THE SWEDISH NATIONAL COUNCIL ON MEDICAL ETHICS

Smer comments

In this document series, the Swedish National Council on Medical Ethics (Smer) summarises and comments on national and international reports concerning topical medical ethics issues. The ethical analyses presented here, and any positions taken, are simplified.

Opportunistic genomic screening

Smer 2022:3. Published 19 December 2022
The document can be downloaded from www.smer.se

About the topic

Whole genome sequencing is expected to become a normal part of future investigations of disease. It aims to detect genetic variants that are important for diagnosis and treatment. When such an investigation is carried out, it can look for other genetic variants not related to the disease that is the subject of the investigation, but which may entail an increased risk of other diseases.

Introduction

The development of next-generation sequencing (NGS) has made it possible to sequence large volumes of genetic material in one and the same analysis. This has contributed to a dramatic drop in the cost of sequencing a person's entire genome. Knowledge about how genetic factors affect the onset and progression of diseases, and how the individual reacts to different treatments, is also expanding. Today, whole genome sequencing is sometimes used as part of the investigation and treatment of serious disease. It is expected to become more and more common in the future.

The question is: should such investigations also look for genetic variants linked to other unrelated diseases, which is termed opportunistic genomic screening (OGS)? One purpose of such an investigation can be to enable early preventive or therapeutic interventions when diseases have no or limited symptoms, but the prospects of successful treatment are greater. Another purpose may be to provide information that could have an impact on future reproductive decisions. Since whole genome sequencing will be done regardless of whether OGS is performed or not, the cost per patient will be lower with OGS compared to what it would be if screening for the same genetic variants were to be offered to the whole population.

OGS raises a number of ethical questions. Some concern the fact that OGS is a form of *screening*, meaning an investigation done without any concrete suspicion of disease. One of these questions concerns what demands should be placed on the trade-off between the expected benefit and risk with this kind of investigation, and how respect for autonomy will be safeguarded when the initiative comes from the healthcare system and not the patient. Other issues are related to *genetic* testing in general, such as how strong the link should be between a genetic variant and a disease. The fact that genetic information is also relevant for blood relatives also raises ethical questions. Finally, the *opportunistic* element, meaning that not everyone who could benefit from the investigation will receive the offer, can raise questions relating to justice and the principle that healthcare should be provided according to need.

This comment concerns

de Wert, G., Dondorp, W., Clarke, A. et al. (2021). Opportunistic genomic screening. Recommendations of the European Society of Human Genetics. *European Journal of Human Genetics*, 29, 365–377. Available from: https://www.nature.com/articles/s41431-020-00758-w

Terminology

Whole genome sequencing means determining the complete sequence of base pairs (A, T, C, and G) in the DNA of an individual. If the sequencing is limited to the protein-encoding portions of the genome (the exome), the term used is *whole exome sequencing*. In the following, the term whole genome sequencing is used to refer to both types of sequencing, unless stated otherwise.

Screening means investigations whose purpose is to detect disease or the risk of disease in persons

with no concrete suspicion (no clinical indication) of the disease. Screening is often done as part of screening programmes where all people in a predetermined target group are offered the investigation. When screening is not carried out as part of a screening programme, the term opportunistic screening is used. Opportunistic screening can be done at the individual's request or offered by the healthcare system to patients who have presented for other reasons.

Findings related to the indication that led to (genetic) testing are referred to in the following as *primary findings*, whereas findings that do not relate to this indication are referred to as *secondary findings*. This latter term refers to findings that the healthcare system has actively chosen to look for and should not be confused with unintentional or incidental findings.

Summary of the report

The European Society of Human Genetics (ESHG) previously recommended that genetic analyses in healthcare should focus on the original test indication. The article to which this comment relates reviews the previous recommendations in light of the rapid development in this area. The article provides some examples of how OGS is used or is recommended to be used in different parts of the world. It discusses the advantages and disadvantages of OGS and examines its ethical aspects. The article concludes with updated recommendations for how OGS should be used in healthcare.

