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Strategies for prevention of gastrointestinal cancers in developing countries: opportunities and challenges

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Gastrointestinal cancers account for one third of total cancer incidence and mortality in developing countries. Among others, gastric, liver and colorectal cancers are currently the three most common gastrointestinal cancers (GICs) in these countries. Despite extensive efforts to improve treatment outcomes of the metastatic disease, even in the developed world, 5-year survival rates for these cancers are low. This situation highlights the need to further explore the potential of primary prevention and early detection strategies, especially in developing countries where treatment of advanced stage cancers is additionally limited due to infrastructure and economic constraints. This project aimed to explore strategies used for prevention of gastric, liver and colorectal cancers in the context of developing countries and then to estimate the effectiveness of a selected strategy that is most promising.

In a first step, a comprehensive systematic literature review was conducted to provide an overview of studies evaluating strategies for prevention or early detection of the three most common gastrointestinal cancers (gastric, liver and colorectal cancer) in developing countries. MEDLINE, Web of Science and WHO Global Index Medicus databases were searched for relevant articles published until October 2016. Original studies that reported long–term health outcomes (e.g. reduction of incidence or mortality) or intermediate outcomes that are expected to be associated with long–term effects (e.g. detection rates or vaccine efficacy), were included. Details on preventive measure, country, study design, study population (sample size, sex distribution and age), outcomes under study and results was extracted. Overall, 73 articles reporting on 54 studies (several articles refer to the same study but report on different follow-up periods or outcomes) met the inclusion criteria providing information on short- and long-term outcomes (up to 30 years) of various, mostly randomized intervention studies. Trials on HBV vaccination consistently showed vaccine efficacy over time and indicated long-term preventive effects on liver cancer (~80% incidence reduction) that start to become measurable at the population level. Studies on anti-H.pylori treatment suggested a reduction in stomach cancer incidence (~40%) reaching statistical significance after long-term follow-up, while evidence regarding a preventive effect in persons with precancerous lesions is still inconclusive. Regarding colorectal cancer there were several studies on early detection, but mostly restricted to intermediate endpoints. There were a number of studies on gastric and liver cancer prevention in developing countries showing promising results after long-term

follow-up. Important next steps include pooled meta-analyses as far as possible given the heterogeneity between studies as well as implementation research.

In the second stage, given the insights gained by the literature review regarding effectiveness of HBV vaccination in protecting against chronic infection and potential for the prevention of liver cancer, the research project further explored the feasibility of evaluating population-wide HBV vaccination program in preventing liver cancer. Most HBV vaccination programs started mainly in mid 1990s or later; hence the effect of the programs currently could be assessed in children and adolescents (0-19 years of age) only. To avoid inclusion of hepatoblastoma, a liver cancer of fetal origin, the age group 0-4 years was excluded from the analysis. Liver cancer incidence data was obtained from Incidence in Five Continents (CI5) databases from International Agency for Research on Cancer (IARC) up to the year 2007 (latest published volume of CI5). Data regarding HBV vaccination was retrieved from WHO and UNICEF estimates of national infant immunization coverage. Availability of at least 15 years incidence data for liver cancer up to 2007 i.e. 5 years prior to introduction of HBV universal vaccination and 10 years afterwards; and at least 10 years time since start of hepatitis B vaccination was assumed as inclusion criteria. Only 17 of 194 countries met the inclusion criteria. In view of low incidence of liver cancer in 5-19 year age group, statistical analysis procedures was applied to the country with the highest liver cancer incident cases (the US) among the included countries, using estimates of age-specific incidence rates in 5-19 years age groups from 9 SEER cancer registries.

The study showed that extensive lack of liver cancer incidence data and insufficient HBV vaccination coverage data limit the feasibility of evaluating population HBV vaccination programs at this point of time. For example, 114 of 194 WHO member states (95% of them developing countries) lack cancer registries at all or have registries that do not meet inclusion criteria of CI5 databases. The study also demonstrated that on contrast to studies from Taiwan, the incidence of liver cancer in children and adolescent in the US surprisingly did not decrease and rather showed a non-statistically significant increase. While low number of incident cases in the registries from the US (compared to Taiwan) might be a reason for this variation, other potential hypotheses could also be responsible for this trend. For instance, child and adolescent overweight has tripled between 1976-1980 and 2003-2004 in 6-19 years age group in the US and might contribute to the trend.

Overall, in view of diverse strategies used for prevention of gastrointestinal cancers, generating robust evidence (e.g. by pooled meta-analysis) followed by context-oriented implementation research is critical to inform cancer prevention policy and programs in developing countries. Future research should also explore how health systems in developing countries can be supported generate data to estimate cancer burden and evaluate cancer prevention programs effectively.