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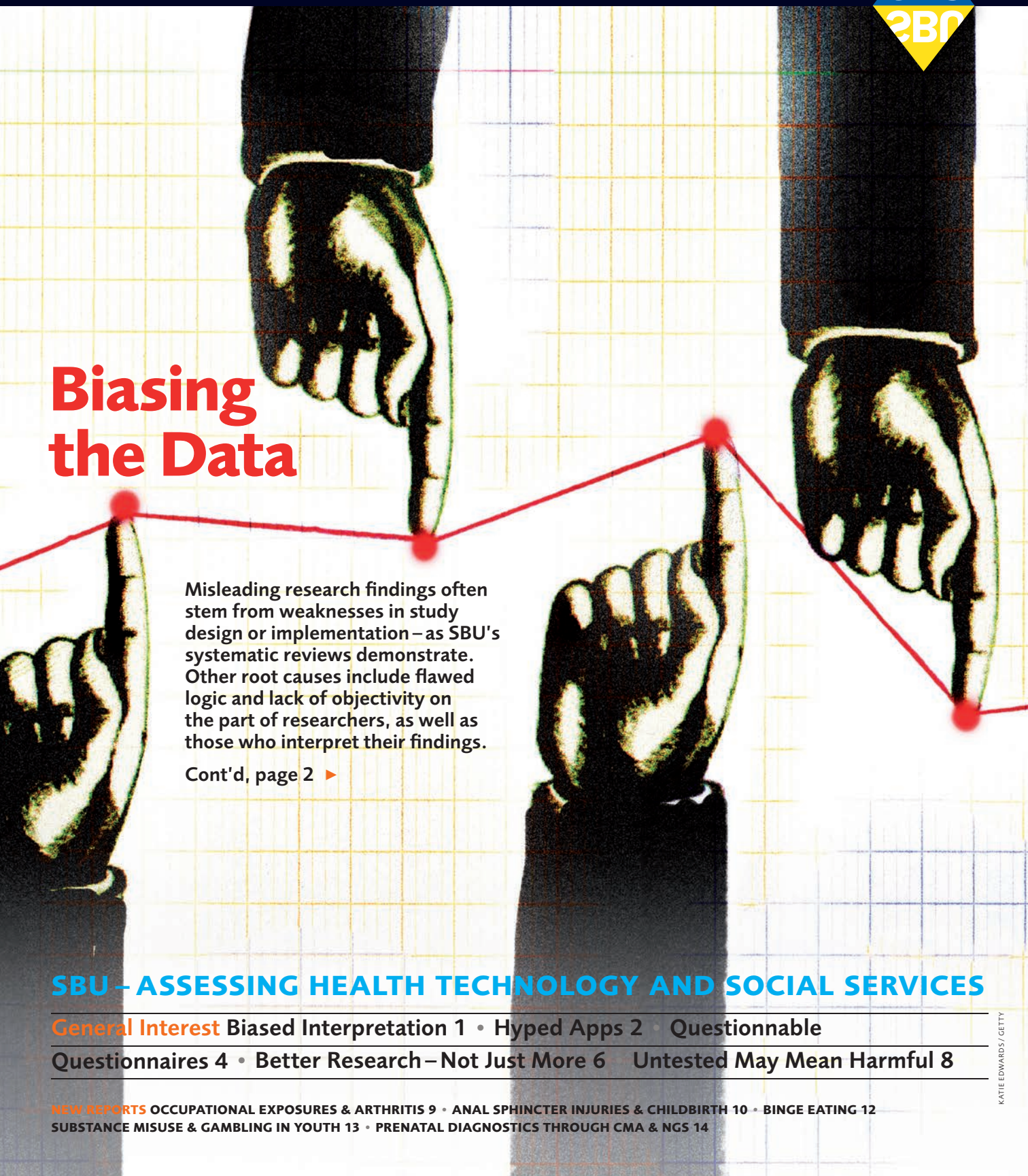

Biasing the Data

Misleading research findings often stem from weaknesses in study design or implementation – as SBU's systematic reviews demonstrate. Other root causes include flawed logic and lack of objectivity on the part of researchers, as well as those who interpret their findings.

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KATIE EDWARDS / GETTY

SBU – ASSESSING HEALTH TECHNOLOGY AND SOCIAL SERVICES

Health App Hype: Help or Harm?

HEALTH APPLICATIONS FOR smartphones and tablets are mushrooming year by year. By 2015 they had grown to more than 165,000 – a whole battalion of digital would-be doctors prepared to combat not only exercise and lifestyle issues, but crucial medical problems as well. While health apps are hyped, very few have undergone any kind of quality assurance. One review (Ben-Mussa A et al, 2016) found that they rarely meet the basic requirements for proper information to patients. Most health apps that qualify as medical devices have not even obtained statutory CE marking to verify that they are not harmful. Rapid development of mobile apps does hold great promise. But we must remain vigilant about dubious health advice and quackery, no matter how impressive the packaging may be.

Many future health apps and decision support tools will be based on the kind of big data that many experts believe will revolutionize the world of medicine. Digital pedometers, location information, and calling and data traffic statistics from our mobile devices already provide businesses with invaluable insights into our daily habits. If we also allow them to see our medical history and genetic makeup – not to mention our dietary, smoking and drinking habits – they will be able to combine it with information from social media about our family, friends, education and job to predict the health problems that we need to watch out for and to suggest products to allegedly minimize the risk.

"Very few have undergone any quality assurance."

THE TECHNOLOGY IS exciting, but the ability of businesses to store and coordinate personal information also poses a serious challenge to data security and reliability. And the evidence base of the advice is hazy. Even when health apps and decision support tools are marketed as evidence-based, the underlying research and the conversion of evidence to specific advice may be hard to pin down. It is as though somebody rubs a bottle stuffed with statistics and out pops a genie with a stethoscope and prescription. Determining how special economic interests are at play here is no easy task.

Transparency is a cornerstone of all research. The trail of evidence that has led to a conclusion must be crystal clear. The scientific community has been subject to increasing requirements for openness and data sharing over the past few years (Ross JS. Systematic Reviews 2016;5:159). Clinical researchers have long been expected to report their funding sources, affiliations and potential conflicts of interest. They should also present their hypotheses and study plans in public databases. Institutions and other users are starting to demand that research reports, along with basic data whenever feasible, be made widely available.

Without this kind of transparency, credibility will always be in question. The health apps and decision support tools of the future are no exception. We may trust a genie to offer us three wishes, but we should probably not expect him to think critically about the prospect of fulfilling them. This remains our job.

Ragnar Levi Editor

NOT ALL RESEARCH is reliable – far from it. Cases of conspicuous fraud and irregularities are relatively rare but, when exposed, often hit the headlines. By contrast, common problems that do not qualify as fraud are often tacitly overlooked. Yet they skew results and lead to false conclusions.