The application of OGS – examples

Recommendations from the American College of Medical Genetics and Genomics

In 2013, the American College of Medical Genetics and Genomics (ACMG) published recommendations concerning the reporting of secondary findings in whole genome sequencing.[1] According to these recommendations, laboratories that carry out whole genome sequencing should check a minimum list of genes and – if genetic variants associated with disease are detected – report the finding to the ordering physician. The diseases on the ACMG's minimum list should have a long asymptomatic period and be medically actionable, i.e. possible to treat or prevent, according to these recommendations. The ACMG also recommended that only genetic variants with a high likelihood of causing disease should be reported as secondary findings.[2] For genetic variants that fit the criteria, ACMG's view is that the large benefits and minimal risks make it unethical not to offer OGS. These findings should be reported regardless of the patient's age, which is justified by the great potential gain in health for the individual or their family members. Initially, ACMG did not favour offering the patient the option to opt out of OGS if they consented to whole genome sequencing. But since 2015, an opt-out model has been advocated, whereby the patient is given the opportunity to opt out of the analysis of genes unrelated to the indication for the testing.[3]

Guidelines from Société Française de Médecine Prédictive et Personnalisée

The second example taken up by the article from ESHG is the *Société Française de Médecine Prédictive et Personnalisée* (SFMPP), which published guidelines for reporting secondary findings in whole genome sequencing in connection with cancer diagnosis in 2018.[4] Based on assessment criteria that include the risk of severe disease, medical actionability and the level of evidence, SFMPP recommends that 36 genes linked to cancer in adults should be investigated and reported. Informed consent should be obtained in a two-step process. When deciding to perform whole genome sequencing, the patient should be given the opportunity to decide on the option of looking for secondary findings. When the primary findings are reported, the patient should then be asked again if they want to be told about any secondary findings. SFMPP believes that OGS should only be offered to adult patients pending further ethical discussion concerning OGS in children.

---

[1] Green, R. C. et al. (2013). ACMG recommendations for reporting of incidental findings in clinical exome and genome sequencing. *Genetics in medicine: official journal of the American College of Medical Genetics*, 15(7), 565–574.
[2] The original list contained 57 genes. After a number of updates, the list (October 2022) contains 78 genes, most of which are linked to either specific forms of cancer or cardiovascular disease.
[3] ACMG Board of Directors (2015). ACMG policy statement: updated recommendations regarding analysis and reporting of secondary findings in clinical genome-scale sequencing. *Genetics in medicine: official journal of the American College of Medical Genetics*, 17(1), 68–69.
[4] Pujol, P. et al. (2018). Guidelines for reporting secondary findings of genome sequencing in cancer genes: the SFMPP recommendations. *European Journal of Human Genetics*, 26(12), 1732–1742.

100,000 Genomes Project

The third example is the *100,000 Genomes Project* in the UK, which was aimed at stimulating the implementation of genetic technology methods in routine healthcare. The project involved 100 000 patients with rare diseases or cancers whose genome was sequenced to detect genetic variants associated with their condition. Participants were offered the option of receiving information on potential secondary findings in two categories: conditions that are medically actionable, and carrier status concerning genetic variants that pose a risk that a future child will suffer from a serious genetic disease. The genetic variants selected were to have high penetrance, meaning that a large proportion of carriers do develop the disease, and there should be strong evidence for the efficacy of interventions. In order to avoid burdening the healthcare system unnecessarily, there also had to be a clinical benefit from obtaining genetic information before any symptoms appear.

Ethical analysis

The ESHG notes that the ACMG regards OGS as part of regular patient care, and as such that it should be assessed on the basis of traditional medical ethics standards – in this case the obligation to provide information on matters that may have a decisive impact on the patient's future health. This is in contrast with the ethical standards for screening developed by the WHO, for example, where the public health perspective is more decisive. However, whether screening is carried out as a public health measure or as patient care is, according to the ESHG, not crucial. What is central from a normative perspective is that in the case of screening, there is no medical indication for the specific investigation. This circumstance makes the trade-off between risk and benefit more complex in screening compared to investigations where there is an indication and thus a medical need for the patient. According to the ESHG, three fundamental requirements must be met for screening:

1. there must be evidence that for those being screened, the benefits-to-risks balance is clearly favourable (proportionality),
2. there must be explicit informed consent (autonomy), and
3. the investigation must be justifiable in terms of distributive justice, especially if it is publicly funded.

Proportionality

The ESHG notes that a study has shown that more than one person in 40 may be the carrier of one of the genetic variants on the ACMG's list. According to the ESHG, OGS thus has a significant potential health benefit. Prerequisites for this are that a large proportion of those who test positive for a genetic variant in screenings will go on to develop the disease (unless they receive treatment)[5], that proven effective treatments exist – and that the patient has access to them – and that the patient is offered relevant counselling.

