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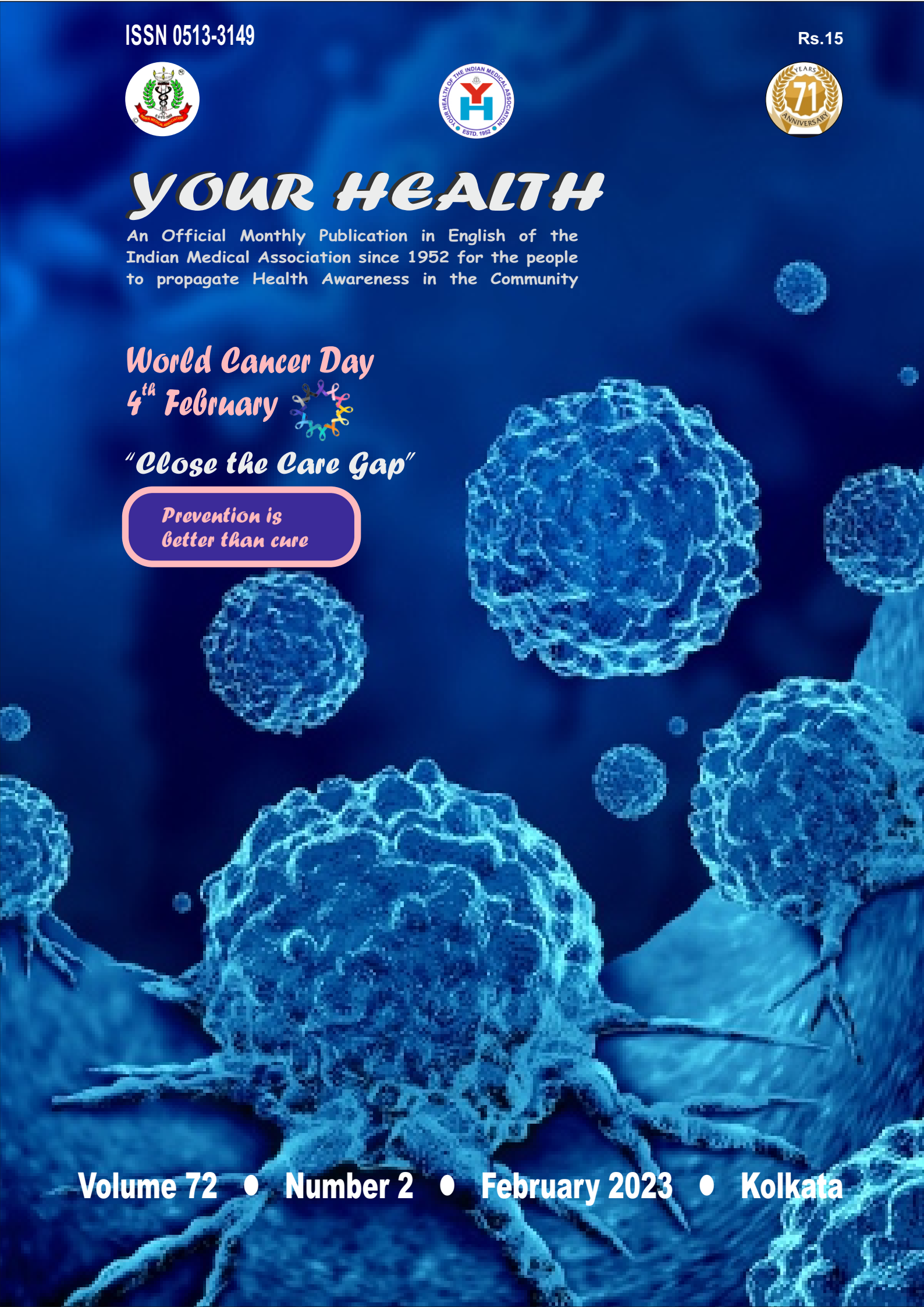
YOUR HEALTH

An Official Monthly Publication in English of the Indian Medical Association since 1952 for the people to propagate Health Awareness in the Community

World Cancer Day
4th February

"Close the Care Gap"

Prevention is better than cure



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Editorial

Dr Kakali Sen
Hony. Editor, Your Health

Taboos in Cancer Care:

What matters to patients..... "Weaving the cultural beliefs about Cancer as a "God-forsaken" disease in many cultures to the success of modern cancer therapeutics is a critical definition of complementary culturally based cancer care". – Dr. Kakali Sen, the Hony Editor, Your Health of IMA

In the play Hamlet, William Shakespeare wrote “Diseases desperate grown, by desperate measure are revealed, or not at all.” June Goodfiled, the British Historian, also quipped, “Cancer begins and ends with people. In the midst of scientific abstraction, it is sometimes possible to forget this one basic fact.....Doctors treat diseases, but they also treat patients, and this precondition of their professional existence sometimes pulls them into two directions at once”.

Millennia's old cultures and taboos across the globe continue to shape humans' present-day lives across the globe. It is a badge of honor, blessing, curse, or identity for many. Many of these taboos and practices continued to evolve and dissipate over the years, but what is more important is, which ones remain to the present day and how it affects all spheres of our lives. I bring up this medieval yet poignantly modern and important topic of taboos and cultural practices because while we can easily think of them as "peculiar" and rush to patronize and "discard them," some remain critically and exclusively important to patient identity, a badge of cultural or religious honor and belief a reapproachment. Cancer, colloquially known as the big C, is as old a disease as the taboo itself and is as modern as the many present-day taboos. As an oncologist practicing in India, the cradle of humankind and possibly the only continent with the highest level of taboos, practices and beliefs to this date, this topic hit home differently.

"Now it is cancer's turn to be disease that doesn't knock before it enters,”

In its very own etymology as a disease, Cancer is highly heterogeneous and a complex topic for my patients. From the various tumor types to the treatment modalities, to the treatment facilities, to cancer patients, to the different social determinants of health, and the insights and beliefs about Cancer, this disease remains a global scourge. Like many other unique or not so unique daily life practices, taboos also spill into the corridors of hospitals or cancer wards and clinics, to be precise.

Cancer is, by far the only disease in the history of mankind that is highly aligned to negative taboo beliefs and connotations. From the Greek mythology and Latin word "crab" referring to Cancer, Greek physicians Hippocrates and Galen noted the similarity of the sea animal crab to some tumors with swollen veins, to the vivid descriptions of medieval times as "a curse from God" to the sorcery and bewitchment connotation, the cancer disease has been described globally in every passing millennium, including the modern times. But what is more important to modern cancer care is the patient's insight into their disease. In other words, how much does the patient know about their cancer diagnosis, what caused it, what is their belief on the outcome of such disease, do they believe in modern science and novel therapies, or will they rather resort to traditional healers and herbals or seek spiritual intervention?

In many instances, usually stemming from patients' education level, income bracket, age, and cultural background, the answers to the aforementioned questions are heterogeneous. Patients in rural India might not holistically believe their cancer diagnosis as a "curse from God" or as an "outcast." Still, at some point, mainly due to circumstantial health inequities and disparities compounded by social-economic gaps and financial toxicity, they will resort to traditional ways of treating Cancer. These include but are not limited to; exenteration of the tumor, consumption of oral or topical herbs, physical burning of the tumor in the hope of shrinking, spiritual healing through the background faith and many more.

Appreciating the cultural nuances and sociodemographic differences among cancer patients is the first step in empowering patients. Educating patients on the harms and ineffectiveness of the kept beliefs of outdated traditional home-based treatment strategies while engaging them as decision partners is the second critical step in improving treatment compliance. Weaving the cultural beliefs about Cancer as a "God-forsaken" disease in many cultures to the success of modern cancer therapeutics is a critical definition of complementary culturally based cancer care.

Dr Samarendra Kumar Basu
Hony. Secretary, Your Health

From the Desk of Secretary

History of Singular Research on Cancer

Research on Cancers started almost 200 years back. A few judicious observers were ahead of their time, including Rudolf Virchow, who with the benefit of a microscope deduced the cellular origin of cancer in 1863,and Stephen Paget, who in 1889 wisely mused about the seed-and-soil hypothesis of metastatic disease, a theory that is coming into its own today. Other key advances were the discovery of a viral cause of avian cancer by Peyton Rous in 1911 and the proposal by Theodor Boveri in 1914 that cancer can be triggered by chromosomal mutations.

Singular Discoveries and Major Events in the Cancer Field and Changing Relative Survival Rates for Patients with Cancer in the United States, 1863–2006.

Year	Discovery or Event
1863	Cellular origin of cancer (Virchow)
1889	Seed-and-soil hypothesis (Paget)
1914	Chromosomal mutations in cancer (Boveri)
1937	Founding of NCI
1944	Transmission of cellular information by DNA (Avery)
1950	Availability of cancer drugs through Cancer Chemotherapy National Service Center
1953	Report on structure of DNA
1961	Breaking of the genetic code
1970	Reverse transcriptase
1971	Restriction enzymes Passage of National Cancer Act
1975	Hybridomas and monoclonal antibodies Tracking of cancer statistics by SEER program
1976	Cellular origin of retroviral oncogenes
1979	Epidermal growth factor and receptor
1981	Suppression of tumor growth by p53
1984	G proteins and cell signaling
1986	Retinoblastoma gene
1990	First decrease in cancer incidence and mortality
1991	Association between mutation in APC gene and colorectal cancer
1994	Genetic cancer syndromes Association between BRCA1 and breast cancer
2000	Sequencing of the human genome
2002	Epigenetics in cancer MicroRNAs in cancer
2005	First decrease in total number of deaths from cancer
2006	Tumor stromal interaction

**Data are from the National Cancer Institute (NCI) Survival, Epidemiology, and End Results (SEER) program. APC denotes adenomatous polyposis coli.*

The eminent doctors of Chittaranjan National Cancer Institute have agreed to undertake an issue on this important speciality and illustrated to the best of the understanding of the readers.

We are extremely thankful for their contribution.

Releasing of Your Health January 2023 Edition at Sir Nil Ratan Sircar IMA House, Kolkata by Dr. Sharad Kumar Agarwal, National President of IMA, in presence of office bearers of JIMA, Your Health and IMA Hqs at Kolkata

Guest Editorial

Dr. Ranajit K Mandal, MD,DNB,PGDHHM
Prof. & HOD Gynaecological Oncology, CNCI Kolkata

It is a proud privilege to write a foreword for the IMA dedicated to the cause of Cancer Elimination. This booklet outlines the debate about cancer prevention with the primary focus on three most preventable cancers- Cervical, Breast and Oral Cancer. This book is a comprehensive summary of the benefits and strategies for cancer prevention. It is an important addition to any library serving those involved in policy development and clinical prevention. The goals of cancer prevention are to reduce the incidence, morbidity and mortality due to cancer through the identification and elimination of precancerous lesions or the early detection of minimally invasive cancers. For this reduction in cancer death to continue, it is extremely important that we continue to prioritize efforts in cancer prevention and control

The audience is primarily those involved in thinking about, planning for, and implementing prevention strategies who wish to have a comprehensive book that explores current theories and proven models.

Books have the power of transformation and with good content, they have the potential to impart confidence and a feeling of support amongst the readers. I hope the pearls of knowledge in this book will help at every step in learning something new and guide you in your decision making for a better patient outcome

The content of the focus is of high quality and reading the words from stalwarts will surely ignite young minds to focus on the preventive aspects of cervical, breast and oral cancer which is the need of the day. The chapters have been aptly chosen to cover most of the relevant areas in cancer screening and early detection.

