"A Return to Cancer Screening"

Developed By the Medical Society of the State of New York's Heart, Lung, Cancer Committee

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"RETURN TO CANCER SCREENING"

The impact of Covid on early detection and cancer screening in NY state

In 2019 and early 2020, the Medical Society of the State of New York's Heart, Lung Cancer Committee began development of a prevention and screening tool that could be used as a guideline for MSSNY to advocate for insurance coverage and to compile the evidence-based guidelines into one "document" for its members. MSSNY Policy 125.996 *Screening Programs and Interventions Most Beneficial in Improving the Overall Public Health* is the result of many years of advocacy for the rights of patients to have access to various screening services and interventions most beneficial in improving the overall health of the public. Obviously access to these important health care service recommendations is dependent upon the acceptance, agreement and availability by relevant private and public insurance entities, which is why MSSNY continues to support and advocate for insurance coverage for all these screening programs. MSSNY physicians recommend prevention, screening, and early detection as important factors in achieving good public health.

MSSNY Policy 125.999 states the following:

MSSNY has long advocated for the rights of patients to have access to various screening services and interventions most beneficial in improving the overall health of the public. Obviously access to these important health care service recommendations is dependent upon the acceptance, agreement and availability of them by relevant private and public insurance entities, which is why MSSNY continues to support and advocate for insurance coverage for all of these screening programs. MSSNY Policy 125.996 was developed and put forward to the MSSNY Council in 2010 and was also reaffirmed by the MSSNY Council in 2011. **(PLEASE SEE APPENDIX A FOR COMPLETE POLICY).**

"The Pandemic"

However, as the coronavirus pandemic raged in 2020, the number of people getting screened for cancer in the United States dropped dramatically. Medical offices and other screening facilities closed in 2020 and some of those facilities are now facing severe staffing shortages. At the height of the pandemic, many patients were afraid to go to these facilities and hospitals for fear of exposure to COVID 19.

An estimated 9.4 million cancer screening tests that normally would have taken place in the United States in 2020 did not happen. Ref: Chen, RC, Haynes, K, Du, S et al. JAMA Oncol 2021;7(6): 878-884. These missed screenings raised concerns that this could lead to cancers being diagnosed at a more advanced stage with increased cancer mortality. Recent information from the National Cancer Database (NCDB), the largest cancer registry capturing 74% of us cancer cases showed a decline of 14% in new cancer cases in 2020. (REF: Lum SS et al JAMA Surg. 2023; doi:10.1001/jamasurg.2023.0652). A recent publication (Changes in cancer diagnosis and stage distribution during the first year of the Covid pandemic in USA: a cross sectional national assessment (Han, X et al: Lancet Oncol 2023; 24: 855-867) identified a substantial cancer underdiagnosis and decrease in the proportion of early-stage disease in 2020 with significant disparities noted in the medically underserved.

Currently, physicians have indicated that there has not been a "return to prevention screening" by their patients. This paper discusses the reasons why cancer prevention, screening and early detection are important to the health and welfare of all patients.

CANCER PREVENTION AND EARLY DETECTION FOR SPECIFIC POPULATIONS

We are now in an exciting evolution of healthcare delivery - while there is an increased focus on population and public health, we have entered an era of precision, targeted approaches and individual risk stratification. The public health messages and guidelines for prevention and screening are broad, developed for the general population. This is crucial since ½ US men, and 1/3 American women will be diagnosed with cancer during their lifetime. However, the appreciation of the impact of social determinants of health and recognition of diverse communities has highlighted the need for inclusion and consideration of the additional barriers the following groups face:

LGBTQ+ Community

In February 2023, a Gallup poll reported that about 7.2% of the US population self-identified as belonging to a sexual orientation/gender identity (SOGI) minority. There is a lack of data about cancer incidence and prevalence in the sexual and gender minority (SGM) since SOGI information is not routinely collected. At a December 2022 patient advocacy summit held by the NCCN (National Comprehensive Cancer Network), the National LGBT Cancer Network estimated that approximately 500,000 LGBTQ+ individuals have missed cancer screenings since the Covid pandemic began. The underlying sense of discrimination, insensitivity, and past experiences that this population experiences were further negatively impacted by Covid reductions in staffing and availability of screening services, as well as patient fear of Covid exposure. Cancer screenings that are gender directed such as breast, cervical and prostate or invasive (cervical, colorectal) add further barriers to testing. Multiple recommendations for clinicians, office staff and institutions have been developed to help the SGM feel safe and welcome.

CULTURALLY DIVERSE COMMUNITIES

New York State is rich in cultural, racial, and ethnic diversity. Although many of the lessons learned from the LGBTQ+ population can also be applied to asylum refugees and immigrant populations, there are additional cultural norms. There needs to be recognition that these groups may not have participated in cancer screenings in their homelands, have increased sensitivity about breast, pelvic and rectal exams and discomfort with providers of the opposite sex. Cultural competencies can enhance appropriate services and care for diverse populations.

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CANCER SURVIVORS

With more than 1.2 million cancer survivors in New York State, most providers will have the privilege of providing or sharing the care of this population. As Covid impacted the health care team and impeded services for all, it was particularly stressful for survivors who had their screening and timeliness of surveillance test schedules disrupted. With a risk of 10 – 16% to develop a second primary cancer as well as the fear of recurrence of their first cancer, adult cancer survivors reported high stress levels. There is a communication and knowledge gap between the oncology and PCP team that needs to be addressed as the survivorship population grows. These challenges can be best addressed with education, coordination, and shared care.

RURAL POPULATION/SOCIAL/GEOGRAPHIC INEQUITIES

The challenges of transportation, lack of access to providers, limited services and costs are underlying for this population and increased with Covid. The NYS Cancer Services Program is a network in all regions of NYS with more than 5000 providers, facilities, and laboratories. Onsite as well as multiple mobile cancer services were provided to more than 53,000 New Yorkers in the 2 years prior to Covid. These individuals were screened for breast, cervical or colorectal cancers with 1166 found to have cancer or pre-cancerous conditions. Most of the NYS Cancer Services Program's screenings were halted during Covid and the impact on cancer diagnoses and stage

is yet to be determined. With focused efforts from the NYSCSP and community groups such as the American Cancer Society and the 65 NYS Commission on Cancer accredited hospitals committed to return to prevention and early detection, the deficit in screenings will hopefully be eliminated. However, this will require additional support and funding from NYS.