Another potential benefit of OGS is that it may reduce the risk of serious adverse reactions to various drugs associated with certain genetic variants.[6] A third type of potential benefit is that patients will be able to make informed decisions about future reproductive choices, for example in order to avoid serious genetic disease in a future child. The benefits of OGS may turn out to be even greater in the future as it becomes possible to treat additional serious genetic disorders.

According to the ESHG, adverse effects can occur if OGS is introduced without sufficient evidence regarding the health impact of a genetic variant that is screened for. This may include lack of clarity regarding penetrance (the proportion of those carrying the genetic variant who develop the disease), the severity of the disease, or how the severity of the disease varies from one individual to another. In the case of penetrance, the ACMG has been criticised because its recommendations are based on knowledge of the link between genetic variants and diseases mainly derived from families where some member is affected by the disease. Such data could overestimate the risk of developing the disease for carriers without a family history. A consequence of overestimating the risk of disease may be that the individual is unnecessarily exposed to the medical risks involved with prevention. It can also lead to psychological harm in the form of unnecessary anxiety. According to the ESHG, psychological harm can also occur if people are informed that they are at risk of suffering

[5] This means that the positive predictive value must be high.
[6] Genetic variants of this type are included in the ACMG's minimum list.

from a serious disease that cannot be treated or prevented. Such a risk may arise if the requirement that the disease be medically actionable is compromised or the bar is set too low. Furthermore, psychological harm may occur if the individual is not offered adequate information and advice.

The ESHG emphasises that the assessment of whether the proportionality requirement for a screening offer is met must be evidence-based. At present, there are many questions and gaps in knowledge concerning the effects of OGS. According to the ESHG, this means that currently, the proportionality requirement is not met.

Autonomy

The ACMG advocates an opt-out model for consent to OGS, in which the patient is informed that they can opt out of OGS when whole genome sequencing is performed. Presenting screening in this way as the default option runs, according to the ESHG, counter to established screening standards, where every screening offer requires full and explicit consent. A problem with an opt-out model for consent pointed out by the ESHG is that the patient may not be aware that looking for secondary findings has nothing to do with the investigation of their original medical problem. The mere fact that OGS is presented as standard procedure can affect the patient's ability to make an autonomous decision, according to the ESHG.

According to the ESHG, OGS brings into focus two principles that may come into conflict: respect for the patient's autonomy, in particular the right not to know; and the obligation to communicate information that may be crucial for the patient's future health. By only providing the information requested by the patient, such a conflict can be avoided. Although not always feasible in genomics, the aim must be to minimise this conflict as far as possible. This can be done by means of a multi-step consent model such as the one advocated by the SFMPP, where the patient is given a subsequent opportunity to decide whether they want to be informed about any secondary findings when the primary findings are discussed. By awaiting renewed consent before analysing the raw data from the sequencing, the risk of a conflict between these principles can be further reduced.

Justice

The basis for offering OGS is that an indication for whole genome sequencing already exists. Patients have no greater anticipated risk of being carriers of the genetic variants included in the screening (those not covered by the indication) than the general population. In light of this, it may be considered problematic from a justice perspective not to offer the investigation to the whole population. If this is not possible for reasons of cost, the ESHG nevertheless is of the view that it may be justifiable to offer OGS to a particular group if the cost of the investigation in this particular group is low in relation to the benefit. But the ESHG also points out that OGS may further widen existing health gaps, since people from socio-economically advantaged groups are generally more inclined to seek medical care than others. The ESHG further points out that if the treatment to avoid severe disease is so expensive that many cannot afford it, screening for the genetic variant in question will be of greater benefit to some people than to others.

The ESHG emphasises that in the genetic variant databases available today, people of European descent are greatly over-represented. For people from groups for which there are less data, the assessment of whether a particular genetic variant causes disease or not is less certain, which may lead to an increased risk of harm to individuals.