The concept of cancer prevention is changing gradually as we gain a greater understanding of the genetic and molecular basis of carcinogenesis. Certainly, it is understood that the cancer patient is not well one day and the next day diagnosed with cancer.

Oncologists have the potential to be a large and important group of activists for cancer prevention measures, and faced, as we are daily, with the failure of cancer prevention we have more incentives than many others to see them implemented. Seen in this light, this handbook is both timely and necessary, and it is my sincere hope that you will find it both a practical tool and guide to thinking about this vital subject.

Dr Jayanta Chakrabarti
Director, Chittaranjan National Cancer Institute

Cancer is a generic term for a large group of diseases that can affect any part of the body. Other terms used are malignant tumours and neoplasms. One defining feature of cancer is the rapid creation of abnormal cells that grow beyond their usual boundaries, and which can then invade adjoining parts of the body and spread to other organs; the latter process is referred to as metastasis. Widespread metastases are the primary cause of death from cancer. Cancer arises from the oncogenic transformation of normal cells into tumour cells in a multi-stage process that generally progresses from a pre-cancerous lesion to a malignant tumour. These changes are the result of the interaction between a person's genetic factors and three categories of external agents, including: physical carcinogens, such as ultraviolet and ionizing radiation; chemical carcinogens, such as asbestos, components of tobacco smoke, alcohol, aflatoxin (a food contaminant), and arsenic (a drinking water contaminant); and biological carcinogens, such as infections from certain viruses, bacteria, or parasites.

Cancer is a leading cause of death worldwide, accounting for nearly 10 million deaths in 2020, or nearly one in six deaths. In India around 2.7 million (2020) people are suffering from cancer. Every year around 13.9 lakhs new cancer patients are registering. Total deaths in our country due to cancer in last year were 8, 51,678 (men: 4, 38,297; women: 4, 13,381). Cancers of oral cavity, stomach and lungs account for over 25% of cancer deaths in males and cancer of uterine cervix, breast and oral cavity account for 25% cancers in females. Around one-third of deaths from cancer are due to tobacco use, high body mass index, alcohol consumption, low fruit and vegetable intake, and lack of physical activity. Cancer-causing infections, such as human papillomavirus (HPV) and hepatitis, are responsible for approximately 30% of cancer cases in low- and lower-middle-income countries. The top five cancers in men and women account for 47.2% of all cancers (men: Lip, Oral cavity, Lung, Stomach, Colorectal and Oesophagus; women: Breast, Cervix uteri, Ovary, Lip, Oral cavity and Colorectal); these cancers can be prevented, screened for and/or detected early and treated at an early stage. This could significantly reduce the death rate from these cancers.

Cancer risk can be reduced by: not using tobacco; maintaining a healthy body weight; eating a healthy diet, including fruit and vegetables with high antioxidant; doing physical activity on a regular basis; avoiding or reducing consumption of alcohol; getting vaccinated against HPV and hepatitis B if you belong to a group for which vaccination is recommended; avoiding ultraviolet radiation exposure (which primarily results from exposure to the sun and artificial tanning devices) and/or using sun protection measures; ensuring safe and appropriate use of radiation in health care (for diagnostic and therapeutic purposes); minimizing occupational exposure to ionizing radiation; and reducing exposure to outdoor air pollution and indoor air pollution, including radon (a radioactive gas produced from the natural decay of uranium, which can accumulate in buildings — homes, schools and workplaces).

Correct cancer diagnosis is essential for appropriate and effective treatment because every cancer type requires a specific treatment regimen. Treatment usually includes surgery, radiotherapy, and/or systemic therapy (chemotherapy, hormonal treatments, Immunotherapy, and targeted biological therapies). In this evolving field the personalised medicine is playing an increasingly important role in cancer prevention, diagnosis, prognosis and therapeutics from studies of patient's genome by next-generation sequencing. The primary goal of cancer treatment is generally to cure cancer or to considerably prolong life. Improving the patient's quality of life is also an important goal. This can be achieved by support for the patient's physical, psychosocial and spiritual well-being and palliative care in terminal stages of cancer. Some of the most common cancer types, such as breast cancer, cervical cancer, oral cancer, and colorectal cancer, have high cure probabilities when detected early and treated according to best practices. Some cancer types, such as testicular seminoma and different types of leukaemia and lymphoma in children, also have high cure rates if appropriate treatment is provided, even when cancerous cells are present in other areas of the body. Social responsibilities are important including giving monetary & financial help to poor cancer patients irrespective of caste & creed and spreading awareness of cancer amongst the public. Awareness includes quarterly bulletin, screening of cancer film in schools, arranging lectures by eminent doctors on different type of cancers, use of social media to promote cancer screening and early diagnosis.

On the Day of World Cancer Day

Dr Sankar Sengupta
Hony. Associate Editor, Your Health

Cancer arises from three different kind of factors including physical (ultraviolet and ionizing radiation), chemical (tobacco smoke, alcohol etc) and biological (viruses, bacteria, or parasites) carcinogens. Nearly 609,360 deaths and 1,918,030 new cancer cases in united states and 14,61,427 new cases and 8,08,558 deaths in India were recorded in the year 2022. Every 1 in 68 males and 1 in 29 females developed risk of cancer. Cancer mortality is reduced when cases are detected and treated early. For this we have to aware people by providing correct information about the early symptoms of cancer, thus enabling them to seek treatment at an early stage.

There are several screening test for cancer considered effective like mammography for Breast Cancer, HPV Test for Cervical Cancer, colonoscopy, CT scan etc. Molecular diagnostics play a vital role in clinical oncology. Quantitative PCR has widespread application in the detection of DNA/RNA/miRNA abnormalities for initial diagnosis of cancer. These would also be applicable in surveillance, follow-up and monitoring treatment outcome of cancer patient. The development of massively parallel next-generation sequencing facilitates the analysis of multiple genes and now is being used to sequence the coding regions of the genome (the exome) for clinical testing. Recently gene mutational Signature analysis taking the lead for better applicability in cancer treatment and cancer prevention. More recently, multiplexed immunohistochemistry (mIHC)-based analysis, compared with other cutting-edge technologies, has been shown to provide unique insight into the three-dimensional relationships among cells within the complex tumour microenvironment (TME) including infiltrating immune cells, cancer cells, and stromal cells. Using the TSA Opal mIHC protocol, multiple immune biomarkers can be detected in a single tissue section through sequential staining, regardless of the species of the primary antibodies. Therefore, this protocol can overcome the hurdle of conventional mIHC, which normally uses a cocktail of primary antibodies raised in different types of cancer. Fluorescence-activated cell sorting (FACS), Artificial Intelligence (AI) based metabolomics and AI based heat map are new edge methods used nowadays to identify a particular type of cancer.

After diagnosis of cancer, a proper selection of a treatment regimen takes into consideration both the cancer and the individual being treated. Treatment usually includes surgery, radiotherapy, and/or systemic therapy (chemotherapy, hormonal treatments, targeted biological therapies). To reduce the risk of developing cancer by not using tobacco, maintaining healthy body, not consuming alcohol, do physical activities as much as possible, getting vaccinated against HPV and hepatitis B if someone belong to a group for which vaccination is recommended. Besides all of these information, being a health care worker we should take some social responsibilities towards the patient who suffered by the disease and to improve the quality of life of patients and their families. Relief from physical, psychosocial, and spiritual problems through palliative care is possible for more than 90% of patients with advanced stages of cancer.

Inauguration of 82nd BIMACON 2023 at Hotel Stadel, Saltlake City, West Bengal

HPV Vaccination - A Step Forward to Cervical Cancer Elimination

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The World Health Organization has recommended the three strategic approaches for eliminating the cervical cancer by 2030 which includes cervical cancer vaccination as a key element : 90% vaccination coverage of the adolescent girls; twice in a lifetime screening coverage of 70% of women between 35 and 45 years using a high-performance test and appropriate treatment of up to 90% of screened positive women Before the end of the present millennium, this strategy is anticipated to successfully lower cervical cancer incidence to a threshold of four per 100,000 woman-years (i.e., levels no longer regarded as a public health hazard).

Human Papilloma Virus high-risk genotypes are responsible for more than 95% of cervical cancer cases. An estimated 70% of occurrences of invasive cervical cancer globally are thought to be caused by HPV strains 16 and 18.

Currently, Cervarix ® (bivalent, Glaxo Smith Kline), Gardasil ® (quadrivalent, Merck), and Gardasil-9 ® are the three vaccines offered in the Indian market (nona-valent, Merck). The Serum Institute of India will soon offer Cervavac®, a quadrivalent vaccine that is inexpensive and developed in India.

Cervarix®	Gardasil®	Gardasil-9®
16,18	6, 11,16,18	6,11,16,18,31,33,45,52,58

Cervical cancer vaccines contain virus-like particles (VLP) without any pathogenic DNA. This does not cause a new HPV infection and does not cure an existing HPV infection. The vaccination guards against female cancers and pre-cancers of the cervix, vagina, vulva, and anal regions. Additionally, the nonavalent and quadrivalent vaccines offer defence against genital warts brought by by HPV 6 and 11. With the bivalent vaccine, there is cross-protection against serotypes 31 and 45. [1]

Whom should we vaccinate?

Although females between the ages of 9 and 15 are the major focus of the HPV vaccine, it is approved for use in anybody between the ages of 9 and 45 years. Upto the age of 15, two doses are advised; beyond that, three doses is recommended. The Two doses should be spaced out by six months interval. In the event of three doses, the bivalent vaccine requires 0, 1, and 6 months, while the quadrivalent vaccine requires 0, 2, and 6 months.

Vaccination from 15 to 26 years is referred to as "catch-up vaccination".[1] Counselling regarding reduced efficacy and the significance of cervical cancer screening starting at the age of 25 to 30 years should be provided to the people in this age group as well as women older than 26 years who are willing for the vaccination.

Women who have received the vaccine will still require routine cervical cancer screening because not all HPV strains that cause cervical cancer are covered by the vaccine. Consequently, cervical cancer screening and vaccination are complimentary.

Vaccination in Boys

In 2013, Australia was the first country to include boys in their national immunisation schedule. HPV vaccination of boys offers protection against anogenital HPV infections, genital warts and cancer precursors of the anal region. Recently, HPV vaccination has also been found to protect against HPV infections of the oropharynx.[2]

Is there any role of Single dose vaccine?

According to a recent WHO position paper published in December 2022, a single dosage of the cervical cancer vaccination can offer equal protection to a two- or three-dose strategy. SAGE, an independent expert advisory panel for WHO first recommended this alternate single-dose timing in April 2022 .[3]

WHO now recommends
A one or two-dose schedule for girls aged 9-14 years as well as for girls and women aged 15-20 years
Two doses with a 6-month interval for women older than 21 years

WHO now recommendsA one or two-dose schedule for girls aged 9-14 years as well as for girls and women aged 15-20 yearsTwo doses with a 6-month interval for women older than 21 years

Is the vaccine safe?

Globally, more than 270 million doses of the vaccine

have been given, and there have not been any significant adverse events associated with it, according to the vaccine's good safety statistics. Minor occurrences including discomfort at the injection site, tenderness, edema, fever, headache, myalgia, and gastrointestinal problems have all been documented. Even compared to regularly provided vaccines like tetanus toxoid, the reported anaphylaxis rate is significantly lower.

How effective is this HPV vaccine?

According to studies like the FUTURE I[4], FUTURE II[5], and PATRICIA[6] trials, the cervical cancer vaccination is about 99% effective in preventing cervical cancer and 90–94% effective at avoiding cervical precancers like CIN 3.

