Almost 40 years ago, WHO commissioned a report on screening from James Maxwell Glover Wilson, then Principal Medical Officer at the Ministry of Health in London, England, and Gunner Jungner, then Chief of the Clinical Chemistry Department of Sahlgren's Hospital in Gothenburg, Sweden. The report[1], published in 1968, was entitled: *Principles and practice of screening for disease* and it has since become a public health classic.

Revisiting Wilson and Jungner in the genomic age: a review of screening criteria over the past 40 years

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At the time when Wilson and Jungner wrote their report, there were many technological advances in medicine, which made screening a topic of growing importance and controversy. With the recent sequencing of the entire human genome,[2,3] screening is re-emerging as a timely issue. Genetic screening is being proposed as a major vehicle for translating genetic and genomic advances into population health gains.[4,5] However, the ever-widening gap between what is technologically possible and the services available is creating pressure to introduce or expand screening programmes, often before adequate safeguards and regulatory frameworks are in place.[6,7]

The main difficulty, as observed by Wilson and Jungner in 1968, was that "in theory, screening is an admirable method of combating disease … [but] in practice, there are snags".[1] In their landmark publication, the authors were fundamentally preoccupied with the notion that:

"The central idea of early disease detection and treatment is essentially simple. However, the path to its successful achievement (on the one hand, bringing to treatment those with previously undetected disease, and, on the other, avoiding harm to those persons not in need of treatment) is far from simple though sometimes it may appear deceptively easy."

For this reason, Wilson and Jungner attempted to define screening criteria to guide the selection of conditions that would be suitable for screening, based, among other factors, on the capacity to detect the condition at an early stage and the availability of an acceptable treatment (Box 1). They considered these criteria "especially important when case-finding is carried out by a public health agency, where the pitfalls may be more numerous than when screening is performed by a personal physician".

Just as forty years ago, Wilson and Jungner wrote their treatise amidst a great deal of controversy surrounding the early detection of disease, there are now similar debates with respect to genetic screening. A growing number of diseases can now be detected in the pre-clinical stage, and even in the pre-pathological stage, using molecular and non-molecular diagnostic techniques.

Large-scale screening for genetic conditions began around the time of the Wilson and Jungner publication. There was newborn screening for inborn errors of metabolism such as phenylketonuria, later followed by prenatal screening for Down syndrome and neural tube defects using ultrasound and biochemical markers. Once individual disease genes started to be identified using novel molecular techniques, pilot screening programmes were established for several rare genetic conditions such as Tay Sachs disease and cystic fibrosis. With the advances in genetic technology, the rate at which new disease genes are being identified is out-pacing the ability of professionals and

Box 1. **Wilson and Jungner classic screening criteria[1]**

1. The condition sought should be an important health problem.
2. There should be an accepted treatment for patients with recognized disease.
3. Facilities for diagnosis and treatment should be available.
4. There should be a recognizable latent or early symptomatic stage.
5. There should be a suitable test or examination.
6. The test should be acceptable to the population.
7. The natural history of the condition, including development from latent to declared disease, should be adequately understood.
8. There should be an agreed policy on whom to treat as patients.
9. The cost of case-finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole.
10. Case-finding should be a continuing process and not a "once and for all" project.

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policy-makers to assess the potential benefits and pitfalls of introducing or expanding genetic screening programmes.[8–10]

Due to the complexity involved in genetic screening policy-making, many advocate the use of criteria. The Wilson and Jungner criteria have long been considered the gold standard in making such decisions.[11–13] However, a growing number of approaches to genetic screening policy-making are in use,[14,15] based on an even greater number of different sets of criteria.[16–19] Many are variations on the classic criteria of Wilson and Jungner. However, when different jurisdictions use diverse methods of decision-making for the same screening decisions, it can lead to inconsistencies: "The lack of even broad concordance at the level of national policy is extremely disturbing. Though all discussion is nominally founded on the ten principles laid down by Wilson and Jungner in 1968, there seems no generally accepted way of using these principles, or derived criteria, as objective decision tools."[20]

Even when the same criteria are used, these have at times been criticized for being too vague or theoretical,[21] and thus difficult to assess in a consistent manner.[22,23] Furthermore, even when criteria are met, there may still be logistical, social or ethical reasons that preclude screening.[24] Research is therefore needed to determine which criteria should be used and what processes are required to ensure that new and expanded genetic screening programmes best serve the public interest.

