life (such as interventions aimed at reducing psychiatric disorders), the authors noted.
They conclude that for primary prevention, cost-utility ratios that include the costs and effects of unrelated medical care should be used, even if that means collecting substantially more data.

Baal PH van, Feenstra TL, Hoogenveen RT, Wit GA de, Brouwer WB Unrelated medical care in life years gained and the cost utility of primary prevention: in search of a "perfect" cost-utility ratio. Health Econ. 2007 Apr;16(4):421-33

counted savings in treatments for lung cancer and cardiovascular disease as a direct consequence of quit-smoking interventions. Following that, he also included extra healthcare costs caused by the expected rise in "unrelated", age-related ailments. For this he used RIVM's chronic-diseases model, upgraded for the occasion with costs related to Alzheimer's and similar diseases. The grand total was divided by the number of "quality-adjusted life years" (QALYs) gained by the program.
Helping smokers quit would cost about 4,400 euros per extra QALY including everything, Van Baal says. Without considering the costs of unrelated diseases, it would have been 1,500. "Either way, it's a bargain," he says. "Whichever cost-utility ratio you use, prevention costs far less than many hospital treatments, which are easily between 50,000 and 80,000 euros per extra QALY."
In retrospect, the exercise was rather moot because the costs of unrelated diseases added little. "I spent a year of my life answering a question that hardly alters the fact that prevention is very cost-effective," Van Baal says.

Politics

Economically speaking, governments should help all smokers quit before moving into curative healthcare. Obviously, other factors are at play as well. "Pretty soon our government will launch an advertising campaign against youth drinking. We know it won't work, while making drinks more expensive definitely does," says Van Baal.
"The better I get in understanding the field, the easier it becomes to explain things in clear language," Van Baal says. "I'm still learning in that respect. But I've also discovered that finding the right way to tell your story takes just as much time as doing the research itself."

Danny Houthuijs
Environment and Safety
Division (RIVM-MEV)

Keeping up annoyances

For a researcher, having an impact can have advantages and drawbacks. For more than 10 years, RIVM helped shape the debate on the health effects of Schiphol Airport. Being close to public policy, however, also invites scrutiny from people other than peers.

Nowhere on earth has the continuous growth of an international airport been accompanied by so much health research.
As early as 1993, when the Dutch government announced plans to build a new runway, a need for research into the health effects was established. Between 1995 and 2005, researchers analysed birth weight registrations and pharmacy records, measured blood pressure, wake-up times and lung capacity, and performed allergy and cognition tests. Thousands of people living near old or new runways filled out a questionnaire about their health and the quality of their environment.
All the while, political debate about the new runway raged on. “It has been a highly interesting experience,” says Danny Houthuijs, who led RIVM’s contribution to the research since 2001. The work, together with research at other institutes and universities, produced a wealth of data on the health impact of modern-day international airports. It also helped lay the foundation for a position paper by the Dutch government, published in April 2006, in which more attention was paid to the annoyance of people living farther away from runways.
Yet for a researcher, Houthuijs discovered, politics can come almost too close.

Downward trends

The research data taken around Schiphol in 1996, 2002, and 2005 tell the story of a rapidly growing airport and its impact on millions of people, living close by or at greater distances from the runways. Suddenly rising noise levels related to the opening of a new runway in 2003 caused a sharply increased incidence of people reporting annoyance, the research showed; of those reporting severe annoyance, many also reported high blood pressure and reduced general health.
But the number of people reporting severe annoyance decreased markedly over the years. The same trend was seen in different parameters, including the number of people reporting severe sleep disturbance and the number of people filing complaints about high noise levels.
“The downward trend differs radically from what was reported in the news media,” Houthuijs says. “There, you just heard about growing numbers of complaints filed after the runway had opened,

Fewer people losing much sleep over new runway

The health status of people living near Schiphol Airport did not change substantially after the opening of a new runway, the authors of this report conclude. However, spatial shifts did occur in the noise exposure and the occurrence of annoyance and sleep disturbance.
There is growing evidence of an association between exposure to air traffic noise and the prevalence of high blood pressure around Schiphol Airport.
The monitoring program was part of the Health Impact Assessment Schiphol Airport (HIAS), designed to study environmental burden, health and perceptions around the airport.
Opening a fifth runway in 2003 has led to spatial shifts in noise exposure, the study found. Fewer people were exposed to high levels of noise in 2005 than in 2002, though on average noise levels increased for people exposed to relatively low levels.
The authors also see associations between aircraft noise and poor self-perceived health and the use of sedatives. No relation was observed between aircraft noise and mental health.
Neither do the authors see evidence of air traffic contributing to the occurrence of respiratory disorders.
Since 1996, severe annoyance and severe sleep disturbance around Schiphol Airport have decreased. On the other hand, the number of people reporting moderate sleep disturbance increased after 2002.