Special scenarios

1. Pregnancy: Cervical cancer vaccine is not recommended in pregnancy. However, termination of pregnancy is not required in women who have been inadvertently vaccinated during a previously undiagnosed pregnancy.

2. Lactation: HPV vaccination is not contraindicated.

3. Interrupted or missed doses: FOGSI good clinical practice recommendation (GCPR, 2020) recommends two doses of HPV vaccine at least 6 months apart for girls aged 9 to <15 years of age, although the interval between two-doses can be extended to 12–15 months in circumstances where the second-dose is not repeated within 6 months. There is no need to restart the reschedule in case of missed or interrupted doses.

4. Immunocompromised population like HIV infection: The FOGSI GCPR committee, (FOGSI GCPR 2020) recommends that HIV-positive girls should be offered three doses even below 15 years of age.

Problems in the Implementation of HPV vaccination programs on a larger scale and the Current scenario of vaccination in India

The WHO Strategic Advisory Group of Experts (SAGE) Working Group on *Vaccine Hesitancy* defined vaccine hesitancy as "delay in acceptance or refusal of vaccination despite the availability of vaccination services."[6]

Vaccine hesitancy is fuelled by a lack of evidence-based knowledge and motivation among the general public, administrative and political stakeholders, and even some segments of the medical community. In the past, rumours and false information have damaged the vaccine's reputation. Acceptance of the cervical cancer vaccine is influenced by sociocultural as well as financial considerations. The affordability and vaccine availability has been the other deterring elements.

Despite the aforementioned obstacles, the widespread adoption of HPV vaccination in India on a larger scale in the future is encouraged by the successful HPV vaccination programmes in Punjab and Sikkim (with high coverage and safety), government-sponsored opportunistic vaccination in Delhi, prospects of a single dose providing adequate and acceptable protection, and the availability of the affordable Indian vaccine (Cervavac) in the near future.[7]

In spite of the above hurdles, the successful HPV vaccination programmes in Punjab and Sikkim (with high coverage and safety), government-sponsored opportunistic vaccination in Delhi, prospects of a single dose providing adequate and acceptable protection, and availability of the affordable Indian vaccine (Cervavac) in the near future shows promise for widespread implementation of HPV vaccination in India on a larger scale in the future.[8]

Indian HPV vaccine- a ray of light

On July 12, 2022, the Drugs Controller General of India approved Cervavac for market authorization to females and males aged 9 to 26 years based on promising results from a significant phase 2/3 clinical research. On September 1, 2022, the vaccine had its public debut. Compared to currently available licenced HPV vaccines, Cervavac will be significantly less expensive.

Despite the fact that different HPV vaccinations have been accessible in India since 2008, efforts to develop a nationwide vaccination programme have restrictions, primarily due to worries about side effects and cost. Although the final confirmations are still pending, the new vaccine will be funded by the Indian government and provided through state-run services. Initially, enough doses will be produced to vaccinate nearly 50 million girls between the ages of 9 and 14; there are also plans to make it available to private providers and eventually export it to other underdeveloped countries.[9]

Contribution of Chittaranjan National Cancer Institute in cervical cancer vaccination in the state of West Bengal

Chittaranjan National Cancer Institute has been in the major role for the cervical cancer screening projects and conducted various community based projects with the involvement of the multiple screening agencies, NGOs and government of India since inception. Since 2017, 2654 girls from rural Bengal from the age of 9-15 years have received vaccination.

67 girls defaulted to receive the second dose of vaccine, resulting in a 97.5% uptake rate. No significant negative effects were observed.

Continued on page 23...

Guidelines on Cervical Cancer Screening

Dr. Sreeya Bose, Consultant (Preventive Oncology)
Dept. Gynaecological Oncology, CNCI Kolkata

Dr. Bijoy Kar, (DrNB Resident)
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In the recently published Globocan 2020 data, India is contributing 20.51% of new cases and 22.62% of deaths globally due to cervical cancer.[1] These numbers show an upward trend as compared to Globocan 2018 data.[2] It is now a known fact that cervical cancer is a preventable cancer if detected early.

On 17th November 2019, World Health Organization (WHO) launched a global strategy to accelerate the elimination of cervical cancer by 2030.[3] WHO set the 90:70:90 target to be met by 2030 : 90% vaccination coverage of the adolescent girls; twice in a lifetime screening coverage of 70% of women between 35 and 45 years using a high-performance test and appropriate treatment of up to 90% of women.[4]

The fundamental principle of cervical cancer screening program are based on the adopting a screening test

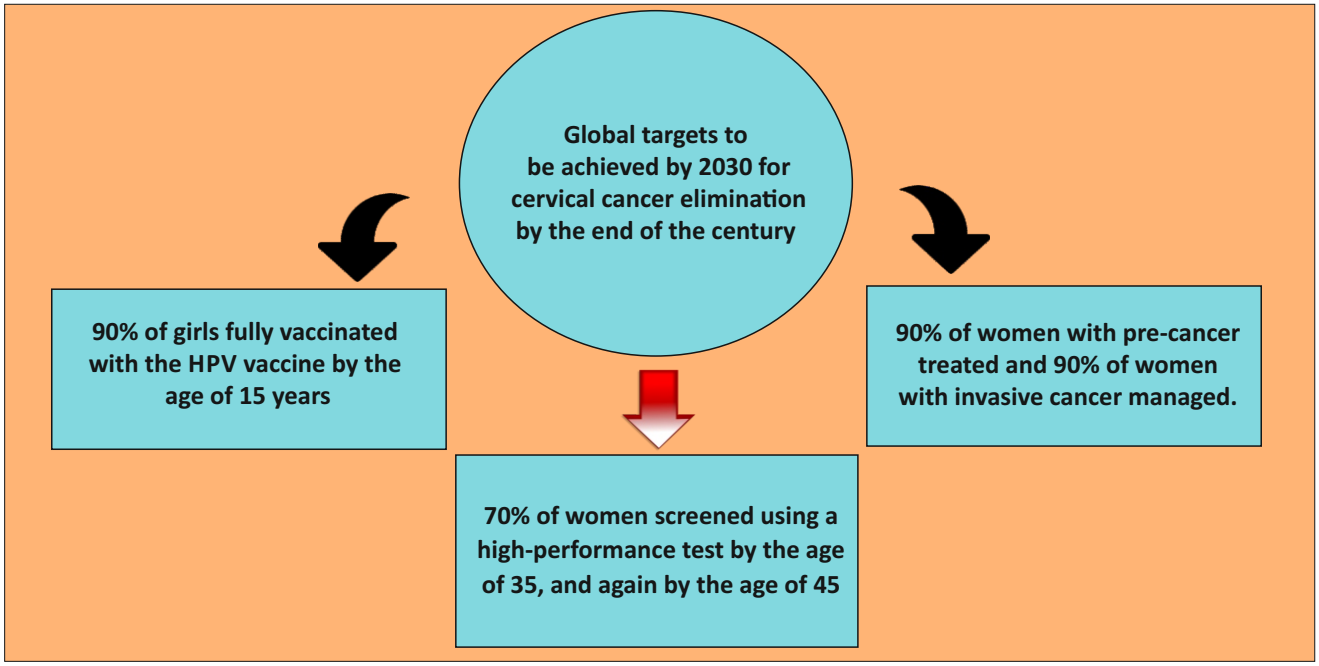

Figure 1 : Components of WHO's global strategy for cervical cancer elimination.

having high sensitivity (i.e. the ability of a test correctly to identify women who are at risk) and high negative predictive value (that the women are truly diagnosed as negative i.e. not having disease). HPV DNA detection meets these requirements compared to other cervical cancer screening tests such as Pap smear, visual inspection with acetic acid (VIA), VIA with magnification and Visual inspection with Lugol's iodine (VILI).

The limitations of cytology/Pap smear testing are well documented in various publications. One study from the United Kingdom reported 27% of cervical cancer diagnosed patients having negative Pap smear report.[5] Pap smear has lower sensitivity (50%-60%), and may miss pre-cancer lesions and hence the recommendations are for frequent testing every 3 years. VIA tis a subjective test and also has challenges with suboptimal sensitivity, high false positivity, and poor performance in post- menopausal women. It needs intensive training of healthcare workers on the interpretation of results, negatively influencing the scaling up of see and treat approach using VIA based cervical cancer screening program.[6]

Various clinical studies has established superiority of HPV DNA detection test over cytology. The large, prospective, landmark ATHENA study was conducted in more than 47,000 women aged 21+ years which lead to US FDA approval of the first clinical validated HPV test – Cobas® HPV. In ATHENA study, the sensitivity of HPV test

was 92% compared to 53% of Pap cytology for ≥ CIN3 detection.[7]

HPV DNA test as primary screening test: Guidelines and recommendations

1) WHO recommendations[4] (Figure 1.)

a. WHO recommends HPV DNA detection as the primary screening test rather than VIA or cytology in screening and treatment approaches among both the general population and women with HIV infection. WHO recommendations suggests transition to the currently ongoing VIA or cytology based programs to HPV test.

b. WHO also provides conditional recommendations for a 'screen-and-treat' approach and 'screen, triage and treat approach' using HPV test as the primary screening test and suggested partial genotyping, colposcopy, VIA or cytology to triage women after a positive HPV test.(Table 1.)

c. Recommendations are also given for starting regular cervical cancer screening at the age of 30 years among the general population of women and from 25 years of age among women living with HIV.

d. Recommendation are given for regular screening interval of 5-10 years in general population and 3-5 years for women living with HIV, when using HPV test as primary screening test.

e. General population of women who have screened positive on an HPV DNA primary screening test and then negative on a triage test are to be retested with HPV DNA testing at 24 months and 12 months for women living with HIV.

	Screen-and-treat approaches
1.	VIA as the primary screening test followed by treatment 11
2.	HPV DNA (self- or clinician-collected) as the primary screening test followed by treatment
	Screen, triage and treat approaches:
3.	Cytology (conventional or liquid biopsy) as the primary screening test, followed by colposcopy triage, followed by treatment
4.	HPV DNA as the primary screening test, followed by HPV16/18 triage (when already part of the HPV test), followed by treatment, and using VIA triage for those who screen negative for HPV16/18
5.	HPV DNA as the primary screening test, followed by VIA triage, followed by treatment
6.	HPV DNA as the primary screening test, followed by colposcopy triage, followed by treatment
7.	HPV DNA as the primary screening test, followed by cytology triage, followed by colposcopy and treatment

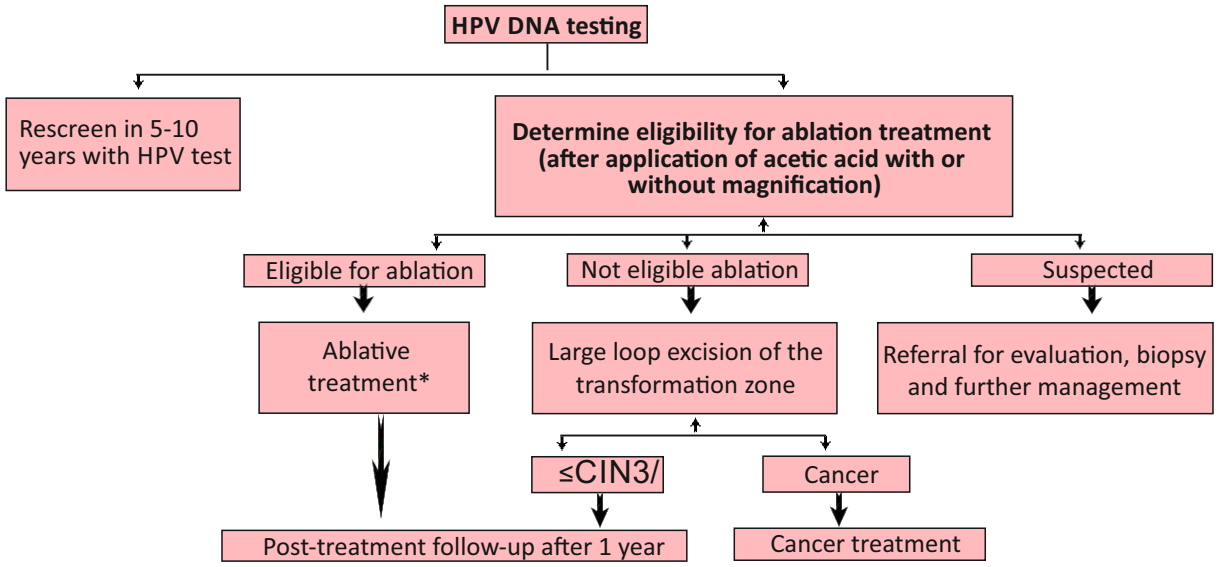

Figure 2. Algorithm of See and treat approach using HPV DNA as a primary screening test

Role of colposcopy in the new WHO guideline

The HPV positive women may be triaged with cytology or colposcopy. Further management based on colposcopy (which is not part of the WHO guidelines) is described in Figure 3.

