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Recommendation 12 for Policy-makers on Cancer-causing infections and related interventions

- **Strengthen hepatitis B virus (HBV) vaccination programmes to maximize their effect on reducing the prevalence of HBV infection. This can be achieved, according to the epidemiological burden, by ensuring that:**
  - All children receive their first dose of HBV vaccine as soon as possible after birth.
  - HBV vaccination programmes are resourced to reach the 95% coverage target.
  - Catch-up vaccinations are offered to people at increased risk of acquiring HBV infection.
- **Strengthen human papilloma virus (HPV) vaccination programmes to maximize their impact by ensuring that:**
  - The vaccine is given at the youngest age possible to the priority target age group (between 9-14 years) as decided at the national level.
  - HPV vaccination programmes are resourced to reach the 90% coverage target for girls and boys.
  - Catch-up vaccination opportunities are provided to people older than the priority target age but at least until age 18 years, when feasible.
  - Individuals at high risk of HPV infection, including immunocompromised individuals and people who experienced sexual abuse, are considered for vaccination against HPV as a priority. Individuals known to be immunocompromised or infected with human immunodeficiency virus (HIV) should receive at least two HPV vaccine doses and, where possible, three doses.
- **Strengthen the importance of HBV and HPV vaccination as cancer prevention tools. This includes identifying behavioural determinants of vaccine uptake, addressing obstacles to vaccination, and implementing awareness-raising campaigns to increase confidence in these vaccines among health professionals, teachers, parents, and (pre-)adolescents. Monitor progress in vaccination programmes against HBV and HPV in a timely manner.**
- **Introduce sustainable initiatives of testing and treating:**
  - Adopt policies facilitating the offer of an affordable, ideally free of charge, test for HBV, hepatitis C virus (HCV), HIV and *Helicobacter pylori* (*H. pylori*) to adults in low-threshold settings using a non-stigmatizing approach.
  - Treat individuals with confirmed HCV, HIV or *H. pylori* infection as early as possible. For HBV, treatment should be provided to selected individuals, according to the clinical guidelines.
  - Offer pregnant women HBV and HIV testing, and consider offering also HCV testing based on individual risk assessment.
  - For HIV, the offer of testing should prioritize individuals with HIV indicator conditions and people at increased risk of sexual acquisition of HIV or exposure to blood and blood products.
  - Develop and coordinate public health awareness campaigns related to all infections that cause cancer and interventions that avoid their acquisition or progression to disease.
  - Monitor progress in test-and-treat strategies in the population, including low-literacy and vulnerable groups.

Executive summary

Five infectious agents – four viruses HPV, HBV, HCV, and HIV) and one bacterium (*H. pylori*) – are responsible for 5% of cancer incidence in the European Union (EU). Of the most frequent types of cancer associated with these infectious agents, HPV-induced cervical cancer is the only one for which organized cancer screening programs are widely available in the EU.

This policy brief describes international policies and guidelines that support policy-makers and other stakeholders to implement the European Code Against Cancer, 5th edition (ECAC5) policy recommendation on vaccinations to address the cancer burden caused by HBV and HPV infections and test-and-treat strategies to address the cancer burden caused by HBV, HCV, HIV, and *H. pylori* infections.

Vaccination for HBV and HPV

Almost all EU Member States have implemented a national policy for universal HBV vaccination, including antenatal screening combined with new-born vaccination. A safe and effective vaccine against HBV has been available since the early 1980s. HBV vaccinations prevents HBV infection and, thus, HBV-associated liver diseases and liver cancer. Newborns and young children are at high risk of developing chronic HBV if infected at birth or in early childhood.

Safe and highly effective vaccines against HPV have been licenced since 2006 in the EU and can prevent new HPV infection, associated precancerous lesions, and invasive cancers in women and men. The 9-valent vaccine is used in most EU Member States. Current HPV vaccines have no therapeutic effect, and therefore the efficacy of HPV vaccination is highest when the vaccine is given at a young age (i.e. before exposure to HPV). By 2024, all EU Member States had introduced HPV vaccination girls and boys. In girls, HPV vaccination coverage in 2023 was above 90% in Denmark, Sweden, and Portugal, less than 50% in five EU countries and not reported in two other countries. A reduction in the incidence of cervical cancer has already been observed among young women in a few EU Member States where HPV vaccine coverage is high and where high-quality cancer and vaccination registries exist to monitor cancer trends.