SBU's systematic reviews of the scientific literature show that study design often falls short. Statistical methods may be misused, critical information may not be reported, and endpoints may be manipulated to ensure less ambiguous results. Insufficient knowledge or sloppy use of research methodology may be the culprit. But problems can also be due to conscious departures from the ethical foundations of research. Instead of comprehensively exploring a topic or testing a hypothesis, researchers may be tempted to shape their questions and answers to a personal agenda. Political considerations, personal career ambitions, scientific disputes, professional jealousy, hubris and pride can all jeopardize accuracy.

POWERFUL ECONOMIC interests impact the field of medicine. In the early 2000s, the editors of several leading medical journals published critical articles about the pharmaceutical industry's influence on scientific publications. Several years later, a comprehensive review by the Institute of Medicine in the United States reported that an unholy alliance of the pharmaceutical industry, medical technology companies, individual scientists and research institutions was accompanied by a clear risk of bias.

Vested interests are the rationale behind the established set of ethical imperatives in scientific work. These ground rules include not manipulating research results to promote profit or to push an agenda. Scientific conclusions must be open to scrutiny and subject to observed facts – not special interests. The factual content of hypotheses and criticisms should be considered regardless of the individuals or institutions that present them.

Researchers do not always meet these ethical standards. When describing and discussing the evidence base, many experts tend to ignore findings that run counter to their pet hypotheses while paying disproportionate attention to corroborating their results. As early as the seventeenth century, English

ROBERT NYBERG

philosopher Francis Bacon described this type of distortion or "confirmation bias". He noted that people prefer to stick to their opinions despite evidence to the contrary. They overlook or ignore information that flies in the face of their initial interpretation.

WELL-KNOWN PROBLEMS to which this type of bias might contribute appear in scientific contexts. For example, it has been shown that publication of a substantial percentage of studies is delayed, sometimes indefinitely. Frequently scientists do not write or submit research reports for publication because they are not satisfied with the results. Meanwhile, other findings are overemphasised due to duplicate or "salami" publication, misleadingly magnifying the findings of a single study. Although the scientific community is addressing these problems, they have not gone away.

When presenting new findings, researchers often refer to a limited selection of previous studies instead of offering an overview. A systematic review in 2011 that covered various fields of medicine revealed that fewer than one-quarter of randomised trials are subsequently cited in similar research. Positive findings are referred to more frequently than negative ones. Inflated expectations of new and promising treatment methods may also lead to poor study design. For instance, unrealistic hopes of dramatic, immediate effects lead to trials that are too small or too short. Even with a small sample of subjects, some researchers recklessly generalise their findings.

THE RISK FOR biased reasoning and interpretation is particularly high in the discussion sections of research publications, but one-sided interpretations and erroneous conclusions also find their way into other parts of scientific articles. While modestly favourable and non-significant treatment outcomes may be presented as promising, for example, correspondingly unfavourable outcomes of the same magnitude are not described as discouraging. Such wishful thinking becomes apparent when research is unable to demonstrate an anticipated difference and the investigators conclude that the problem was inadequate study size. They conveniently ignore the possibility that no substantial difference exists.

Researchers may also confuse correlation and causation – assuming, on chronological grounds only, that event A caused event B. It goes without saying that two phenomena may occur concurrently or sequentially even though there is no causal relationship between them.

ANOTHER COMMON ERROR is overinterpreting the absence of evidence. Just because there is no proof for an assumption, it is not necessarily false. Conversely, the lack of disproof does not verify an assumption. The absence of reports concerning adverse effects of a treatment does not mean that it has none. Similarly, a method may be effective even though no evidence has yet been found to support the hypothesis.

The history of medicine is replete with advocates of various unproven methods who persistently sought to buttress their assumptions without any intention to be biased, but who nevertheless neglected to adequately question them.

The ability to think critically and test hypotheses is a cornerstone of scientific endeavour. Such thinking must be applied and encouraged, not only in research but in all evidence-based practices.

The challenge is to accept the uncertainty that is inherent to many fields of research and resist the temptations of both overconfidence and unwarranted scepticism. ◆ **RL**

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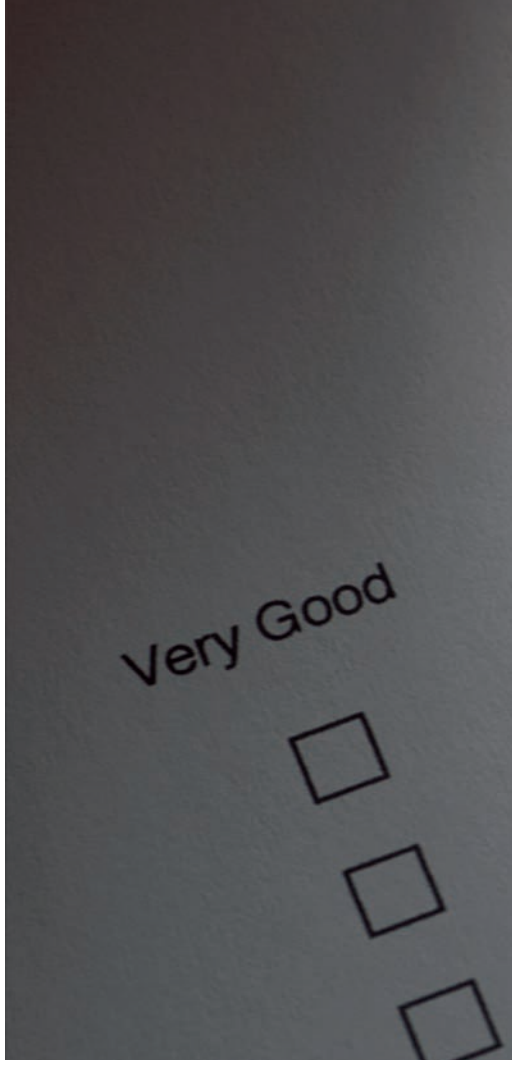
Biased Views of Facts – Some Examples

- Anchoring – using a single detail to shape an overall view
- Antipathy – rejection due to personal dislike of a source
- Authority – blind trust in power or conventional opinions
- Automated thinking – accepting an interpretation without reflecting on it
- Bandwagon – excessive effort to reach consensus or conformity, "groupthink"
- Clique building – allowing a few influential experts to determine an interpretation
- Confirmation – seeking support for current beliefs despite contradictory information
- Conflict of interest – bias due to economic or other gain, career, status, etc.
- Familiarity – trust due to previous exposure while ignoring that which is unfamiliar
- Framing – allowing context to distort the facts
- Hasty (premature) conclusion – erroneously viewing additional facts as extraneous
- Ignorance – insufficient knowledge of alternatives, etc.
- Inertia – following old patterns even when new facts emerge
- Narrow-mindedness – failure to accept views other than one's own
- Novelty – excessive emphasis on new or unexpected possibilities
- Omission – intentional nonreporting of information that challenges a desired outcome
- Overconfidence – overestimating one's own judgement and underestimating that of others
- Oversimplification – going too far in boiling down complicated phenomena
  Sunk cost – unwillingness to change views due to previous investment
- Wishful thinking – overrating benefits and underrating harms

Questionable Questionnaires

A plethora of appraisal instruments for health risks and social needs have been introduced by healthcare and social service institutions. Some tools provide valid information about an individual's condition, but others may be wholly misleading. While adding structure to the diagnostic process can be useful, scientific testing is needed to establish the potential benefits and risks of such instruments.