Houthuijs DJM, Wiechen CMAG van (eds)
Monitoring of health and perceptions around Schiphol Airport
RIVM report 630100003/2006

increases that continued throughout 2004 and 2005." More complaints, however, were filed by fewer people. "Our overall conclusion has been that for people most affected by the new runway, the annoyance level subsided after an initial jump. Policies to limit the number of people experiencing annoyance have been successful," he says. "It's sad for people who suddenly found themselves living under a new approach route, but for many more people noise exposure decreased substantially. The policy worked, although most of the gains had already been established before the new runway opened, likely due to less noisy aircraft and optimisation of routes."
The research also highlighted a certain arbitrariness of government policies, Houthuijs says, by showing that in absolute numbers, much more severely annoyed people were living far from the airport than were living nearby. Although at greater distances the annoyance risk is much smaller, the overall impact is bigger because many more people live farther away than nearby.
RIVM had flagged the issue several times, he says, before the government in its 2006 position paper mentioned reducing annoyance farther away from the airport as a policy priority. The paper did not revise the general policy to concentrate annoyance on a small number of people rather than spreading it out over a great many of them.

Columns and peers

However, being very close to policy can have its downside, Houthuijs and co-workers discovered when a press release about multi-centre research around international airports into performance of primary school children raised the eyebrows of one newspaper columnist. The release had stated that an estimated 50 to 3,000 high school students living near Schiphol had lower reading comprehension scores because of loud aircraft.
Volkskrant columnist Ronald Plasterk, later appointed as Minister of Education, Culture, and Science, was quick to blame the researchers for inaccurate reporting because the figures for Schiphol did not show the effect. "RIVM provides many politically relevant figures," Plasterk wrote, "making it crucial that publicity and research match perfectly." Houthuijs still fully supports the work. "In fact, the research has since been published in The Lancet and The American Journal of Epidemiology, two leading journals; our scientific peers had no comments," he says.
The experience could tempt a researcher to refrain from informing large audiences and report only to scientific peers, Houthuijs acknowledges. It did make him wish for a bit more distance between his research and policy. "Having a consensus report or a commission that evaluates many separate studies, for example, might prevent one study from suddenly landing in the middle of political debate."

Becoming a reliable source

Industries and governments world-wide are embracing nanotechnology and preparing an endless array of applications, but risk assessment procedures are falling behind. In 2006, the Dutch government asked researchers at RIVM to help fill the gap.

Adriënne Sips
Nutrition, Medicines and Consumer Safety Division (RIVM-VGC)

If there is one thing that RIVM will have to be in the area of nanotechnology, says Adriënne Sips, then it is a reliable source that carefully monitors products and applications with respect to possible risks. “As an institute, we should not stand in the way of technical development and innovation,” she says. “But neither should we let ourselves be carried away by Star Trek-like applications or governments looking only for economic growth.”
At RIVM, Sips heads a toxicokinetics research group that, among other things, advises the Dutch Medicines Evaluation Board on preclinical pharmacokinetics of drugs awaiting market authorisation. Within her immediate line of work, Sips encounters nanotechnology only sporadically. However, by bringing together all parts of RIVM that were dealing with it in bits and pieces, she has been an instrumental force.
“The strength of an institute such as RIVM is its ability to bundle the work and the expertise of many different disciplines in public health and environment,” she says. “Before, a number of us were handling small projects and budgets separately. Now that we’ve come together, we form a large and highly visible group. By using our different roles and networks and by acting as part of RIVM rather than just ourselves, we have managed to become the country’s biggest player when it comes to assessing the risks of nanoparticles and nanotechnology products.”
In the fall of 2006, the strategy paid off when the Dutch government published a position paper. It named RIVM as the site of a future “observation post” for potential risks of nanoparticles and nanotechnology products. “That paper gave us a real boost,” Sips says.

