

Cancer Expert Working Group on Cancer Prevention and Screening

Recommendations on Prevention and Screening for Nasopharyngeal Cancer For Health Professionals

Local epidemiology

1. In 2014, nasopharyngeal cancer (NPC) was the sixth commonest cancer in men and the 13th commonest cancer in women. A total of 834 NPC cases were recorded, accounting for 2.8% of all newly diagnosed cancer cases. The age-standardised incidence rate (ASIR) was 12.6 for male and 3.9 for female per 100,000 standard population. The median age at diagnosis was 54 for males and 52 for females.¹

2. NPC was the 10th leading cause of cancer death in 2015. There were 327 deaths caused by NPC, constituting 2.3% of all cancer deaths. The total age-standardised mortality rate (ASMR) of NPC was 2.8 per 100,000 world standard population. After adjusting for population ageing, both the ASIR and ASMR for both sexes showed a downward trend in the past three decades.² The ASMR has decreased by a greater magnitude than the corresponding ASIR, attributable to improvements in treatment outcome.³ More information on nasopharyngeal cancer statistics can be found at the Centre for Health Protection (CHP) website: <http://www.chp.gov.hk/en/content/9/25/54.html>.

Risk factors

3. Risk factors for NPC include:

- (a) family history of NPC (the relative risk of first-degree relatives of NPC patients varying from 6.3 to 21.3)⁴
- (b) smoking (for keratinizing NPC)^{4,5}
- (c) high intake of preserved (salted) and fermented food with high nitrosamine content (for non-keratinizing NPC)^{4,5}
- (d) Epstein-Barr virus (EBV) reactivation^{5,6}
- (e) occupational exposure to wood dust, formaldehyde, and chemical fumes^{5,7,8,9}
- (f) practice of burning incense sticks, which contain carcinogenic polycyclic aromatic hydrocarbon compounds¹⁰
- (g) immunocompromised state such as Acquired Immune Deficiency Syndrome (AIDS) which doubles the risk for both keratinizing and non-keratinizing NPC¹¹

Primary prevention

4. Some preventive measures can help reduce the risk of NPC:
 - (a) Do not smoke
 - (b) Do not eat preserved and fermented food
 - (c) Observe occupational safety and health rules and take precautionary measures to minimise exposure to causative agents for NPC at workplace
 - (d) Avoid burning incense sticks

Early detection

5. Common signs and symptoms of NPC include swollen neck lymph nodes, decreased hearing, tinnitus, recurrent ear infection, unexplained headache, double vision, stuffiness, nose bleeding, facial paralysis, hoarseness of voice and dysphagia. Individuals with these signs and symptoms should be investigated for NPC.

Screening

Screening tests

6. As preclinical phase of NPC is commonly associated with EBV reactivation, the assessment of EBV serological status constitutes an important tool in predicting subsequent symptomatic development. High IgA viral capsid antigen (VCA), IgA diffuse early antigen (D-EA), and EBV DNase with increasing titers correlate with subsequent diagnosis of NPC.^{12,13,14} However, a false-positive rate of 2% to 18% has been noted with these serologic testing alone.^{15,16} Regarding the risk associated with individual EBV marker to identify NPC susceptibles within high risk NPC families, it has been reported that EBV nuclear antigen-1 (EBNA1) IgA seropositivity was the marker most strongly associated with NPC risk.¹⁷

7. EBV DNA is shed consistently from NPC tumor cells and can be routinely detected in the plasma of patients with NPC with more than 95% sensitivity, though with limited specificity as shown in a local study.¹⁸ An expanded phase II project by the same group is currently undertaken.

8. Other important advances in the early detection of NPC include serum protein profiling, measurement of plasma tumor-specific methylation, detection of multiple gene methylation and EBV copy number from brushing samples collected directly from the nasopharynx. However, the performance of all these methods as a screening test on asymptomatic individuals has not been adequately evaluated.

9. To date, there is lack of evidence on the effectiveness of screening by EBV DNA or IgA against EBV viral antigens in reducing NPC mortality among the general population.

Effectiveness of NPC screening for people at high risk

10. A local study on NPC screening on family members ($n=1,199$) of NPC patients was carried out between 1994 and 2005. Significant shift in stage distribution to earlier stage could be achieved by annual screening with EBV serology test and nasopharyngoscopy. The screening-detected NPC patients had significantly higher proportion of stage I disease (41% versus <1%) and better disease-free survival compared with patients with symptomatic NPC referred during the same period.¹⁹

11. However, due to a small sample size, this survival result should not be overstated. First, the other estimates of survival, namely cancer-specific survival rate and overall survival rate did not reach statistical significance. Secondly, there might be lead-time bias and length-time bias as this study was not a randomized controlled trial. The Cochrane systemic review in 2015 concluded that there was lack of methodological rigour in available studies to determine the effectiveness of screening of asymptomatic individuals in reducing the mortality of NPC.²⁰

12. After taking into consideration local epidemiology, emerging scientific evidence, local and overseas screening practices, the Cancer Expert Working Group on Cancer Prevention and Screening (CEWG) made the following recommendations on NPC screening at its 26th meeting in June 2016:

For persons at average risk	
1.	There is insufficient evidence to recommend a population-based nasopharyngeal cancer (NPC) screening programme using IgA against specific Epstein-Barr virus (EBV) viral antigens and EBV DNA test.
For persons at high risk	
2.	Family members of NPC patients may consider seeking advice from doctors before making an informed decision about screening.

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