Overview of Cancer and Cancer Screening in AI/AN People with Diabetes

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Objectives

As a result of completing this training, participants will be able to:

- Identify the most commonly diagnosed cancers among diabetic and AI/AN populations.
- Implement strategies for cancer risk reduction.
- Examine current guidelines for cancer screening.
- Refer patients for cancer screening to improve outcomes.
Diabetes & Cancer

Common Chronic Diseases

• Significant impact on health
  • Physical, psychological, spiritual
• Genetic and epigenetic factors
• Environment and lifestyle influence development and outcomes
  • Increased risk with overweight, obesity
  • Increased risk with smoking, and increased risk of complications in smokers
• Screening can result in better outcomes
Improving Trends in AI/AN People

Diabetes Prevalence

Adults Diabetes – Prevalence has decreased since 2013

- BMJ Open Diab Res Care 2020;8:e001218. doi:10.1136/ bmjdr-2020-001218

Cancer

- National Cancer Institute SEER Cancer Statistics database reports: overall decline in incidence and mortality rates

*National Cancer Institute* Surveillance, Epidemiology, and End Results Program
Diabetes Prevalence Trends

Figure 2. Diabetes Prevalence in AI/AN Adults

Diabetes prevalence decreased from 15.4% in 2013 to 14.6% in

Source: IHS National Data Warehouse
Cancer in American Indians/Alaska Natives

• American Public Health Association (APHA) Journal Supplement 2014 reviewed data 1990-2009 cancer incidence, mortality in AI/AN people
  • Higher incidence compared to white US population of liver & bile duct, gallbladder, esophagus, stomach, colorectal, kidney, larynx, lung, uterine, cervix, prostate, myeloma
  • Higher mortality rates compared to white US population for prostate, kidney, bladder, breast, cervix, uterus, stomach, colorectal, Hodgkin’s Disease
• Significant regional variation in incidence, mortality and patterns of cancer
# Office of Minority Health: Cancer in AI/AN Population in US – Men

## Top Cancer Sites for American Indian/Alaska Natives (2012-2016)

<table>
<thead>
<tr>
<th>Cancer</th>
<th>American Indian/Alaska Native Men</th>
<th>Non-Hispanic White Men</th>
<th>American Indian/Alaska Native /Non-Hispanic White Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Sites</td>
<td>315.3</td>
<td>505.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Colon &amp; Rectum</td>
<td>41.2</td>
<td>44.1</td>
<td>0.9</td>
</tr>
<tr>
<td>Esophagus</td>
<td>5.9</td>
<td>8.3</td>
<td>0.7</td>
</tr>
<tr>
<td>Kidney</td>
<td>21.2</td>
<td>23.1</td>
<td>0.9</td>
</tr>
<tr>
<td>Liver &amp; IBD</td>
<td>19.3</td>
<td>10.8</td>
<td>1.8</td>
</tr>
<tr>
<td>Lung</td>
<td>43.3</td>
<td>67.5</td>
<td>0.6</td>
</tr>
<tr>
<td>Oral Cavity &amp; Pharynx</td>
<td>11.8</td>
<td>19.3</td>
<td>0.6</td>
</tr>
<tr>
<td>Pancreas</td>
<td>11.4</td>
<td>15.1</td>
<td>0.8</td>
</tr>
<tr>
<td>Prostate</td>
<td>55.4</td>
<td>104.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Stomach</td>
<td>11.5</td>
<td>8.2</td>
<td>1.4</td>
</tr>
</tbody>
</table>


Office of Minority Health: Cancer in AI/AN Population in US – Women

<table>
<thead>
<tr>
<th>Cancer</th>
<th>American Indian/Alaska Native Women</th>
<th>Non-Hispanic White Women</th>
<th>American Indian/Alaska Native/Non-Hispanic White Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Sites</td>
<td>306.0</td>
<td>448.0</td>
<td>0.7</td>
</tr>
<tr>
<td>Breast</td>
<td>79.5</td>
<td>136.6</td>
<td>0.6</td>
</tr>
<tr>
<td>Cervical</td>
<td>7.4</td>
<td>6.6</td>
<td>1.2</td>
</tr>
<tr>
<td>Colon &amp; Rectum</td>
<td>37.9</td>
<td>34.3</td>
<td>1.1</td>
</tr>
<tr>
<td>Esophagus</td>
<td>1.7</td>
<td>1.9</td>
<td>0.9</td>
</tr>
<tr>
<td>Kidney</td>
<td>13.1</td>
<td>11.1</td>
<td>1.2</td>
</tr>
<tr>
<td>Liver &amp; IBD</td>
<td>8.5</td>
<td>3.7</td>
<td>2.3</td>
</tr>
<tr>
<td>Lung</td>
<td>33.9</td>
<td>56.0</td>
<td>0.6</td>
</tr>
<tr>
<td>Oral Cavity &amp; Pharynx</td>
<td>5.3</td>
<td>7.0</td>
<td>0.6</td>
</tr>
<tr>
<td>Pancreas</td>
<td>8.0</td>
<td>11.5</td>
<td>0.7</td>
</tr>
<tr>
<td>Stomach</td>
<td>6.4</td>
<td>3.8</td>
<td>1.7</td>
</tr>
<tr>
<td>Uterus</td>
<td>19.7</td>
<td>28.5</td>
<td>0.7</td>
</tr>
</tbody>
</table>