Technology celebration

The current state of affairs in nanotechnology resembles a technology celebration, Sips says, in which often the sky seems to be the limit. Industry has introduced hundreds of products using nanoparticles and is investing heavily in what is projected to be a multi-billion-dollar market. Governments, especially those of highly industrialised regions such as the United States and Europe, are mostly cheering their efforts, keenly aware of the need for highly advanced technological sectors to grow now that manufacturing jobs are being moved to lower-wage countries.
“As a government institute, RIVM has an obligation to investigate whether some of those applications could carry risks,” Sips says. “At the same time, however, people should not start seeing us as spoiling

Giving nanoparticles better visibility

In 2006, the RIVM nanotechnology working group, which had been launched the year before, raised its profile. Twelve RIVM staffers who had previously acted alone or in small groups now started operating together, bundling knowledge, efforts and visibility to the outside world. All of them acted as ambassadors for a joint RIVM effort to become a strong player in nanotechnology.
The group got a boost from a 2006 position paper of the Dutch government in which RIVM was named as a future "observation post" for nanotechnology risks assessment.
According to Adriënne Sips, the nanotechnology working group aims to focus on risk assessment and bundling of expertise. Some laboratory work should be included to gain hands-on experience. The group is involved in setting up several research agendas and participates in several grant proposals at the EU's Seventh Framework Programme.

The nanotechnology working group: Nynke Brouwer, Susan Dekkers, Robert Geertsma, Cees de Heer, Evelyn Heugens, Willie Peijnenburg, Diana van Riet, Maaike van Zijverden, and – from left – Wim de Jong, Dik van de Meent, Flemming Cassee and Adriënne Sips.

the party. There could be great applications of nanotechnology, and perhaps RIVM should even engage in efforts to develop applications that are useful for activities of our own. Also, we should explain to companies that it's not in their interest if, at some later stage, their products suddenly attract negative media attention or will have to be pulled off the market."
To operate in such a high-stakes, multi-stakeholder environment can be complicated, Sips says, especially in a country such as The Netherlands where the public has not been informed about nanotechnology. "We need to be careful when publicly talking about potential risks, since some stakeholders won't necessarily like it. However, we also have to make sure our credibility is not compromised. At the end of the day, we should deal with nanotechnologies like we handle all others — check carefully whether there could be potential risks involved."
RIVM will focus its efforts on potential human and ecotoxicological risks. Conventional titanium oxide particles, for instance, used in cosmetics, can't reach the brain from the bloodstream.
Although thus far it does not seem to be the case, for titanium oxide nanoparticles theoretically things could be different. "We know nanoparticles have the potential of behaving differently than bigger particles of the same composition," Sips says. "We cannot trust the chemical and physical criteria used for conventional compounds, such as size and lipophilicity. More research is needed to explore such basic questions."

Consumers

Many stakeholders publicly acknowledge this need, Sips says, but not much funding is following such promises. "More than 95 percent of research budgets is spent on product development, less than 5 percent on risk assessment research."
"In policy circles, many people say they don't want to see the history of biotechnology being repeated," Sips says, referring to food and agricultural applications of biotechnology that ran into trouble with European consumers. Yet some similarities are starting to show, Sips says, such as hundreds of products reaching the market while risk assessment procedures are still in the making. "That's why I'm happy to see rising awareness of the importance of collecting toxicological data, both at the national and international level," she adds.

Getting the best of two worlds

"Public Health Status and Forecasts" is a book published every four years by RIVM to map the health status of The Netherlands and to suggest ways to address major public health concerns. Designed to maximise the impact of research on policymakers, the project also manages occasionally to grab newspaper headlines.

At the Centre for Public Health Forecasting, all everyone thinks about is increasing the impact of scientific research. The centre's mission is to integrate and to interpret other people's research and to disseminate the results to Dutch policymakers. For Nancy Hoeymans, a nutritional scientist, working at the centre has been great because she likes to operate in both worlds. "Digging deeper and deeper into one question is not my thing," she says. "I like translating basic research into ideas that can be put to work. At the centre, we gather all available research and tell our client: This is what we know; this is what we don't know. This is what you can do; this is what it will cost; and this is what you can expect to come out of it. That's the kind of work I like very much."