Though the guideline does not specify, all suspected cancer cases should ideally be evaluated with colposcopy (unless there is a frank growth) and all LLETZ procedures should be performed under colposcopy guidance. Women positive on HPV 16 and/or 18 (when such information is included in the HPV test results) may be managed in a different way compared to those positive for other oncogenic HPV types that are not as virulent as HPV 16/18. As per the recent WHO guidelines, the HPV 16/18 positive women are to be treated immediately while the others may be sent for triaging with colposcopy or other means

2. American Society of Clinical Oncology guidelines for cervical cancer secondary prevention.[8]

In 2017, ASCO resource-stratified guidelines for screening women for secondary prevention of cervical cancer was published and the key recommendations are:

a. HPV DNA testing in all resource settings (maximal, enhanced, limited or basic resource strata)

b. The screening interval and the age ranges-

1. Maximal settings- 25 to 65 years, every 5 years interval,
2. Enhanced settings-30 to 65 years, if two consecutive negative tests at 5 year intervals, then 10 years,
3. Limited settings-30 to 49 years, every 10 years; and
4. Basic-30 to 49 years, one to three times in a lifetime.

3. FOGSI Good Clinical Practice Recommendations (FOGSI GCPR)[9]

FOGSI GCPR also recommends HPV test in all resource settings.

a. Primary HPV testing for women aged 30-64 years with 5 years of screening interval .

b. Primary HPV testing, triaging with cytology, HPV genotyping or VIA , depending on availability.

c. When HPV positive women are triaged with cytology, a normal cytology report should be followed up by a repeat HPV test at one year. Colposcopy and directed biopsy recommended for women with ≥ ASCUS cytology.

Global adoption of HPV test as primary screening test

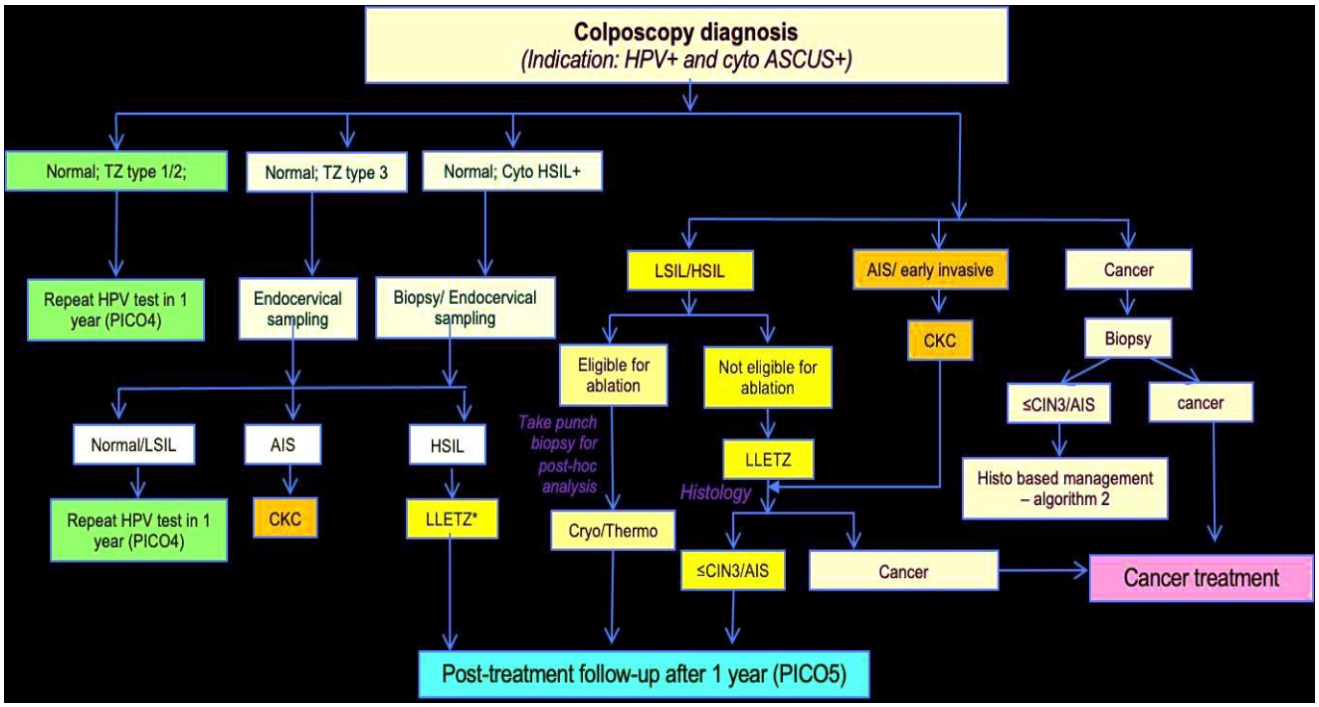

Figure 3. Management of HPV positive women (cytology ASCUS or worse when cytology is used for triaging) based on colposcopic suspicion of disease

The transition to HPV testing from cytology or VIA based testing has taken momentum in recent years. Many countries in Europe namely, Norway, United Kingdom, The Netherlands, Germany, Belgium, France, Denmark, Malta, and Turkey have decided to adopt HPV testing as a primary screening test. Turkey and Netherland have already implemented national program with primary HPV Screening and Germany has opted for Co-testing model.[10] In later part of year 2017, the Australian National Cervical Cancer Screening Program underwent a major paradigm shift switching from biennial cytological Pap testing of asymptomatic women to primary HPV testing (20) and provided 100% screening coverage with HPV testing. Countries like Argentina, Chile, Malaysia, Thailand and Vietnam are transitioning gradually to HPV based program. We expect, this will take strong momentum with the WHO's call for action towards cervical cancer elimination.

Efforts and accomplishments of our Institute: The journey so far

Chittaranjan National Cancer Institute, Kolkata is a premier Regional Cancer Center (RCC) in eastern India registering more than 6000 cancer patients per year. It's preventive oncology department initiated HPV detection based cervical cancer screening since the year 1999 with the launch of the collaborative study with International Agency for Research on Cancer. The Institute was the first to instal Hybrid Capture II technology in India in 1998. The Integrated Programme on Non-Communicable diseases (IPNCD), is the latest project being run at our institute, under the Ministry of Health and Family Welfare, Government of India since 2017. HPV testing is being done at our institutes laboratory using Hybrid capture technique.

Project	Year	Total women screened	Method of screening	Sample collection
Cancer Early Detection and Screening (CEDS)	1999-2003	10,123	Hybrid Capture	Provider Collection
Cervical Cancer Prevention and Control Initiative (CPCI)	2007-2010	48,740	Hybrid Capture	Provider Collection
Cervical Cancer Screening And Prevention (CCSP)	2010-2015	6,336	Hybrid Capture	Provider Collection
Integrated Programme on Non-Communicable Diseases (IPNCD)	2017-November, 2022	35,994	Hybrid Capture & Cobas	Provider Initially-Now converted to self sampling
PRESCRIP-TEC (The Prevention and Screening Innovation Project Toward Elimination of Cervcial Cancer)	2021-Ongoing	1005	Cobas	Self sampling

Table 2. Summary of the past and ongoing projects in our Institute

- Study sites were chosen 30–120 km away from Kolkata and were selected based on the logistic convenience
- Prior to initiation of the project, the key stakeholders governent as well as non- government were identified to develop a partnership
- Initially, in the selected areas all the households were surveyed by trained field workers to identify the eligible women and invite them for screening.
- Women aged between 30 and 60 years with intact uterus, married, not pregnant and with no history of CIN or cervical cancer were eligible to undergo screening
- The core team consisted of four female health workers (Hws), two female social workers, 1 laboratory technicians and one/two clinicians
- Test samples were collected by a health workers and transported in ice-boxes.
- Samples were subjected to HPV testing in Institute laboratory.

Figure 4. Methodology followed for cervical cancer screening by our Institute

Screening practices have been modified with time, and during the recent pandemic situation there has been a shift from outreach camps to door to door awareness and self-sample collection. Where on one hand the ongoing pandemic resulted in widespread mortality and exposed the frailties of the healthcare system world wide, the Preventive Oncology department of Chittaranjan National Cancer Institute, Kolkata upheld its cervical cancer screening activities, by reaching out to the hard to reach, socio-economically disadvantaged and unscreened women at the community setting.(Figure 5.) Several measures were undertaken, including innovating screening techniques by shifting from provider-collected vaginal sampling performed by health workers in camp settings to participant self-collected vaginal smears during the 'door to door' visits by health workers. Dedicated health workers had visited several rural and semi-urban communities in South 24 Parganas. In the comfort of their homes the participants were educated and explained about the procedure of collecting their vaginal samples by themselves, while maintaining COVID safety protocols. The collected samples were then taken to the laboratory at CNCI, Kolkata for testing. High risk HPV positive participants were thereafter transported by hospital provided vehicles in batches for colposcopy and treatment. (Figure 6.) In this manner more than 14,000 participants have already been screened by vaginal self-sampling high risk HPV testing since the onset of the pandemic. This has occurred at a time when non-emergency health services had been scaled down and screening services in several developed nations worldwide have been withheld. It has been found that the high risk HPV positivity rate among participants screened in this manner has been similar to provider collected samples. The compliance to follow up for their treatment in hospital has also remained unchanged hence proving the efficacy, acceptability and success of this screening strategy in the community.

Figure 5. Screening camps held in the community followed by provider collection of samples before the pandemic.

