Identification and Management of Persons with Chronic Viral Hepatitis in Europe

Meeting Report

Budapest, Hungary, 18–19 March 2010

David FitzSimons,[1] Greet Hendrickx,[2] Alex Vorsters[2] and Pierre Van Damme[3]

1. Chief Editor, Documentation and Communications, Office of the Governing Bodies, World Health Organisation; 2. Researcher, Secretariat Viral Hepatitis Prevention Board, Vaccine and Infectious Diseases Institute, University Antwerp; 3. Full Professor and Chairman, Vaccine and Infectious Disease Institute, University of Antwerp

Abstract

The Viral Hepatitis Prevention Board organised a meeting on the identification and management of persons with chronic viral hepatitis in Europe in Budapest, Hungary (18–19 March 2010). The objectives of the meeting were to review screening of chronic diseases, evaluate the applicability of the Wilson and Jungner screening criteria to chronic hepatitis, report on health technology assessments of such programmes, weigh the benefits of screening against costs and potential harm that may ensue and define conditions for screening and its strengths and weaknesses, and public health and social implications, including impact on individuals.

Keywords

Chronic viral hepatitis, identification, screening, management, prevention

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Correspondence: Greet Hendrickx, Viral Hepatitis Prevention Board, Centre for the Evaluation of Vaccination, Vaccine & Infectious Diseases Institute, University of Antwerp, Universiteitsplein 1, B-2610 Antwerp, Belgium. E: greet.hendrickx@ua.ac.be

In 1968, Wilson and Jungner published a set of 10 criteria for screening of a condition. As medical practice has changed over the years, numerous other criteria have been proposed and in recent years these have reflected non-paternalism, evidence-based decision-making and results-based management, with elements such as defined objectives and target populations, proven effectiveness of the screening method, informed choice, equity and access, minimisation of harm and evaluation (see *Annex*).

Changing epidemiology, better knowledge of the natural history of chronic infection, new vaccines and treatments, and clinical developments have been seen in viral hepatitis. In the case of hepatitis B, however, there has been no change since 1982 in surveillance for markers of hepatitis B virus (HBV) infection in risk groups: no new risk group has been identified and recommendations for screening remain the same.

Current approaches to prevention and control of viral hepatitis are seen as not being sufficient for the purpose. Part of the problem is that not all decision-makers, professionals or even the public are aware that available measures can be effective when they are strategically planned and taken in a co-ordinated manner. A few weeks before the meeting, the Institute of Medicine of the National Academy of Science in the US published a consensus report on a national strategy,[2] concluding that "the current approach to the prevention and control of chronic hepatitis B and hepatitis C is not working". Several reports presented at the meeting noted that integration of viral hepatitis prevention and control into other existing programmes can strengthen health systems generally. One of the driving forces for prevention is the increasing cost of treatment resulting from the growing number of cases found through screening.

Limited surveillance programmes for hepatitis B and/or hepatitis C reportedly exist in many countries, but in form and practice they show wide variations[3] and large proportions of the populations in low-income countries are not covered by any surveillance. Harmonisation of surveillance across the EU will be difficult given the differences in national surveillance systems. Basic data, let alone comparable and validated reliable prevalence data, are missing in numerous countries. Similarly, access to testing varies substantially in correlation with a country's wealth.

The European Centre for Disease Prevention and Control (ECDC) commissioned a review on the effectiveness of screening for hepatitis

B and hepatitis C in some 34 countries. The findings provide some evidence of cost effectiveness and indicated that secondary prevention could considerably improve health status. It confirmed, however, the lack of prevalence data in the general population as well as the wide diversity of prevalence patterns. Indeed some 'low-prevalence' countries may harbour populations among whom prevalence is high. Little information is also available about incidence rates among such groups.[4]

The results of studies on the health economics and computerised modelling of viral hepatitis will depend on the accuracy of the data on prevalence, incidence, natural history and treatment outcome. Lessons are being learnt from other screening programmes such as those for HIV and chronic kidney disease.