Professional services begin by analysing an individual's problem and describing it accurately. Such an approach is crucial to offering proper health care and social services. An initial inaccurate diagnosis or needs assessment may lead to ineffective interventions followed by unnecessary suffering and waste of scarce resources.

Many different types of health and social services suffer from this problem. The need for better diagnostic measures attracted international attention following the release of a report by the Institute of Medicine at the United States National Academies. Also in Sweden, critics have argued that diagnostic errors are common and are not taken seriously enough as part of efforts to improve patient safety. Documents issued by the Swedish National Board of Health and Welfare and other sources point to the need for more reliable and uniform appraisals of both health and social services.

APPRAISING A PERSON'S circumstances, needs and ability to function under the constraints of time may be difficult. For instance, SBU's assessment in 2012 of diagnostic measures for depression and mania showed that clinicians miss every other case during the first appointment. Because these conditions are complicated, they are occasionally confused with other psychiatric problems or physical disorders. The result may be delayed or inappropriate treatment.

The aim of structured and uniform appraisal methods is to reduce the risk of arbitrary or incomplete information and to clarify the basis for each evaluation. The standardised instruments that have been developed contain questions for the staff or individual to answer in accordance with a manual. These instruments are intended to improve professional appraisals, identify high-risk situations and further assess unclear cases.

Not all tools work well, however. Calling an assessment instrument "standardised" does not make it reliable. Determining whether an instrument is serving its intended purpose requires rigorous testing. But many instruments have never been scientifically evaluated.

To assess diagnostic methods for depression and mania, SBU identified over 60 different appraisal tools that are used in Sweden. Only a few of them had been evaluated in a scientifically acceptable manner that clarified the magnitude of risk that either cases would be overlooked or false alarms would be triggered.

According to the body of research, only a couple of instruments were shown to be both sensitive and specific for addressing adult depression and mania. Whether an instrument was reliable or misleading could not generally be determined.

Risks and Needs Appraisal Tools

Appraisal tools are used in health care and social services to help identify health problems and social needs. Such questionnaires and checklists can be used by professionals to gather relevant information through interviews and observations, or by patients through self-assessment. A manual should clarify purpose, intended use, scientific basis, training requirements and costs. Some tools are intended for education or research rather than for clinical practice. Adapting tools to national or regional conditions can be a delicate task.

DAVID GOULD / GETTY

AN SBU ASSESSMENT in 2015 reviewed instruments for assessing suicide risk and showed that one of the methods used at several psychiatric departments (Sad Persons Scale) is highly insensitive, frequently missing predisposition for suicide. The result can give staff a false sense of security and ultimately do more harm than good. Even though most diagnostic rating scales are intended to complement rather than replace other procedures, they can encourage overconfidence in the results. It is important to keep in mind that these instruments are no more than assistive tools.

EVALUATING METHODS FOR diagnosis and needs assessment entails several thorny challenges. Most studies address a method's sensitivity so as not to miss any cases, as well as its specificity so as not to generate false alarms. Sensitivity and specificity add up to accuracy.

Accuracy depends not only on the design of the instrument itself, but on the group of individuals examined, including the frequency and severity of the condition among them. Various models for interpreting outcomes may also be important, and the accuracy of an instrument may vary with the presence or absence of other diagnostic procedures. There may also be good reason to determine whether the instrument affects the relationship between the client and staff in health care and social services. The actual benefit of such tools is a function of their impact on decision-making and ultimately on the wellbeing of the people they are meant to benefit, but such studies are rarely performed.

AN EXAMPLE THAT SBU called attention to in 2013 concerned ADHD. Swedish clinicians use 15 different diagnostic instruments to identify the condition. Not a single instrument had been scientifically documented for accuracy, and no studies had been published concerning the value of the extensive diagnostic process as a whole.

The key question for patients and clients is always: Which instruments and tests will ultimately help improve my symptoms, function, quality of life and living conditions? Many systematic reviews by SBU suggest that researchers, as well as health and social service professionals, should be asking such questions – much more often than has typically been the case. ◆ **RL**

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KERSTIN WAURICK / GETTY

Better Research Is Needed – Not Just More

Many efficacy trials in health care and social services leave clients, providers and decision-makers asking, "So, now what?" The reason is that the studies are inappropriately designed. Going forward, they must be larger, longer and more relevant.

When researchers identify important, unanswered questions related to health care and social services, they typically call for further research. But frequently the real need is not for more, but better, studies.

"Simply adding more studies has been shown to be an ineffective way of resolving scientific uncertainty," Associate Professor Susanna Axelsson says. She has many years of experience assessing scientific quality and has recently been named Director-General of SBU.

"Of all the treatment studies that have been performed and regarded as essential, only a few have successfully shown that an intervention impacts wellbeing. Although some studies have addressed other important issues or raised vital new questions, surprisingly few have satisfactorily answered the most fundamental concerns."

An estimated 1 million clinical trials and tens of thousands of systematic reviews have been published to date.

"**OUTCOMES STUDIES** in many areas should be able to offer more," Axelsson says. "Many of them have too few participants and are not conducted for long enough. Far too often they fail to focus on whether the interventions actually improve life and health."

John Ioannidis, Professor of Medicine, Health Research, and Statistics at Stanford University in California, has long pointed out serious deficiencies in both medical and psychological research. His widely-read article in 2005 used mathematical models to show that the probability of misleading results is particularly high when studies are small, expected effects are minimal or many hypotheses are conceivable but only a few are considered. Risks are also greater in areas where study design, definitions, endpoints and analytical methods vary considerably. The same is true when it comes to fields of research beholden to powerful special interests and consisting of many teams that are striving to confirm their pet hypotheses. Many findings that are ascribed statistical significance and appear in scientific journals cannot be repeated in later studies. Such failures are more common than can be attributed to chance. Among the primary reasons is systematic error that would be avoided if study design were better.

IF A RESEARCH PROJECT is to be of clinical value, it is not enough for the findings to be valid. An important health problem must also be addressed. According to Ioannidis, most clinical trials do not meet this criterion.

There needs to be a clear link between

the burden that an illness places on an individual and the amount of clinical research that is conducted, he writes. Research initiatives in many fields of medicine are fuelled by various people and organisations that are trying to promote new diagnoses.

Instead of rewarding researchers for the number of scientific articles they publish, colleges and universities should favour important studies. And rather than trying to turn every clinician into a prolific researcher, academic institutions should invest in improving the methodology and critical thinking of scientists, Ioannidis writes.

ONE POSSIBLE APPROACH would be to regularly begin a clinical trial with a systematic review of current findings. Researchers could then identify what types of studies are needed and how large they should be to yield useful answers. Many current studies are simply too small. A 2010 analysis of randomised studies in the PubMed medical research database reported that the median number of participants in a treatment or control group was 36.