HPV vaccination is most effective when high levels of coverage in women are reached at the youngest possible age. This also generates strong herd protection, which means that reducing the circulation of the virus protects individuals without the vaccine. Vaccinating both girls and boys generates a strong herd protection against HPV infection in women, in addition to providing direct protection against HPV-related cancer in men.

Test-and-treat programmes

All EU Member States screen blood donors for HBV, HCV and HIV infection and pregnant women for HBV infection, while most EU Member States also screen pregnant women for HIV. Data on coverage of these programmes are limited. Diagnostic tests, antiviral drugs and antibiotics are available in all EU Member States, but testing has been primarily risk-based, or directed at symptomatic individuals with limited success. No organized national screening programmes of testing and treating of HBV, HCV, HIV or *H. pylori* are in place in the EU. Expanding testing and treatment in different healthcare and community settings in relatively low-prevalence countries could improve coverage and cost-effectiveness, while also reducing stigma. Testing could also be offered when patients are already having a blood test for other reasons. EU-level guidance exists for three testing strategies that can be implemented within existing healthcare settings in the EU to enhance coverage and diagnosis: (1) population prevalence-based testing, (2) birth-cohort testing, and (3) indicator condition-guided HIV testing. Current treatments can cure HCV and *H. pylori* infections and prevent clinical progression and transmission of HBV and HIV infections. This means that testing and treating for these infections can decrease the cancer burden.

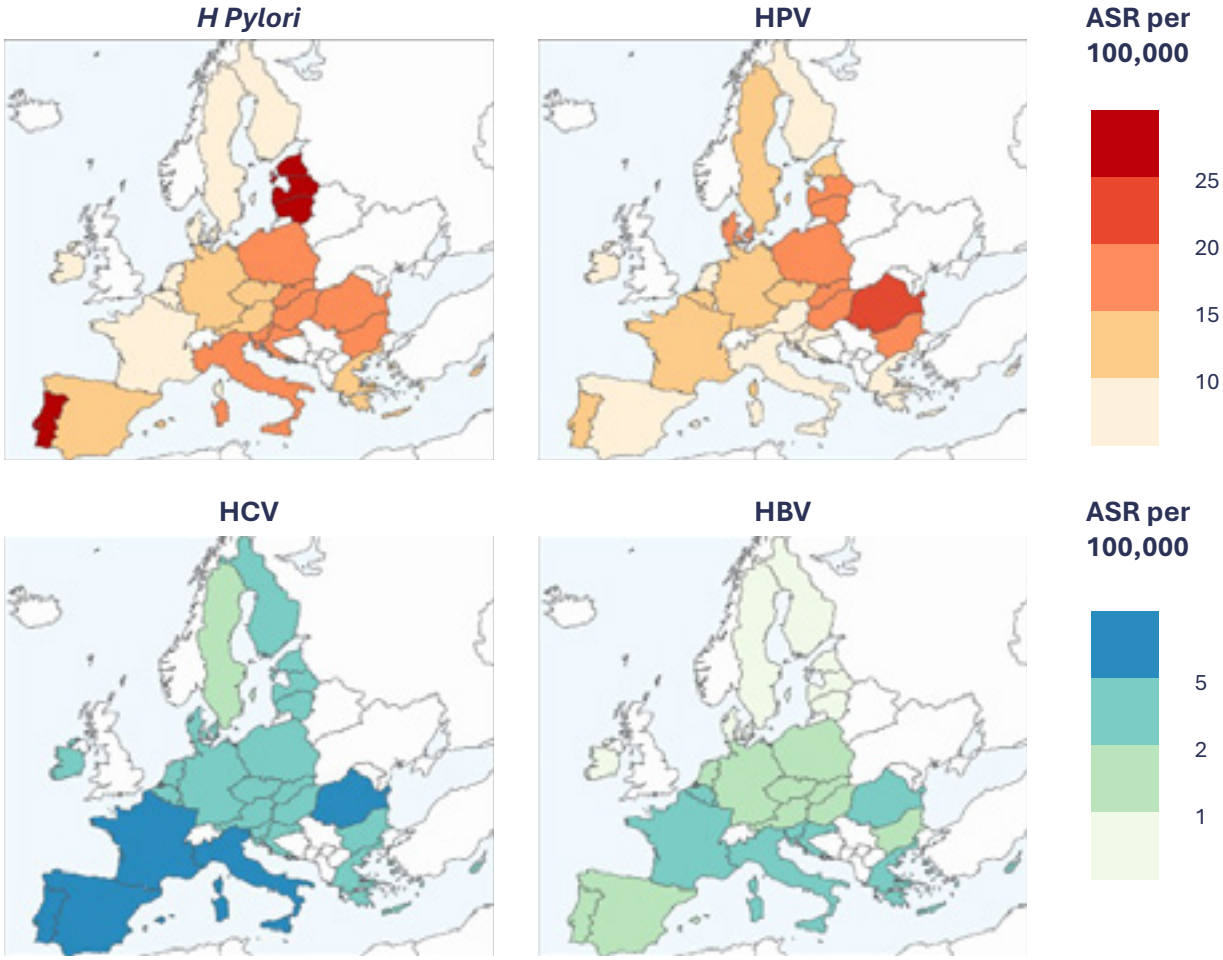
Testing and treatment programmes for these infections should be based upon locally developed protocols with practical factors, including: **When** (frequency and timing of the service); **Where** (location of service and mobilization); **Who** is providing service (health workers, peers, or self-testing); and **What** should be included in the package of services. Good participation in population-based interventions, especially HCV testing in the EU and elsewhere (such as the United Kingdom, Spain, the USA and Australia) indicates that testing for HBV, HCV, and HIV is acceptable and can disclose infections that were not known or had not been treated.

