THE EVOLVING EPIDEMIC OF HPV-RELATED MALIGNANCIES IN TEXAS

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Objectives
- Identify the prevalence of HPV and HPV-related malignancies across Texas
- Understand the impact of HPV vaccination on HPV-malignancies
- Describe cancer survivors’ risk for HPV-related malignancies compared to the general population

Disclosures
- No relevant financial or industry interests to disclose

HPV: Quick Facts
- Most common sexually transmitted infection
- 79 million currently infected (1 out of 4)
- 14 million new cases every year
- HPV virus can be shed from asymptomatic carriers
- Symptoms may not present for years
- Most infections resolve without treatment
- Some develop persistent infection

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HPV: Quick Facts
- >150 HPV serotypes
- “Low risk” types not associated with cancer
- “High risk” types = associated with malignant transformation of mucosal skin cells (carcinomas)

HPV-Related Cancers
- HPV is implicated in:
  - 91% of cervical cancers
  - 75% of vaginal cancers
  - 69% of vulvar cancers
  - 63% of penile cancers
  - 91% of anal and rectal cancers
  - 70% of oropharyngeal cancers

HPV High Risk Types

<table>
<thead>
<tr>
<th>16</th>
<th>18</th>
<th>6</th>
<th>11</th>
<th>31</th>
<th>33</th>
<th>45</th>
<th>52</th>
<th>58</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bivalent Vaccine: Cervarix</td>
<td></td>
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<tr>
<td>Quadrivalent Vaccine: Gardasil</td>
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<tr>
<td>9-Valent Vaccine: Gardasil9</td>
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HPV-related Cancers
- ~30,000 new cases/year in US
- ~4,000 new cases/year in Texas
HPV-Cancers: Age at Diagnosis

Financial Burden of HPV

- **Direct Costs:**
  - Total direct cost to State of Texas from HPV-associated cancers in 1 year = $77.7 million
  - $51.4 million for diagnosis & treatment
  - $26.3 million for consequences from treatment

- **Indirect Costs:**
  - Evaluated in terms of present value of lifetime earnings (PVLE) lost due to cancer mortality
  - PVLE = (Total #HPVdeaths) x (expected future earnings based on age & life expectancy)
  - 2013 PVLE = (362) x ($543,277) = $196.6 million

Fiscal Year 2013 Medicaid Costs Associated with Consequences of Cancer Treatment in Texas (HBSC Medicaid)

<table>
<thead>
<tr>
<th>HPV-Related Cancer</th>
<th>Number of Cases</th>
<th>Treatment Cost</th>
<th>Adjusted Cost</th>
<th>Consequence Cost</th>
<th>Adjusted Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arousa</td>
<td>1,895</td>
<td>$4,358,170</td>
<td>$4,129,780</td>
<td>$1,714,297</td>
<td>$1,560,931</td>
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<tr>
<td>Rectal</td>
<td>8,849</td>
<td>$13,238,987</td>
<td>$13,834,110</td>
<td>$8,155,336</td>
<td>$3,748,310</td>
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<tr>
<td>Cervix</td>
<td>9,676</td>
<td>$15,713,839</td>
<td>$16,361,671</td>
<td>$8,386,808</td>
<td>$7,749,617</td>
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<tr>
<td>Oropharyngeal</td>
<td>6,723</td>
<td>$23,078,752</td>
<td>$25,656,116</td>
<td>$11,690,880</td>
<td>$10,515,139</td>
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<tr>
<td>Puts</td>
<td>395</td>
<td>$736,857</td>
<td>$742,920</td>
<td>$408,702</td>
<td>$380,702</td>
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<tr>
<td>Vulva and Vagina</td>
<td>1,535</td>
<td>$2,906,400</td>
<td>$2,676,812</td>
<td>$1,495,159</td>
<td>$1,495,159</td>
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<tr>
<td>Total</td>
<td>19,823a</td>
<td>$51,419,580</td>
<td>$52,113,747</td>
<td>$26,113,747</td>
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HPV-Cancer Prevention

- HPV Vaccination
  - Current CDC Recommendation revised in December, 2016

HPV Vaccination: CDC Guidelines 2016

- Catch-up vaccines
  - Males up to 21 (although can still receive it up to age 26)
  - Females up to 26

HPV Vaccination: CDC Guidelines 2016

- 2-dose series:
  - Age 11 to 12
  - 0, 6-12month schedule
  - Rule applies to all who initiate at age 9-14

- 3-dose series:
  - Age 15-26 who are first initiating the series OR Immunocompromised persons
  - 0, 1-2, 6 month schedule

HPV Vaccination Barriers

- #1 Barrier = NO provider recommendation
- Only 53% of Texas teens received a recommendation

(MD Anderson HPV Vaccine Uptake in Texas Pediatric Care Settings: 2014-2015 Environmental Scan Report)
Why No Recommendation?
- Lack of provider knowledge of HPV-diseases
- Low awareness of the relationship between age of vaccination and immune response
- HPV recommendations not well understood
  - Number of doses in series
  - STI testing not required
- Perceived lack of time to discuss HPV vaccine

Texas HPV Vaccine Coverage
- How are HPV vaccine coverage levels measured?
  - Behavioral Risk Factor Surveillance System (BRFSS) survey
  - National Immunization Survey-Teen (NIS-Teen).

