Community-based prevention of hepatitis-B-related liver cancer: Australian insights

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Problem Although most primary hepatocellular cancers (HCCs) are attributable to chronic viral hepatitis and largely preventable, such cancers remain a leading cause of cancer-related mortality wherever chronic hepatitis B is endemic.
Approach Many HCCs could be prevented by increasing awareness and knowledge of hepatitis B, optimizing the monitoring of chronic hepatitis B and using antiviral treatments – but there are gaps in the implementation of such strategies.
Local setting The "B Positive" programme, based in Sydney, Australia, is designed to improve hepatitis-B-related health outcomes among immigrants from countries with endemic hepatitis B. The programme offers information about disease screening, vaccination and treatment options, as well as optimized access to care.
Relevant changes The B Positive programme has been informed by economic modelling. The programme offers culturally tailored education on chronic hepatitis B to target communities and their health practitioners and regular follow-up through a population-based registry of cases.
Lessons learnt As the costs of screening for chronic hepatitis B and follow-up are relatively low and less than one in every four cases may require antiviral drugs, optimizing access to treatment seems an appropriate and cost-effective management option. The identification and accurate staging of cases and the judicious use of antiviral medications are predicated upon an informed and educated health workforce. As establishing community trust is a lengthy process, delaying the implementation of programmes against chronic hepatitis B until antiviral drugs become cheaper is unwarranted.

Abstracts in عربي, 中文, Français, Русский and Español at the end of each article.

Problem

In May 2010, the Sixty-third World Health Assembly adopted a resolution calling for a comprehensive approach to the prevention and control of all forms of viral hepatitis – which kills over 1 million people each year. Human infection with hepatitis B virus is highly endemic in many Asian countries.[1] Such infection is generally acquired early in life and leads to lifelong chronic hepatitis B that has life-threatening complications – such as cirrhosis and hepatocellular cancers (HCCs) – in 25 to 40% of cases.[2–4]

Over 200 000 Australians are estimated to have chronic hepatitis B[5] and liver cancer is now the seventh most common cause of cancer-related death among Australian men.[6] In Australia, despite these observations, there is no systematic screening for chronic hepatitis B, even among at-risk groups, and many cases are only detected late, after the onset of complications. In New South Wales – Australia's most populous state – 46% of HCCs occur among immigrants, particularly those born in countries with endemic hepatitis B.[7] Compared with individuals born in Australia, immigrants from China, Indonesia, the Republic of Korea or Viet Nam have a six- to 12-fold greater risk of developing HCCs.[7]

In addition to vaccination, the public health response to hepatitis B requires screening for the chronic form of the disease, improved access to care and support and improved provider training, education and disease surveillance. To address these challenges as they apply to New South Wales, a local cancer charity – Cancer Council New South Wales – planned and implemented a multi-pronged intervention designed to reduce the incidence of hepatitis-B-related liver cancer among the state's high-risk migrant communities. The main pillars of this intervention, known as the "B Positive" programme, comprise economic modelling to ascertain the programme's costs and benefits, educational outreach for both the at-risk migrant communities and their primary-care providers, and establishment of a chronic hepatitis B registry. The registry has been developed to improve not only our understanding of the epidemiology of chronic hepatitis B, but also the follow-up of participants in the B Positive programme. The programme's key activities and some of the lessons learnt as a result of the programme are summarized below.

Approach

The programme was approved by the Institutional Ethics Committee of the Sydney South West Area Health Service and developed in three phases. In Phase 1, economic modelling was used to investigate the feasibility of the programme. The target population was defined, a screening and treatment algorithm for chronic hepatitis B was developed and the types of data to be recorded in the disease registry were determined.

The programme's target population consists of residents of south-west Sydney born in countries with high prevalences of hepatitis B and who receive primary health care from local general practitioners. However, the programme has also been made available to all local residents with confirmed diagnoses of chronic hepatitis B – irrespective of their countries of birth and modes of disease acquisition. Cases of chronic hepatitis B are identified by general practitioners through medical record checks and opportunistic screening of at-risk patients. Each case is then followed up twice a year. Blood