Cancer is a condition where normal tissues develop genetic mutations that can over time result in uncontrolled cell growth. Cancer by its nature can dissolve typical tissue boundaries and spread through lymph node channels and blood vessels into other organs of the body and can become life-threatening if not treated. Thankfully, there are interventions that can be done to prevent the cancerous mutations from beginning in the first place, and if a cancer is identified early through cancer screening, it can be treated at an earlier, more curable stage. Cancer prevention and early detection with cancer screening should form the foundation of the public health initiatives for cancer care.

CANCER PREVENTION, RISK REDUCTION AND HEALTH PROMOTION

The potential to eradicate the increasing numbers of HPV-associated cancers with early HPV vaccination and risk reduction by avoiding exposures which cause the initial cancerous genetic mutations to occur in the first place is significant. The most well-known cancer-causing mutagen is cigarette-smoking, and due to extensive public health efforts, the toll of smoking related cancers has decreased significantly. Several lifestyle factors which will be discussed later in this document include tobacco avoidance, alcohol use, weight control, physical activity, processed meat consumption, all of which impact cancer risk. Additionally, cancer prevention vaccines such as the HPV vaccine, provide immunity to infection from multiple HPV viruses which are associated with cancers of the cervix, head and neck, anus, and other genital cancers in individuals.

Cancer screening on the other hand, is intended to detect cancers early or catch them in a precancerous state where intervention at earlier stage is associated with superior clinical outcomes than treatment for advance stage disease. Great strides have been achieved with cervical cancer screening, with cytology and HPV testing which detect precancerous, treatable conditions. Because of effective screening and prevention with the HPV vaccine, cervical cancer incidence and mortality have decreased. Successful efforts to reach the unvaccinated, under-screened or unscreened population will facilitate the elimination of cervical cancer. Lung cancer screening has been shown to reduce lung cancer mortality by 20%, yet less than 5% of the eligible NYS population has been screened. Further gains in screening acceptance need to be made to improve early detection of breast, colon, rectum, prostate, lung, and skin cancers.

The reason that people should take advantage of prevention, and early detection of cancer, is to simply improve their chances of avoiding cancer in their lifetime, or detecting a cancer before it can impact their lifespan and health span. Lifestyles which are cancer preventative, are also the same lifestyles which reduce the risk of heart disease and other medical conditions and are powerful overall low-cost interventions compared the cost of treatment or lost productivity from illness and early death.

Barriers to prevention and screening are due to multiple systems, provider, or patient factors. These include knowledge gaps for patients and medical practitioners; insurance coverage; economic and transportation limitations; time constraints for healthcare providers to educate and make strong recommendations and order tests; obtaining prior authorization; follow-up of abnormal results; and cultural/social factors which limit access to healthcare. A recent survey from the Prevent Cancer Foundation reported that 65% of Americans over age 21 were not up to date with at least one routine cancer screening. This was further exacerbated during the years of the Covid-19 Pandemic, with the additional >9.4 million deficit in breast, cervical and colorectal

cancer screenings. (Ref as above, Chen et al). The concern that this will lead to patients presenting with more advanced stages of cancer has now been documented by Han et al.

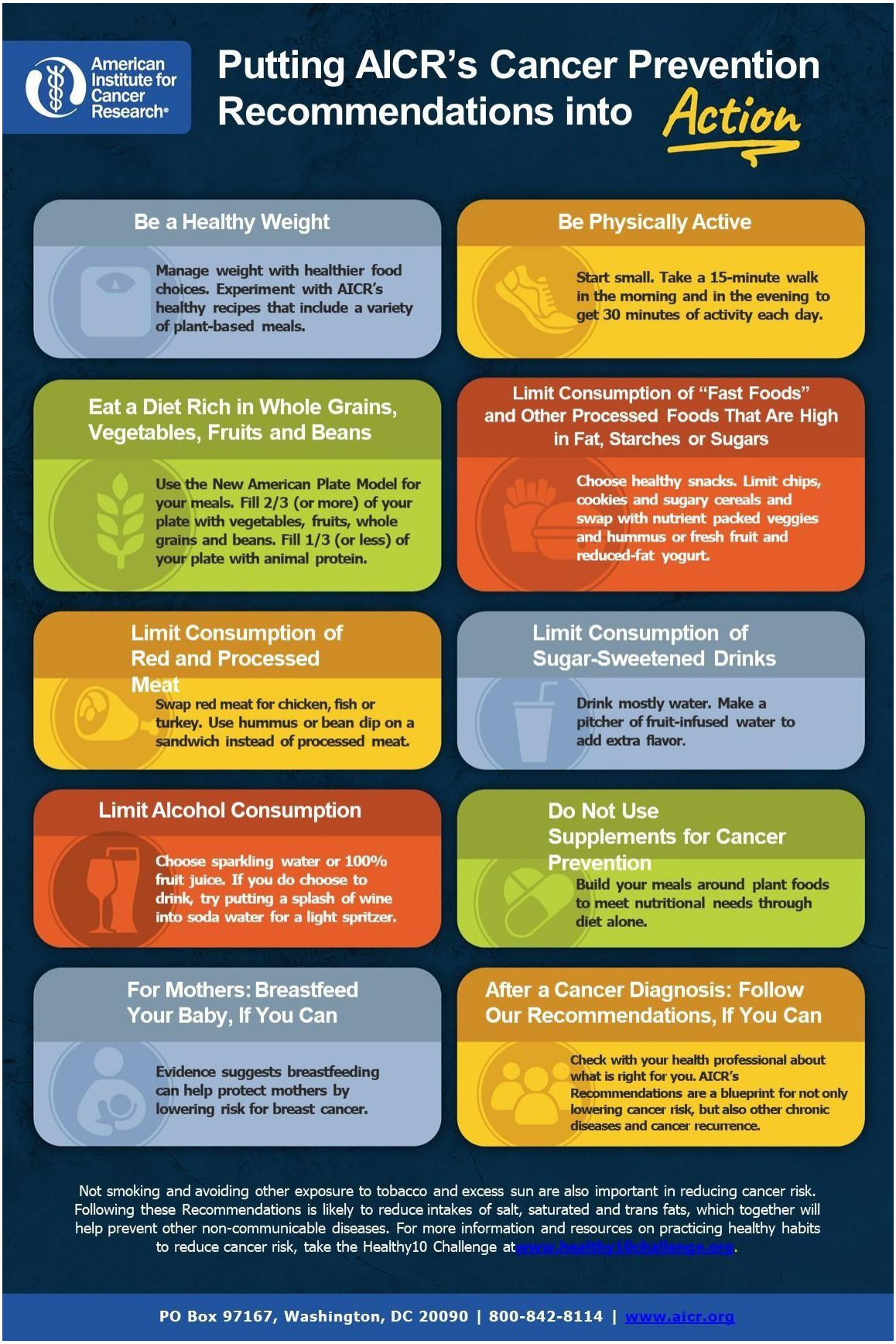
Cancer is a disease were genetic changes lead to abnormal cell growth. Even though cancer is a condition which affects the genes, only a small minority of cancers, around 20 percent, are heritable. Most of the genetic changes in cancer are due to external factors impacting the genome not heritable factors. Most cancers may be caused by external exposures and the most modifiable contributors are lifestyle factors. Lifestyle factors include diet, exercise, healthy habits (such as avoidance of alcohol, tobacco and substance use) good sleep, mental health, healthy relationships and vaccinations.