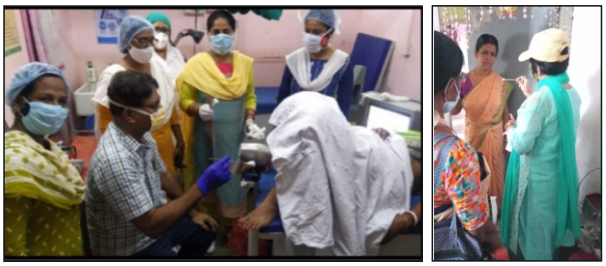

Figure 6. During the pandemic , the health-workers went door to door for self vaginal sample collection followed by colposcopy and treatment at CNCI

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Treatment modalities of Cervical Intra-epithelial Neoplasia

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Introduction

Cervical intraepithelial neoplasia (CIN) is a premalignant lesion which is the sequel of persistent Human Papilloma Virus infection that is diagnosed by histology as CIN1, CIN2, or CIN3.[1] If left untreated, CIN2 or CIN3 can progress to cervical cancer. It is estimated that approximately 1–2% of women have CIN2+ each year, with higher rates reported for women of HIV-positive status, at 10%.

There are three principal treatments available in low- and middle-income countries to treat CIN: cryotherapy, large loop excision of the transformation zone (LLETZ or LEEP), and cold knife conization (CKC). Treatment methods need to be effective but also minimally damaging and uncomplicated. Treatment methods of actual or suspected CIN should be both effective and safe. *Effective* treatment of CIN implies eradicating the TZ and reducing risk of cancer to nearly zero. *Safe* treatment implies reducing the risk of complications to an absolute minimum.

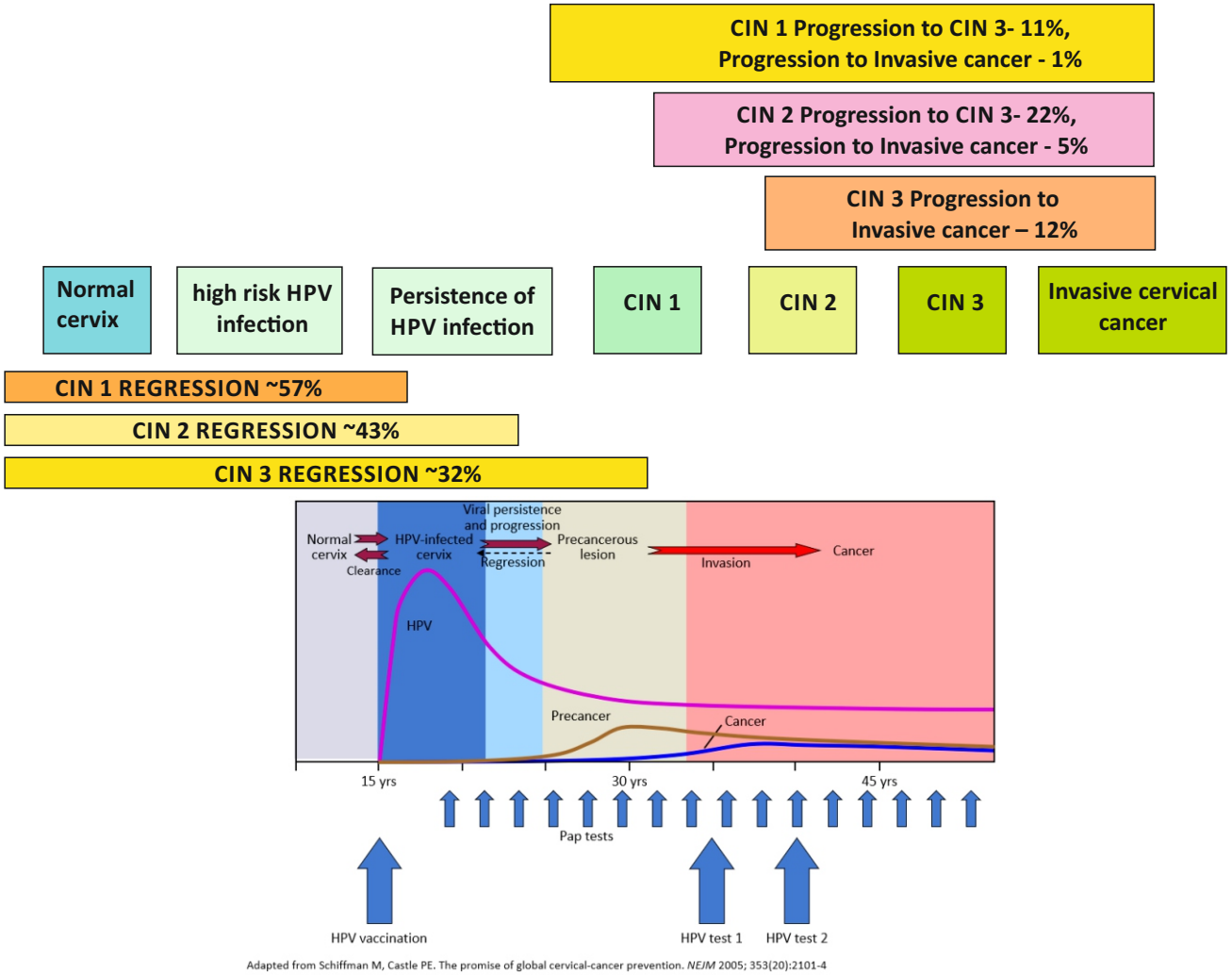
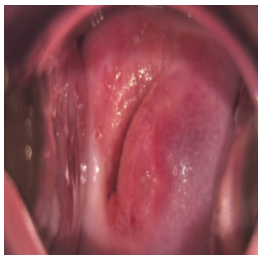
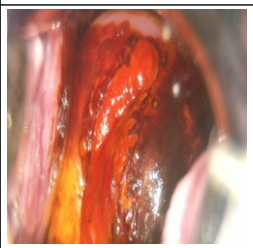
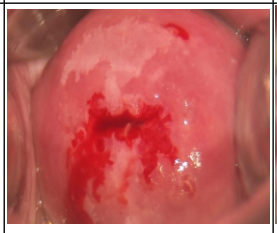
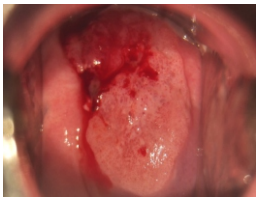
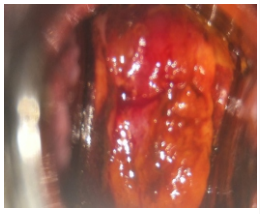


Figure 1: Natural History of Cervical Intraepithelial neoplasia[2]

CIN classification	Corresponding Bethesda Cytology	HPE Description	After Acetic acid	After Lugol's iodine
CIN1	LowGrade squamous intraepithelial lesion (LSIL)	Mild dysplasia Confined to 1/3 rd of the epithelium		
CIN2	High Grade squamous intraepithelial lesion (HSIL)	Moderate dysplasia Confined to 2/3 rd of the epithelium		
CIN 3	High Grade squamous intraepithelial lesion (HSIL)	Dysplastic epithelium may involve full thickness		

Natural history of HPV and CIN

Each individual case of cervical cancer arises from persistent infection with a specific high risk HPV (most common being 16,18,31,33). It may take decades from the time of acquisition of HPV to invasive cervical cancer. Dysregulated expression of E6 and E7 in replicating basal cells leads to disturbances of cell-cycle regulation and apoptosis. The changes include disruption of the retinoblastoma protein (pRB) family regulatory pathway by E7, which results in accumulation of p16 and the P53 pathway by E6 viral oncoprotein. CIN 1, 2 and 3 lesions are identified on the basis of nuclear abnormality with respect to the position in the epithelium in thirds, in ascending order from the basal layer.

Diagnosis of CIN

CIN lesion arises from squamo-columnar junction (SCJ) within the transformation zone (TZ) of the ectocervix. The transformation zone is defined as the Table 1 summarizes the CIN and the different terminologies. CIN can start in any of the three stages and can either progress or regress.

Treatment

Treatment of cervical precancers depends on age of the patient, preceding screening test abnormalities, colposcopy findings and patient compliance. *"Screen and Treat"* and *"Screen, triage and treat"* are accepted methods of managing cervical precancers. In population where compliance is an issue, *"Screen and treat"* is preferred. In the *"Screen, triage and treat"* approach, while using HPV DNA detection as the primary screening test among the general population of women, partial genotyping, colposcopy, VIA or cytology may be used to triage women after a positive HPV DNA test. There may be slightly more treatments and preterm deliveries with a *"screen-and-treat"* approach. [2]

CIN 1 is best managed by follow up. In case of persisting CIN 1 for more than 2 years, treatment may be considered.

CIN2 is in grey zone and these lesions may be triaged by Immunohistochemistry (IHC) markers p16INK4A or Ki 67. Evidence suggests that p16 is strongly over expressed in dysplastic cervical cells because of the transforming

activity of the E7 oncogene of all high-risk human papillomavirus (HR-HPV) types.[3] Ki 67 is a proliferative marker and is directly proportional to degree of dysplasia. Women with negative baseline dual staining (DS) results have significantly lower 5year risk of CIN 2 or higher.[4] Therefore, CIN2 lesions with DS positive may undergo immediate treatment whereas follow up is an option for young women who are DS negative and willing for future child bearing.

As **CIN3** is considered as the true cancer precursor, immediate treatment is recommended.

Two types of treatment are available: Ablative and Excisional

Ablative procedures which include Thermal ablation (TA) Cryotherapy (CT) and Laser ablation (LA). Ablation to a depth of 7 mm is considered optimal as CIN may be found in the crypts of the glands as deep as 4 mm. Ablative methods are considered when they fulfil the following criteria:

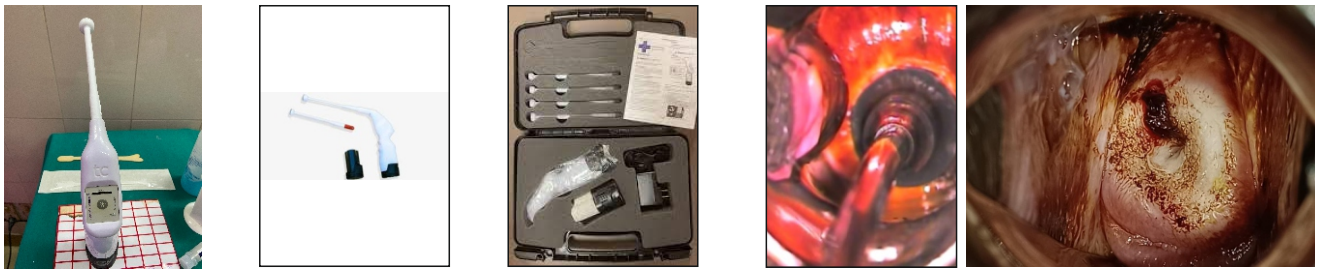
- The entire lesion should be visible and on ectocervix or TZ type 1
- No endocervical extension
- Less than three quadrant involvement
- No suspicion of Invasive cancer or glandular abnormality on cytology.

Thermal ablation : It was developed by Kurt Semm of Kiel, Germany in 1966 when it was called cold coagulator. It is also called thermocoagulator. It has been used worldwide, but most notably in the UK. It utilizes electricity to heat a thermosound to temperatures of 100–120°C, allowing for ablation of cervical epithelial lesions by "boiling." Clinically, it is acceptable as outpatient department (OPD) procedure, especially for small lesions. No anaesthesia is required and it is currently available in India.

In 2019, WHO published special guidelines for the use of thermal ablation for cervical precancer as this method was not included in the earlier guidelines of 2011.[5] This is an ablative procedure for CIN 2+ disease. Colposcopic evaluation or Lugol's iodine test are mandatory to plan the procedure.