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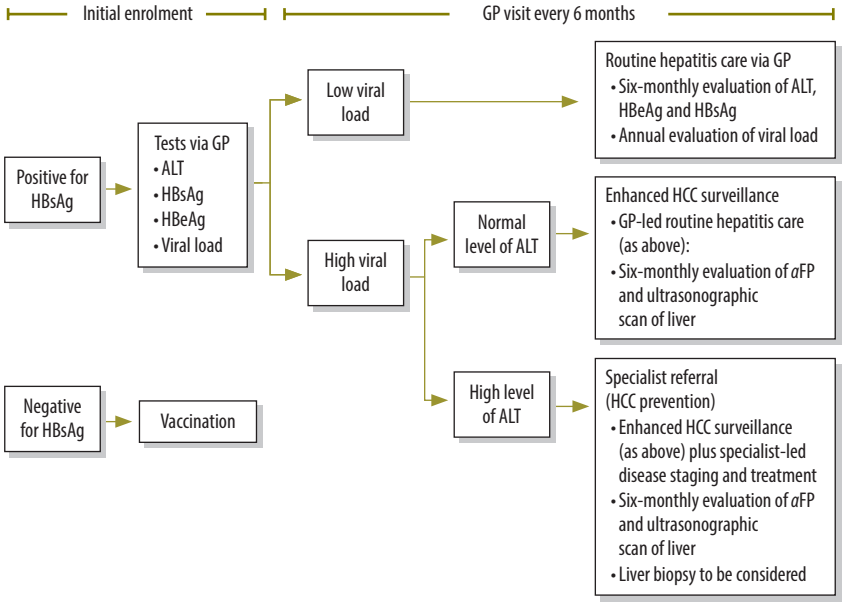
levels of alanine aminotransferase (ALT) and alpha-fetoprotein are determined at each follow-up visit, while levels of hepatitis B virus DNA are measured annually. The programme's management algorithm is used to categorize the cases as being at high, intermediate or low risk for HCC (Fig. 1). "Low-risk" cases have low viral loads and "normal" levels of ALT; "high-risk" cases have high values for both viral load and ALT; and the cases at "intermediate" risk" have high viral loads but normal levels of ALT. General practitioners are encouraged to refer the high-risk cases for specialist assessment and to continue to follow up the other cases.[8]

In Phase 2, the programme's acceptability to key stakeholders was ascertained. In addition, opportunities for the education of local general practitioners and target communities about hepatitis B testing, prevention and treatment were provided.

In Phase 3 of the programme's development, an extensive programme redesign was implemented based on consultation with the relevant stakeholders. The monitoring and evaluation tools were refined and the data collected in the case registry were compared against the assumptions made in the economic modelling.

Fig. 1. **The B Positive programme's management algorithm for cases of chronic hepatitis B, Australia, 2007–2014**



αFP, alpha-fetoprotein; ALT, alanine aminotransferase; GP, general practitioner; HBeAg, hepatitis B e antigen; HBsAg, hepatitis B surface antigen; HCC, hepatocellular cancer.
Notes: Levels of ALT were categorized as high when they were at least two-fold higher than the upper limit of the "normal" range. Viral loads were categorized as high when the amount of hepatitis B virus in the serum exceeded 2000 international units per ml.

Local setting

Phase 1 commenced in 2007 with a literature review and a collation of clinical and epidemiological data on which the economic modelling could be based. A Markov economic model was then developed to compare three management strategies: enhanced surveillance for HCC; HCC prevention – in which enhanced HCC surveillance was combined with the optimized management of chronic hepatitis B; and maintenance of the status quo – which was characterized by low levels of treatment uptake for chronic hepatitis B and only opportunistic screening for HCC. For each modelled strategy, case stratification and management were based on age, viral load and ALT level. We modelled a hypothetical cohort of 10 000 Asian-born adults with chronic hepatitis B; all were aged 35 years at enrolment and were followed up for 50 years. The cost of HCC cases, the number of deaths averted and the number of quality-adjusted life years gained over the entire follow-up period were estimated for each strategy. We adopted a health-care funder perspective and discounted all future costs and health outcomes by 5% per year.

Only one of the three strategies modelled – HCC prevention – appeared to be cost-effective and able to deliver substantial health benefits. In the model, this strategy reduced cases of cirrhosis, HCC diagnoses and hepatitis-B-related deaths over the 50 years of follow-up by 52%, 47% and 56%, respectively, at an estimated cost of 12 956 Australian dollars for each quality-adjusted life year gained.[8] As a consequence of this modelling work, the B Positive programme used the HCC-prevention approach.