The International Agency for Research on Cancer (IARC) is a specialized part of the World Health Organization focused on cancer research and prevention. The IARC reviews large volumes of scientific and medical literature and publishes documents of carcinogens to better inform the public and policy makers and include a grading scale on the likelihood of the exposure causing cancer. Many of the IARC's reports are focused on chemical exposure through industry, but some key reports on lifestyle factors are shown below:

Factor	IARC Grade	Cancer Risks
Alcohol use	Group 1 Carcinogenic to humans	Oral Cavity, Pharynx, Larynx, Esophagus, Liver
Smoking Cigarettes	Group 1 Carcinogenic to humans	Head and Neck, Esophagus, Lung, Pancreas, Bladder, Kidney
Processed Meat Consumption	Group 1 Carcinogenic to humans	Colon, Rectum, Stomach
HPV Viral Infection	Group 1 Carcinogenic to humans	Cervix, Vulva, Vagina, Penis, Anus, Oral Cavity, Oropharynx
Red Meat Consumption	Group 2A probably carcinogenic to humans	Colon, Rectum, Pancreas, Prostate
Night Shift Work	Group 2A probably carcinogenic to humans	Breast, Prostate, Colon, Rectum

Obesity is a major factor associated with certain cancers. While the causes of obesity are many, the presence of extra body fat and the impact it has on metabolism and hormones results in obese people having a higher risk of the following cancers: meningioma, thyroid, esophagus, breast, multiple myeloma, liver, gallbladder, stomach, pancreas, kidney, uterus, ovary, colon, rectum according to the CDC.

There are lifestyle factors that can contribute to reducing the risk for cancer. The American Institute of Cancer Research (AICR) and American Cancer Society publish guidelines to reduce the risk of cancer for individuals and cancer survivors based on reviews of medical and scientific literature. Generally, these recommendations are consuming a diet rich in whole grains, fruits, vegetables, and beans, while limiting processed foods and processed and red meat; modest physical activity; maintaining a healthy weight; avoiding or limiting cancer inducing substances like alcohol and tobacco. Additionally, the AICR and US Preventative Task force recommend against the use of supplements for the sake of cancer prevention. The general lifestyle patterns which reduce the risk of cancer from these bodies are outlined below:


American Institute for Cancer Research
Putting AICR's Cancer Prevention Recommendations into Action
Be a Healthy Weight
Manage weight with healthier food choices. Experiment with AICR's healthy recipes that include a variety of plant-based meals.
Be Physically Active
Start small. Take a 15-minute walk in the morning and in the evening to get 30 minutes of activity each day.
Eat a Diet Rich in Whole Grains, Vegetables, Fruits and Beans
Use the New American Plate Model for your meals. Fill 2/3 (or more) of your plate with vegetables, fruits, whole grains and beans. Fill 1/3 (or less) of your plate with animal protein.
Limit Consumption of "Fast Foods" and Other Processed Foods That Are High in Fat, Starches or Sugars
Choose healthy snacks. Limit chips, cookies and sugary cereals and swap with nutrient packed veggies and hummus or fresh fruit and reduced-fat yogurt.
Limit Consumption of Red and Processed Meat
Swap red meat for chicken, fish or turkey. Use hummus or bean dip on a sandwich instead of processed meat.
Limit Consumption of Sugar-Sweetened Drinks
Drink mostly water. Make a pitcher of fruit-infused water to add extra flavor.
Limit Alcohol Consumption
Choose sparkling water or 100% fruit juice. If you do choose to drink, try putting a splash of wine into soda water for a light spritzer.
Do Not Use Supplements for Cancer Prevention
Build your meals around plant foods to meet nutritional needs through diet alone.
For Mothers: Breastfeed Your Baby, If You Can
Evidence suggests breastfeeding can help protect mothers by lowering risk for breast cancer.
After a Cancer Diagnosis: Follow Our Recommendations, If You Can
Check with your health professional about what is right for you. AICR's Recommendations are a blueprint for not only lowering cancer risk, but also other chronic diseases and cancer recurrence.
Not smoking and avoiding other exposure to tobacco and excess sun are also important in reducing cancer risk. Following these Recommendations is likely to reduce intakes of salt, saturated and trans fats, which together will help prevent other non-communicable diseases. For more information and resources on practicing healthy habits to reduce cancer risk, take the Healthy10 Challenge at www.healthy10challenge.org.
PO Box 97167, Washington, DC 20090 | 800-842-8114 | www.aicr.org

It is very important to realize that lifestyle recommendations to reduce cancer incidence also impact other co-morbidities. The common theme among healthy lifestyle factors is that the same behaviors which reduce the burden of cancer also reduce the burden of heart disease, lung disease, diabetes, and obesity which collectively cause significant impact on the lifespan and health span of New York residents.

The results of lifestyle factors can be quite striking. In a large study conducted by Harvard University titled "Impact of Healthy Lifestyle Factors on Life Expectancy in the US Population" the authors' analyzed 5 low risk lifestyle factors: never smoking, maintaining a healthy body weight, 30 minutes of moderate to vigorous exercise a day, moderate alcohol consumption and a healthy diet similar to that described above. The results showed that lifestyle factors are found to be dose dependent. Those participants who had the best adherence to these lifestyle modifications reduced their risk of cancer mortality by 65%, reduced cardiovascular mortality by 82% and lived between 12-14 years longer than their expected average lifespan. Personal and public health actions aimed to improve lifestyle factors will not only reduce cancer risk but improve overall health of a population.