As part of a larger research programme,[25] a series of literature reviews and consultations were used to develop a systematic and transparent approach for guiding genetic screening policy decisions. The initial step involved a literature review to systematically identify and synthesize over 50 lists of screening criteria that have been proposed over the past 40 years. The majority of these criteria overlap with the classic Wilson and Jungner criteria, particularly with regard to screening for health conditions at an early stage, where there exist effective interventions to improve outcomes compared to standard care. However, several adaptations have been made to the classic criteria, and several new criteria have also emerged (Box 2). Many adaptations of classic criteria reflect issues raised by the growing interest in genetic screening (e.g. the importance of serious genetic conditions even if they are rare, implications of genetic information for family members, need for analytical and clinical validity of screening tests, possibility of interventions that offer reproductive options, etc.). In contrast, many of the emerging criteria reflect broader trends that have shaped both Western medicine and society more generally over the past generation (e.g. increased consumerism, the shift away from paternalism towards informed choice, a focus on evidence-based health care, and the rise of managed care models that emphasize cost-effectiveness, quality assurance, and accountability of decision-makers).

Box 2. **Synthesis of emerging screening criteria proposed over the past 40 years**

- The screening programme should respond to a recognized need.
- The objectives of screening should be defined at the outset.
- There should be a defined target population.
- There should be scientific evidence of screening programme effectiveness.
- The programme should integrate education, testing, clinical services and programme management.
- There should be quality assurance, with mechanisms to minimize potential risks of screening.
- The programme should ensure informed choice, confidentiality and respect for autonomy.
- The programme should promote equity and access to screening for the entire target population.
- Programme evaluation should be planned from the outset.
- The overall benefits of screening should outweigh the harm.

Following a series of consultations with local and international stakeholders and experts, the modified Wilson and Jungner criteria and newly emerging criteria transformed into a more elaborate decision support guide.[25] The guide consists of three levels of analysis that contribute to integrating various types of scientific and contextual evidence, making explicit the iterative nature of decision-making, balancing different perspectives (e.g. individual versus population viewpoints), comparing various alternatives (e.g. different screening strategies as compared to routine clinical care), considering whether implementation in a given context will allow the benefits of the screening programme to be realized, and emphasizing that adequate governance and regulatory frameworks are required. This approach to screening policy-making encourages documentation of evidence, trade-offs, and the reasoning underpinning recommendations, thus promoting greater transparency, and allowing decisions to be revisited over time.

Ultimately, the decisions to develop, implement and continue to fund genetic screening programmes are political.[26] On the one hand, governments want to support the biotechnology sector which provides jobs and fuels the economy, while on the other hand, governments are also responsible for organizing health services and protecting consumers.[27] Although genetic services and screening programmes aim to improve the health of the population, there is growing concern that the increasing number of genetic tests becoming available at lower costs could compromise the viability of the health care system. Even though the tests themselves may be inexpensive and suitable for large-scale use, the infrastructure and human resources needed to provide appropriate education, counselling, interventions and follow-up are likely to be far more costly. When it comes to the allocation of scarce resources, economic considerations must be considered alongside "notions of justice, equity, personal freedom, political feasibility, and the constraints of current law".[28,29]

Governments are therefore faced with the difficult task of managing the use of new genetic information and technologies while balancing the many different perspectives and needs of society. Even beyond the field of genetics and genomics, there is a growing understanding that population-level policy decisions should be based both on high quality evidence and on the values of the population,[30,31] as well as contextual considerations.[32,33]

The criteria of Wilson and Jungner are still upheld today as "classics",[34] the "gold standard of screening assessment",[35] having "stood well the test of time".[36] However, the authors never expected their criteria to remain unchanged over time, but rather hoped that their publication would provoke further reflection and debate in this complex area:

"If anywhere we have appeared dogmatic, we hope this may serve to stimulate discussion, since, in the end, real development depends on an exchange of views."

Indeed, an exchange of views has occurred over the last four decades, and many other authors have attempted to adapt or reinvent the Wilson and Jungner criteria to better fit within their particular context of screening and with the changing times. In particular, a great deal has been written with regard to screening criteria as applied to the rapidly growing field of genetics. Although the value of the Wilson and Jungner criteria remains undisputed to this day, newer policy tools are now available,[25] bringing new life to the longstanding debate that Wilson and Jungner started on how best to tackle perennial challenges relating to screening policy decisions. ■

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