The programme has only led to a slight increase in the workloads of the general practitioners who serve the target communities. It is expected, however, to increase the local demand for specialist services needed in the management of HCC,[9] even though most cases of chronic hepatitis B enrolled in the programme can be managed at the primary-care level. Only 8 to 25% of cases – the exact proportion depending on the guidelines that are followed for treatment initiation – require antiviral treatment.[10] However, in the economic modelling, the cost of antiviral drugs accounted for most (54–76%) of the estimated total cost of the programme.[10] The economic modelling showed that the estimated costs attributed to surveillance for chronic hepatitis B (4–30% of the programme's total cost) and HCC screening and surveillance (5–9%) were relatively small.[10]

All local general practitioners were invited to free "continuing medical education" seminars on hepatitis B and provided with tailored educational resources. A quarter of the local general practitioners attended at least one seminar in the 18 months following the programme's launch. Approximately 2500 members of the target communities attended at least one of the hepatitis-B-themed events run by the programme, with educational talks delivered in Cantonese, English, Mandarin and Vietnamese. At the same events, fact sheets on hepatitis B – in Arabic, Chinese, English, Indonesian, Korean and Vietnamese – were also distributed. Low programme uptake in the first 18 months – when only six general practitioners and 32 patients were enrolled in the case registry – prompted a wide stakeholder consultation to ascertain the reasons for the low enrolment and to seek suggestions for the redesign and improvement of the programme.

Semi-structured interviews with 88% of the general practitioners who attended the seminars helped to identify some options to improve programme enrolments. The interviewees suggested reducing the number of data fields in the registry, offering enrolment via the World Wide Web and providing administrative support and a small financial incentive to the primary-care practices of participating general practitioners. Other suggestions for improving the programme came from community health workers and Vietnamese- and Cantonese-speaking residents of south-western Sydney.

The B Positive programme was re-launched in 2011, with an improved patient reminder and recall system, enhanced practitioner support and the introduction of incentive payments for general practitioners and a nurse educator to facilitate case identification and strengthen linkages with the tertiary sector. The minimum number of data fields to be completed for each case recorded in the case registry was reduced from 36 to 14 and provisions were made for online enrolment. The algorithm used for the management of chronic hepatitis B was simplified, in line with recommendations of the Gastroenterological Society of Australia.[11] The continuing medical education scheme for general practitioners has recently been expanded and seminars are now offered more frequently, with funding and additional resources provided by the Australasian Society for HIV Medicine.

The programme's relaunch also entailed revisions to our interventions for improving community engagement. We consulted widely to ensure that our community-level educational activities were culturally sensitive and adequately tailored to the target communities. We also established collaborations with key community-based organizations, local councils and schools. Messages designed to improve screening for hepatitis B are now widely disseminated at community meetings, festivals and fairs and marketed through "ethnic" newspapers, newsletters and radio programmes. Differential messaging is used for specific audiences – such as students attending English-language classes, school students, the elderly and recently arrived migrants – and we provide education on hepatitis B in an increasing number of languages, including Assyrian, Cambodian, Khmer and Laotian. New hepatitis-related resources have been developed, tested and translated, including a travelling hepatitis library, posters detailing hepatitis myths and misconceptions and a cartoon video. With the support and collaboration of local immigrants from Viet Nam, we produced a soap-opera-style film in Vietnamese. The actors in this film were local residents and important messages about hepatitis B were woven into the storyline. Although this film has only been shown in two cinemas, it is envisaged that it will be distributed more widely and, perhaps, broadcast on at least one local television channel. Local high-school students learn about hepatitis B as they are taught about film animation and they convey messages about hepatitis B prevention to their peers, families and communities.

Over the last 12 months, the number of individuals enrolled in the hepatitis registry has increased substantially. At the time of writing, more than 1200 cases – approximately 15% of the entire target population – are enrolled and being followed up by more than 50 local general practitioners.

The recent effectiveness of the B Positive programme was highlighted by the results of a nationwide survey on the uptake of treatment by those with cases of chronic hepatitis B in Australia. The percentage of such cases in south-west Sydney who were receiving treatment (7%) was found to be higher than that in any other surveyed area and double the nationalaverage.[12]

Box 1. **Summary of main lessons learnt**

- As the costs of screening for chronic hepatitis B and follow-up are relatively low and less than one in every four cases may require antiviral drugs, the facilitation of treatment access is a rational, appropriate and cost-effective option in the management of the disease.
- The identification and accurate staging of cases of chronic hepatitis B and the judicious use of antiviral medications are predicated upon an informed and educated health workforce.
- Programmes for the population-based management of chronic hepatitis B should not be delayed until antiviral drugs become cheaper, as establishing community trust in such programmes is likely to be a lengthy and involved process.