Office of Minority Health: Cancer in AI/AN Population in US – Death Rate for Men

<table>
<thead>
<tr>
<th>Cancer</th>
<th>American Indian/Alaska Native Men</th>
<th>Non-Hispanic White Men</th>
<th>American Indian/Alaska Native/Non-Hispanic White Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Sites</td>
<td>176.3</td>
<td>197.3</td>
<td>0.9</td>
</tr>
<tr>
<td>Colon &amp; Rectum</td>
<td>19.1</td>
<td>16.6</td>
<td>1.2</td>
</tr>
<tr>
<td>Kidney</td>
<td>8.1</td>
<td>5.7</td>
<td>1.4</td>
</tr>
<tr>
<td>Liver &amp; IBD</td>
<td>14.4</td>
<td>8.3</td>
<td>1.7</td>
</tr>
<tr>
<td>Lung</td>
<td>42.0</td>
<td>54.1</td>
<td>0.8</td>
</tr>
<tr>
<td>Prostate</td>
<td>19.2</td>
<td>18.1</td>
<td>1.1</td>
</tr>
<tr>
<td>Stomach</td>
<td>6.9</td>
<td>3.3</td>
<td>2.1</td>
</tr>
</tbody>
</table>

Source: NCI 2020. Seer Cancer Statistics Review. 1975-2016. Table 1.20
### Cancer Death Rates per 100,000 – Women (2012-2016)

<table>
<thead>
<tr>
<th>Cancer</th>
<th>American Indian/Alaska Native Women</th>
<th>Non-Hispanic White Women</th>
<th>American Indian/Alaska Native/Non-Hispanic White Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Sites</td>
<td>124.9</td>
<td>141.9</td>
<td>0.9</td>
</tr>
<tr>
<td>Breast</td>
<td>14.3</td>
<td>20.6</td>
<td>0.7</td>
</tr>
<tr>
<td>Cervical</td>
<td>2.8</td>
<td>2.1</td>
<td>1.3</td>
</tr>
<tr>
<td>Colon &amp; Rectum</td>
<td>13.0</td>
<td>11.9</td>
<td>1.2</td>
</tr>
<tr>
<td>Kidney</td>
<td>3.8</td>
<td>2.4</td>
<td>1.6</td>
</tr>
<tr>
<td>Liver &amp; IBD</td>
<td>7.4</td>
<td>3.4</td>
<td>2.1</td>
</tr>
<tr>
<td>Lung</td>
<td>29.4</td>
<td>38.0</td>
<td>0.8</td>
</tr>
<tr>
<td>Stomach</td>
<td>3.6</td>
<td>1.7</td>
<td>2.0</td>
</tr>
<tr>
<td>Uterus</td>
<td>3.5</td>
<td>4.4</td>
<td>0.8</td>
</tr>
</tbody>
</table>

Cancer in AI/AN Men and Women

University of Oklahoma Study: Cancer incidence 1999-2015 breast, prostate, lung, colorectal cancer by IHS region from CDC WONDER Data Source

- Incidence of these cancers were lower for AI/AN than non-Hispanic white (NHW) population, but over time period of study rates for breast and lung cancer declined more for NHW
- Regional variations were observed
  - Breast cancer: higher rates for women in Alaska
  - Colorectal cancer: higher rates reported in Alaska, Southern Plains (higher than NHW) Overall decline observed over 17 years
  - Lung cancer: higher in Alaska and Plains regions, but persistent decline in incidence observed since 2005
  - Prostate cancer: higher in Plains regions, continued decrease for all populations since 2008
- From 2012-2016, AI/AN men were almost twice as likely to have liver & IBD cancer as compared to non-Hispanic white men.
- AI/AN men are 40 percent more likely to have stomach cancer than non-Hispanic white men and are over twice as likely to die from the same disease.
- AI/AN women are 2.3 times more likely to have, and twice as likely to die from, liver & IBD cancer, as compared to non-Hispanic white women.
- AI/AN Native women are 20 percent more likely to have kidney/renal pelvis cancer than non-Hispanic white women.
Diabetes and Cancer

• UK Clinical Practice Research Databank Study
  • Total mortality declined 32% in males, 31% in females, similar to persons without diabetes
  • Marked decline in deaths due to cardiovascular causes, more pronounced in population with diabetes.
  • Cancer surpassed vascular diseases as leading cause of death for people with diabetes in 2018.