Forecasting

In 2006, the Centre for Public Health Forecasting (VTV) published its fourth "Public Health Status and Forecasts," the centrepiece of a portfolio that includes several Web sites, as well as a series of thematic reports, for example, on the future of care for the elderly. Nancy Hoeymans was a member of the editorial board, together with four of her colleagues: Guus de Hollander, Johan Melse, Hans van Oers and Johan Polder. "Never before have I worked so hard for so long to get something completed," she says. "But never before have I had so much fun doing it."
To maximise the study's impact, the editors worked with policymakers at the Dutch government's Ministry of Public Health, Welfare and Sports (VWS). Their co-operation led to a government report,

Nancy Hoeymans
Public Health and Health Services Division (RIVM-V&Z)

"Choosing Healthy Living" in which several priorities highlighted by the RIVM study had been translated into policy plans. Programmes to help prevent alcohol abuse and mental disorders, for instance, had gained prominence.
"We had concluded that these were important health problems, that there are significant opportunities for prevention and that therefore they made excellent policy priorities," Hoeymans says. "We didn't make the policy choices, but we did bring them up with the government."
It is not the only way the centre tries to make sure the work will reach its target. Before beginning to work on thematic reports, Hoeymans says, clients are asked how the outcomes will be put to use. "If the client can't answer such questions, we won't even start," she says. "We will not write a report that ends up just being shelved. For us, it's important to know our work will actually land."
Another way to maximise impact is to limit the size of the four-yearly reports. "In 2006, we were determined to keep it at 100 pages," Hoeymans says. "We failed — we ended up making 350." Reducing the size is difficult, in part because new questions keep being added, she notes. Yet she knows that although many people heaped praise on the book, almost no one had read it.
For the future, Hoeymans wonders whether it could be useful to produce two books: one rather thin, summing up everything for policymakers, and another, more voluminous, to satisfy the research community. "It's easier, though, to write a thick book than a thin one," she acknowledges. "Usually you don't have the time to cut the number of pages."

Media attention

Hoeymans vividly remembers one telling example of how very little information can have significant impact. "Someone suggested I should make a press release about a map showing how life expectancy varies across Dutch regions, with differences up to 12 years. I did, and it attracted immense media attention. I was on national television, and all newspapers carried big headlines. In the media, that one press release carried more weight than the 350 pages so many people had worked on so hard. From this, I learned that news media need one clear message, not 20 messages in a hefty report. That is important because what gets into the media will often also end up in the heads of policymakers."

Dutch health is okay, but it could be better

As was done in 1993, 1997 and 2002, a large amount of information on health, prevention and health care in The Netherlands was collected for the fourth edition of the VTV public health forecast. Public health in the Netherlands is improving, the authors conclude, but there is room for improvement. For example, at birth Dutch women have a lower life expectancy than the average woman in Europe; In The Netherlands, smoking is more popular than in the rest of Europe.
Unhealthy behaviors and conditions, including obesity, especially among young people, are undermining the future of Dutch public health. Aging of the population could lead to a surge in demand for health care. Furthermore, large differences in health and health risks exist across regions and neighbourhoods within cities. Public health problems are often associated with socioeconomic deprivation.
According to the authors, prevention efforts should not focus only on individuals, but also on social and spatial factors surrounding them. To improve public health, other areas of government policy, including education, spatial planning and socioeconomic development, should be involved.
The report was written with the assistance of hundreds of Dutch researchers. Many detailed maps and figures can be found at the VTV Web site.

Hollander AEM de, Hoeymans N, Melse JM, Oers JAM van, Polder JJ (eds)
Public Health Forecast 2006, RIVM report 270061003/2006
http://www.rivm.nl/bibliotheek/rapporten/270061003.pdf (in Dutch)
Website: http://www.rivm.nl/vtv (in Dutch)

Bringing 30,000 chemicals within REACH

The Chemical Substances Bureau mandate from the Dutch government is to perform executive tasks under chemical substances legislation. In 2006, the bureau prepared for the launch of European rules called REACH. The result: thousands of pages of legislation, guidelines for authorities and industry, a Web site, a video and a help desk.

Dick Sijm started his career as an academic. For many years, he tested toxicity levels of chemical compounds in university labs. Since then, however, his focus has shifted to work that brings him more into contact with the rest of the world.
"I think RIVM has to serve all parts of the chain: from basic research to its application," Sijm says. "For me personally, the latter parts are the most exciting these days — interacting with players outside, witnessing the impact our research is having. That's what gets me going here at RIVM. As a scientist, setting up a help desk for the industry is about as close as you can get to applying your research."