Another improvement would be to place greater emphasis on studies that do not show a difference between the treatment and control group. Assuming that the studies address an important clinical issue and are sufficiently large to detect a relevant difference, "negative" results also provide valuable information. It is often more important to compare an effective treatment option with another than with placebo or with a presumably ineffective option for the purpose of highlighting the differences.

Research findings would also improve substantially if more randomised trials had a pragmatic design, rather than an explanatory design intended to isolate the effects of a single intervention in a homogeneous sample.

A pragmatic clinical trial aims to compare realistic treatment options as a foundation for healthcare decisions. As opposed to many explanatory studies, pragmatic randomised trials include a broad, diverse, timely sample of subjects in different care environments and the effects under consideration are clinically important.

Although many observers have called for randomised pragmatic trials, they remain relatively rare. According to one systematic review, the pharmaceutical industry sponsored only nine drug trials of this type between 1996 and 2010. During the same period, explanatory studies numbered in the thousands.

FINALLY, CLINICAL RESEARCH would provide better payoffs if it targeted questions that patients themselves rank as most important.

"Investigators and their sponsors often set the agenda as things are now," Axelsson says.

"Greater client influence on research resources could help close the gap between the agenda and the interests of patients."

Clients do not benefit from studies that ask the wrong questions. For researchers to effectively address issues that impact health care and social services, their findings must be both valid and relevant – not just one or the other. ◆ **RL**

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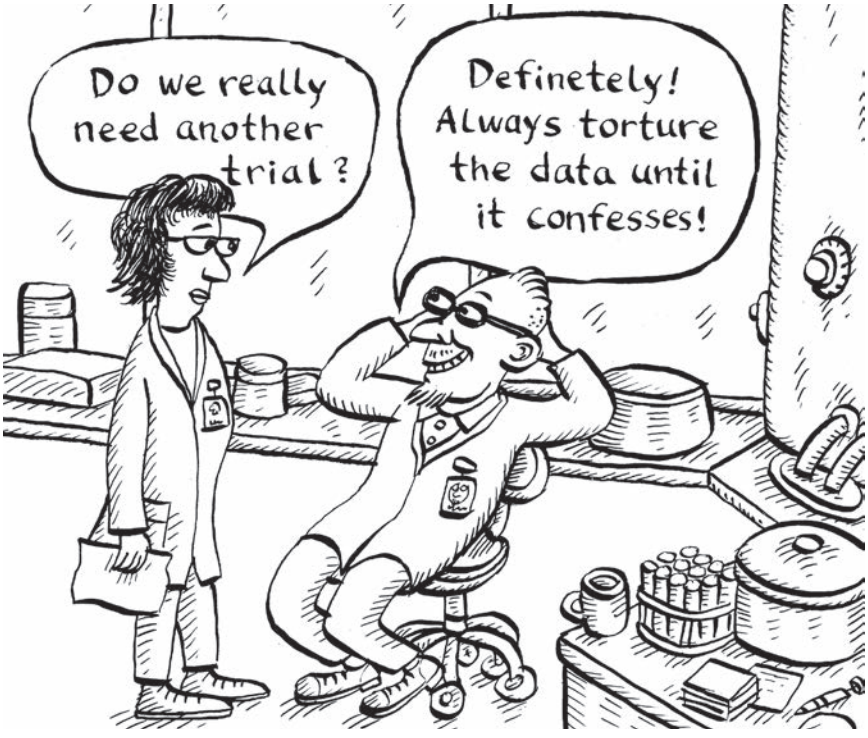

Considerations for assessing the value of an additional clinical trial include:

- **the importance of the research question:** Does the study explore a high-priority clinical problem?
- **current knowledge:** Have previous studies been systematically reviewed such that the value of an additional trial can be assessed?
- **the adequacy of basic trial features:** Will the trial be large enough and will follow-up be long enough to acquire important new knowledge?
- **the relevance of the trial design and setting:** Can the trial provide relevant and useful new knowledge of population, intervention, control group, outcomes and setting?
- **patient/user priorities:** Will the trial address issues that patients and users identify as key?
- **opportunity costs:** Would a different trial provide more knowledge in relation to cost? Will the research budget be used cost-effectively?
- **trial feasibility:** Is it likely that the trial can be conducted in accordance with the protocol?
- **transparency:** Do the study protocol and report of findings provide sufficient detail for reproducing the trial if necessary and for assessing the internal and external validity of the results?

Untested May Mean Harmful

MARTIN BARRAUD /GETTY

Unless the benefits and risks of new treatments are tested scientifically, they may not only be ineffective or useless, but do more harm than good.

New treatment methods are often viewed as innovative and promising – and occasionally they are. But the fact that an intervention or therapy is new also means that it has not been tested for very long or only with surrogate endpoints.

The balance between the benefits and risks of a new method is often uncertain as compared to existing options. Generally speaking, whether or not the new intervention is safer or more effective remains to be established. Recently approved drugs are not always superior to those already in use. Many new products that have been in use for a while and subject to clinical trials turn out to be no better, sometimes even worse, than what is already available.

The pharmaceutical committee of the Stockholm County Council recently offered several examples of drugs that the manufacturer initially marketed intensely but that were later withdrawn after serious adverse effects had been discovered.

THE FIRST EXAMPLE is rosiglitazone, approved in 2000 to treat type 2 diabetes, which can eventually lead to stroke or myocardial infarction. The mechanism of action was new and deemed to be interesting. Approval was based on short-term studies showing that HbA1c, which reflects long-term blood glucose levels, decreased by one percentage point compared to placebo. No evidence indicated that the risk of stroke or myocardial infarction – the primary objective of treatment – would be reduced. The substance was later found to increase the risk of myocardial infarction and heart failure.

In fact, there had been early indications of increased risk for fluid retention and heart failure. But the focus remained on blood glucose levels. Several analyses subsequently heightened suspicions of potential adverse effects. WHO asked the manufacturer to review the scientific evidence in 2004, but the European Medicines Agency did not withdraw rosiglitazone from the market until 2010.

A second example is sibutramine, which was approved for treatment of obesity in 2001. Short-term studies showed a weight reduction of 3–5 kg compared to placebo, but the substance was also found early on to potentially raise both blood pressure and heart rate. Eight years after approval, a large study with several years of follow-up demonstrated that the treatment group did indeed lose weight but was more prone to stroke and myocardial infarction than the placebo group. The regulatory agencies withdrew sibutramine from the market shortly afterwards.

THE THIRD EXAMPLE is rimonabant, which is also for treating obesity and was approved in 2006. The mechanism of action was new, and approval was based on studies during which obese subjects lost 5 kg more with rimonabant than with placebo. The substance also appeared to have a positive effect on blood lipid levels, although adverse psychological effects were approximately twice as common. Two years later, a large study was discontinued when adverse effects such as anxiety, depression and sleep disorders were found to increase despite the ab-

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sence of risk reduction for cardiovascular disease. The EMA withdrew the licence.