Women who are eligible are those where the entire lesion is seen, either on ectocervix or slightly in the endocervix where the probe can reach. A patient is considered unsuitable if the lesion is high in the endocervix beyond the reach of the probe. Multiple applications of 20–30 seconds each at a temperature of 100°C till the entire abnormal area undergoes ablation. Thermal ablation provides an advantage of multiple applications. The battery-operated device is easier to use and carry which is an advantage while using in outreach camps. (Figure 2)

Nurses and paramedicals may be trained to undertake the procedure. The recommendation states that if both LLETZ and thermal ablation are available, suggest LLETZ. If after thermal ablation, the patients' tests turn out to be positive, WHO recommends LLETZ.



2a **2b** **2c** **2d**

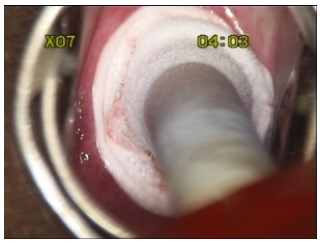
Figure 2a+b+c : Battery operated thermal ablator from Liger(R) 2d: Cervix following thermal ablation
(2d image courtesy: IARC atlas of VIA of cervix with acetic acid for screening, triage and assessment for treatment)

Cryotherapy: It is an ablative procedure. Liquid nitrogen is used to destroy abnormal tissue (Fig. 3). There is cryonecrosis, dehydration of cells which leads to vascular stasis and protein denaturation. Double freeze-thaw cycle is recommended. It takes about 20–30 minutes. Anaesthesia is not required. It is extensively used worldwide and has excellent results. The paramedical staff can be trained to do the procedure. It is the mainstay of "see and treat" policy.

The recommendation of WHO guidelines (2013, 2014) states that "the expert panel's strong recommendation is for cryotherapy over no treatment for women who have histologically confirmed CIN 2+ disease".[3],[12] However, the available evidence is low. There is some uncertainty related to the preterm delivery in future pregnancies. The benefits outweigh the risks. Further, this technology is possible in low resource settings. There is lower risk of

developing cervical cancer and related mortality due to cervical cancer.

In cryotherapy, nitrous oxide (N_2O) or carbon dioxide (CO_2) gases are used to induce the freezing effect on the cervix. The temperature of either of the gases, when released to atmospheric pressure, drops to -60 to -80 °C. The tissue temperature is reduced to -20°C, causing permanent damage to the epithelial cells in the transformation zone. 3 minutes "freeze"- 5 minutes "thaw"- 3 minutes "freeze" method is generally used. It is however cumbersome to carry nitrous cylinder and equipment around and it takes longer time for the entire process of cryotherapy.

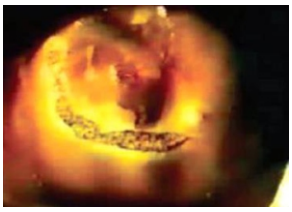


Cryotherapy probe application on the cervix

Cryotherapy probe and cylinder unit

Figure 3

The CO2 laser: This can be used for ablation or for excision. It is a powerful tool, used by oncologists and ear, nose, and throat (ENT) specialists, and is expensive. If it is available, it should be used for the treatment of CIN. Its advantage is that it can be used to treat HPV lesion in the entire genital tract. Vulval, vaginal, and perianal warts can be successfully treated. For young patients who have yet to complete their families CO_2 laser ablation is most suitable (Fig. 4).



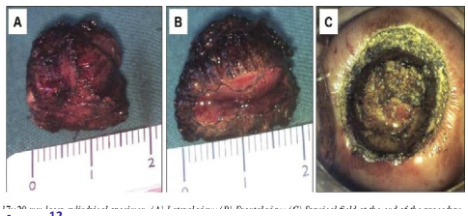


Fig 4: CO_2 laser procedure[12]

2. Excision procedure is by loop excision of transformation zone (TZ) or LLETZ, Straight wire excision of transformation zone (SWETZ), laser excision and Cold knife conisation. In case where the lesion does not fulfil any of the criteria, excision is preferred.

Large loop excision of transformation zone: This terminology is preferred over loop electrosurgical excision procedure (LEEP) as it qualifies that transformation zone is the target as LEEP is often used in taking multiple small biopsies with small loops. It is mainly an excisional therapy and very suitable for high grade lesions. Follow-up is still needed and the tissue excised should be sent for histopathology. It can be done under local anaesthesia. A number of loops of different sizes and a good electrocoagulation machine must be available (Fig. 5). A prior colposcopic evaluation is recommended. The entire abnormal area is to be excised. A second "pass" may be done if some tissue is left behind. Adequate training in this procedure is necessary. The base is cauterized and the patient is observed for 2–4 hours for any hemorrhage. Follow up is done after 4–6 weeks. This procedure is strongly recommended by WHO. The benefits outweigh the risks. At 6 months, HPV clearance is 89.1%, but drops to 64.7% at 1 year. The major complications are hemorrhage at 2/1,000, Infection at 1/1,000 and preterm deliveries may go up to 37 more preterm per 1,000. Hence, it may be restricted to women who have completed their families. The risks are low in good setting. However, the facilities for LLETZ are limited and they need to be expanded. The referral system also needs to be strengthened.

After positioning and a local anesthetic injection, a suitable sized loop is used to glide through the cervix "like hot knife on butter" in a side-to-side or above-downwards direction. Hemostasis is achieved with ball cautery. The specimen is taken out preferably in one piece.

Figure 5a: Table layout for LLETZ : includes Sponge-holding forceps, insulated speculum, Cotton-tipped swabs, freshly prepared 5% acetic acid, Lugol's iodine, Monsel's solution/paste, Local anaesthetic injection, Dental syringe (preferred) or 22 G spinal needle or 10 cc syringe and needles, vials containing 10% formaldehyde for

collecting tissue for biopsy and sutures to control bleeding.

Conization: This is also known as Cold Knife Conization (CKC). In the absence of any equipment, it is still possible to do a conization of the cervix. Lugol's iodine may be applied to denote the abnormal epithelium on the ectocervix. Circular incision is taken all around the lesion and a cone-shaped area excised (Fig. 6). It is possible to take a small cone and not suggested to go deep into the endocervix to avoid brisk hemorrhage. Cauterization of the base is needed. The patient should be kept under observation for at least 6 hours and called for a follow-up after 10 days. It is both diagnostic and therapeutic.

Currently, it is not practiced much in view of high morbidity due to hemorrhage and infection. The WHO recommends CKC when no other treatment is available. Benefits still outweigh the harms which include both hemorrhage and infection both 9/1,000. Subsequent obstetric complication of premature labor is significant at 100 more preterm deliveries per 1,000. Ortoft et al. in 2010, reported that perinatal mortality and preterm delivery increases in subsequent pregnancy after conization of the cervix.[6] Similar experience has been reported by Bruisma and Quinn (2011).[7]

The easy availability in low resource setting makes it acceptable to the patients. The WHO guidelines also recommend CKC over LEEP in cases of adenocarcinoma in situ.

Cold knife conization may result in fewer recurrences, and the panel felt that this benefit outweighed the additional resources required for CKC. Kim et al. have stated in 2011 that it is a single procedure for the treatment of adenocarcinoma in situ.[8]

(Image courtesy: IARC atlas of VIA of cervix with acetic acid for screening, triage and assessment for treatment)

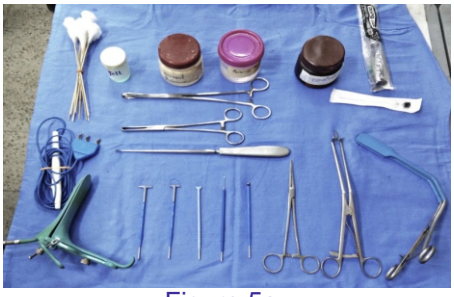


Figure 5a

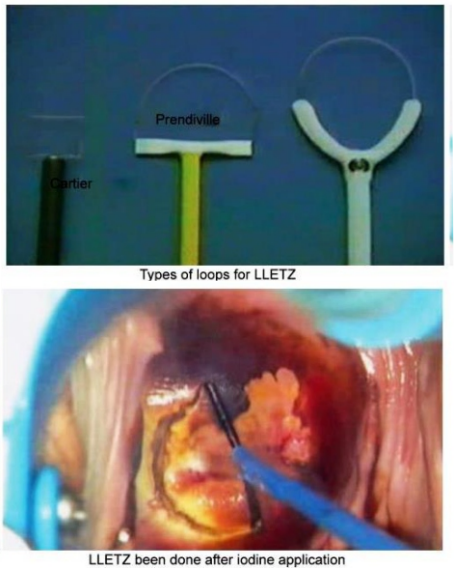


Fig 5b: LLETZ procedure[12]

Hysterectomy is best avoided for CIN except for associated benign gynaecological disorders or Adenocarcinoma in situ (AIS). Details of the treatment is summarized in Figure 7.

Adenocarcinoma in situ : Unlike Squamous cervical precancer where HPV independent entities are not recognised in the who classification, adenocarcinoma precursors may be HPV dependent and independent. The HPV independent precancers behave more virulently. The HPV-associated lesions, termed AIS, constitute the majority of cases. Excision methods (CKC and LLETZ) are preferred over ablation. Hysterectomy is an option for women who have completed family.

Special situations

CIN in pregnancy n: Majority of CIN lesions regresses in postpartum period. This may be either due to natural history of the disease itself or misinterpretation of histopathological findings in antenatal period. In case of absence of invasive disease, treatment of even CIN2, CIN3 can be deferred till 6 weeks postpartum with re-evaluation by colposcopy and/or biopsy.