Radical transition

As a government-mandated body, the Chemical Substances Bureau, which Sijm heads, has been heavily involved in preparations for a radical transition in chemical substances legislation. In December 2006, the European Union formally adopted the laws to make industry responsible for demonstrating

Dick Sijm
Environment and Safety Division (RIVM-MEV)

Getting ready to answer questions 24/7

The Chemical Substances Bureau spent much of 2006 drafting a handbook and preparing material for a help desk to assist companies in finding answers to questions about the new REACH framework. The help desk, along with a Web site filled with explanations, guidance, questions and answers and a "role identification tool," was produced in co-operation with SenterNovem, an agency of the Dutch government's Ministry of Economic Affairs.
The official language of the Web site is Dutch because under the REACH regulations all enterprises, whether large or small, should be able to fully understand the rules.
As of January 1, 2007, the help desk can be reached every morning by phone. RIVM and SenterNovem staff members take turns answering the questions or forwarding them to experts.

REACH help desk
www.reach-helpdesk.nl

the safe use of chemicals it brings to the market and which, through its products, eventually end up in the environment. The new regulation is called REACH, an acronym for Registration, Evaluation, Authorisation and restriction of Chemicals.
REACH will require manufacturers and importers to centrally register applications of some 30,000 chemical substances and supply toxicological data showing that their use is safe. Governments will get to check the quality of the data and ban chemicals or specific applications when they find that the benefits do not outweigh the risks. In shifting the burden of proof from the government to industry, the legislation means a radical change.

As their country's prime experts, Sijm and his colleagues assisted the Dutch government during years of negotiations over the legislation, especially when The Netherlands acted as the EU's president in 2004, as well as the year after when Luxembourg took up that role. Later on, Sijm's bureau took up key tasks in preparing its implementation, primarily in The Netherlands.
The work consisted mostly of translating extensive legislation into practical guidelines to be used by companies and the government. "My department has worked tirelessly to write thousands of pages, all in close co-operation and consultation with the European Commission, national ministries and industry partners," Sijm says. "It was a very constructive but highly pressurised process, since it was imperative that these handbooks are ready when REACH will go into effect."
The same expertise was used to prepare the REACH help desk that includes a Web site (see box) to answer many questions that companies have. The help desk is a joint effort of RIVM and SenterNovem, an agency of the Dutch ministry of Economic Affairs. "Talking to industry will help companies and will help us to further improve our handbooks and alert policymakers to problems. We very much wanted to be part of that monitoring," Sijm says.
As a general rule, he adds, the help desk will tell companies what to do to comply with the rules, not how they should do it. "REACH makes companies responsible for implementation, so if they need help filling in forms, we will refer them to trade organisations or consultants, not help them ourselves," Sijm says.

Weighing claims

Has having so many conversations with stakeholders changed his outlook on how toxicology should be applied? "Yes," Sijm says. "Since my days at the university, I have gained more realistic insights into how we should deal with chemical substances. Of course, we have to keep looking at risks for people and the environment, but we also have to take arguments from industries and non-governmental organisations into account."
"For me, it's important that thanks to REACH our bureau will get to weigh the toxicological risks of certain substances against the benefits of their actual use. Certainly, some plastic softeners carry great health risks, but does that mean we should not allow their use in equipment that can treat kidney patients? I think it is important to give society a more firm place at the table.
"We won't do toxicological tests here at the bureau, but we will stay in close contact with scientists and their work. Sometimes, we will determine that new research needs to be done. In the end, our work will be about interpreting the data and weighing the claims from all relevant parties. If we come up with the best arguments, we could have immense impact doing that."