The Biden Administration's Cancel Panel identifies high-priority issues that are impeding progress against cancer and has developed recommendations addressing these issues that one may want to consider. The new report Closing Gaps in Cancer Screening: Connecting People, Communities and Systems to Improve Equity and Access was released on February 2, 2023.

LUNG CANCER SCREENING

The US Preventive Services Task Force (USPSTF) recommends annual screening for lung cancer with low-does computed tomography (LDCT) in adults over aged 50 to 80 years of age who have a 20 pack-year smoking history and currently smoke or have quit within the past 15 years. Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or willingness to have curative lung surgery. MSSNY has strongly supported screening of patients for lung cancer. **(MSSNY Policy** 125.994 Use of CT scans for Early Detection of Lung Cancer The Medical Society of the State of New York supports screening for lung cancer with low dose computed tomography for patients who meet current nationally recognized guidelines. (HOD 2014-157)

BREAST CANCER SCREENING

The COVID-19 pandemic negatively impacted breast cancer screening. During the pandemic peak in 2020 there was near complete cessation of many cancer screening services including screening mammography. State mandated social distancing orders, restriction of nonessential travel and cessation of elective medical procedures deterred patients from addressing routine and emergent medical needs that were not COVID-19 related. The impact of this perceived and physically imposed medical care isolation disproportionately impacted underserved and vulnerable populations further exaggerating disparate health care access (AMRAM JAMA 2021).

Despite guidelines on a safe return to imaging as early as May 2020, the pandemic effects have led to decreased breast cancer screening by approximately 20-58% and more dramatically so for underserved groups (AMRAM JAMA 2021). While screening mammography volumes began to rebound in the months after the pandemic peak, rates are still recovering to reach pre-pandemic baseline and hover at approximately 85% of pre-COVID for screening mammography (ZULEY JACR 2022). Cancer screening and care provider location play important roles in utilization of such services. As the pandemic wanes but continues, bringing patients back for their health care needs requires a shift in mindset for healthcare systems.

There were an estimated 9.4 million missed cancer screening tests across the United States in 2020 alone (JOUNG CANCER 2022). The National Cancer Institute projected that there may be 10,000 additional cancer deaths from breast and colon cancers due to missed screening during

the pandemic. In response, many professional medical societies launched national campaigns to encourage patients to return to screening. Such programs provide toolkits and guidelines to encourage a return to screening including the “Get Screened” campaign from the American Cancer Society.

With the significant deficit of mammographic screening and potential for additional breast cancer cases and deaths related to missed screening during the pandemic, a conservative approach to breast cancer screening is prudent. Healthcare systems need to support screening mammography recovery and expand access to breast cancer screening services to minimize the negative impact of delayed care. Geography plays an important role in the utilization of screening services. Practices and facilities have adopted a wide variety of strategies to encourage patients to return for screening including expanding hours, switching to electronic intake forms, improved cleaning and sanitation practices, and rearranging workflows of clinics (ZULEY JACR 8/2022). As the effects of the pandemic linger on, meeting patients where they are for their breast health care, both physically and mentally, will be of utmost importance.

For breast cancer screening, conflicting screening guidelines led to confusion even before the onset of the COVID-19 pandemic. Multiple professional societies have published or supported a variety of guidelines. The United States Preventive Services Task Force (USPSTF) recommendations serve as the basis for Medicare and Medicaid coverage of services. The USPSTF last completed an update to its breast cancer screening recommendations in 2016. Recently, in May of 2023, new draft USPSTF recommendations for breast cancer screening were released and open for public comment. These guidelines reportedly considered how breast density, breast cancer risk and comorbidity level affect the balance of benefit and harm of screening mammography. However, these only apply to asymptomatic individuals aged 40 years or older who do not have preexisting breast cancer, previously diagnosed high-risk breast lesion and who are not at high risk for breast cancer because of a known underlying genetic mutation (BRCA 1 or 2 or other familial breast cancer syndrome) or history of chest radiation at a young age (Annals of Internal Medicine 2/2016). These guidelines do not consider other factors such as race, ethnicity, or social determinants of health.

As the era of personalized screening evolves, a comprehensive approach to breast cancer screening considering risk factors and other determinants of health is needed. A comprehensive screening approach inclusive of all individuals at average risk for breast cancer has been published by the American College of Radiology (ACR) and Society of Breast Imaging (SBI) in 2021. These guidelines expand on previously published guidelines which have largely been supported by the American Society of Breast Surgeons (ASBrS), American College of Obstetricians and Gynecologists (ACOG), American Medical Association (AMA) and National Comprehensive Cancer Network (NCCN) with some modification outlined by the American Cancer Society (ACS) (SMETHERMAN JACR 2021). Most recently, in 2023, the ACR published updated guidelines for breast cancer screening in higher-than-average risk individuals (Monticciolo et al JACR MAY 2023)

SCREENING MAMMOGRAPHY AVERAGE RISK INDIVIDUAL:

Screening mammography begins at age 40 for average risk individual.
Screening should begin at age 40. Beginning at this age results in the greatest mortality reduction, the most lives saved, and the most life years gained. The years of life lost to breast cancer are higher for individuals in their 40s. Breast cancer incidence increases substantially around age 40 with the incidence rate for ages 40-44 twice that for ages 35-39. One in six breast cancers occur in individuals aged 40-49. The largest and longest running breast cancer screening trials found that regular mammography screening cuts breast cancer deaths by roughly a third in all individuals ages 40 and over.

Despite differences regarding preferred age for initiating mammographic screening, all guidelines advocate in favor of access to screening mammography beginning at age 40 for individuals who are asymptomatic and have average risk in the US (ASBrS 2019 Official Statement). Mammography remains the principal modality of early detection for individuals at average risk. Early detection allows for diagnosis of tumors of smaller sizes with fewer nodal metastases and less histologic grade progression, making treatment more effective. Early detection is directly related to substantial declines in breast cancer mortality. The ACR and SBI recommend annual mammography screening starting at age 40 to maximize these benefits. The ACR and SBI affirm that weighing the benefits and risks of mammography should be done by individuals, not for individuals and shared decision making a goal in a more personalized screening climate. The method of detection is an independent prognostic factor for breast cancer mortality with increased mortality associated with cancers presenting with clinical findings over those that are detected with screening mammography. Mammography detected tumors are more effectively treated and treatment advances alone do not account for improved mortality. Efforts to reduce risks of mammography screening, including false positives, overdiagnosis and perceived patient anxiety, have been made through improvements in mammographic technology. For example, digital breast tomosynthesis (DBT) decreases false positive mammograms while simultaneously increasing cancer detection.