*Lancet Diabetes Endocrinol* 2021; 9: 165–73 Published Online February 4, 2021 [https://doi.org/10.1016/S2213-8587(20)30431-9](https://doi.org/10.1016/S2213-8587(20)30431-9)
Diabetes and Cancer (con’t)

- Increased risk of certain cancers in diabetes:
  - Liver, pancreas, endometrium 2x risk
  - Breast, colorectal, esophagus, kidney, bladder 1.2-1.5x risk

- Hyperglycemia associated with increased risk of cancer in population studies in Europe and Korea
  - Linear association with FBS, A1C elevations

- Increased mortality for people with diabetes and breast and colon cancers
Obesity and Increased Cancer Risk

• Cancers associated with obesity
  • endometrial* 2-4x risk (up to 7x in severely obese)
  • stomach, esophagus*, liver*, kidney* 2x risk
  • others*: colon, gallbladder, breast, pancreas

• Study of Cancer Trends in Young Adults in US 1995-2014
  • identified increasing incidence of obesity related cancers
  • (kidney, uterine corpus, colorectal, gallbladder, pancreas, and multiple myeloma) in ages 25-49
  • steeper rises in younger cohorts

Emerging cancer trends among young adults in the USA: analysis of a population-based cancer registry Lancet Public Health 2019
https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667(18)30267-6/fulltext
*share increased risk with diabetes
Obesity and Increased Cancer Risk (con’t)

Rate of New Obesity-associated Cancers by Race/Ethnicity

All Obesity-associated Cancers, Male and Female, United States, 2017

Rate per 100,000 people


Obesity associated cancers—adenocarcinoma of the esophagus; cancers of the breast (in postmenopausal women); colon and rectum; endometrium (corpus uterus); gallbladder; gastric cardia; kidney (renal cell); liver; ovary; pancreas; thyroid; meningioma; and multiple myeloma.
Diabetes, Obesity, and Cancer
Diabetes Meds and Cancer Risk

Metformin

• Lower incidence of gastric, colorectal, liver, breast, and endometrial cancer
• Longer survival/lower mortality in colorectal, lung, breast, endometrial, prostate, and pancreatic cancers
• Anti-neoplastic effects: inhibits tumor cell and blood vessel growth, can enhance effect of some chemotherapy drugs
Diabetes Meds and Cancer Risk (con’t)

Sulfonylureas (glipizide, glyburide, glimepiride)
  • Neutral cancer risk

Thiazolidinediones (pioglitazone, rosiglitazone)
  • Overall cancer risk reduction
  • Anti-neoplastic effects: slows cancer cell growth, may decrease risk colon cancer
  • Pioglitazone associated with increased bladder cancer risk in some studies (rare, time and dose dependent)
Diabetes Meds and Cancer Risk (more)

DPP-4 inhibitors (linagliptin/Tradjenta®, saxagliptin/Onglyza®, sitagliptin/Januvia®)
  • Neutral or decreased colorectal cancer risk

SGLT-2 inhibitors (canagliflozin/Invokana®, dapagliflozin/Farxiga®, empagliflozin/Jardiance®)
  • In vitro: tumor inhibition effects described
  • Recent meta-analysis – no difference in cancer risk
  • Long term data is limited
Diabetes Meds and Cancer Risk (addt’l)

GLP-1 receptor agonists (liraglutide/Victoza®, semaglutide/Ozempic®, dulaglutide/Trulicity®, exenatide ER/Bydureon®)

- Increased thyroid C cell tumors in rats
- Recent meta-analysis no elevated risk of thyroid, pancreas, or overall cancer rates

Insulin

- Theoretical risk due to insulin and insulin growth factor (IGF) receptors on cancer cells
- Longstanding endogenous hyperinsulinemia common in T2DM
- Concern re: increased risk with use of insulin analogues but evidence inconclusive
Cancer Prevention and Risk Reduction