Non-pharmaceutical interventions may also have negative effects and carry serious risks. A dramatic example in the 1970s and 1980s involved attempts to improve mechanical prosthetic devices for severe heart valve disease. When early models of the Björk-Shiley valve were introduced, the formation of blood clots impaired their function. Construction was then modified to include a disc that was held in place by two metal struts. During the initial tests prior to launch, the developers discovered by chance that the struts could fracture but attributed it to poor welding. The cause was never fully investigated. Nevertheless, the FDA assumed that the new valve models represented an improvement. The valves were not taken off the market until 1986 following hundreds of avoidable deaths.

Although systems for product control have improved and now include better follow-up after the launch of a product, not to mention the use of large quality databases, benefits still need to be weighed against risks when new medical technology is introduced.

The same logic applies to psychological treatment and interventions by the social services. New is not necessarily better – not even when theoretical reasoning and surrogate endpoints seem to suggest that it is. ◆ **RL**

EXPOSURE ON THE JOB
ARTHRITIS LINKED TO SOME KINDS OF WORK

Osteoarthritis develops more commonly in the knees and hips of people with physically demanding jobs that require heavy lifting or climbing ladders or stairs. Working in standing or kneeling positions increases the risk of knee osteoarthritis. Hip osteoarthritis develops more often in those who often work in a bent or twisted position. Gender does not matter if exposure is the same.

Osteoarthritis is a chronic joint disorder characterized by pain and reduced joint function. It is a major cause of physical disability, primarily affecting older adults.

SBU's systematic review clearly indicates that some kinds of work increase the likelihood of developing osteoarthritis in the knee, hip or both. Knee osteoarthritis occurs less frequently in people with jobs that allow them to sit much of the time and more frequently in those who spend much of their workday standing, kneeling or squatting.

Although hip osteoarthritis has not been researched as thoroughly, the available evidence shows that it occurs more often in those who spend their days working in bent or twisted postures. In general, those with physically demanding jobs that involve manual labour, such as lifting, carrying, walking or climbing, more commonly develop osteoarthritis of the knee, hip or both.

The systematic search performed for this assessment was designed to be very broad such that the relationships between any form of osteoarthritis and as many working conditions as possible could be evaluated.

AMONG THE THOUSANDS of identified articles, the team found 476 relevant studies. After systematically examining the articles, only 35 studies were found to have sufficiently high methodological quality to be used in the assessment. Some of the included research consisted of prospective cohort studies that explored the working conditions and health of a group of people and then followed them over a long period of time, recording changes to their health. The others were case-control studies that compared the working conditions of people who had developed osteoarthritis with a control group. ▸

SBU'S CONCLUSIONS ARTHRITIS AND WORK

▸ A substantial body of evidence exists showing that there is an increased risk of developing osteoarthritis in the hip, knee or both associated with some working conditions. Efforts for prevention are warranted.

▸ People who have physically strenuous jobs, or who have jobs that require a lot of walking, climbing, lifting or carrying run a higher risk of developing osteoarthritis in the hip, knee or both than others.

▸ People who spend much of their workday standing, kneeling or squatting run a higher risk of developing knee arthritis, especially when combined with heavy lifting. Knee osteoarthritis develops less frequently in people who are primarily seated while working.

▸ People who work in bent or twisted postures develop hip osteoarthritis more often than others.

▸ Women and men with similar occupational exposures develop osteoarthritis to a similar extent.

▶ Of the 35 high-quality studies identified, nearly all dealt with osteoarthritis of the hip and/or knee. Furthermore, they all focused on physical postures or movements. No high-quality evidence was found for any of the other potentially important work-related variables, such as the psychosocial environment, noise, vibration, risk of infection, or other physical factors.

LOOKING AHEAD, SBU identified the need for studies that address ways that employers can modify working conditions to protect their employees from the known harms associated with various physical postures and movements.

It is important to note that just because certain types of work-related physical strain are associated with an increased risk for osteoarthritis does not mean that physical inactivity is good. Too little physical exertion can contribute to osteoporosis, muscle atrophy and impaired metabolic function.

MODERATE LEVELS of physical exertion are important for everyone's health and wellbeing. However, it is difficult to say how much is enough or excessive. SBU earlier summarized and analysed a systematic review that showed that well-planned and highly structured training can improve mobility and reduce pain for those suffering from hip and knee osteoarthritis. In order to prevent and relieve suffering, it is important that healthcare professionals and decision-makers keep the evidence that links working conditions to osteoarthritis in mind. ◆ **RL**

About the Report

Occupational exposures and osteoarthritis (2016). SBU report no 253 (in Swedish). Project Manager SBU: Karin Stenström, karin.stenstrom@sbu.se. Chair: Prof Emer Eva Vingård, Occupational and Environmental Medicine, Uppsala University.

An English language translation of the summary for this report can be found on SBU's website. http://www.sbu.se/253e

The full report is only available in Swedish: http://www.sbu.se/253

CHILDBIRTH MORE WOMEN COULD AVOID FAECAL INCONTINENCE AFTER DELIVERY

According to an SBU review, injuries to the pelvic floor incurred during childbirth can be detected and prevented more often. Current postpartum examinations often miss injuries to the anal sphincter, which is linked to an increased risk that new mothers will develop faecal incontinence and reduced quality of life. Changing examination routines could increase the number of women who are correctly treated in time.

It is well-known that the anal sphincter muscles can be damaged during childbirth. Many professionals work to prevent, detect and treat these injuries today. However, a systematic review and assessment performed by SBU indicates that they occur more often than expected and that the situation could improve in several ways.

In 2004, more than 3,300 Swedish women, or 3.4% of those who gave birth vaginally, were diagnosed with anal sphincter injuries. However, according to the research identified by SBU, another 3,000 women may have incurred such injuries that were not detected before they left the delivery ward.

Injuries to the anal sphincter can be detected earlier and more often when a few additional examinations are routinely performed immediately after delivery.

Today midwives and doctors routinely examine the woman's pelvic region both visually and manually to detect possible injuries. If this standard procedure were supplemented with an ultrasound examination of the anus, one out of thirty new mothers could receive appropriate treatment in time to avoid suffering from severe faecal incontinence one year after her child was born.

Faecal incontinence is rarely noticed before the new mother leaves the maternity unit – and the attending doctors and midwives rarely receive any feedback regarding injuries the woman may have sustained.

RESEARCH ALSO SHOWS that there are ways to prevent birthing injuries. For instance, an incision (episiotomy) in the tissue between the vaginal opening and the anus can provide some protection if performed before vacuum assistance is used for a woman who gives birth for the first time. Warm compresses applied to the perineum during the pushing stage of childbirth can also provide some protection.

Anal sphincter injuries can also be prevented when the delivery ward staff is trained to promote a slow delivery, manually protect the perineal region with various hand-holds and use episiotomies, but only when it is best for the child's health. The evidence indicates that such training programmes can reduce anal sphincter tearing – although it is not clear which aspects of the training are responsible for the effect. For instance, the specific effects of the various techniques for manually supporting both the baby's emerging head and the woman's perineum during delivery remain unclear.