Screening Intervals:
Annual screening is recommended as this interval results in more screen-detected tumors, tumors of smaller size and fewer interval cancers than biennial screening, the latter a key determinant of survival (Smetherman JACR 2021).

Impact of delayed screening on specific population groups:
Though race has not yet been proven to be a predictor of breast cancer diagnosis outcome, black individuals have more advanced disease and adverse prognostic indicators at diagnosis and are significantly more likely to have triple negative (estrogen receptor negative, progesterone receptor negative and Her2neu nonamplified) breast cancers. Further research is necessary to understand the differences in tumor biology associated with race. (GEMIGNANI CANCER 2019) Recommendations to delay screening until age 50 adversely affect minority individuals as one-third of all breast cancers in Black, Asian and Hispanic individuals are diagnosed under age 50. Among all individuals with breast cancer, minority individuals are 72% more likely to be diagnosed with invasive breast cancer under age 50 and 58% more likely to be diagnosed with advanced - stage disease under age 50 than non-Hispanic white individuals (NHW). Among individuals dying of breast cancer, minority individuals are 127% more likely to die under age 50 than NHW individuals.

In addition, a greater proportion of younger individuals are diagnosed at late stages compared with older individuals and a significant 54.5% of younger non-Hispanic Black (NHB) individuals and 52.9% of younger Hispanic individuals are diagnosed with late-stage disease compared with 46.0% for younger NHW individuals. In addition to being diagnosed at younger ages, NHB individuals have 40% higher breast cancer mortality than NHW individuals. NHB individuals have a higher incidence of BRCA1 and BRCA 2 mutations and twice the incidence of aggressive, triple negative breast cancers in NHB individuals. Breast cancer specific mortality for Hispanic Black, Hispanic White and NHB individuals ranges from 10-50% higher than for NHW individuals (Smetherman 2021 JACR).

The age distribution of breast cancer is younger, and the stage distribution is more advanced in NHB individuals. Population based breast cancer mortality rates are higher among NHB individuals and population-based incidence rates of triple negative breast cancer are twofold higher among NHB individuals. Mammography screening, in addition to improved access to care, can be a valuable weapon in achieving health equity with the benefits of early detection through

screening for all breast tumor phenotypes including improved survival and reduced need for adjuvant chemotherapy. (ASBrS statement)

Screening in individuals who identify as lesbian, gay, bisexual, transgender or queer:
Individuals who identify as lesbian, gay, bisexual, transgender or queer are less likely to present for cancer screening. Work must be done to provide a respectful environment that welcomes all people. For average risk transgender patients, recommendations depend on sex assigned at birth, use and duration of hormones, surgical history are based on limited data and expert opinion. Annual screening at age 40 is recommended for transfeminine (male-to-female) patients who used hormones for greater than 5 years. Annual screening at age 40 is recommended for trans-masculine (female-to -male) patients who have not had mastectomy.

Risk Factors: a characteristic, condition, or behavior that increases the possibility of getting a disease.
Risk factors for breast cancer include age, personal history of breast cancer, family history of breast cancer, genetic predisposition, early menstruation, late menopause, age at first pregnancy, benign breast disease, oral birth control, hormone replacement therapy, being overweight or obese and radiation exposure (mantle radiation by age 30). Having dense breast tissue is an independent risk factor for breast cancer.

Risk Assessment and Risk Based Screening: Lifetime risk for breast cancer.
Risk assessment for all individuals should be performed at age 25, and no later than age 30. This is especially important for individuals at higher-than-average risk for breast cancer including for minority individuals to ensure that they are not in a higher risk category (Monticciolo JACR 2023). This allows for those individuals at higher risk to be identified and begin screening before age 40. An estimated breast cancer risk using current validated models including the current Tyer-Cuzick model is recommended however all models have limitations in minority populations. Based on risk assessment modeling, individuals may fall into categories of average, intermediate and high risk for breast cancer and screening approaches adapted to address risk including age to begin screening and screening modalities. Performing risk assessment allows for identification of individuals who may be at elevated risk, education of individuals about their risk for shared decision making and allows for risked based screening.

Average Risk: less than 15%. Annual screening mammography. Digital breast tomosynthesis particularly for those with heterogeneously dense or dense breasts. For individuals with dense breast who desire supplemental screening, breast MRI is recommended (Monticciolo JACR 2023)
Intermediate Risk: between 15-19%. Annual screening mammography with digital breast tomosynthesis particularly for those with heterogeneously dense or dense breasts. Consider supplemental screening with screening breast ultrasound or contrast enhanced mammography. MRI may be appropriate in some individuals that fall into this risk group.

High Risk: greater than 20%. Annual screening mammography +/- digital breast tomosynthesis and MRI regardless of breast density. Screening begins by age 30. If not able to undergo MRI, other supplemental screening with contrast enhanced mammography or screening breast ultrasound (Monticciolo JACR 2023).

Prevention: Healthy habits to reduce risk of breast cancer
Providing education on lifestyle management to reduce the risk of breast cancer plays a role in health maintenance. While some risk factors like genetic predisposition to cancer, age and sex are not controllable, actively taking part in self-care addressing factors that are controllable can help.

Maintaining a healthy weight with regular exercise, a nutritious diet and limiting sugar intake are advisable. Breast feeding should be encouraged to aid in minimizing risk for breast cancer.

Individuals should not smoke and should limit alcohol intake. Regular health check-ups and self-breast awareness should be encouraged. Being educated about individual breast cancer risk and getting screened for breast cancer with annual mammography is essential.

GENETIC ISSUES

The emerging understanding of precision medicine plays an integral role in the treatment of cancer. Multiple biomarkers have been identified and clinically validated that are both prognostic and predictive in cancer therapy to optimize patient care. Cancer is a genetic disease that reflects an individual's unique genome – in fact a tale of 2 genomes – our germline (genes we inherit) and our somatic (changes occurring during our lifetime due to environmental exposure). This genome then interacts with a complicated network of multi -omics (transcriptomic, proteomic, epigenomic, metabolomic, etc.) that is unique within each person.