Numerous guidelines on screening and testing for viral hepatitis exist, but some are inconsistent (e.g. those of the US Preventive Services Task Force and the US National Institutes of Health). At the same time, many European countries are planning to introduce national screening programmes, but questions remain about whom and how to test.

The year 2010 clearly became the 'year of hepatitis'. Besides the publication of the Institute of Medicine report,[4] the World Health Organization (WHO) and the World Hepatitis Alliance have published the results of a comprehensive analysis and overview of the policies and programmes in place for viral hepatitis across the world.[5] WHO is finalising its update of the estimated global burden of disease due to hepatitis B and hepatitis C. WHO's governing bodies considered viral hepatitis, and in May 2010 the Sixty-third World Health Assembly adopted resolution WHA63.[18] which urges improvements in surveillance, cost effective and integrated prevention, control and management programmes with strengthened health systems and evaluation of programmes as well as the designation of a World Hepatitis Day. Major conference on viral hepatitis were due to be held, including the Summit Conference on Hepatitis B and Hepatitis C (Brussels, October 2010). ECDC is discussing proposals for enhanced surveillance of hepatitis B and C across the EU with plans for a new surveillance network.

Burden of Disease

Chronic viral hepatitides have been described as 'silent' diseases – slow, burdensome and costly illnesses – because, frequently, those infected have no obvious symptoms until serious liver disease ensues. Global estimates in 2004 indicated that 350 million people were chronically infected with HBV, and 500,000–700,000 people died annually. Figures for the US are 0.8–1.4 million and 3,000, respectively. Globally about 130–170 million people are chronically infected with the HCV, with more than 350,000 deaths/year: figures for the US are 2.7–3.9 million people infected and 12,000 deaths. Some 2 % of the US population are living with chronic hepatitis B or hepatitis C, although most of these people are unaware that they are infected until they develop liver disease many years later (as many as two-thirds of chronically infected Asian-Americans are thought not to know their HBV status). Together the two diseases are more common than HIV/AIDS in the US and cause more deaths (15,000 in 2006) than HIV (14,000 in the same year).[2] HIV co-infection poses a problem for both progression and treatment of chronic viral hepatitides. Although incidence rates of hepatitis D are falling, it still causes a considerable disease burden: an estimated 15–20 million people are infected worldwide, and chronic infection leads to more severe liver disease.

A repeated observation concerned the weakness of baseline data. For instance, some 10 million migrants, one of the main groups among whom high prevalence rates had been detected, are officially registered in the EU, but the actual figure may be closer to 20 million. Data from the UK suggest a doubling of cases of hepatitis B in this group in the next five years, and in Ireland and the Netherlands estimates of the number of migrants infected with HBV exceed the estimated number of infected people in the two countries. The pace of new diagnoses of hepatitis C in migrants is also growing. The trends are likely to be similar in other European countries. Even in countries with reported high prevalence rates, data on burden of disease and mortality are not readily available.

ECDC has underlined the paucity of published information on policies, prevalence and effectiveness of screening programmes. Gaps in knowledge also exist about prevalence of markers of hepatitis B and C virus infection in the general population and in groups at risk (including prisoners) mostly in countries where overall the prevalence is low, as well as in blood donors and pregnant women. Rates of infection with HCV tend to be higher than those for HBV markers, particularly notable examples being the rate of anti-HCV antibodies in first-time blood donors in Spain and pregnant women in Greece and Italy. Prevalence rates for HCV infection are increasing, although this is possibly due to improved surveillance, intensified screening and the availability of accurate testing methods.

The natural history of chronic hepatitis C is becoming clearer, although long-term outcome of asymptomatic HCV infection is unknown (for instance, who progresses cannot be predicted). The long-term outcome of successful treatment of hepatitis C is also unknown beyond 5–10 years.