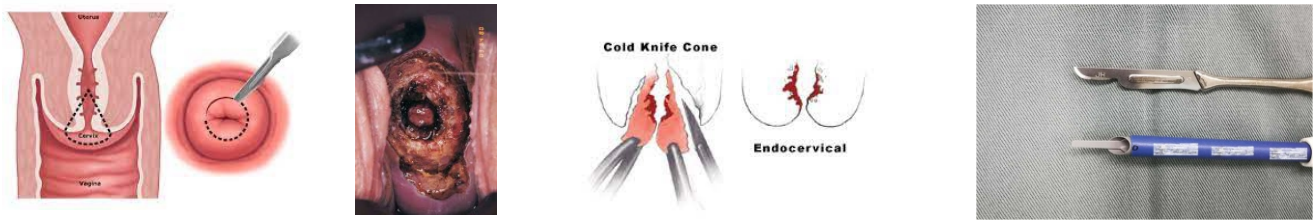


Fig 6: conization procedure

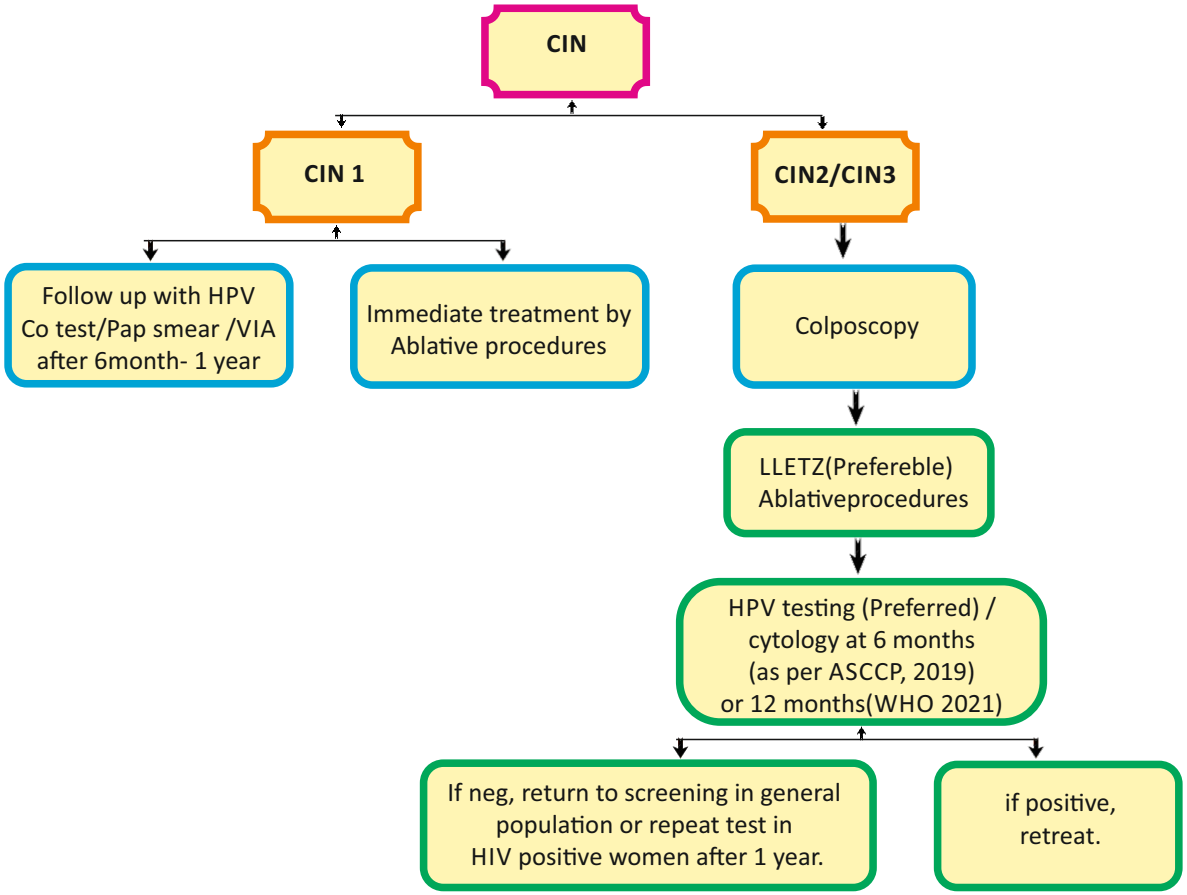


Figure 7: Simplified Management of Cervical Intra epithelial Neoplasia (CIN)

CIN in HIV infected women : Higher rates of persistent HPV infection and CIN are seen in adolescents with HIV, regardless of whether HIV was acquired vertically or horizontally.[9] *"Screen triage and treat"* approach is recommended and the management is similar in line with the non-immunocompromised women.[10] The chance of treatment failure and progression to higher grade is high in these women and therefore requires more stringent follow up as seen in figure 2.

Post treatment follow up : Women with CIN are at greater risk of developing invasive cancer than the general population and the risk persists as long as 20 years. Overall, the rate of recurrent or persistent CIN is reported to be 5-17%[11]. Most of the failures occur within 2 years after treatment. HPV testing has a high negative predictive value therefore can be used as a test of cure.

Experimental modalities of treatment : Studies have shown that HPV vaccination may be used to prevent recurrences of CIN2+ lesions after treatment in previously unvaccinated women. Trials of topical therapy with immune-modulating agents (imiquimod), anti-proliferative agents (5-FU), and anti-viral agents (cidofovir) therapies have had the most promising results, but there is need for more evidence.

Conclusion : In the context of young women, the aim is to treat women with high risk of developing invasive disease. Those who are not at high risk are observed and kept on follow-up as the treatment can have adverse consequences on the future pregnancy. The aim is also to protect them for harms of over-treatment. These good clinical practice recommendations (GCPR) have taken into consideration the available resources, clinical conditions, population preferences, and research evidence in the Indian context and are suitable for adoption in other low and low-middle income countries.

Finally, many good treatment modalities are available today which have revolutionized the management of pre-invasive cervical carcinoma. Conservative procedures can avoid a hysterectomy but the need for life-long follow-up is difficult to achieve. With the increasing role of screening of Asian population, many more cases of CIN will be detected. Globocan (2020) has given us encouraging picture of decreasing Incidence and mortality in cervical cancer the world over. However, the total number of cases shows an increase due to rise in population. This in turn may lead to higher number of CIN being detected globally.

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HPV Vaccination- A step Forward to Cervical cancer Elimination

Abbreviations

WHO- World Health Organisation

HPV- Human Papilloma Virus

SAGE- Strategic Advisory Group of Experts

FOGSI- Federation of Obstetric and Gynecological Societies of India

GCPR- Good Clinical Practice Recommendations

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Breast Cancer Screening

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Breast is considered to be the epitome of female beauty in all of the cultures. Yet this tissue harbors the commonest cancer for women which accounts for the second leading cause of oncological deaths in female bodied persons, in our country. Data shows that, India had approximately 1,82,000 breast cancer patients by the end of 2022.

Indeed, a fearful statistic, but not as sinister as it should have been. Fortunately the modern treatment of breast cancer has a very good outcome, resulting in cure or long term remission, if diagnosed and treated early, and here comes the importance of screening.

Breast screening like every other screening, is performed on women without any signs or symptoms of breast cancer, to diagnose the disease in early stage. Although traditionally assessed by triple assessment, i.e., breast awareness, clinical breast examination and mammography, case specific ultrasonogram and/or MRI can also be used as screening tests.

So, we got three unfamiliar terms. Let's see what those are...

1. Breast Awareness :

- Breast awareness is nothing but familiarity with one's own breast. It *includes breast self-examination, i.e., using one's hands and eyes to look* for any abnormality in any of the breasts, for which the following steps should be taken.

Begin with visual examinations: One should inspect her own breasts, in a *sitting or standing* position, in front of a mirror.

- What should be looked for?

Puckering, dimpling, or changes in size/ shape and symmetry.

Any inversion or retraction of nipple.

- *Repeat the same, with,*

a. Hands pressed down on her hip.

b. Arms raised overhead.

c. Palms pressed together.

d. Lifting the breasts.

- *Next use hands: the person should lie down/ lather her fingers in a shower for easier feeling.*
- *The pads of the middle three fingers should be used.*
- *The goal is to feel distinct levels of breast with change of pressure with the fingers.*
- *The feel should be performed in a systematic way, so that no partof breast is left unexamined,*
- *The best time of palpation is the first few days of menstrual cycle.*

It is to be remembered that, breast awareness is just an initial test. It doesn't mean anything, unless confirmed by a qualified doctor. Any lumps/ knots/skin changes/FNAC changes/discharges should be immediately reported to a clinician, for further examination.

2. Clinical Breast Examination :

It should be done by a qualified doctor, where the doctor makes a detailed evaluation of patient's history and performs a body checkup. This should not be delayed when the patient &/or the party suspects some abnormality.

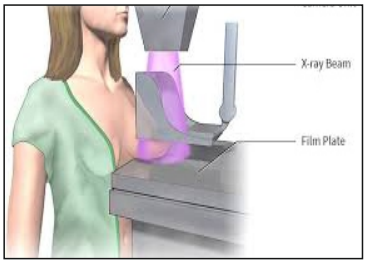

Fig. 5: Mammography Unit

Mammography :

A special kind of x ray, which is performed in 2 directions, to show up and small hidden lump in breast which is non-palpable or barely palpable by hand. An age-old method of screening. But this test is less sensitive to young, dense breasts, where we often replace it with ultrasound/MRI.

For screening, the women are divided into two major groups, those of normal risk and those with increased risk. **Females *with family history of breast, ovary, endometrial cancers, females with one sided treated breast cancer, with history of chest radiation, with diagnosed genetic predisposition* are considered high risk.**

The second factor considered for screening is age.

Age	Normal risk	Elevated risk
<25	▪ Nothing as such	▪ Breast Awareness ▪ Clinical Breast Examination every year
25-40	▪ Breast Awareness ▪ Clinical Breast Examination every 1-3 years	▪ Breast Awareness ▪ Clinical Breast Examination every year ▪ Mammography once a year
>40	▪ Breast Awareness ▪ Clinical Breast Examination every year ▪ Mammography once a year	▪ Breast Awareness ▪ Clinical Breast Examination twice every year ▪ Mammography once a year

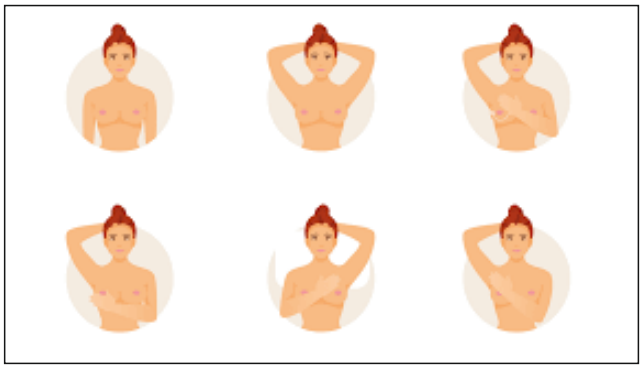

Fig. 1: Different position of breast examination

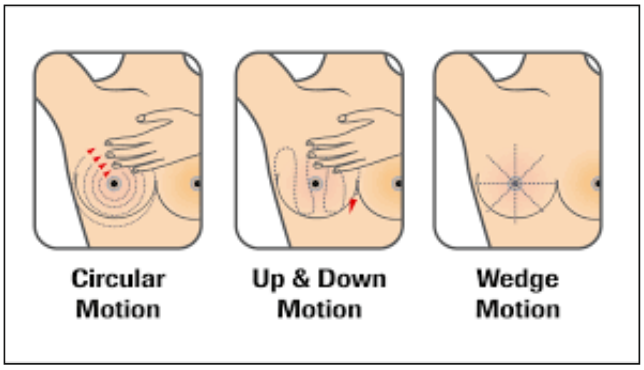

Fig.2: Direction of movement of hands during palpation

Screening protocol is usually as the following chart depicts:

So, to conclude,

Here are four key points to remember.

- The risk is assessed by a doctor and only by a doctor.
- Mammography should be done under supervision and with advice from a doctor. A patient shouldn't go on her own to do her mammography.
- Yes, there is radiation exposure during Mammography, so for screening the minimal possible frequency of tests has been advised assessing the risk/ benefit ratio.
- No screening test can confirm the presence of a cancer. So, if the doctor suspects then he will confirm the disease with a biopsy before treatment.

Often patients do neglect their initial signs or suspicions of breast cancer, due to shame or fear of losing one or both of the breasts, which psychologically presents as loss of womanhood, for them a few points are to be remembered.

1. Breast cancer is a curable disease in most of the early cases, while when presented late it often results in death. WHO 2020 data shows 6,85,000 of 2.3 million patients had died, due to this cancer. Where there were 7.8 million 5 year or more survivors present worldwide on that specific year.

2. For those who are afraid of losing their breast, early detection is helpful, as only the lump and the surrounding small amount of tissue is removed in early breast cancer.

3. The screening of breast cancer is quite efficient and can diagnose 8 of 10 early cancers.

Screening is a tool for choosing a healthy life over death... at least for breast cancer....

Choose life.... Screen....

Prevention of Oral Cancer : Myth or Reality?

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Prevention of oral cancer has been a much-written topic with many Global and National initiatives. But across the world a successful reproducible model for Oral Cancer Prevention is yet to materialize.