Cutting infection rates by increasing feedback

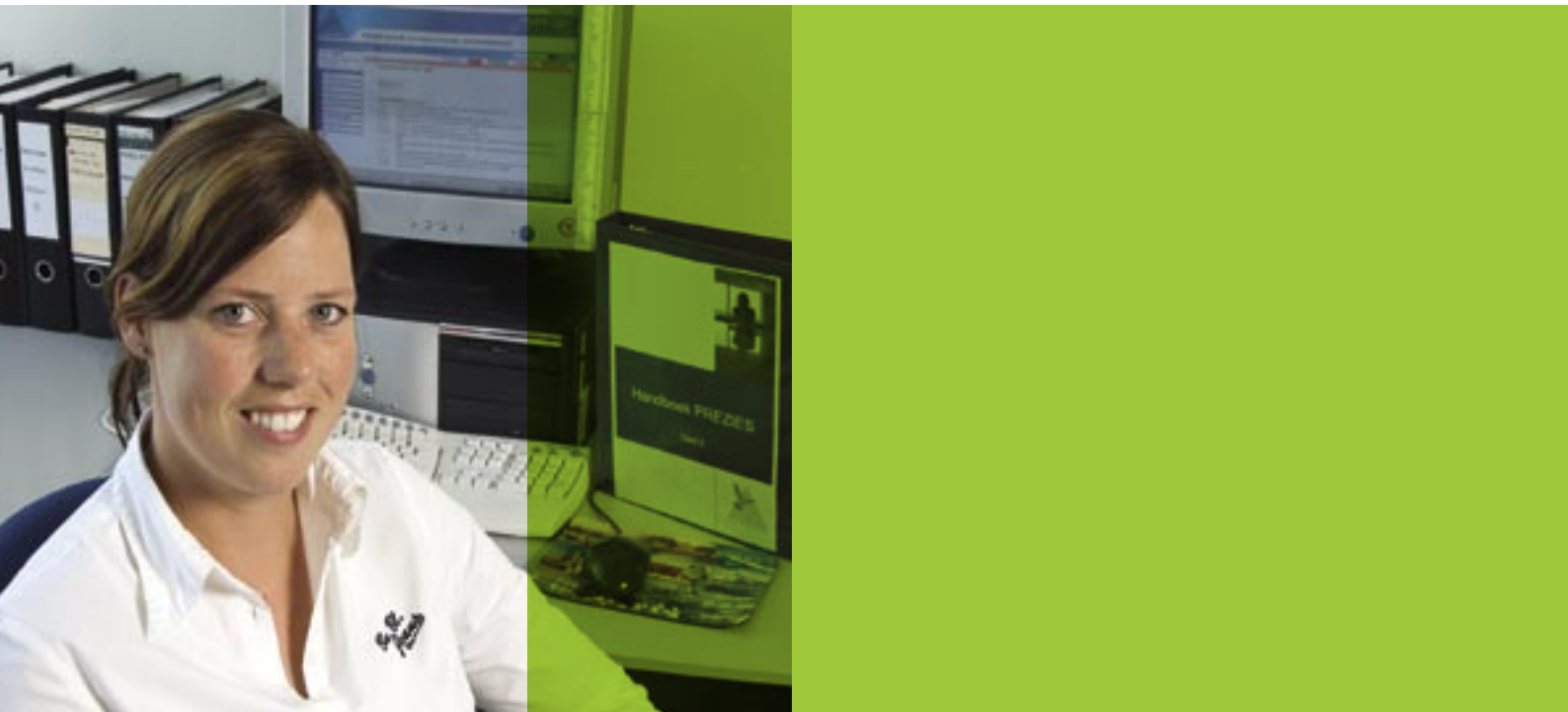
For 10 years, researchers at RIVM have quietly provided feedback to a growing number of Dutch hospitals, informing them about their nosocomial infection rates. Increasingly, their measurements are being used to evaluate the success of attempts to bring rates down.

Of every 100 patients entering a Dutch hospital, five to 10 will acquire some sort of infection in the hospital. Many get urinary tract infections; others come down with pneumonia. Three to four percent of patients who undergo surgery will develop post-operative wound infections.
In 1996, staggering figures like these led to the launch of PREZIES, a surveillance network in which the National Institute for Public Health and the Environment (RIVM), the Dutch Institute for Healthcare Improvement (CBO) and many Dutch hospitals took part. In Dutch, the acronym resembles the word "precies" (precise); its characters stand for Prevention of Hospital Infections through Surveillance.
In 2006, 10 years after the network was launched, 90 percent of Dutch hospitals have taken part in PREZIES. In 2006, more than 75 percent of hospitals participated in one of four surveillance programs: post-operative wounds, wound infections after heart surgery, central venous catheter-associated sepsis, and ventilator-associated pneumonia were monitored. The Netherlands Health Care Inspectorate (IGZ) now routinely asks hospitals whether they take part in PREZIES as one of several performance indicators. In 10 years, PREZIES has become the primary tool for recording hospital-acquired infections in the Netherlands.