The prevalence for *H. pylori* infection in the EU is very high (approximately 40%) and testing and treatment has been carried out on a relatively large scale in nearly all EU Member States using urea breath test or faecal samples.

Several EU Member States have developed programmes of testing and treatment for HBV and HCV infections (to prevent liver cancer), HIV infection (to prevent a range of cancers increased by immunosuppression), and *H. pylori* infection (to prevent stomach cancer). Programmes initially targeted populations at high-risk of infection but the focus is moving to the general population (as exemplified in studies from Spain and the UK). In addition, there have been substantial improvements in the efficacy, safety and affordability of diagnostic tests and treatments for these infections, especially for HCV.

To apply the ECAC5 recommendation, diagnostic and treatment services will have to be strengthened. Although an infection can be diagnosed in various primary-care settings, specialized centre may be needed for treatment and follow-up of individuals with infections. A sudden overload of national health system can, however, be avoided by gradually upscaling the interventions as done in the past for the introduction of other cancer screening programmes. The introduction of testing and treatment may start with a region and/or (as done in the United States) by age-cohorts. Finally, awareness of the strong link between certain (chronic) infections and cancer risk in the general population, health workers and policy-makers should be increased. Efforts should focus on the South and East of the EU where the incidence rates of infection-associated cancers are highest.

In conclusion, ECAC5 proposes making preventive interventions against cancer-associated infections the default option in the general population, facilitating healthier choices for individuals across EU countries.



Source: Plummer et al. (2025)

Figure 1: Age-standardized incidence rate (ASR) of infection-attributable cancer in the EU, by infection and country
This figure shows the age-standardized incidence rate (ASR) of cancer attributable to *H. Pylori*, HPV, HBV, and HCV among men and women. Overall, approximately 144.000 cancer cases of all cancer cases in the EU in 2022 can be attributed to five infectious agents, i.e., about 5% of all cancer cases. *H. pylori* and HPV were had the most significant contribution, followed by HCV and HBV. ASR attributable to HIV are not estimated separately as the virus typically acts in combination with the other carcinogenic viruses.

Monitoring progress in the reduction of infection-associated cancers

Monitoring coverage: EU-wide monitoring of vaccination coverage, as well as testing and treatment of cancer-causing infections is needed to implement the ECAC5 recommendation. Investment in reporting systems, such as interactive dashboards with regional- and communal-level data, can generate highly detailed data to inform strategies to improve coverage and other key performance indicators.

Record Linkage: Investments in linkages between vaccination registries and screening and cancer registries can enhance impact measurement and boost vaccination efforts. Improving legal frameworks for data-sharing arrangements or federated analyses to facilitate this linkage is essential in the EU.