Strategies for Cancer Risk Reduction

- Tobacco Cessation
- HPV vaccination
- Hepatitis B vaccination
- [Hepatitis C screening and treatment]
- [Aspirin for colorectal cancer prevention]
- [Treatment of helicobacter pylori infection]
Population Based Screening, Chronic Disease Management & Health Outcomes

IHS Standards of Care and Clinical Practice Recommendations for Type 2 Diabetes

- Recommendations for screening and clinical care
- Flowsheets/ Clinical Reminders
- IHS Diabetes Care and Outcomes Audit

Improving Trends

- End Stage Renal Disease
- Retinopathy
Cancer Screening in 2020 and COVID-19

Reported rates of cancer screening decreased in 2020

- Mass General – Brigham and Women’s Hospital system – abrupt decline in cancer screenings during spring and summer, resulting in fewer cancer diagnoses; Partial rebound in screening observed in fall of 2020. (JAMA Oncol. 2021;7(3):458-460.)

- Kaiser – Southern California - 80% decline in cervical cancer screening rates from 1/1/19-9/30/19 vs. 1/1/20-9/30/20, greatly improved but did not return to normal after stay-at-home order lifted (MMWR Morb Mortal Wkly Rep 2021;70:109–113)

COVID-19 Vaccine and Breast Cancer Screening

“Being vaccinated against COVID-19 may cause temporary swelling of the lymph nodes in the armpit, according to several recent studies. Because this side effect of the vaccine may be mistaken for a sign of breast cancer, several oncology groups are recommending that people wait 4-6 weeks after completing COVID-19 vaccination before getting a mammogram.”

National Cancer Institute
Cancer Screening Guidelines in US

- Screening goals: Identify cancer in asymptomatic, early, or precancerous stage
- Professional society guidelines (USPSTF, American Cancer Society, American College of Obstetrics and Gynecology, American College of Physicians, American Academy of Family Practice and others)
- Guidelines vary. Organizations assess available tests, risks, benefits, test performance in US population at average risk, often age and/or sex specific, reviewed and updated frequently
- Basis for health policy, quality indicators, reimbursement
- Government Performance and Results Act (GPRA) measures and reporting in IHS
Cancer Screening Guidelines in US (con’t)

• Guidelines different for people at higher risk
  • Personal history of cancer
  • Family history (esp. breast, colorectal cancer)
  • Known cancer gene (BRCA1, BRCA2, p53, TP53)
  • Exposures to known carcinogens – environment, occupational, radiation, smoking
  • Cirrhosis, nonalcoholic fatty liver disease (NAFLD)
  • People on transplant medications
Breast Cancer (Mammogram) Screening Guidelines in US for women at average risk (2021)

<table>
<thead>
<tr>
<th></th>
<th>Age 40-49</th>
<th>Age 50-74</th>
<th>Age 75 and older</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>US Preventive Services Task Force</strong></td>
<td>Shared decision making</td>
<td>Every 2 years</td>
<td>Insufficient evidence for continued screening</td>
</tr>
<tr>
<td><strong>American College of Obstetricians and Gynecologists</strong></td>
<td>Offer every 1-2 years (individual decision)</td>
<td>Every 1-2 years</td>
<td>Shared decision making based on health status and life expectancy</td>
</tr>
<tr>
<td><strong>American Cancer Society</strong></td>
<td>Offer annual to age 45, then annually</td>
<td>Annually age 50-54, then every 2 years option annually ages 55-74</td>
<td>Continue screening if in good health and life expectancy is at least 10 years</td>
</tr>
</tbody>
</table>

GPRA (2019): Women ages 52 to 75 with mammogram within 2 years
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Pap Smear</td>
<td>Ages 21-29: every 3 years</td>
<td>Ages 25-65: every 3 years</td>
<td>Ages 21-65: every 3 years</td>
</tr>
<tr>
<td></td>
<td>Age 30-65: every 3 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pap Smear with HrHPV test (co-test)</td>
<td>Ages 30-65: every 5 years</td>
<td>Ages 25-65: every 5 years</td>
<td>Ages 30-65: every 5 years</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary HPV test (specific high-risk strains)</td>
<td>Ages 30-65: every 5 years</td>
<td>Ages 25-65: every 5 years</td>
<td>Ages 25-65: every 3 years (consider)</td>
</tr>
</tbody>
</table>

GPRA (2019): Women ages 24-64 (without hysterectomy) with Pap Smear in the past 3 years, or if 30-64 years old, either a Pap Smear in the past 3 year or a Pap Smear and an HPV DNA on the same day in the past 5 years.
Colon Cancer Screening Guidelines in US for people at average risk (2021)