Minors

Many guidelines for genetic testing state that minors should only be tested for genetic disorders where treatment needs be initiated early in life in order to be effective. The reasons usually put forward for this are the right to autonomy when it comes to information about one's own health and the risk of adverse psychological effects if the child learns that they have a high risk of future disease. Advocates for children also being offered OGS (for diseases with onset in the adult years) claim that this reasoning is applicable where there is a known family history of late onset genetic disease, since it is possible to postpone the test without adverse effects for the child. However, for children without a known family history (and their relatives) OGS is a unique opportunity to get potentially life-saving information. The ESHG's view is that there is a need for further discussion on the benefits of OGS for children in relation to potential adverse effects and disregard for the child's autonomy. In addition, the ESHG does not believe that the claim that OGS represents a unique opportunity for the child is convincing, given that genetic analysis may become 'routine' in healthcare of the future. If it is primarily the child's relatives who benefit from the investiga-

tion, the question arises as to whether their reproductive and health-related interests justify setting aside the child's future right to autonomy.[7]

Recommendations

The ESHG emphasises that not all forms of OGS are a priori unsound. Nevertheless, given the many complex issues that OGS raises, the position of ESHG is that if OGS is offered, it should take the form of pilots with rigorous evaluation. On the basis of its analysis, the ESHG presents a number of recommendations and positions:

1. Performing a broader analysis than needed to answer the diagnostic question amounts to a form of screening. The general framework of screening criteria is therefore applicable to OGS.
2. Since OGS is an investigation done without medical indication, there is a strong burden of proof that it is on balance beneficial for the patient. More research is needed on possible psychological harm, and it is thus too early to recommend OGS as the professional standard.
3. In view of the many uncertainties impacting the required proportionality of OGS, any OGS should be embedded in pilot and evaluation studies to determine its proportionality.
4. Clear criteria are needed for which genetic variants are to be included in OGS. All relevant stakeholders, especially patients, should be included in the debate on these criteria.
5. Informed consent should be the norm when OGS is offered. Opt-out models are problematic. The patient's right not to know should be respected as far as reasonably possible, while allowing professionals to still inform the patient about specific findings of great importance for the patient's own health or that of their close relatives.
6. When counselling for OGS, the provisional nature of current knowledge on penetrance should be addressed as well as options for re-contacting in case new scientific evidence of clinical relevance arises.
7. OGS pilots may be justified to generate data for comparative analysis of OGS and its main alternatives such as universal genomic screening for highly penetrant, actionable variants.
8. The question of OGS in children for later-onset actionable variants needs further ethical scrutiny.

The Swedish perspective

Whole genome sequencing within the healthcare system is currently performed at primarily three regional centres for genomic medicine (Karolinska University Hospital, Sahlgrenska University Hospital, and Skåne University Hospital). During 2021, approximately 7 000 analyses were performed involving whole genome or whole exome sequencing as part of clinical practice in Sweden.[8] The need for whole genome sequencing in healthcare is expected to increase and more centres for genomic medicine are in the process of being established.

At present, whole genome sequencing is used primarily to diagnose rare diseases in patients. Another area where whole genome sequencing is anticipated to be of great importance is in diagnosing cancer.[9] In the Swedish healthcare system, disease-causing genetic variants are not actively looked for where there is no link to the original indication (secondary findings). However, broad analyses in connection with investigations for rare diseases that are difficult to diagnose may lead to such genetic variants being detected as incidental findings.[10]

Smer's comments

OGS entails an active decision to look for secondary findings unrelated to the original indication for the investigation. This means that from an ethical point of view, OGS cannot be compared to reporting incidental findings. OGS is a form of screening and, according to Smer, should be assessed on the basis of the same ethical principles as other forms of screening.

All screening involves a trade-off between the possibility of helping those who will benefit from

[7] According to the ESHG, the need for a discussion of these issues is further strengthened by the fact that whole genome sequencing in the future may become part of the standard offer in newborn screenings.
[8] Genomic Medicine Sweden. (2022, 11 April). Sequencing of 7,000 genomes in Swedish clinical practice in 2021 for better diagnosis and treatment.
[9] Already today, all children who develop cancer are offered whole genome sequencing in the context of an ongoing research study. See Genomic Medicine Sweden (2021, 23 March). *Ny studie för bättre behandling av barn med cancer*. (New study to help improve treatment of children with cancer).
[10] Source: The Swedish Society of Medical Genetics and Genomics.

early treatment for an unknown risk of disease, and the risk of harm to those who do not need nor will benefit from treatment, for example through false positives, over-treatment of individuals who will not become seriously ill, or learning of the risk of a disease that is not medically actionable. This means, as the ESHG points out, that screening requires strong evidence that the potential benefits to those screened exceed any risks, i.e. proportionality.