Little can be said about many other methods that have been proposed to prevent birthing injuries, since they have not been assessed well enough to reliably determine their benefits or harms. For instance, the report found there was not enough evidence to determine whether ▶

About the Report

Anal sphincter injuries associated with childbirth – a systematic review and evaluation of the health, economic, social, and ethical aspects (2016). Project Director SBU: Sigurd Vitols, sigurd.vitols@sbu.se Find the full report and summary at www.sbu.se

NORDIN / NORDIC PHOTOS

perineal preparation techniques, such as massage, pelvic floor training or a balloon to stretch the perineum (Epi-No) prior to the onset of labour were effective. Evidence gaps were also identified for the effects of labour and birthing positions, injections of hyaluronidase in the perineal region or birthing aids, such as fundal pressure belts and leg supports.

Women giving birth for the first time run the highest risk of sustaining anal sphincter injuries. Other risk factors include the use of vacuum or forceps to assist vaginal delivery, giving birth to a big baby, the top of the baby's head not descending into the birth canal first (abnormal presentation), or the woman having been genitally mutilated.

The SBU report also discusses the potential consequences of increasing the detection of anal sphincter injuries. For instance, improvements in the detection and diagnosis of anal sphincter injuries could change the need for episiotomies. ◆ **RL**

FROM SBU'S CONCLUSIONS ON BIRTHING INJURIES TO THE ANAL SPHINCTER

▸ Current postpartum examination methods miss injuries to the anal sphincter because they are not sensitive enough. This has led to an underestimation of how often these injuries happen. If left undetected and untreated, they can lead to faecal incontinence and reduce the woman's quality of life. Existing techniques that are better at detecting these injuries are not being routinely used.

▸ Fewer anal sphincter injuries are reported when the delivery ward staff are trained using programmes that focus on promoting a slow delivery, manually protecting the woman's perineal region, and performing episiotomies only when necessary. It is unclear which aspects of the training are responsible for the effects. For instance, manual perineal protection could lead to fewer tears, according to some, but not all of the studies assessed.

▸ An episiotomy may offer some protection against anal sphincter tears if done before vacuum assisting a women delivering her first baby. On the other hand, routine episiotomies of these women will always result in a grade 2 injury to the pelvic floor. Warm compresses applied to the perineum during the pushing phase helps prevent anal sphincter tears to some extent and likely has no negative effect.

▸ More research is needed to understand which postpartum examination methods should be used to insure that no injuries go undetected. The methods will need to be simple, reliable and sensitive. Studies that use objective methods and measurements as well as clear diagnostic criteria are needed to fully assess how these and other detection and prevention methods affect the incidence of anal sphincter injuries associated with childbirth.

BINGE EATING
THERAPY HELPS EVEN AFTER TREATMENT

Both cognitive behavioural therapy (CBT) and interpersonal psychotherapy (IPT) can help people with binge eating disorder, according to studies that had follow-ups up to a year after the therapy ended. Some pharmaceuticals medications also help reduce the frequency of binge eating episodes, although it is not known whether this effect continues if the regimen is discontinued.

According to a systematic assessment conducted by SBU, multiple therapies can help people with binge eating disorder (BED). The evidence shows that both psychological and pharmaceutical therapies can suppress binge eating when measured immediately post treatment. CBT and IPT can also reduce binge eating behaviours one year after treatment is concluded. The long-term effects of such regimens have not been studied.

GUIDED SELF-HELP programmes based on CBT may also help people with BED reduce or eliminate binge eating episodes. BED is associated with psychological and physical suffering and is often perceived as shameful by those who have it. Many of them never seek help or wait for a number of years.

As opposed to other eating disorders, people with BED are often overweight or obese. However, doctors who commonly treat overweight patients are not always aware of the symptoms associated with BED.

ALTHOUGH PATIENTS with BED commonly report poor quality of life, most studies have not evaluated whether it improved or changed after treatment, leading SBU to call for more research on life outcomes. SBU also identifies the need for future research that explores long-term and adverse effects, as well as cost-effectiveness, of BED treatments. More research is also needed to determine how well these treatments work for children and adolescents. ◆ **RL**

* A structured form of psychotherapy that focuses on the link between psychiatric health and a person's life situation, especially with respect to their relationships with others.
IPT is a structured form of psychotherapy that focuses on improving an individual's social functioning and support network in order to modify undesired behaviours.

SBU'S CONCLUSIONS BINGE EATING DISORDER

- Several different treatments can help a person with BED stop binge eating, or binge eat less frequently.
- Both CBT and IPT can help a person with BED stop binge eating, or binge eat less frequently up to a year after treatment. Directly post treatment, CBT provided as a guided self-help therapy, can help people with BED binge eat less often, or stop binge eating entirely.
- SSRI antidepressants and the central stimulant lisdexamfetamine can result in remission or decreased frequency of binge eating episodes at end of treatment. The effect of psychopharmacology beyond the end of treatment has not been sufficiently studied to draw any meaningful conclusions.
- Future research should investigate the long term and adverse effects, cost-effectiveness, the effect of treatments for children and adolescents, and the effect of treatments on quality of life.

PAUL DAVID GALVIN/GETTY

Binge Eating Disorder

People with binge eating disorder (BED) consume food even when they are not hungry. They eat more quickly than normal and continue past the point of discomfort. It is common for these people to eat alone due to feelings of shame, and they commonly experience guilt, disgust or depression after binging. BED resembles bulimia nervosa, with the exception that a person with BED will not induce vomiting or misuse laxatives to eliminate excess calories. As a result, this population is often overweight or obese. An estimated 1-4% of them are estimated to have BED at some point in their lives. The estimated lifetime comorbidity with other psychiatric disorders is 70%. BED appears in the eating disorders section of DSM-5.

About the Report

Treatment for binge eating disorder (2016). Chair: Prof Ata Ghaderi, Inst for Clinical Neurosciences, Karolinska Institutet. Project Director SBU: Jenny Odeberg, jenny.odeberg@sbu.se

The full report is available in Swedish: www.sbu.se/248
The executive summary is available in English: www.sbu.se/248E

ADDICTION A FEW PROGRAMMES CAN REDUCE RISK BEHAVIOUR IN YOUTH

ANDREW PATERSON/GETTY

It is possible to persuade young people to drink somewhat less alcohol when broad community coalitions work together to limit access. Although no structured school-based programmes can prevent drug use in general, a few are able to reduce binge drinking or the amount of tobacco or cannabis young people use.

People who engage in risky behaviours, including abusing controlled substances such as alcohol, narcotics, steroids or tobacco, or begin gambling at an early age, can develop problems that last a lifetime.

SBU has assessed the scientific evidence for methods that address the prevention or modification of risky behaviour in young people. The methods identified include structured school-based programmes, parent support efforts and public education initiatives designed for groups or individuals.

There is not enough scientific evidence to draw any conclusions about the effects of most of the programmes that have been identified. Even the studies that were found often turned out to be small with little or no impact on risk behaviours.