Our knowledge of genetics and genomics is advancing at a rate often exceeding our ability to understand clinical utility and integrate new protocols into clinical practice. Tools have been created to educate providers and facilitate the use of this information in caring for patients. Genetic providers have the most up to date repository of clinical information pertaining to risk profiles and relevant testing protocols and as a member of a healthcare team, they provide support for physicians and the families who may be at risk for a variety of inherited cancer predisposition syndromes. They identify individuals at risk, investigate the problem present in the family, interpret information about the disorder, analyze inheritance patterns and risks of recurrence, and review available options.

National Comprehensive Cancer Network (NCCN) guidelines provide recommendations for treatment as well as detection, prevention, and risk reduction for the following cancers: acute leukemia, breast, colon, lung, ovarian, pediatric, prostate, and rectal. Multiple stakeholders participate in creating the guidelines and they are typically updated on an annual basis. Therefore, this is the most up to date resource, but it does have its limitations.

The following is a summary of the 2023 guidelines with recommendations for germline genetic testing for the most prevalent cancers:

Hereditary Breast, Ovarian, GI, Prostate and/or Pancreatic Cancers:

- All individuals diagnosed with breast cancer under the age of 50 • All individuals with triple negative breast cancer (TNBC) at any age.
- All men and individuals diagnosed with breast cancer.
- All individuals diagnosed with Ashkenazi Jewish (AJ) ancestry.
- All individuals with metastatic breast cancer (MBC) to assist with treatment decisions.
- Unaffected with family history (FH) of close blood relatives (first, second, third degree relatives on the same side of the family) with any of the following: breast ca < 50; male breast ca; ovarian cancer; prostate ca that is metastatic (mPC)/high risk group; pancreatic ca; > 3 family members with breast ca; > 2 close relatives with either breast or prostate (any grade); probability of >5% of carrying a BRCA1/2 pathogenic variant (PV) determined on a model
- Any individual (affected or unaffected) with a known PV in the family

Prostate:

- Any individual with metastatic prostate or high/very high-risk grade group and/or histology including cribiform/intraductal.

- Unaffected: >1 close relative with breast ca dx<50: TNBC any age; male breast ca, ovarian ca, mPC or high- risk group;> 2 blood relative with breast/prostate any grade/any age or AJ ancestry
- Pancreas: Any individual with exocrine pancreatic cancer and unaffected individuals with an affected first degree relative (add a separate heading for pancreas?)

Ovarian:

- Any individual with epithelial ovarian (OC) (including fallopian tube or primary peritoneal) diagnosed at any age
- Unaffected with family history only: First or second degree relative with OC or >5% probability on basis of model

Gastrointestinal/ Lynch Syndrome (LS) Guidelines:

- Any individual diagnosed with colorectal or endometrial cancer < 50
- Any individual with synchronous or metachronous LS tumor
- Personal history of tumor with mismatch repair deficiency (MMRD) determined by polymerase chain reaction (PCR), next generation sequencing (NGS) or immunohistochemistry (IHC) at any age.
- Unaffected: Any individual with first degree relative (FDR) or second degree relative (SDR) with CRC or endometrial cancer age less than 50 or a relative with metachronous or synchronous LS related cancer regardless of age; > 3 FDR or SDR affected with LS cancer regardless of age; individual with PREMM score or probability model > 5% (consider 2.5%)
- Any individual with a known pathogenic variant in the family

Providers who order germline genetic testing need to understand that not all labs are created equally. Commercial laboratories are CLIA validated for analytic and clinical validity, but each offer a different selection in the number and type of genes they test for. Some of these panels are targeted for the specific phenotype but other larger panels can identify pathogenic variants that are not driving the development of current cancer in the patient (opportunistic). Importantly, some of the genes on the panels have specific recommendations for management but many genes have questionable clinical utility and gene-disease association remains to be elucidated. Providers need to understand a few key points regarding each lab's capabilities:

· What genes are being tested and is it covering the genes of interest

· Depth of sequencing coverage (coverage 50x preferable)

· Does the lab detect copy number variants/ deletion/ duplications

· Do they offer orthogonal confirmation for detected pathogenic variants (PV's); do they perform RNA sequencing

· How often do they update variants of uncertain significance and how is this communicated to the provider/patient

Currently, oncologists employ somatic testing to target therapies for treatment. Somatic testing is complementary with germline testing. Somatic and germline labs employ different testing platforms as well as different bioinformatic algorithms for interpretation. Somatic testing can identify mutations that are germline but this needs to be confirmed clinically.

Suggestions that a somatic test result is also potentially part of the germline are the following:

· Identification of a gene typically not thought to be a driver of the cancer (ie identifying a BRCA/ Lynch syndrome mutation in a lung cancer) with a high variant allele frequency

· Identification of a founder mutation (i.e., BRCA1 c68-69delAG; CHEK2 c.1100delC)

Tumor testing may fail to identify approximately 10% of clinically actionable PV/LP. This can be due to many factors including filtration, tumor heterogeneity, different nomenclature and different technology that makes it difficult to detect deletions and duplications.

Therefore, if there is any suspicion of a germline predisposition, follow up germline testing is still necessary. Germline testing is critically important for the care of cancer patients and their families. It informs cancer screening and prevention as well as eligibility for clinical trials. Genomic testing is refining our understanding of the drivers of cancer. It will determine decision making, treatment and management by targeting therapies while limiting toxicities to optimize patient care. This technology will be foundational for precision medical approaches applied to all systemic diseases.

Unfortunately, data from whole genome/exome studies of individuals with cancer reveal that we are failing to identify a significant population who do not meet the NCCN criteria. Germline testing is critically important for the care of cancer patients and their families. Failure to test results in “diagnostic misattribution” with incorrect management, lost opportunity for precision medicine, precision prevention and optimal patient care. Studies also demonstrate poor rates of cascade testing once we identify a pathogenic variant in a proband. These represent missed opportunities to prevent cancer.

With testing costs being lowered and results more actionable, we expect that anyone with cancer will eventually have paired germline-tumor testing. This will provide a framework for precision medicine including effective therapies, opportunities to participate in clinical trials, enhanced surveillance for other cancers an individual might be at risk for and potential prevention of cancer in an unaffected, at-risk family member.