It is well known that the more than ninety percent of oral cancer can be directly linked to the consumption of tobacco with or without alcohol. Yet the easy availability and widespread use of these products defeats all attempt to stop the calamity. India is the second largest tobacco producer behind China. The tobacco industry of India employs about 36 million people in farming, labour activities, manufacturing, processing and export activities. The average annual revenue collection, from tobacco products, stands at about Rs 53,750 crore as on August 2021

Hence the question arises, can one prevent a disease which is also actively promoted?

Populations belonging to low socioeconomic status are the main victims of oral cancer due to a combination of lack of awareness regarding the ill-effects of tobacco and alcohol use coupled with the social acceptance, advertisement and the promotions of these products. Strangely the calamity of this disease fails to make any dent on the population consuming tobacco allied products and alcohol. Oral cancer is not a rich man's disease and draws little attention to its devastating consequences across our society. Compare that to the media discussion on the pros and cons of car-seatbelts to save lives. Hence preventive interventions for oral cancer have been has been left to government initiatives and NGO's working with these categories of people of the lower social rungs.

Primary Prevention of Oral Cancer: policies on cessation of exposure to risk factors & cessation interventions

Govt. of India ratified the WHO Framework Convention on Tobacco Control (WHO FCTC) in 2004, for various measures to reduce the demand as well as supply of tobacco. Under this framework, the various strategies adopted can be listed as successful strategies or failed strategies:

We can list four successful strategies for primary prevention:

- Price and tax measures to reduce the demand for tobacco.
- Protection from exposure to second hand tobacco smoke.
- Packaging and labelling of tobacco products.
- Education, communication, training and public awareness.

Equally we can list four failed or unsuccessful strategies of primary prevention

- Tobacco content and product regulation.
- Tobacco advertising, promotion and sponsorship.
- Demand reduction measures concerning tobacco dependence and cessation.
- Provision of support for economically viable alternative activities.

The two almost negate each other and hence the aims of primary prevention for oral cancer have not been able to achieve much results.

Secondary Prevention of Oral Cancer: screening for oral cancer

Clinical oral examination and palpation of the oral cavity mucosa and the external facial and neck regions is the only screening method that is routinely used for the detection of oral cancer. It is reasonable to conclude that unlike breast or cervical or gastric cancer, the oral cavity is quite accessible for examination and hence oral cancer should be possible for early detection. The crux of the problem is that detecting oral cancers early is easier said than done. There exists insufficient data on the success of preventing oral cancer through early detection. Even with the best manpower utilization present early detection programs have been a logistic nightmare for almost every country even with best utilization of resources. Despite oral cavity being accessible for examination, individuals report to a clinician only in later stages of the disease, thus no improvement in

survival rate for oral cancer over the decades have been observed.

Images of common Premalignant conditions :

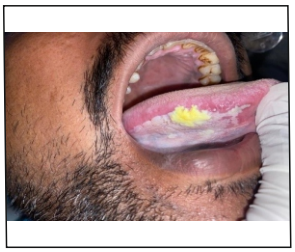

Fig-1 leukoplakia on tongue

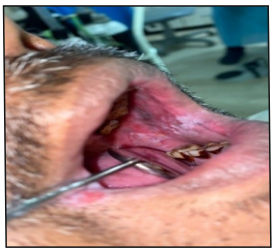

Fig-2- Leukoplakia on Buccal mucosa

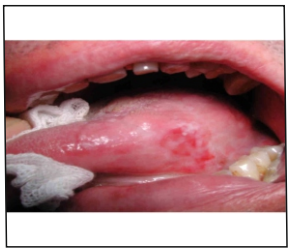

Fig-3- Erythroleukoplakia on tongue

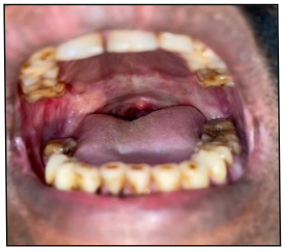

Fig 4- Oral submucous fibrosis

Tertiary Prevention of Oral Cancer: early diagnosis and treatment Since

Primary and Secondary prevention have not been successful, we must fall back on the science of early diagnosis and treatment to reduce the catastrophic consequences of oral cancer on our society. This approach results in waste of precious resources and merely converts a preventable disease into a chronic mutilating illness with long term consequences on our society. There are very few cancers where the relationship between cause and effect is so well documented yet even with a million deaths a year due to oral cancer, we continue to ignore the science. Even when we know that prevention offers the most cost-effective long-term strategy for the control of oral cancer, we seem to flounder when the strategies are to be implemented.

So how do we approach this vexing subject of prevention of oral cancer?

First we must accept that the concepts of Primary Prevention need enforceable clauses and penalty clauses to make them realistic goals. Second our health system will have to conceptualize a practical reproducible Oral Cancer Screening Program especially for high-risk population. Access to early biopsy and histopathology facilities would be crucial for early diagnosis and treatment. And lastly due to the paucity of data in the area of oral cancer prevention, focussed research in all aspects of preventive intervention for Oral Cancer needs our urgent attention.

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Dr. Sharad Kumar Agarwal, National President of IMA and Dr. Santanu Sen, MP, Past National President of IMA, and Hony Secretary IMA Bengal State giving their valuable speeches at 82nd BIMACON, Hotel Stadel, Salt Lake City, West Bengal,

The Role of Research in the Modern Management of Cancer

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The study of cancer has been one of the most interesting journeys in the vast landscape of medical research. Over the last few decades the diagnostic and therapeutic aspects of cancer management have gained tremendously from various areas of research in both medical and non medical sciences. The cross utilization of appropriate technologies have given unforeseen benefits to patients and added to the armamentarium of treating doctors alike. Yet the challenges ahead dwarf the substantial achievements made in this regard and act as a continuous impetus to generations of basic and clinical science researchers across the globe.

Research is the most important area of modern medicine. The proper understanding of research methodologies and their judicious implementation remain the cornerstones for advancements in modern medicine. Needless to say that the giant steps mankind has taken in the field of oncology were begotten by the small steps taken by generations of research workers toiling tirelessly at the cutting edge of medical science. It is due to their relentless efforts that a number of cancers without hope have now been tamed into treatable and controllable diseases.

One of the earliest evidences in this regard was from the treatment of Chronic Myeloid leukemia (CML). CML accounts for 15-20 percent of all Leukemias, primarily affecting adults. The only curative therapy for this disease was a bone marrow transplant, but that treatment carried numerous risks and was available only for those patients who found a matching donor. Basic science researchers identified the precise abnormality that caused the white blood cells to grow uncontrollably in this leukaemia. This abnormality is an enzyme, called a tyrosine kinase that normally regulates cell growth. In CML, due to an exchange of genetic material between two chromosomes (known as a translocation), a mutated enzyme is produced. Instead of regulating cell growth, this enzyme now signals the cells to grow continuously, thus leading to leukaemia. Imatinib is a drug which was developed in late 1990-early 2000 which works by completely shutting down this specific abnormality at the molecular level. This once-a-day pill treatment has been well tolerated, with minimal side effects. In short, it is a simple, effective treatment that disables the cancer without disabling the patient. In May 2001, the FDA approved Imatinib for the treatment of CML in record time. This opened the flood gates for what is today known as Biologically Targeted therapy in the treatment of cancer. Today a variety of cancers including Leukemias, Lung cancer, sarcomas, Renal cell cancer, Hepatocellular cancer, Cholangiocarcinoma amongst others have been encompassed in the purview of targeted therapies, This list keeps growing by the day and the efforts of years of research have finally begun to bear fruit.

Radiotherapy has come a long way since the olden days of deep XRAY and Radium machines. Today both external beam radiotherapy and brachytherapy; the two main modalities of radiotherapy, have become more safe and effective compared to the older generation machines. The advent of modern machines like the Cyberknife, MR LinAc, Proton Beam therapy, Helical Tomotherapy, coupled with improved software for adaptive and AI Based segmentation have madelife much easier for the practising radiation oncologist. All this has been a result of continuous innovation and development being pursued in various fields of science including medical physics, computer science, AI as well as Radiobiology. The culmination of all these efforts is evident in the results being obtained in modern radiotherapy wherein the side effects are minimal compared to historical data and higher doses are being delivered safely without causing untoward effects to the patients.

Ultra-high dose rate (FLASH) radiotherapy is a new way of treating tumours caused by cancer. Higher doses of radiotherapy are associated with trauma to the healthy tissue surrounding the tumour, whereas FLASH radiotherapy demonstrates a sparing effect of the healthy tissues without compromising the anti-tumour action. The very short radiotherapy time compared to that of conventional dose-rate radiotherapy is another advantage of FLASH-RT. Although still in trial phase the future looks bright for this form radiotherapy.

Surgical Oncology has also been striving to achieve newer heights with the advent of modern technologies. Robotic surgery (also called robotic-

assisted surgery) is perhaps the most cutting-edge medical technology of modern times. The most widely used system today involves a camera and the use of very small surgical tools attached to robotic arms. A specially trained surgeon controls the robotic arms from a viewing screen, which is usually situated in the same room as the operating table. But the viewing screen could be located far away, allowing surgeons to perform telesurgery from remote locations. The screen is part of what is referred to as a console, which allows surgical procedures to be performed from a seated position, while the surgeon views a magnified three-dimensional view of the patient's surgical site.

Finally the newest entrant in this area is cancer immunotherapy. It is also an excellent example of the value of research in cancer. Researchers began to think that activating the immune system could fight tumours more than 100 years ago. But efforts to develop treatments based on this idea—with vaccines, for example—foundered in part because researchers didn't understand enough about how the immune system works. Years of research finally culminated in the 2018 Nobel Prize in Physiology or Medicine being awarded jointly to James P. Allison and TasukuHonjofor their discovery of cancer therapy by inhibition of negative immune regulation. This literally changed the approach of cancer therapy across thousands of patients in hundreds of centres across the world.

Immunotherapy is a broad category of cancer therapies that triggers the body's immune system to fight cancer cells. Cancer cells are different from normal cells, in that they do not die normally. These abnormal cells frequently change, or mutate, helping them evade the immune system, which protects the body from disease and infections. Cancer immunotherapy drugs are designed to alert the immune system about these mutated cells so it can locate and destroy them. Several types of immunotherapy are used to treat cancer. These include:

- Immune checkpoint inhibitors, which are drugs that block immune checkpoints. These checkpoints are a normal part of the immune system and keep immune responses from being too strong. By blocking them, these drugs allow immune cells to respond more strongly to cancer.
- T-cell transfer therapy, which is a treatment that boosts the natural ability of T-cells to fight cancer. In this treatment, immune cells are taken from the tumour. Those that are most active against the cancer are selected or changed in the lab to better attack cancer cells, grown in large batches, and put back into the body using the intravenous route. T-cell transfer therapy is also being called adoptive cell therapy, adoptive immunotherapy, or immune cell therapy.
- Monoclonal antibodies, which are immune system proteins created in the laboratory that are designed to bind to specific targets on cancer cells. Some monoclonal antibodies mark cancer cells so that they will be better seen and destroyed by the immune system. Such monoclonal antibodies are a type of immunotherapy.
- Treatment vaccines, which work against cancer by boosting the immune system's response to cancer cells. Treatment vaccines are different from the ones that help prevent disease like HPV and Hepatitis B vaccine.
- Immune system modulators like interleukins and interferons which enhance the body's immune response against cancer.

To summarise, the role of cancer research is invaluable in our global war against cancer. Researchers around the world are in a race to find better ways to prevent, detect and treat cancer and ensure that survivors live longer, better lives. But they know that this race is a marathon, not a sprint. Cancer research won't stop until cancer does.

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