Lessons learnt

The main lessons learnt from the B Positive programme (Box 1) indicate that a public health intervention to tackle chronic hepatitis B and its complications can be feasible, acceptable to the target communities and effectively delivered by trained general practitioners. The initial problem of low programme uptake was corrected by a wide consultation and a substantial redesign of the programme – highlighting the critical role of ongoing monitoring and stakeholder consultations in the success of this and similar programmes.

The interventions implemented in the B Positive programme are similar to those followed in similar large-scale, community-based programmes in New Zealand[13] and the United States of America.[14,15] The B Positive programme has been seeking to reduce hepatitis-B-related health disparities in migrant populations through community-based screening, linkage to care and increasing community-level awareness of hepatitis B and participation in disease surveillance. Meaningful community engagement has played a critical role in the programme's success. Without such engagement and adequate input from the "recipient" communities, programme uptake would probably have been too poor to have had a significant impact on any hepatitis-B-related health problem. Whitehead identified a spectrum of community-based interventions – ranging from those where the community is the driver and funding agent to those controlled by external agencies – in which the establishment of equitable and mutually rewarding partnerships represented the "ideal" scenario.[16] The original B Positive programme was launched with limited community involvement, with the target communities being the programme's recipients but having little opportunity to contribute to the programme's design. Only after the programme's goals were clearly communicated and the scope of community consultation was widened did the programme's aims become relevant to the target communities – resulting in increased programme uptake.

As far as we are aware, B Positive is the only population-based programme for chronic hepatitis B mitigation guided by economic modelling and using a case registry to support patient follow-up and linkage to treatment. In

the absence of systematic surveillance for chronic hepatitis B in Australia, data collected in our case registry are helping to characterize the clinical features, staging and treatment needs of people with the disease.

In chronic hepatitis B, the high cost of antiviral therapy currently makes the treatment of all cases identified in population-based screenings unaffordable in many countries. However, it appears that only a relatively small proportion of those diagnosed with the disease require antiviral treatment and that cases needing antiviral therapy can be effectively identified using a relatively simple screening and follow-up algorithm. The data collected in the B Positive programme indicate that, among high-risk groups, such a system can be fairly readily implemented at primary-care level, at an acceptable cost. We envisage that community-based screening for chronic hepatitis B and community-based treatment will soon become a reality, even in resource-limited settings.

As the building of adequate community trust requires careful planning and much lead time, it appears unreasonable to defer public health action against chronic hepatitis B until antiviral treatment becomes less costly. Today's challenge is to move beyond demonstration projects to full-scale implementation. This is reminiscent of the state of affairs seen in the management of human immunodeficiency virus (HIV) a decade ago, as summarized by Moatti et al.: "Scaling up access to antiretroviral drugs (ARVs) for HIV-infected adults and children in developing countries can no longer be refused for medical or economic reasons, or on the grounds of inequality, lack of infrastructure, risk of viral resistance or alternative priorities. Access to ARVs is an appropriate, rational and cost-effective investment choice in developing countries."[17] ■

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ملخص

التوقي المجتمعي لسرطان الكبد ذي الصلة بالتهاب الكبد "باء": رؤى أسترالية

المشكلة رغم أن معظم السرطانات الكبدية الخلوية الأولية (HCCs) تعزى إلى التهاب الكبد الفيروسي المزمن ويمكن توقيها على نطاق واسع، إلا أن هذه السرطانات تظل سبباً رئيسياً للوفيات ذات الصلة بالسرطان في مناطق توطن التهاب الكبد "باء" المزمن.

الأسلوب يمكن توقي العديد من السرطانات الكبدية الخلوية عن طريق إذكاء الوعي والمعرفة بالتهاب الكبد "باء" وتحقيق الاستفادة القصوى من رصد التهاب الكبد "باء" المزمن واستخدام العلاجات المضادة للفيروسات– ولكن ثمة ثغرات في تنفيذ هذه الاستراتيجيات.

المواقع المحلية تم تصميم برنامج "بي بوزيتيف" في سيدني بأستراليا بغية تحسين الحصائل الصحية ذات الصلة بالالتهاب الكبدي "باء" بين المهاجرين من البلدان التي يتوطن بها الالتهاب الكبدي "باء". ويقدم البرنامج معلومات عن تحري المرض وتطعيمه وخيارات علاجه بالإضافة إلى الوصول إلى الرعاية على الوجه الأمثل.