Until now, with the results being issued of different reviews, information about national policies on viral hepatitis has been lacking, as has evidence on the effectiveness of policies.

Surveillance

ECDC is currently conducting a survey of surveillance systems and prevention programmes, and preliminary results underline a wide variation on reported data and in surveillance methodology.

Surveillance has not generated sufficiently good data for sound policy-making decisions. Collection of data at national and regional levels responds to different needs and requests from bodies at different policy-making levels, and sources of data differ. Validation of data can be problematic: case definitions are inconsistent between countries and intergovernmental or international agencies, and a EU version is not universally used; application of the International Classification of Diseases for coding has its limitations; and examples were cited in which disease data were coded with a view to reimbursement of costs.

Comparison of surveillance data is hampered by differences in the surveillance systems, the population under surveillance, the sources of data and the unknown proportion of infections that are undiagnosed or missed because they are asymptomatic or (if diagnosed) unreported. Also, there is no clear distinction in the overall reporting between acute and chronic cases.[4]

Co-ordination of surveillance for viral hepatitis is lacking.[3] Not only is reporting incomplete but reporting systems differ widely. ECDC is

preparing to co-ordinate enhanced surveillance for hepatitis B and C and develop standardised behavioural surveillance. In particular, it is establishing a new surveillance network, pilot testing a methodological study of the cost effectiveness of HCV screening and producing estimates for burden of disease in Europe. A protocol for surveillance of viral hepatitis, with a defined set of criteria, is being finalised.

Screening

Screening is just one strategy for improving population health. Perennial issues include where a programme fits into the continuum between mass screening and clinical testing; the need to consider added benefits; whether benefits outweigh the harm, which historically has been underestimated; what are the opportunity costs; whether it meets the needs and reflects the perspectives of individuals, target populations and society in general; being transparent about choices; and producing evidence to support decisions to screen. Screening is much more than just a test. Programmes must be co-ordinated with overall management, delivery of services (from education and informed consent to intervention and follow-up) and laboratory testing.

The process for making policy decisions on screening is complex. Those involved need to share a common understanding. In particular, decision-making must be based on three conceptual aspects: that it be patient-centred, evidence-based and system-driven (in order to ensure practicality and enable the use of routine screening). A guide is developed to support decisions for population-based screening emphasises the following three elements: the importance of determining the utility of a proposed screening programme through an analysis of the extent of the problem, in this case viral hepatitis, and evaluating alternative strategies; the need to evaluate the relevance, feasibility and acceptability of implementing a screening programme in a specific context; and assessing the societal implications.[6]

In some areas, such as the screening of pregnant women, much work has already been done, but lessons learnt need to be applied: for example, such screening protects against neonatal infection but follow-up of the infected women and their partners is not always adequate. Questions need to be answered: how are those screened going to be followed-up? Incarcerated populations, for instance, may be relatively easy to screen but may be lost to follow-up after their release. How can compliance with any prescribed treatment be ensured? Reviews of effectiveness have shown, inter alia, that screening is cost-effective for HCV infection in injecting drug users and migrants and for HBV infection in pregnant women, high-prevalence target groups could thus be selected on the basis of risk factor profiles. A literature review concluded that screening and early treatment of HCV infection had the potential to improve average life expectancy, but should focus on populations in which the prevalence was elevated in order to be cost effective.[7]

In the US, primary health-care providers have met to design a simple, clear algorithm (based on existing guidelines) for screening and initial evaluation and management of HBV-infected patients and referral for evaluation for treatment. The Centers for Disease Control and Prevention (CDC) issued a national strategy for prevention of HCV infection in 2001 which recommended routine testing for people with an increased risk of infection.[8] Considerable emphasis is being put on secondary prevention (early diagnosis and treatment) and reducing the risk of infection converting into chronic liver disease.