Confidential

Judith Manniën, who once studied food and health at Wageningen University, has been a part of PREZIES for six of those 10 years. Since 2001, she has closely monitored post-operative wound infections, the longest-running of the four programs.
"It is remarkable how scores of individual hospitals can vary wildly from the national average", Manniën

Judith Manniën
Centre for Infectious Diseases Control (RIVM-CIb)



says. “For some types of surgery, the average infection rate nationally hovers somewhere between 1 and 3 percent, while individual hospitals vary between zero and 7 percent. Obviously, that tells you that there is room for improvement.”
Hospitals take part voluntarily in the network’s confidential surveillance. That, according to Manniën, is a better recipe for success than using their infection rates as a public benchmark. “We will never publish data for individual hospitals, only national averages and variances,” she says. “If we did, many hospitals might not participate in the network. What’s more, they could be tempted to subtly squeeze the registration data in order to prevent bad publicity, for instance by underreporting infections or refusing to treat high-risk patients. Or they would just monitor types of surgery they knew to run perfectly, instead of those they suspected of causing problems. As a researcher, I’m sure it would make my data less reliable and the surveillance less effective.”
In any case, using infection rates as performance benchmarks would be complicated, Manniën says. “It’s very hard to reliably compare rates across hospitals. For example, our research shows that actively following-up with patients after discharge, as some hospitals do but others don’t, almost doubles the number of infections they find. Also, patient populations can differ substantially.”

Germany

The same is true for international comparisons, Manniën says. Monitoring infection rates started in the United States, and like many other countries The Netherlands has based its protocols and risk definitions on those of the United States. “I myself have tried to compare Dutch numbers with those in Germany. That turned out to be harder than expected because many factors vary. For instance, German patients remain in the hospital longer, so higher infection rates at the time of discharge don’t tell you much.”
Publishing details on hospital procedures and improving them is probably more effective than publishing infection rates, Manniën believes. “How is the operating room being ventilated? How do they remove body hair? Is antibiotic prophylaxis administered correctly? Those things already tell you a lot about how well a hospital is performing.”
To Manniën’s delight, hospitals increasingly use PREZIES data to evaluate the effects of attempts to bring nosocomial infection rates down. “We have seen projects in which hospitals try interventions, such as opening the door to operating rooms less often. Such studies proved to be highly successful, and it would be great to see more.”
This year, Manniën will try to assess whether infection rates in participating hospitals have declined over the first 10 years of PREZIES. “My predecessor found an effect after five years, so hopefully the outcome will be the same,” she says.

Most nosocomial infections found after patients have checked out

The authors compared the number of surgical site infections registered in Dutch hospitals using active post-discharge surveillance versus hospitals that did not use active surveillance systems following discharge. Of all 98 hospitals in The Netherlands, 64 took part in the study. The study included data on 131,798 surgical procedures between 1996 and 2004. For about half of these procedures, active post-discharge surveillance was done.
Doing such surveillance the recommended way almost doubled the chance of finding post-surgical infections, the study found. On average, for the 14 surgical procedures that were studied, 3.1 percent of all patients were registered as developing site infections by hospitals not doing active surveillance. In hospitals doing surveillance the recommended way, the infection rate was 3.7 percent.
In hospitals doing active surveillance, 76 percent of surgical site infections following appendectomies were found after the patient had been discharged. For knee prosthesis surgery, the rate was 64 percent; for mastectomies 61 percent.
The study demonstrates that, without actively carrying out high-quality post-discharge surveillance, hospitals will seriously underestimate post-surgical site infection rates.

Manniën J, Wille JC, Snoeren RL, Hof S van den
Impact of post-discharge surveillance on surgical site infection rates for several surgical procedures: results from the nosocomial surveillance network in The Netherlands
Infect Control Hosp Epidemiol 2006; 27(8):809-16

No major barriers for new medicines

Many people think that regulation causes undue delays when companies try to get new pharmaceuticals to market. Surprisingly, companies themselves have no major complaints. Companies and government agencies would like to see more transparency and better co-operation, however.

Last year, when Marjolein Weda started interviewing representatives from the Dutch pharma-ceutical industry, she braced for a long list of complaints. Like many people, she suspected that companies do not look favourably at strict regulation and time-consuming procedures. In fact, such notions had prompted the Ministry of Public Health, Welfare and Sports (VWS) to commission RIVM to find out whether things could be improved.
To Weda's surprise, pharmaceutical companies did not complain about overly tight regulation or long procedures. "In fact, government bodies and industry mostly agreed on the issues," she says. "Companies acknowledge that registration of medicinal products needs to be done meticulously. In a way, it even protects them from competitors quickly making similar products. For industry, it's most important that procedures are clear and transparent."

Priority medicines

With Ingrid Hegger, Weda interviewed about 20 representatives of government bodies and industry, all dealing with regulation of newly developed drugs and vaccines. The project was driven in part by the Dutch government's intention to lower companies' administrative burden. Another reason came from a 2004 conference of the World Health Organisation (WHO) "Priority Medicines for Europe and the World," suggesting which medicines should fill companies' pipelines and stressing the need to get them to market as quickly as possible.