Monitoring the feasibility of test-and-treat strategies for cancer-associated infections and defining key performance indicators are essential to estimate the cost–effectiveness of interventions and to determine whether to scale up these strategies. Such monitoring requires a data system to collect, manage, and securely store data.

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Key policy actions to strengthen HBV and HPV vaccination programmes

To effectively enhance HBV and HPV vaccination programmes for cancer prevention, the following steps should be taken:

- Expand vaccination programmes, incorporating HBV and HPV vaccines into national immunization efforts, ensuring that vaccines are free of charge or fully reimbursed, especially for vulnerable groups.
- Integrate vaccination into cancer prevention strategies by promoting integrated health communication and operational support within broader prevention programmes.
- Increase vaccine uptake by providing vaccines free of charge and carrying out awareness-raising campaigns on safety and importance of HBV and HPV vaccination.
- Monitor vaccine coverage in the target population and fight against misinformation.

For HBV vaccination, it should be ensured that:

- All children receive their first dose of HBV vaccine as soon as possible after birth. The optimal schedule includes a birth dose given within 24 hours after birth, followed by 2 or 3 doses to complete the primary series in the first year of life.
- HBV vaccination programmes are resourced to reach: 95% vaccination coverage (third dose) in children, 95% of new-born babies receiving the HBV birth-dose vaccination within 24 hours of birth, and 95% of pregnant women screened for hepatitis B surface antigen.
- Catch-up vaccination opportunities are provided of other groups, including offering vaccines to unvaccinated adults at increased risk of acquiring HBV infection, for example, health-care professionals, people who inject drugs, and migrants from areas with high HBV rates.

For HPV vaccination, it should be ensured that:

- The vaccine is given at the youngest age possible recommended in their country, prioritizing the target age group of 9–14 years in both sexes as effectiveness in prevention of HPV-related cancers diminishes rapidly with increasing age at vaccination. School-based programmes tend to have highest coverage.
- HPV programmes are resourced to reach the 90% coverage target for girls and boys and, on account of the relative novelty of the vaccine, must include communication strategies to maintain or increase confidence in the HPV vaccine among parents, adolescents, and other stakeholders. Programmes should be responsive to any safety-related events or mistrust in vaccination and prepare a crisis communication strategy and budget to deploy the strategy.
- Catch-up vaccination opportunities are provided to older women until at least age 18, when feasible. Providing catch-up vaccination in older age groups is not a replacement for achieving high coverage in early childhood but rather offers additional value by potentially accelerating the reduction in the incidence of HPV-related cancers and promoting equity by reaching groups that were previously missed.
- High risk individuals including immunocompromised and individuals living with HIV as well as those who have experienced sexual abuse as priority groups. They should be vaccinated against HPV as soon as their status is known.

Risk of cancer

HBV

- Chronic HBV is usually asymptomatic (has no symptoms) but may progress to cirrhosis and, subsequently, liver cancer in people who have been infected for more than 20 years.
- An infection contracted during childhood is the most likely to develop into a long-lasting infection (chronic infection) and progress to liver cancer.

HPV

- Oncogenic types of HPV, mainly types 16 and 18, are the cause of nearly all cases of cervical cancer and the majority of anal cancer.
- HPV is also responsible for a significant proportion of cases of vulvar, vaginal, penile, and oropharyngeal cancers.

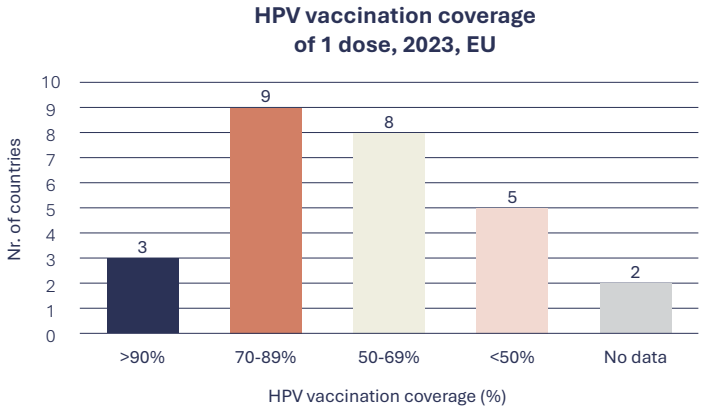

Figure 2: Coverage 1st dose HPV vaccination among females by the age of 15 years in 2022 in EU countries. © WHO/UNICEF Joint Reporting.