Appendix A

MSSNY Policy 125.999 states the following:

MSSNY has long advocated for the rights of patients to have access to various screening services and interventions most beneficial in improving the overall health of the public. Obviously access to these important health care service recommendations is dependent upon the acceptance, agreement and availability of them by relevant private and public insurance entities, which is why MSSNY continues to support and advocate for insurance coverage for all of these screening programs. MSSNY Policy 125.996 was developed and put forward to the MSSNY Council in 2010 and was also reaffirmed by the MSSNY Council in 2011. These revisions pertained to various updates from medical specialties or organizations throughout the last ten years and represent only recommendations, but not practice guidelines, for physicians.

MSSNY supports and advocates for insurance coverage for all these screening programs:

Essential Behavioral Changes:

1) ***Tobacco Cessation Counseling*** – Tobacco cessation counseling on a regular basis is recommended for all persons who use tobacco products. Providers are advised to use the 5-A approach (Ask, Advise, Assess, Assist, Arrange). Information on how to access free support services should be provided, and nicotine replacement, nicotine receptor partial agonist (varenicline) or bupropion therapy should be offered. Pregnant individuals and parents with children living at home also should be counseled on the potentially harmful effects of smoking on fetal and child health. (US Preventive Services Task Force) http://www.ahrq.gov/professionals/clinicians-providers/guidelinesrecommendations/tobacco/5steps.html

2) ***Healthy Diet and Nutritional Intervention Counseling*** – Dietary counseling is recommended for adults and parents of children over the age of 2, to emphasize fiber-rich produce (i.e., fruits and vegetables) and minimally-processed grains, limiting the dietary intake of refined sugar and saturated fats and encouraging intake of mono-unsaturated fats. (http://www.cochrane.org/CD009825/VASC_mediterranean-diet-for-the-prevention-of-cardiovasculardisease; http://www.mayoclinic.org/healthy-lifestyle/nutrition-and-healthy-eating/in-depth/mediterraneandiet/art-20047801; http://www.nhlbi.nih.gov/health/health-topics/topics/dash/)

3) ***Exercise Promotion***–Counseling patients to incorporate regular physical activity into their daily routines is recommended to prevent coronary heart disease, hypertension, obesity, and diabetes. General recommendations for adults are to do 150 minutes (more is advisable) of aerobic physical activity a week, preferably at moderate-to-vigorous intensity but at light-to-moderate intensity for persons with chronic conditions who are unable to do moderate intensity activity; strength training of all large muscle groups is recommended for two days a week. These recommendations are based on the proven benefits of regular physical activity (Department of Health and Human Services, Centers for Disease Control and Prevention, American College of Sports Medicine, National Physical Activity Plan, National Center for Education in Maternal and Child Health, American Academy of Family Physicians, American Academy of Pediatrics, The American Heart Association, and The American College of Obstetricians and Gynecologists).

Essential Preventive Screening

1) ***Hypertension Screening and Treatment***–Screening for hypertension in adults in adults aged 18 and older should occur.

Blood pressure categories are:

- Normal: Less than 120/80 mm Hg;
- Elevated: Systolic between 120-129 *and* diastolic less than 80;
- Stage 1: Systolic between 130-139 *or* diastolic between 80-89;
- Stage 2: Systolic at least 140 *or* diastolic at least 90 mm Hg;

Hypertensive crisis: Systolic over 180 and/or diastolic over 120, with patients needing prompt changes in medication if there are no other indications of problems, or immediate hospitalization if there are signs of organ damage. (2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: Executive Summary Paul K. Whelton**,** Robert M. Carey**,** Wilbert S. Aronow**,** Donald E. Casey**,** Karen J. Collins**,** Cheryl Dennison Himmelfarb**,** Sondra M. DePalma**,** Samuel Gidding**,** Kenneth A. Jamerson**,** Daniel W. Jones**,** Eric

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2) ***Diabetes Screening and Treatment*** – The US Preventive Services Task Force recommends screening for abnormal blood glucose as part of the cardiovascular risk assessment in adults 40 to 70 years who are overweight or obese. Clinicians should offer or refer patients with abnormal blood glucose to intensive behavioral counseling interventions to promote a healthful diet or physical activity. (USPSTF Recommendation: https://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/screening-for-abnormal-blood-glucose-and-type-2-diabetes?ds=1&s=diabetes

3) ***Primary Prevention of CVD in Adult*** – *Frequency of Screening* In general, a comprehensive assessment of risk factors should be performed at least every 5 years starting at 18 years of age, and a global risk score should be calculated at least every 5 years starting at the age of 35 years for men and 45 years for women. Those with increased cardiovascular risk, for example, those with diabetes, cigarette smokers, or those with obesity, should have their risk factors and cardiovascular risk assessed more frequently. (J Am Coll Cardiol, 2009; 54:1364-1405, doi:10.1016/j.jacc.2009.08.005 © 2009 by the American College of Cardiology Foundation). Journal of the American College of Cardiology March 2018 DOI: 10.1016/j.jacc.2018.01.004 2018 ACC/AHA Clinical Performance and Quality Measures for Cardiac Rehabilitation; A Report of the American College of Cardiology/American Heart Association Task Force on Performance Measures Writing Committee Members, Randal J. Thomas, Gary Balady, Gaurav Banka, Theresa M. Beckie, Jensen Chiu, Sana Gokak, P. Michael Ho, Steven J. Keteyian, Marjorie King, Karen Lui, Quinn Pack, Bonnie K. Sanderson and Tracy Y. Wang)

4) ***Primary Prevention of Stroke*** – Guidelines include well-known prevention measures such as controlling high blood pressure, not smoking, avoiding exposure to secondhand smoke, being physically active and treating disorders that increase the risk of stroke such as atrial fibrillation (a type of irregular heartbeat), carotid artery disease and heart failure. The guidelines suggest physicians consider using a risk assessment tool such as the Framingham Stroke Profile to assess patients' risk. (American Heart Association/American Stroke Association; US National Institute of Neurological Disorders and Stroke).