التغيّرات ذات الصلة تم وضع برنامج "بي بوزيتيف" في ضوء معلومات النمذجة الاقتصادية. ويقدم البرنامج تثقيفاً موجهاً لمختلف الثقافات حول الالتهاب الكبدي "باء" المزمن بغية استهداف المجتمعات المحلية والممارسين الصحيين التابعين لها والمتابعة المنتظمة من خلال السجل السكاني للحالات.

الدروس المستفادة نظراً للانخفاض النسبي في تكاليف تحري الالتهاب الكبدي "باء" المزمن ومتابعته واحتمال احتياج ما يقل عن حالة واحدة من كل أربع حالات مرضية إلى الأدوية المضادة للفيروسات، يبدو أن تحقيق الاستفادة القصوى من الوصول إلى العلاج أحد خيارات التدبير المناسبة وذات التكلفة الفعالة. ويعتمد تحديد الحالات وتصنيف مراحلها بدقة واستخدام الأدوية المضادة للفيروسات بحكمة على القوى العاملة الصحية المستنيرة والمثقفة. ولما كان بناء الثقة المجتمعية عملية طويلة، يصبح إرجاء تنفيذ البرامج المضادة للالتهاب الكبدي "باء" المزمن إلى أن تصبح الأدوية المضادة للفيروسات أرخص إجراءً لا مبرر له.

摘要

基于社区的乙肝相关肝癌预防：澳大利亚的启示

问题 尽管大多数原发性肝癌（HCC）可归因于慢性病毒性肝炎，并且很大程度上可以预防，但是只要是慢性乙型肝炎流行的地方，这种癌症就依然是癌症相关死亡的头号原因。

方法 许多 HCC 可通过增加乙肝的意识和知识、优化监测慢性乙型肝炎和使用抗病毒治疗来预防，但是这种策略在实施中存在差距。

当地状况 在澳大利亚悉尼推行的"B Positive"计划被设计用来改善来自乙肝流行国家移民人群中乙肝相关健康结局。该计划提供疾病筛查、疫苗接种和治疗方案的相关信息，以及经过优化的就医途径进行优化。

相关变化 B Positive 计划汲取经济建模的结果。该项目

向目标社区及其健康从业者提供在文化上量身定制的慢性乙型肝炎教育，并通过以人群为基础的病例登记进行定期随访。

经验教训 筛查慢性乙型肝炎和后续随访的成本相对较低，每四例病例中不到一个病例可能需要抗病毒药物，优化治疗途径似乎是适当且具有成本效益的管理方案。有了了解情况并受到良好教育的卫生工作队伍，病例的识别和准确分期以及合理使用抗病毒药物水到渠成。建立社会信任是一个漫长的过程，没有理由将针对慢性乙型肝炎的计划拖下去，空等抗病毒药物变得便宜。

Résumé

Mesures de prévention communautaires du cancer du foie lié au virus de l'hépatite B: aperçu australien

Problème Bien que la majorité des cancers hépatocellulaires primaires (CHC) soient attribuables aux hépatites virales chroniques et qu'ils puissent être évités en grande partie, ces cancers restent une des principales causes de mortalité liée au cancer partout où l'hépatite B chronique est endémique.

Approche De nombreux CHC pourraient être évités par une sensibilisation et une connaissance accrues de l'hépatite B, l'optimisation du suivi des hépatites B chroniques et l'utilisation de traitements antiviraux – mais il existe des lacunes dans la mise en œuvre de ces stratégies.

Environnement local Le programme «B Positive», basé à Sydney en Australie, est conçu pour améliorer l'état de santé lié à l'hépatite B chez les immigrants venus de pays où l'hépatite B est endémique. Le programme offre des informations sur le dépistage de la maladie, la vaccination et les options de traitement, ainsi qu'un accès optimisé aux soins.

Changements significatifs Le programme «B Positive» a été élaboré par modélisation économique. Le programme offre un enseignement sur l'hépatite B chronique culturellement adapté pour cibler les communautés et leurs professionnels de santé, et un suivi régulier via un registre de cas basé sur la population.