Treatment

In the US, the American Association for the Study of Liver Diseases has recently published practice guidelines that cover diagnosis and management as well as treatment for both hepatitis B[9] and hepatitis C.[10] CDC does not issue treatment guidelines. The European Association for the Study of the Liver (EASL) has also recently issued extensive clinical practice guidelines for hepatitis B, which include aspects such as co-infection (hepatitis B, C and D viruses, and HIV), the goal and end-points of therapy, definitions of response, indications and strategies for treatment, monitoring, finite and life-long treatment with different antiviral agents and treatment in special groups (including children).[11] The publication also lists unresolved issues and unmet needs.

Hepatitis B

For hepatitis B, several drugs are now available. Seven antiviral agents are licensed for treatment: interferon-α; pegylated interferon-α; lamivudine; adefovir; entecavir; telbivudine; and tenofovir. (Pegylated interferon also leads to sustained suppression of hepatitis D viral RNA in about 25 % of patients.) Interferon-α and lamivudine have been approved for children infected with HBV, and adefovir shows good pharmacokinetics and is well tolerated.[12] With this arsenal of drugs, treatment has become simpler and safer – it improves quality of life and most patients respond to treatment. Continued treatment is needed for most patients and the outcome may be jeopardised by suboptimal treatment. Treatment slows disease progression but is not curative.

Reliance continues to be placed on treatment with pegylated interferon-α and nucleos(t)ide analogues, which act on different targets. However, resistance is a serious and growing problem, and after discontinuation of treatment the relapse rate is high. Resistance develops most rapidly with lamivudine, the cheapest drug, but so far, experience with tenofovir and entecavir shows that resistance to those agents develops rarely.

The rapid development of resistance to lamivudine raises the question of whether it should continue to be used as a first-line drug. Questions remain about the indications for, and timing of, treatment. Small-scale studies and models point to the clinical benefit of long-term treatment but these need confirmation, through cohort studies in order to validate the models and in case-control studies to determine the effect of non-compliance. For hepatitis B, few if any new drugs or new treatment approaches are in development.

Overall, at present, too many uncertainties exist to allow sound public health decision-making about screening for hepatitis B.

Hepatitis C

In contrast to the case for hepatitis B, for which treatment can suppress the virus and control infection, treatment can result in cure of hepatitis C. Moreover, some 30 compounds are in development for the treatment of hepatitis C, with two being licensed in 2011. Although acute hepatitis C is generally mild, recent work shows that treatment benefits those patients in whom it was instituted early, but the optimal timing and form of treatment for acute disease are not yet established.

All patients with chronic hepatitis C, irrespective of the degree of fibrosis, are potential candidates for treatment. Patients with mild

disease do not need immediate treatment, but those with compensated cirrhosis are candidates for treatment. Half of patients with chronic hepatitis C are eligible for treatment and, of those who receive therapy, half will benefit from treatment, including cure. In other words, in the case of hepatitis C, one of the criteria of Wilson and Jungner relating to treatment is met and screening may be considered but investigation of other criteria is advisable.

Issues

Should use of lamivudine be eliminated because of its propensity to induce resistance? How long should treatment last? If it is for life, where is the evidence for the value of long-term therapy, what are the consequences for development of resistance and what are the policy and cost implications? What is the cost effectiveness of the various therapies? Although studies have suggested that treatment of both hepatitis B and C should save costs and be cost effective, more health economic analyses are needed in order to assess the value of treatment. Also, criteria for treatment of active chronic hepatitis B need to be defined.

Evaluation of treatment needs representative cohort studies to define the natural history of hepatitis B and large randomly controlled trials of monotherapy and combination therapy that measure the long-term effects and safety.[13] But it is difficult to undertake these trials once drugs are already licensed, and often the data are limited to initial efficacy trials.