On the bright side, a few programmes can reduce risky behaviour in young people. Such programmes may be based on building broad community coalitions that bring together local authorities, schools, police officials and businesses in a coordinated effort to limit access to alcohol.

HOWEVER, COMMUNITY programmes aimed at changing attitudes, values or behaviours may show little or no effect on the amount of alcohol, cannabis or tobacco young people use. Furthermore, most studies that evaluated legislative initiatives such as tax had a high risk for bias and no conclusions could be drawn.

Some kinds of counselling may help young people who have already developed hazardous drinking habits to consume less. Motivational interviewing, for instance, can help them recognize the need to change their drinking habits and focus on what they have to gain by doing so. Personalized normative feedback approaches can be useful in settings such as universities where the amount peers drink is commonly overestimated.

Although none of the identified structured school-based programmes could prevent drug use in general, and some studies even reported increased consumption after the completion of school or parental support initiatives, some specific programmes can reduce the consumption of specific substances such as tobacco or cannabis, or reduce binge drinking. A few programmes might even be able to postpone the age at which young people start to smoke by a year or two. ◆ **RL**

About this report

Interventions to prevent misuse of alcohol, drugs and gambling in youth (2015). Chair: Prof Kent Nilsson, Center for Clincal Research, Uppsala University. Project manager SBU: Agneta Pettersson, agneta.pettersson@sbu.se
The executive summary of this report is available: www.sbu.se/243E
The full report is available in Swedish: www.sbu.se/243

FROM SBU'S CONCLUSIONS
PREVENTING SUBSTANCE MISUSE AND GAMBLING IN YOUTH

▸ None of the structured school based programmes can prevent drug use in general. A few programmes can reduce the consumption of tobacco or cannabis, or reduce binge drinking. The effects are usually between 1 and 5%. There was insufficient evidence to draw any conclusions on programs using structured family support groups. Some studies reported increased consumption after school or parental support programs.

▸ When implemented correctly, broadly coordinated community coalitions that limit young people's access to alcohol in multiple ways (ie, licensing, restricting opening hours), may reduce their alcohol consumption. However, multimodal community programmes aimed at changing attitudes, norms or behaviours, have little or no effect on the amount of alcohol, cannabis or tobacco young people consume.

▸ Brief interventions such as motivational interviewing and personalized normative feedback may reduce alcohol consumption by young people who engage in hazardous drinking.

▸ SBU's health economic analysis of alcohol prevention estimates that two preventive interventions may provide health effects at a reasonable cost. Structured school based programmes may be cost effective, provided that the proportion of binge drinking youth is reduced by at least 5%. Motivational interviewing may be cost effective provided that the proportion of binge-drinking youth is reduced by at least 2.5%.

▸ Despite the vast number of studies evaluating interventions to prevent or reduce drug and alcohol abuse, there continue to be significant evidence gaps. There is a need for interventions other than the structured programmes evaluated to be developed and assessed in well-designed studies. Further research is also needed that focuses on young adults in non-school settings, as well as research focused on the hazardous use of performance-enhancing drugs, prescription medications and gambling.

PRENATAL DIAGNOSTICS
QUESTIONS SURROUNDING MORE EXTENSIVE TESTING OF FOETAL DNA

A blood sample from a pregnant woman can be analysed with modern techniques to provide detailed information about the genetic makeup of the baby she is carrying. For some techniques, even the smallest genetic changes can be detected. However, there is still very little evidence regarding the accuracy of DNA sequencing techniques. According to SBU's analysis, considerable ethical problems may also arise if indications are widened.

Until recently, prenatal detection of genetic changes relied on examining cells from the foetus through a microscope. To obtain foetal cells, an invasive procedure was used to sample amniotic fluid or placenta, increasing the risk of miscarriage. Following the time-consuming process of isolating and growing the foetal cells, a microscopic analysis could reliably detect large changes in the chromosome structure.

WITH MODERN methods such as chromosomal microarray analysis (CMA) and next generation sequencing (NGS), it has become possible to detect very small genetic changes that are not visible through even the most powerful light microscopes. Furthermore, a technique referred to as non-invasive prenatal testing (NIPT) enables a detailed NGS analysis of foetal genes to be performed on a single blood sample from the pregnant woman. NIPT has the advantage of eliminating the extra time needed for the tests while avoiding the risks of miscarriage associated with invasive sampling.

SBU HAS SYSTEMATICALLY reviewed the accuracy of both CMA and NGS for prenatal diagnosis and examined whether these tests are better than other established methods at detecting genetic changes that affect the anatomy, function or development of a foetus.

SBU compared the reliability of the results of NGS to other established methods for detecting known genetic aberrations.* The report concludes that there is not enough evidence to determine how often any technique that uses NGS, regardless of whether or not the test sample was obtained invasively, provides incorrect or misleading information. In other words, it is not yet understood how often NSG results lead to false alarms or important genetic aberrations being missed. Despite not being able to combine the results, however, the identified studies suggest that false alarms may occur, indicating that positive test results based on NGS should be confirmed by means of another established method.

SBU's assessment of the reliability of CMA results indicates that it can identify all genetic aberrations detectable by other established methods with the same degree of accuracy, partly because CMA can detect additional changes that are too small to be seen through a microscope. When a prenatal ultrasound examination identifies irregularities, CMA is able to identify relevant genetic aberrations more often than other methods.

THE REPORTS ALSO discuss the need for well-conducted studies that investigate the value that expectant parents ascribe to the information provided by these newer methods.

The ethical analyses were central to the assessment of both CMA and NGS. Prenatal diagnosis is controversial and

SBU'S CONCLUSIONS SEQUENCING-BASED PRENATAL DIAGNOSTICS

For directed diagnostics

- There is not enough scientific evidence to assess the reliability of non-invasive prenatal testing (NIPT) based on next generation sequencing (NGS) to detect trisomies other than 13, 18, or 21, or inappropriate numbers of sex chromosomes. Studies have included too few events. The sensitivity of the method varied significantly between studies that examined monosomy X.
- The included studies differed too much to allow the results to be reliably combined. However, the identified studies indicate that false positives occur more often than false negatives.
- There is not enough scientific evidence to assess the reliability of using NIPT based on NGS to detect microdeletions or microduplications associated with known syndromes.
- The entire genetic makeup of the foetus can be included in some analysis packages even if the primary issue relates to a specific abnormality. This is a potential ethical problem if the woman and her partner are not given the opportunity to decide whether they want such analyses performed.

For analysis of the entire genome

- There is not enough evidence to draw any conclusions about the reliability of sequencing the whole genome with NGS to detect more genetic changes than expected, affecting anatomy, function or development.
- NGS allows the entire genetic makeup of a foetus to be analysed based on a blood sample from the pregnant woman. Since the method can explore the smallest genetic details, it has the potential to provide more information than is useful.
- While NGS might ultimately lead to early detection and treatment of some conditions, it will also generate a large amount of sensitive private data that are often difficult to interpret. This raises questions about genetic changes that should be identified and how the results should be reported. There are also important issues related to how genetic information should be handled by both healthcare professionals and commercial organisations. There is a need for a thorough ethical analysis regarding the management and possible regulation of how information generated by NGS should be used.

touches on some basic social values, such as dignity, autonomy and privacy. When diagnosis is combined with powerful tools that provide potentially unlimited information about the unborn child's genetic makeup, the ethical issues need more attention than usual.