Marjolein Weda and Ingrid Hegger, Nutrition, Medicines and Consumer Safety Division (RIVM-VGC)

Medicines without barriers

After interviewing key players in drug development and registration in The Netherlands, the authors found that there are no significant regulatory barriers obstructing or delaying the registration of new medicines in The Netherlands. Nevertheless, the authors think improvements in the process could be made. Their recommendations are generally aimed at increasing the reliability, predictability and transparency of the role of the government, including consultation procedures in the run-up to new regulation. Some parts of the regulation could be organised more efficiently, such as the formal release of batches of "immunologic pharmaceutical products."
The agencies and committees involved in regulating drug development, clinical testing and market authorisation should communicatie more effectively with industry as well as amongst each other, for instance through setting up Intranet and Internet Web sites where relevant information can be accessed more easily. Applying these measures will help prevent the pharmaceutical industry from moving drug development and market registration to countries other than The Netherlands, the authors conclude.

Weda M, Hegger I
Development and registration of medicines
Are there regulatory barriers?
RIVM report 370001001/2006

“Generally speaking, we have concluded that there are no significant barriers obstructing or delaying the registration of new medicines in The Netherlands,” Weda says. “We did find however that communication between government and industry could be improved, both during development of new regulation as well as during research into new products and during authorisation procedures.”
Adds Hegger: “Communication between the various government bodies can also be improved, we found. Procedures surrounding drug development are rather fragmented in this country, and the agencies which are part of the process could communicate and co-operate more effectively than they currently do.”
Hegger expected complaints about procedures during clinical research. In fact, some of those complaints did materialise, in part because many agencies are involved at this early stage, even more so after laws were revised in March 2006.
In the revised Medical Research Involving Human Subjects Act, committees that had previously overseen only the ethical aspects of clinical trials are now also charged with assessing the safety and quality of pharmaceutical compounds used in the trial. For products involving genetically modified organisms, such as in gene therapy, a second committee (the Committee Genetic Modification or COGEM) assesses risks to the environment, including people other than the patient. Because they operate in different regulatory frameworks, the two committees occassionally come up with conflicting requirements.
A third body would get involved if an immunological medicinal product, such as a vaccine, was investigated in humans: the Health Care Inspectorate (IGZ) would have to check the quality and safety of the experimental vaccine.Finally, during the market authorisation procedure, the European Medicines Agency (EMEA) or the Medicines Evaluation Board (CBG) evaluates whether the research proved the new therapy to be safe and effective.
“All those government bodies do not always communicate and co-operate in the best possible way,” Hegger says. Ethical requirements for clinical studies can be at odds with requirements for market authorisation. That makes it important for government bodies to improve their lines of communication.”

Transparency

In the end, Hegger and Weda mostly recommended better communication, better co-ordination and more overall transparency. Together, those recommendations should increase the reliability and predictability of the Dutch government’s actions and prevent companies from taking their drug development, as well as applications for market authorisations, to countries elsewhere.
One procedure was indeed simplified since the report was published. The Health Care Inspectorate was relieved of its duty to also check the quality and safety of experimental vaccines. Ironically, that decision also affected RIVM’s division, which used to carry out the work on behalf of the Inspectorate.
It did not prevent RIVM investigators from flagging the situation as potentially inefficient, Hegger says. Adds Weda: “Like any agency, we have to be able to also take a critical look at the work we are doing ourselves.”

Research Output

Research output

Centre for Infectious Disease Control (RIVM-CIb)

Professorial Chairs (4)

Coutinho RA
Professor of Epidemiology and Infectious Disease Control
University of Amsterdam

Gründmann H
Professor of Epidemiology of Microbial Diseases
University of Groningen

Koopmans MPG
Professor of Viral Infections in the Gastrointestinal Tract
Erasmus University, Rotterdam,

Mooi FR
Professor of Molecular Microbiology
Utrecht University

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Oers H van
Professor of Public Healthcare, University of Tilburg
Polder, J
Professor of Health Economics, University of Tilburg
Teunis PFM
Professor of Quantitative Microbiology
Emory University, Atlanta, USA
Westert G
Professor of Quality of Healthcare, University of Tilburg

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Loveren H van
Professor of Immuno-Toxicology, University of Maastricht
Slob W
Professor of Toxicology, Utrecht University
Steeg H van
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