Even when treatment options are defined, barriers to treatment remain, for instance: access to and affordability of treatment; the eligibility and desire of patients to be treated; and compliance with and completion of treatment (in a hepatitis C study among US veterans in Alaska only 2 % completed treatment).[14]

The complexities of treating hepatitis in cases of co-infection with HCV and/or HIV as well as resistance all render policy-making difficult. The HIV community is increasingly becoming involved in discussions of treatment and WHO recently convened a meeting on combined treatment approaches to hepatitis B and HIV infection in resource-constrained settings. Such approaches need to be further considered and options evaluated.

Stakeholders

The gamut of interested parties ranges from governments, intergovernmental organisations and nongovernmental organisations (such as patients' associations) to the patients themselves, people who are infected but unaware of the fact, and the families and their contacts. All have different, sometimes overlapping, roles. Greater clarity about their respective roles and the state of cooperation between them would be helpful and a basis for synergies and concerted action. Associations such as EASL and the European Liver Patients Association and national groups (such as the Belgian Association for the Study of the Liver) provide valuable forums and sources of information (from international conferences and other scientific exchanges to publication of guidelines and running networks) as well as powerful advocates and educators (with input into policy at European Union level and raising public awareness). The academic community is deeply involved, through medical and educational institutions, as are health authorities (e.g. the National Institute for Health and Clinical Excellence in the UK and Health Protection Scotland) and the pharmaceutical industry.

Country Studies

Case studies from various countries in Europe, and the US were presented. Several common themes emerged from the presentations. The denominators for many groups of people at risk of infection with hepatitis viruses are not known. Recommendations (for screening, vaccination, management and treatment) vary from country to country but are mostly not followed in practice. Ways need to be found for translating current knowledge into good clinical practice. In most countries, there was no co-ordinated screening (at national or regional level) or federal register of chronic infections, and access to screening and therapy is difficult, creating barriers to prevention and control. Several countries have surveillance systems that can be improved. In some countries screening programmes are in place but they have not been updated for some time or strengthened. In others there was no comprehensive strategy to identify infected prisoners, migrants and other marginalised groups. Reporting systems need improvement with integrated electronic forms and data collection. Interventions and recommendations often have not been evaluated and generally the impact of screening is difficult to assess. Management of viral hepatitis by both general practitioners and specialists together with networking and communication between hospitals, general practitioners and other relevant care providers were often inadequate. Patients receiving therapy often were not compliant with treatment regimens and considerable difficulties were experienced in following up infected people in certain risk groups. The costs of screening for hepatitis B are significant. The cost of chronic liver disease to national authorities is also rising as new diagnostic methods and expensive new treatments are introduced, and more cases of chronic infections are identified.

Interventions are not restricted to treatment. They include measures to change behaviour in order to limit the spread of viruses and to change behaviour related to alcohol consumption. Vaccination against hepatitis B is part of the national immunisation and occupational health programmes in nearly all European countries. Screening of risk groups is being done for HIV and hepatitis B and C virus infection markers in various centres, such as those for injecting drug users and people with sexually transmitted infections, as well as for pregnant women and blood donors. In many countries the costs of screening programmes are covered by state health insurance (for instance, mandatory insurance in the Russian Federation).

In Belgium, good criteria for reimbursement of costs of management and treatment were introduced in January 2010. Besides screening of blood donors and pregnant women, no structured screening is organised at the national or regional level, only opportunistic screening by general practitioners and specialists exists.

France has a network of hepatology reference centres and a national plan for hepatitis B and C for the period 2009–2012. Screening programmes that include campaigns aimed at the general public as well as health professionals are resulting in an increasing proportion of people becoming aware of their HCV or HBsAg seropositivity and showing some encouraging trends in HCV prevalence. The national health insurance scheme covers the costs of screening for HCV (and, imminently, HBV) and treatment of patients with chronic active liver disease or cirrhosis.

In Italy the categories of people to be screened for HBV and HCV are well defined, and follow-up and treatment strategies for both diseases

have been published. There is an active research community and a foundation to support and encourage research was established in 2009.