The proportionality of a screening investigation depends on a number of factors, such as the severity and medical actionability of the disorder, the reliability and validity of the test, and the risks involved in the treatment. According to Smer, a prerequisite for screening is that the disease is medically actionable, since knowing the risk of future diseases that are not medically actionable can lead to considerable suffering over a long period. It is therefore important that the medical actionability requirement is not watered down for OGS, and that the analyses carried out are limited to genetic variants where evidence exists that early detection makes it possible to significantly improve the health outcome.

In genetic screening, validity is mainly related to the proportion of those carrying the genetic variant who develop the disease (the penetrance) and the proportion of individuals who develop the disease who become seriously ill. The ESHG emphasises that there are major gaps in knowledge about penetrance in individuals without a known family history for a number of the genetic variants proposed for inclusion in OGS.[11] If OGS is introduced without reliable evidence concerning the penetrance of the investigated genetic variants in the screened population, there is a risk that healthy people will be identified as ill, which can lead to unnecessary anxiety and have major effects on the individual's life choices, and result in the individual being unnecessarily exposed to treatment risks.

A basic ethical principle in healthcare is that the patient's autonomy should be respected. From the autonomy point of view, care interventions initiated by the healthcare system are more problematic than interventions provided after individuals have sought care themselves for a complaint. The individual can (with good reason) perceive an offer from the healthcare system as a recommendation. Screening, which is usually done on the initiative of the healthcare system, therefore places particular demands on how the offer is designed. Informed and explicit consent is a long established standard in screening investigations designed to safeguard the individual's autonomy and their right not to know, As the ESHG points out, it is problematic from this perspective to propose OGS as a routine procedure with an opt-out option for the patient, as the ACMG recommends.[12] This risks further reinforcing the message that the investigation is something that the patient is being urged to undergo and that it does not pose any risks. In addition, the patient is in a vulnerable position because they already have a serious condition when OGS is performed. In this situation, it can be difficult to absorb the information, and an opt-out model can lead to the patient consenting to screening without fully understanding the consequences. If OGS is to be offered to patients undergoing whole genome sequencing as part of a clinical investigation, according to Smer they should be clearly informed that OGS may unearth information above and beyond what is needed for the investigation. After having received information about both the risks and potential benefits of seeking this information, they should be given the opportunity to consent to or decline the investigation. To ensure that the patient understands the consequences, the provider of the information should have qualifications in medical genetics. In order to give the patient additional time for reflection, it may be appropriate for them to be given general information initially, and then have the option of determining whether they want more detailed information, and the option to ask questions. Clear informed consent is especially important to ensure that the patient understands that OGS is not part of the investigation of the complaint for which they have presented to their clinician for care, and that they do not decline whole genome sequencing just because they do not want information about their risks of future disease.

[11] See also Isidor, B. et al. (2019). Searching for secondary findings: considering actionability and preserving the right not to know. *European Journal of Human Genetics*, 27(10), 1481–1484 and Turner, H., & Jackson, L. (2020). Evidence for penetrance in patients without a family history of disease: a systematic review. *European Journal of Human Genetics*, 28(5), 539–550.
[12] ACMG Board of Directors (2015). ACMG policy statement: updated recommendations regarding analysis and reporting of secondary findings in clinical genome-scale sequencing. *Genetics in medicine: official journal of the American College of Medical Genetics*, 17(1), 68–69.

Furthermore, according to Smer, an all-or-nothing offer is questionable when the patient cannot choose which secondary findings to look for. The patient should be given choice at least on the basis of general categories such as disease-causing genetic variants, variants that affect reactions to drugs, and disease carrier status. It is also important that genetic counselling is offered when communicating results to the patient in order to support them in making subsequent decisions.

According to Swedish law, healthcare must be provided on equal terms and the healthcare system's resources must be prioritised on the basis of medical need. OGS is not offered to all individuals who can be anticipated to have the same potential benefit from the investigation (for example, all of the population over a certain age) but only to people who have already been offered whole genome sequencing for other reasons. If this screening can lead to a risk of serious illness being detected and actioned, and it meets the requirement of proportionality, according to Smer it may be reasonable to offer OGS in situations where the cost is low, even when it is not possible for resource reasons to offer it to the entire population.