PRESENTING COMPLICATED results of these tests to expectant parents requires balanced and thoughtful communication to ensure that they fully understand all the considerations before making an informed decision. Effective communication is particularly important in the case of findings that are unclear, unexpected or related to genetic changes that may impact the future health of the child to one extent or another. Test results must be communicated and handled with great care to not compromise individual autonomy or other fundamental ethical principles.

While NGS might ultimately lead to early detection and treatment of some conditions, SBU concludes that a thorough ethical discussion is warranted concerning management and possible regulation of this technology, addressing consequences for individuals, healthcare professions, and society.

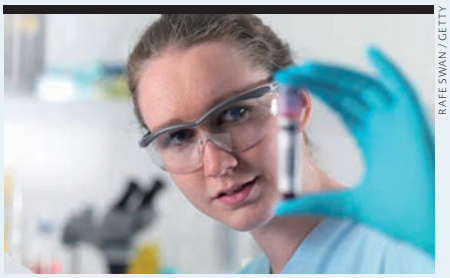
SBU also points out that the entire genetic makeup of the foetus can be included in some analysis packages even if the primary issue relates to a specific abnormality. This is a potential ethical problem if the woman and her partner are not given the opportunity to decide whether they want such analyses performed. For example, NGS is offered to expectant Swedish parents largely as a standard analysis package such that the foetus may be tested for genetic variations that do not interest them.

ANOTHER CRITICAL ISSUE that has been identified is how increased access to CMA and NGS technologies may cause a subtle widening of the indications for genetic testing, driving more prenatal tests for fewer significant genetic variations.

In addition, as access increases and perceptions change of what is preventable or not, expectant parents may experience greater pressure not to bring offspring with genetic aberrations into the world. Such developments could also further stigmatise individuals who have been born with with identifiable genetic conditions. ◆ **RL**

About these reports

Prenatal Diagnosis through Chromosomal Microarray Analysis, (CMA 2016).
Prenatal Diagnosis through next-generation sequencing, NGS (2016).
Project manager SBU: Christel Hellberg, christel.hellberg@sbu.se
Executive summaries are available in English for both reports: (CMA) www.sbu.se/246E and (NGS) www.sbu.se/247E
The full reports are available in Swedish:
(CMA) www.sbu.se/246 and (NGS) www.sbu.se/247E



RAFE SWAN / GETTY

Detailed genetic analysis

Until recently, prenatal identification of certain kinds of genetic changes were identified primarily by visually examining foetal chromosomes through a light microscope (karyotyping). The method is able to detect large genetic changes, such as when a whole chromosome, or a large portion of a chromosome, is missing, has changed places or has been added. For instance, trisomy refers to a situation in which cells have three copies of a particular chromosome rather than the normal two, a genetic anomaly that can be readily detected by karyotyping. Prenatal diagnosis based on chromosomal microarray analysis (CMA) enables a far more detailed exploration of the unborn child's genetic makeup; the method is sensitive enough to allow even very small genetic changes to be identified. Prenatal diagnostics based on next generation sequencing (NGS) provides even more detailed information about the genetic makeup of the foetus. Targeted NGS is designed to limit the amount of information collected by selectively sequencing only stretches of DNA that are known to be linked to specific known birth defects. However, NGS can be used to sequence all of the unborn child's genes, i.e. whole genome sequencing, potentially generating detailed information about the entire genetic makeup.

* Except for trisomies 13, 18, and 21, which are evaluated in a previously published SBU Assessment.

SBU'S CONCLUSIONS MICROARRAY-BASED PRENATAL DIAGNOSTICS

▸ When one or more foetal anomaly is detected by ultrasound, more genetic changes that affect anatomy, development or function can be identified with chromosomal microarray analysis (CMA) than karyotyping, quantitative fluorescence polymerase chain reaction (QF-PCR) or fluorescence in situ hybridisation (FISH) analysis. This applies particularly to anomalies detected in the heart or more than one organ system.

▸ A few additional genetic changes affecting anatomy, development or function can be identified with CMA but not karyotyping when the reason for testing is:

- advanced age of the pregnant woman
- parental anxiety
- high probability of chromosomal abnormality based on maternal serum screening

▸ CMA reveals more genetic changes with unclear significance for anatomy, development or function than karyotyping, QF-PCR or FISH analysis.

▸ For genetic changes that can be resolved with karyotyping, QF-PCR or FISH analysis, CMA has the same diagnostic accuracy as the reference test.

▸ CMA can provide extensive information about an individual's genetic makeup. Thus, it is of the utmost importance that the information be used in an ethically acceptable manner. Due to the extensive and complex nature of the genetic information this test can provide, great tact and patience are required when presenting the results to parents in order to ensure that they fully understand the results. This is particularly true in the case of findings that are unclear, unexpected or related to genetic deviations that impact the future health of the child to one extent or another.

▸ Additional well-conducted studies are needed to investigate the value that expectant parents ascribe to the information that CMA can provide.

ONGOING

Some Current SBU Projects

ALCOHOL SPECTRUM DISORDER (FAS/FASD) IN CHILDREN
Monica.Hultcrantz@sbu.se
Published: Dec 2016

ARM FRACTURES: TREATMENT OPTIONS
Karin.Stenstrom@sbu.se
Expected: Summer 2017

ENDOMETRIOSIS: EVIDENCE BASE FOR NATIONAL GUIDELINES
Jenny.Odeberg@sbu.se
Expected: To be decided

EPILEPSY: EVIDENCE BASE FOR NATIONAL GUIDELINES
Sten.Anttila@sbu.se
Expected: To be decided

HEALTH PROMOTION FOR CHILDREN IN FOSTER CARE
Knut.Sundell@sbu.se
Expected: Autumn 2017

INTERVENTIONS FOR UNACCOMPANIED ASYLUM-SEEKING YOUTH
Pernilla.Ostlund@sbu.se
Expected: Autumn 2017

PARENTING INTERVENTIONS TO PREVENT CHILD ABUSE/NEGLECT
Lina.Leander@sbu.se
Expected: Winter 2017/8

PROSTATE CANCER: COMPLETING PSA TESTS
Helena.Domeij@sbu.se
Expected: Winter 2017/8

PSORIASIS: EVIDENCE BASE FOR NATIONAL GUIDELINES
Anna.Christensson@sbu.se
Expected: Autumn 2017

SURGERY FOR GALLBLADDER SYMPTOMS
Jan.Adolfsson@sbu.se
Published: Dec 2016

TRAUMATIC SHAKING ("SHAKEN BABY") AND THE TRIAD
registrator@sbu.se
Published: Oct 2016

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