<table>
<thead>
<tr>
<th>Ages 45-49</th>
<th>Ages 50-75</th>
<th>Ages 76 and older</th>
</tr>
</thead>
</table>
| American Cancer Society | Consider screening | Stool-based tests/interval  
  Fecal immunochemical test (FIT)/1yr  
  High sensitivity guaiac fecal occult blood/1 yr.  
  Multitarget stool DNA test/3 yrs.  
  or  
  Structural examination  
  Colonoscopy every 10 yrs.  
  CT colonography every 5 yrs.  
  Flexible sigmoidoscopy every 5 yrs. |
| **USPSTF** (in revision) | Tests as noted above  
  or FIT DNA/1-3 yrs.  
  or Flexible sigmoidoscopy every 10 yrs. with FIT every year | Individualize screening decisions for individuals aged 76 through 85 years based on patient preferences, life expectancy, health status, & prior screening history  
  Discourage individuals older than 85 years from continuing screening. |

GPRA (2019): A. Fecal Occult Blood Test (FOBT) or Fecal Immunochemical Test (FIT) during the report period B. Flexible sigmoidoscopy or CT colonography in the past 5 years C. Colonoscopy in the past 10 years D. FIT-DNA in the past 3 years
Lung Cancer Screening Guidelines in US (2021)
Annual low dose Chest CT (LDCT)

**American Cancer Society (2013)**
- Age 55-74 years in fairly good health, and
- Current smoker, or has quit within past 15 years, and 30-pack-year smoking history, and
- Receive smoking cessation counseling if they are current smokers, and
- Have been involved in informed/shared decision making about the benefits, limitations, and harms of screening with LDCT scans, and
- Have access to a high-volume, high quality lung cancer screening and treatment center.

**US Preventive Services Task Force (2021)**
- Age 50-80 years
- Current smoker, or has quit in last 15 years, and
- 20-pack-year smoking history
- Stop screening once person has not smoked for 15 years or develops a health problem that limits life expectancy or the ability or willingness to undergo curative lung surgery.

GPRA: Currently no performance measure
Cancer Screening

• Cancer is a leading cause of morbidity and mortality in people with diabetes
  • Cancers more commonly associated with diabetes include breast, colorectal, liver, pancreas, endometrium, esophagus, kidney, bladder
  • People with diabetes may experience more complications and worse outcomes

• Strategies for cancer prevention include
  • Smoking Cessation
  • Vaccinations: HPV, Hepatitis B
  • Others

• Cancer screening tests can improve outcomes
  • Guidelines for cancer screening continue to evolve
  • GPRA or EMR clinical reminders identify people who might benefit
  • Importance of informed and shared decision making
Questions?
References

• Diabetes, Antidiabetic Medications and Cancer Risk in Type 2 Diabetes: Focus on SGLT-2 Inhibitors

• Disparities in Cancer Mortality and Incidence Among American Indians and Alaska Natives in the United States
  ▪ American Journal of Public Health 104, no. S3 (June 1, 2014): pp. S377-S387 *
    https://ajph.aphapublications.org/doi/full/10.2105/AJPH.2013.301673
  *this APHA supplement was dedicated to mortality trends in AI/AN populations

• Diabetes and Cancer: A Consensus Report

• Diabetes and Risk of Cancer
  ▪ ISRN Oncology Volume 2013, Article ID 583786, 16 pages
    http://dx.doi.org/10.1155/2013/583786
References (con’t)

• Emerging cancer trends among young adults in the USA: analysis of a population-based cancer registry
  • Lancet Public Health 2019 – online 2/4/19
    https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667(18)30267-6/fulltext

• Trends in predominant causes of death in individuals with and without diabetes in England from 2001 to 2018: and epidemiological analysis of linked primary care records
  • Lancet Diabetes Endocrinol 2021; 9: 165–73 Published Online February 4, 2021
    https://doi.org/10.1016/S2213-8587(20)30431-9


• Cancer Screening Tests and Cancer Diagnoses During the COVID-19 Pandemic
Resources

• Office of Minority Health: Cancer and American Indians/Alaska Natives
  • https://minorityhealth.hhs.gov/omh/browse.aspx?lvl=4&lvlid=31

• Trends in Indian Health
  • https://www.ihs.gov/dps/index.cfm/publications/trends2014/

• CDC – Cancer Information and Statistics
  • https://www.cdc.gov/cancer/index.htm

• National Cancer Institute – SEER Program (Cancer Statistics)
  Surveillance, Epidemiology, and End Results Program

• Indian Health Service: Division of Diabetes Treatment and Prevention
  • https://www.ihs.gov/Diabetes/