Even if the cost per patient is lower for OGS compared to what it would be if the entire population were to be screened, OGS nevertheless entails costs for genetic analyses, information and advice to patients before and after the investigation, follow-up analyses, treatments, etc. These costs may arise in various parts of the healthcare system. In assessing the cost-effectiveness of OGS, it is important to take all these costs into account. The risks that OGS can lead to displacement effects and to other groups of patients with greater needs being pushed back in the queue also need to be noted. The introduction of OGS without reliable evidence on penetrance increases the risk that unnecessary follow-ups will take resources away from other patients.

Whole genome sequencing may be considered for children as part of the diagnosis of rare diseases and cancers. When it comes to genetic testing of children who are not able to consent themselves, Smer has previously emphasised that the child's right not to know and to be able to decide on what they want to know about themselves at a later date must weigh heavily.[13] If OGS is to be offered to children, according to Smer the investigation should be limited to genetic variants that cause severe disease with an early onset, where the benefit to the child may be deemed to outweigh the infringement of the child's autonomy.[14] Smer is of the opinion that children should not be tested solely to generate data whose principal value is to provide guidance for parents' reproductive decisions.

Smer's conclusions

In summary, Smer is of the opinion that:

- General ethical criteria for screening should be applied to OGS.
- OGS should be limited to genetic variants where there is evidence that early detection makes it possible to significantly influence health outcomes.
- There should be clear evidence that the screened variants have a high penetrance in the screened population. This is to reduce the risk of individual harm and displacement effects.
- Clear informed consent should be the norm for OGS, and opt-out models should be avoided. Information provided in several steps can be a way of ensuring that the patent is given sufficient time for reflection.
- If OGS is to be offered in the Swedish healthcare system, there should be clear criteria for which genetic variants will be covered. These criteria should be drawn up in dialogue with relevant actors and stakeholders. As with other screening, there should be a structured process for assessing whether a given genetic variant fits the criteria and should be included in the screening.
- If OGS is to be offered to children, the investigation should be limited to genetic variants that cause severe disease with an early onset, where the benefit to the child may be deemed to outweigh the infringement of the child's autonomy.

[13] Swedish National Council on Medical Ethics. (2019). *Smer kommenterar DNA-testning av barn utanför hälso- och sjukvården. (Smer kommenterar 2019:1). (Smer comments: Genetic testing of children outside healthcare)*

[14] According to Smer, screening for medically actionable diseases with onset early in life should primarily be done as part of newborn screening.

Further reading

Johansson Soller, M. et al. (2021, 10 May). Helgenomanalys vid sällsynta diagnoser ger stor patientnytta. (Whole genome sequencing for rare diseases offers great patient benefit) *Läkartidningen*.

National Board of Health and Welfare. (2019). *Om nationella screeningprogram.* (On national screening programmes).

The Swedish National Council on Medical Ethics. (2002). *Genetisk screening – om hälsa och ärftlig sjukdomsrisk. (Genome screening – on health and the risk of hereditary disease)* (Etiska vägmärken 11).

The Swedish National Council on Medical Ethics (2019). *Smer kommenterar DNA-testning av barn utanför hälso- och sjukvården. (Smer comments: Genetic testing of children outside healthcare)* (Smer kommenterar 2019:1).

Läkartidningen. (2021). Tema precisionsmedicin. (Theme: precision medicine) No 19–20/2021.

Uppsala University. (2019, 1 March). *Ska alla få gentesta sig innan de skaffar barn?* (Should everyone be offered genetic testing before having children?) [webpage].

Woudstra, A., Dondorp, W. and de Wert, G. (2021). Stakeholder views on opportunistic genomic screening in the Netherlands: a qualitative study. *European Journal of Human Genetics*, 29(6), 949–956.

Links

Genomic Medicine Sweden

The Swedish Gene Technology Advisory Board. Genetic tests (page in Swedish)

The Swedish National Council on Medical Ethics (Smer) is an all-party advisory board to the Swedish Government whose primary task is to illuminate medical ethics issues from an overall community perspective.

The decision on this Smer comments document was made at a meeting on 28 October 2022.

Smer, Ministry of Health and Social Affairs, SE-103 33 Stockholm, SWEDEN
Phone: +46 8 405 10 00, E-mail: smer@gov.se, website: www.smer.se