Leçons tirées Puisque les coûts de dépistage et de suivi de l'hépatite B chronique sont relativement faibles et que moins d'un malade sur quatre peut avoir besoin de médicaments antiviraux, l'optimisation de l'accès au traitement semble être une option de gestion appropriée et rentable. L'identification des cas, leur triage précis et l'utilisation judicieuse des médicaments antiviraux s'appuient sur un effectif de santé informé et éduqué. L'établissement de liens de confiance avec les communautés est un processus long. Par conséquent, il n'est pas justifié de retarder la mise en œuvre de programmes de lutte contre l'hépatite B chronique jusqu'à ce que les médicaments antiviraux deviennent plus abordables.

Резюме

Методы профилактики связанного с гепатитом B рака печени среди общин: на основе опыта Австралии

Проблема Несмотря на то, что большинство случаев первичного гепатоцеллюлярного рака (ГЦР) вызываются хроническим вирусным гепатитом и приемущественно предотвращаются, такой рак остается основной причиной смертности во всех районах, где хронический гепатит B является эндемическим заболеванием.

Подход Многие случаи ГЦР можно было бы предотвратить путем повышения осведомленности о гепатите B, оптимизации мониторинга хронического гепатита B и применения противовирусного лечения, но для реализации таких стратегий имеются значительные трудности.

Местные условия Программа "B Positive", принятая в Сиднее (Австралия), направлена на улучшение результатов лечения гепатита B среди иммигрантов из стран, где гепатит B является эндемическим заболеванием. Программа предоставляет информацию о методах скрининга заболевания, вакцинации и вариантах лечения, а также оптимизированный доступ к медицинской помощи.

Осуществленные перемены Программа "B Positive" была разработана на основе экономического моделирования. В рамках программы проводится культурно-ориентированное образование по вопросам хронического гепатита B как среди целевых сообществ, так и их практикующих врачей, а также регулярный контроль через популяционный реестр случаев заболевания.

Выводы Поскольку расходы на обследование на наличие гепатита B и на последующий контроль являются относительно низкими, а противовирусные препараты могут потребоваться в менее чем одном из каждых четырех случаев заболевания, то оптимизация доступа к лечению представляется целесообразной и экономически эффективной мерой. Идентификация и точное определение стадии заболевания, а также правильное использование противовирусных препаратов зависят от информированности и образованности медицинских работников. Поскольку учреждение общественного фонда является длительным процессом, затягивание выполнения программ по борьбе с хроническим гепатитом B до тех пор, пока противовирусные препараты не подешевеют, является необоснованным.

Resumen

Prevención con base comunitaria del cáncer de hígado relacionado con la hepatitis B: experiencia australiana

Situación Aunque la mayoría de carcinomas hepatocelulares (CHC) primarios se atribuyen a la hepatitis vírica crónica y son evitables en gran parte, ese tipo de cánceres sigue siendo una de las principales causas de la mortalidad relacionada con el cáncer en aquellos lugares en los que la hepatitis B crónica es endémica.

Enfoque Muchos CHC podrían evitarse con un aumento de la concienciación y el conocimiento sobre la hepatitis B, la optimización de la supervisión de la hepatitis B crónica y el uso de tratamientos antivíricos, pero existen lagunas en la puesta en práctica de estas estrategias.

Marco regional El programa "B Positive", con sede en Sídney, Australia, se ha diseñado para mejorar los resultados sanitarios relacionados con la hepatitis B entre los inmigrantes procedentes de países en los que la hepatitis B es endémica, y ofrece información acerca de la detección de la enfermedad, la vacunación y las opciones de tratamiento, así como un acceso optimizado a la atención.

Cambios importantes El programa "B Positive" se fundamenta en modelos económicos y ofrece educación culturalmente adaptada sobre la hepatitis B crónica para llegar a las comunidades y sus médicos, y realizar un seguimiento regular a través de un registro poblacional de casos.

Lecciones aprendidas Puesto que los costes de detección y seguimiento de la hepatitis B son relativamente bajos y menos de uno de cada cuatro casos requiere medicamentos antivíricos, la optimización del acceso al tratamiento parece ser una opción de gestión adecuada y rentable. La identificación y clasificación correcta de los casos y el uso acertado de los medicamentos antivíricos se apoya en una personal sanitario informado y formado. El establecimiento de la confianza de la comunidad es un proceso muy largo, por lo que retrasar la ejecución de programas contra la hepatitis B crónica hasta que los medicamentos antivíricos se abaraten no tiene justificación alguna.

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