5) ***Breast Cancer Screening Mammography and Appropriate Treatment***—All individuals should be evaluated for breast cancer risk no later than age 30. For individuals at average risk for developing breast cancer, annual mammography should begin at age 40. Mammographic screening should continue as long as an individual is in good health. Regular mammographic screening results in substantial reduction of breast cancer mortality across multiple studies. Individuals should be familiar with the known benefits, limitations, and risks of breast cancer screening. Individuals should also know how their breasts normally look and feel and report any breast changes to a health care provider right away. Breast ultrasound may be used for supplemental screening in addition to mammography in women with mammographically dense breasts. For individuals with dense breasts, supplemental screening may include but is not limited to breast ultrasound, breast MRI or other supplemental imaging modalities (ie contrast enhanced mammography) as recommended by the physician based on the clinical expertise of the physician. Some individuals – because of their family history, a genetic tendency, or certain other factors – should be screened with MRIs along with mammograms and may benefit from beginning to screen earlier than age 40. Individuals should consult with a health care provider about their risk for breast cancer and the best screening plan for them. (ACR, ACOG, NCCN, SBI, ASBrS)

6***) Colon Cancer Screening and Appropriate Treatment***–Colon and rectal cancer Screening–Starting at age 45, all individuals should follow one of these testing plans: Tests that find polyps and cancer. A colonoscopy every 10 years, or CT colonography (virtual colonoscopy) every five years, or flexible sigmoidoscopy every five years, or double-contrast barium enema every five years. Tests that mostly find cancer include yearly fecal immunochemical test (FIT), or yearly guaiac-based fecal occult blood test (gFOBT), or Stool DNA test (sDNA) every three years. If the test is positive, a colonoscopy should be done. The multiple stool take-home test should be used. One test done in the office is not enough. A colonoscopy should be done if the test is positive. The tests that can find both early cancer and polyps should be the first choice if these tests are available, and patients are willing. The most important thing is to get tested, no matter which test is chosen. Patients should talk to a health care provider about which tests might be right for them. If individuals are at high risk for colon cancer based on family history or other factors, they may need to be screened using a different schedule. Patients should talk

with a health care provider about their history and the testing plan that's best for them. (ACS Recommendation)

7) ***Cervical Cancer Screening and Appropriate Treatment***–Cervical cancer testing should start at age 21. Individuals under age 21 should not be tested. Individuals between the ages of 21 and 29 should have a Pap test done every 3 years. HPV testing should not be used in this age group unless it's needed after an abnormal Pap test result. Individuals between the ages of 30 and 65 should have a Pap test plus an HPV test (called "co-testing") done every five years. It is acceptable to have a Pap test alone every three years. Individuals over age 65 who have had regular cervical cancer testing in the past 10 years with normal results should no longer be tested for cervical cancer. Once testing is stopped, it should not be started again. Individuals with a history of serious cervical pre-cancer should continue to be tested for at least 20 years after that diagnosis, even if testing goes past age 65. Individuals who have had their uterus and cervix removed (a total hysterectomy) for reasons not related to cervical cancer and who have no history of cervical cancer or serious pre-cancer should not be tested. All individuals who have been vaccinated against HPV should still follow the screening recommendations for their age groups. Some individuals– because of their health history (HIV infection, organ transplant, DES exposure, etc.) – may need a different screening schedule for cervical cancer and should talk to a health care provider about their history. (ACS Recommendation) Additionally, for transgender or non-binary persons, such screening and testing should be conducted on patients according to their anatomy to ensure that that these individuals are receiving proper screening, until more specific guidelines are available.

8) **Prostate Cancer Screening and Treatment** – Physicians should have an informative discussion about the risk of prostate cancer with their patients at age 40 and identify those patients who are at higher-than-average risk based on family history, race, ethnicity, lifestyle factors and other chronic illnesses. Physicians should offer male patients, at age 45 who are at higher risk and age 50 or average or low risk, yearly testing, including but not limited to, serum PSA and the digital rectal exam. Patients should be referred to a specialist if findings suggest the possibility of prostate cancer. (ACS Recommendation 2010-present) Additionally, for transgender or non-binary persons, such screening and testing should be conducted on patients according to their anatomy to ensure that that these individuals are receiving proper screening, until more specific guidelines are available.

9) ***Immunizations–***-The best way to reduce vaccine preventable diseases is to have a highly immune population. Appropriate vaccinations should be available for all adults including the following: Influenza, tetanus, diphtheria, acellular pertussis, measles, mumps, rubella, varicella, zoster, HPV, pneumococcal, hepatitis A and B, meningococcal, and *Haemophilus Influenzae* type B immunizations. (CDC Recommended Immunization Schedule for Adults Aged 19 Years or Older, United States, 2018)

10) Genetic ***Testing***— All cancer patients deemed at risk for having inherited a recognized cancer predisposition mutation should be seen pre- and post-test by a board-certified genetic counselor or board-certified MD geneticist appropriately trained in cancer genetics. Risk Assessment should include at minimum:

- Full three generation pedigree
- Evaluation of hereditary cancer syndromes and which test is appropriate/indicated.
- Discussion/education of risks, benefits and limitations of genetic testing
- Coordination of optimal individualized specific genetic testing if and when appropriate
- Discussion of genetic test results and all other cancer related implications for patient and at-risk family members

Breast:
Version 1.2019 Screening Guidelines 5/17/19 NCCN
MRI is also indicated for patients with prior history of breast cancer, Gail risk >1.7%, 20% risk defined by personal history of LCIS or ADH/ALH, untested for familial TP53 mutation, untested for familial PTEN mutation. MRI is also a consideration for mutation carriers in the ATM, CDH1, CHEK2, NBN, NF1, and PALB2 genes.
Prostate:

To identify individuals at high risk for prostate cancer: according to NCCN Guidelines Version 1.2018, BRCA1/2 testing is indicated for those with personal history of metastatic prostate cancer or with hi-grade prostate cancer (Gleason score> or= 7) who have a close (1^{st},2^{nd}, or third degree) relative with ovarian cancer, or breast cancer <50, or with 2 relatives with breast, pancreatic, or prostate cancer at any age. Also, by NCCN Guidelines V.2018 Prostate Cancer Early Detection Guidelines screening for those with family or personal history of high-risk germline mutations. Further, MSSNY recommends that physicians concentrate on these interventions for all of their patients and that New York State policy makers devote its limited public resources to these screening and treatment interventions on behalf of those adults unable to afford health care. Also, for each intervention, physician and patient should discuss the positive and negative aspects. (Council 3/8/10; Reaffirmed by Council 1/20/11 in lieu of 2010-163; Revised and Approved by MSSNY Council 3/5/20)

MRI is also indicated for patients with a prior history of breast cancer…. MRI is also a consideration for mutations carriers including but not limited to BRCA, TP53, PTEN, ATM, CDH1, CHEK2, NBN, NF1 and PALB2 genes.

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Source:
(EVIDENCE-BASED, CANCER SCREENING GUIDELINES (ADOPTED FROM MSSNY POLICY 125.996 SCREENING PROGRAMS**.)**

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