In the Netherlands, screening strategies have been regularly revised, most recently in the case of hepatitis B with pilot studies for Chinese and Turkish immigrants in three cities. Pilot projects for screening members of the general public for HCV were begun in 2007–2008 and a national hepatitis C campaign undertaken over five months in 2009–2010. Clinical guidelines for treatment of both hepatitis B and hepatitis C were issued in 2008, and the costs of treatment are covered by health insurance.

In the Russian Federation, screening programmes, mandated by federal regulations, are implemented for various groups, including people attending drug and alcohol abuse clinics, orphanages and military personnel (at hiring and annually thereafter). Reporting works well from health-care facilities up to federal level but less well for outpatient clinics, which are generally overloaded and understaffed. Although the costs of the screening programmes are covered by the State, only some of the costs of evaluation and follow-up are. Tests such as viral load measurement, genotyping, resistance profiles and, in some regions, liver biopsy have to be paid for by the individual. Several treatment programmes exist, including a Federal Target Programme (2007–2011) and six liver transplant centres.

In Scotland, detailed guidelines for testing for HCV infection were issued in 2007, and a costed action plan for diagnosis, treatment and care has been issued that contains defined objectives for 2011. Innovative approaches to encouraging screening are being introduced, with, for instance, promotion activities in mosques, pharmacies and harm-reduction settings. In the UK, the Advisory Group on Hepatitis has submitted for high-level review a report on case-finding for hepatitis B and C in minority populations with a series of recommendations with the responsibilities for implementing those recommendations clearly identified.

In the US, CDC has issued recommendations for the identification and public health management of persons with chronic HBV infection,[15] including the routine testing for HBsAg in populations with HBsAg prevalence of >2 %, people born in geographical regions with HBsAg prevalence of >2 %, men who have sex with men and injecting drug users. In 2001, CDC issued a national hepatitis C prevention strategy (see above under 'Treatment'), which includes education of health-care professionals and the general public, identification and testing of people at risk, preventive programmes, surveillance and research. Data show that the in-peak age prevalence for HCV is shifting in the US to older age groups, suggesting that younger cohorts in recent years are not being infected at the same rate as in earlier periods.

Issues and Needs

Screening programmes need careful preparation, clear objectives, careful design and management, with consideration of ethics and equity at all levels. Reaching some groups at risk is not easy. Screening migrants for viral hepatitis poses several challenges as the term migrant covers a range of people from asylum-seekers and refugees to people with long-term contracts, people from different socio-economic backgrounds and people from areas with different prevalence rates of viral hepatitis. When and where should they be screened? The possible political and ethical issues (e.g. the potential for discrimination) need consideration. Approaches to the various groups need specific tailoring and targeting.

One of several prerequisites for successful programmes for identification and management of patients with chronic hepatitis was a greater understanding of decision-making processes at political levels. Another requirement was co-ordination of surveillance, collection and collation of data, and analysis, all in the context of strong leadership. Furthermore, screening and testing programmes should be integrated into primary health-care and other programmes.

How can programmes and strategies be evaluated for effectiveness? More analyses should be done on the effectiveness of early screening plus treatment. In some countries, screening programmes have been defined in legislation, sometimes with specific targets indicated, although the value of setting goals in legislation was questioned. Not every European country has such legislation or even an action plan and a call was made for such countries to draft an action plan for prevention and control, including screening, especially for groups at risk.

Good-quality data on the extent of infection with hepatitis viruses and the full burden of disease and mortality due to liver disease including hepatocellular carcinoma (especially through registries) are badly needed, not only for clinical practice but also for informing policy-making and for applications in modelling exercises and economic evaluation. Greater efforts are needed to access information published in languages other than English and available only in governmental documents and other such sources – in numerous cases, national information is available (but not always readily accessible) in the national language. Reliance on selected sets for reviews may distort the conclusions drawn for policy-making.