Form on Immunization. From https://immunizationdata.who.int/global/wiise-detail-page/human-papillomavirus-(hpv)-vaccination-coverage

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Key policy actions to test and treat for HBC, HCV, HIV and *H. pylori*

Sustainable initiatives of testing and treating of these infections should be introduced in the EU.

For HBV, HCV and HIV, it should be ensured that:

- Policies are adopted to facilitate the offer of an affordable, ideally free of charge, tests for HBV, HCV, and HIV to adults in low-threshold settings using a non-stigmatizing approach. Only a venous or finger-prick blood sample or a saliva sample is needed to detect the presence of HBV, HCV, or HIV infection. The currently available tests are inexpensive and very accurate.
- Individuals are treated with confirmed HCV or HIV infection as early as possible. For HBV, treatment should be provided according to the clinical guidelines. Antiviral drugs are available in all EU countries and are reimbursed fully or partially by the health system.
- There is availability of timely treatment, which can cure HCV and prevent the long-term effects of an HIV infection, resulting in life expectancies similar to those of people without HIV.
- For HIV testing, individuals with HIV indicator conditions and those at increased risk of sexual acquisition of HIV should be prioritized. In most EU countries, HIV infections are concentrated in men who have sex with men, people who inject drugs, migrants from high-endemic regions, such as sub-Saharan Africa and the Caribbean, and, to a lesser extent, sex workers and prisoners.
- Tasks that should be handled exclusively by a specialist need to be clearly defined to ensure adequate treatment for all people who test positive and to avoid health system overload. Overarching initiatives that can tackle two or three infections at a time may be cost-effective.

For *H. pylori*, this infection can be detected using inexpensive, non-invasive tests, such as a urea breath test and a stool antigen test. It should be ensured that:

- Individuals with confirmed *H. pylori* infection are treated as early as possible. Standard oral treatment typically involves a combination of a proton pump inhibitor, metronidazole, and antibiotics, tailored to an individual's or a community's level of susceptibility to clarithromycin and can cure the infection.
- Eligibility for testing and treatment of *H. pylori* can be defined by age, country of birth and family history. The most effective timing the intervention is before the infection has progressed to severe irreversible conditions.
- Tasks that should be handled exclusively by gastroenterologists need to be clearly defined to ensure adequate treatment for all people who test positive for *H. pylori* infection and to avoid health system overload.

For all infections, it should be ensured that

- Primary care-based protocols make the most appropriate treatment regimens less expensive and easily available to all EU citizens.

Risk of cancer

- HBV and HCV infections are major causes of chronic hepatitis, a progressive disorder that can lead to cirrhosis and cancer (hepatocellular carcinoma). Chronic hepatitis B and C are usually asymptomatic but can progress to cirrhosis in 5–10% of people who have had the infection for more than 20 years. Once cirrhosis is established, the risk is 2-5% per year that hepatocellular carcinoma will develop if the infection is not treated (HCV) or controlled (HBV).
- HIV is not directly oncogenic, but, because it causes immune deficiency, it increases the risk of cancers caused by other viruses. In people with HIV, the risk of cancer is also increased by the chronic inflammation induced by HIV and an increased probability of high exposure to cancer-related viruses (HBV, HCV, or HPV), as well as behavioural risk factors such as tobacco use, alcohol consumption, and for men who have sex with men. Compared with the general population, people with HIV have an increased risk of several types of cancer, including Kaposi sarcoma, lymphomas, and cancers of the liver, cervix, anogenital tract, and throat (HPV-related). Treating HIV infection as early as possible (that is, before profound immunodeficiency has developed) substantially reduces the risk of cancer.
- *H. pylori* is the primary cause of gastric cancer and gastric mucosa-associated lymphoid tissue (MALT) lymphoma. Chronic gastric inflammation may progress to more severe forms of gastritis and ultimately lead to gastric cancer. Most *H. pylori* infections are acquired during childhood and persist lifelong if not treated. This can be exacerbated by an individual's genetic determinants, a high-salt diet, and tobacco smoking.

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This Policy Brief was developed by the Working Group 3 on Infections and related interventions with support from Working Group 5 on Communication and Health Literacy, and the Secretariat of the European Code Against Cancer, 5th Edition project.