There still exist wide gaps in knowledge about viral hepatitis, not just the general public but health-care workers, including physicians and policy-makers are poorly informed. The Institute of Medicine in the US recommended[2] that knowledge and awareness about chronic viral hepatitis should be improved among health-care providers, social-service workers and the public; surveillance for hepatitis B and hepatitis C should be upgraded; and there should be better integration of viral hepatitis services. The fact that numerous criteria and recommendations existed but were not put into practice needed to be rectified.

An extensive body of organisations, associations, charities, academic institutions and even governmental entities undertakes advocacy and health promotion. In recent years, several new patient organisations and advocacy groups have been created and produced striking results,[16] for instance, the Declaration of the European Parliament on Hepatitis C and the formulation of a "European orientation towards the better management of hepatitis B in Europe". Associations for patients have issued guidelines, created websites, and provided printed information, education and support. Issues remain about sustainable funding of such activities, co-ordination of the various bodies and actions, the respective roles of, and relations between, government, civil society and the private sector, ability to reach vulnerable and other at-risk groups, and finding innovative approaches.

Policies, including management of identified hepatitis patients, should be designed for the prevention and control of disease for special populations, in particular prisoners (including community programmes

for continuity of treatment) and migrants. Robust standardised screening methods should be designed, with ethical screening and follow-up of treatment.

The number of top-down decisions and mechanisms should be reduced in favour of patient-based organisations and community-based programmes. A proposal was made for a summary to be prepared for publication of what has been done and of approaches that have been successful and those that do not work.

Concluding Remarks

The Wilson and Jungner criteria for screening remain applicable for chronic viral hepatitides but their continued evolution and adaptation to new technologies and circumstances are desirable.

The following actions were identified as having a high priority:

- Standardise surveillance data and use a common electronic medium for collection of such standardised data.
- Collect good-quality, comparable prevalence data.
- Prepare to build on the adoption by the World Health Assembly of Resolution WHA63[18] on viral hepatitis and the steps it urges.
- Effect a transition from a list of recommendations to a managed programme with an action plan that guarantees assignment of responsibility, setting of priorities, adequate funding, necessary medical resources, monitoring and evaluation.
- Define the purpose of screening, recognising that the multiple benefits come at the price of several potential harms, and, in particular, identify infected subjects who can then enter treatment programmes and whose families may benefit from counselling and relevant prevention services (e.g. vaccination and healthy behaviour) and identify subjects who are not infected but are at risk and offer preventive interventions.
- Do not start screening programmes until preparations for the steps to follow are in place: patient management, treatment, access and feasibility.
- As there is not one-fits-all action plan, adapt any plan to the local epidemiological, infrastructure, defined target group and financial realities.

As in the case of HIV/AIDS, the high cost of existing antiviral drugs and therapy excludes millions of people from treatment of viral hepatitis. The Viral Hepatitis Prevention Board urges lower prices for appropriate medicines and increased financial support for programme implementation. ■

Annex Criteria for Screening[1]

1 – Wilson and Jungner 1968

1 The condition sought should be an important health problem.
2 There should be an accepted treatment for patients with recognised disease.
3 Facilities for diagnosis and treatment should be available.
4 There should be a recognisable 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.

2 – Synthesis of Emerging Criteria for Screening Proposed over the Past 40 Years

1 The screening programme should respond to a recognised need.
2 The objectives of screening should be defined at the outset.
3 There should be a defined target population.
4 There should be scientific evidence of screening programme effectiveness.
5 The programme should integrate education, testing, clinical services and programme management.
6 There should be quality assurance, with mechanisms to minimise potential risks of screening.
7 The programme should ensure informed choice, confidentiality and respect for autonomy.
8 The programme should promote equity and access to screening for the entire target population.
9 Programme evaluation should be planned from the outset.
10 The overall benefits of screening should outweigh the harm.

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