HPV-Cancer Prevention
- Routine Pap screening → cervical cancer detection
  - Age 21-29 → every 3yrs
  - Age 30-65 → every 3yrs, OR Pap-smear + HPV co-testing every 5 yrs
- Condoms

Texas HPV Vaccine Coverage

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State of Texas HPV Strategic Plan
Senate Bill 200, Section 2.32, 84th Legislature
 2015→ Texas State Legislature passes Senate bill directing HHSC to develop strategic plan to significantly reduce morbidity & mortality from HPV-associated cancer
 2015-2016→ HHSC collaborates with Dept of State Health Svcs, CPRIT, stakeholders to draft plan
 HPV Strategic Plan is released in December 2016

Strategic Plan Goals
 Identify actions to:
  • Increase vaccination & screening rates
  • Reduce HPV-cancer morbidity & mortality
 Make policy recommendations to state legislature

Strategic Plan Goals
 Identify barriers to prevention, screening, & treatment for HPV-cancer
 Identify methods to increase vaccination
 Identify methods to increase evidence-based screening
 Develop methods for creating partnerships to increase awareness of:
  • HPV-cancers
  • importance of vaccination education
  • Regular screening

Strategic Plan: Methods for Increased Vaccination
 Educate clinicians on best strategies for counseling & recommending vaccines to patients
 After vaccine initiation, schedule 2nd dose before the patient leaves the office.
 Reminder/recall strategies for remaining doses
  • Improve use of ImmTrac’s reminder/recall functionality to improve second and third dose rates.

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Strategic Plan: Methods for Increased Screening

- **Increase public education** of state programs for screening & diagnostic services
- **Outreach efforts:**
  - Informational cards
  - In-office display posters
  - Digital and social media outreach campaigns
  - Focus on counties identified with low screening rates
- **Increase provider participation** in state programs for screening & diagnostic services

HPV-Malignancies: A 15 Year Review of the Texas Cancer Registry

- **HPV-cancers** = cancers at specific anatomic sites with specific cell types in which HPV DNA frequently is found, as identified by the Center for Disease Control.
  - Cervical carcinomas
  - Squamous cell carcinomas: vaginal, vulvar, penile, anal, rectal, oropharyngeal
- All cancers confirmed histologically & identified by ICD site and histology codes.

Prepared by the Texas Department of State Health Services, Cancer Epidemiology and Surveillance Branch, Texas Cancer Registry.

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**DEFINING THE HPV DISEASE BURDEN IN TEXAS**

**Project Goal 1. Evaluate frequencies of HPV-related cancers by age at diagnosis**
Project Goal 2. Determine frequencies of HPV-related cancers by Texas public health region.

Average Annual Incidence of HPV-Related Malignancies in Texas by Age, 2000-2014

Age

Average Annual Incident Rate

15-19 years
20-24 years
25-29 years
30-34 years
35-39 years
40-44 years
45-49 years
50-54 years
55-59 years
60-64 years
65-69 years
70-74 years
75-79 years
80-84 years
85+

Common Cancers

Oropharyngeal
Rectal
Anal
Penile
Vulvar
Vaginal
Cervical

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Cervical Cancer Across Texas Public Health Regions

Data in Childhood Cancer Survivors (CCS)

- **SEER (1973-2010)** Cancer @Age 0-29
- **64,547 Survivors** of childhood & AYA cancers
- Evaluated standardized incidence ratios (SIR) of HPV-associated subsequent cancers

(Ojha PLoS One, 2013)

HPV-Cancers in Childhood and Young Adult Survivors

- HPV-related cancers INCREASED among childhood and AYA cancer survivors over US general population
  - **Female** survivors → **40% excess** HPV-associated cancers (SIR=1.4, 95% CL: 1.2, 1.8)
  - **Male** survivors → **150% excess** of HPV-associated cancers (SIR=2.5, 95% CL: 1.9, 3.4)

(Ojha PLoS One, 2013)

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HPV-Cancers Post-BMT

- Female survivors of BMT → increased risk for cervical dysplasia
  - Abnormal Pap smears ~3%-6% among healthy women
  - 3 years post-BMT abnormal Paps:
    - AlloSCT = 14% to 54%
    - Auto-SCT = 4% to 33%

Sasadeusz J, Bone Marrow Transplant, 2001

HPV-Cancers Post-BMT

- 2,129 patients s/p BMT for hematologic malignancies (City of Hope, 1976-1998)
- Cumulative probability 2nd solid cancer at 10yrs = 6.1% (± 1.6%)
  - Oropharyngeal Cancer (SIR, 17.4; 95% CI, 6.3 to 34.1)
  - Cervical cancer (SIR, 13.3; 95% CI, 3.5 to 29.6).
- Risk much higher for survivors < 34 yo at time of BMT (SIR, 5.3; 95% CI, 2.7 to 8.6)

Bhatia S, J Clin Oncol, 2001

HPV-Cancers Post-BMT

- BMT recipients → 13-fold increased risk for cervical cancer over general population

Socie G, Journ Clin Oncol, 2000

HPV-Cancers Post-BMT

- Prospective review of Adult SCT survivors: 34% → cervical carcinoma (43% with dysplasia)
  - Median time to HPV-cancer = 51 months post-transplant (range: 22-108)
  - Median age = 42 years (range: 19-62)
  - Most significant in patients receiving chronic IST (OR 4.6)

(Savani, Biology of Bone and Marrow Transplantation, 2008)
HPV-Cancers After Hodgkin Lymphoma
- MD Anderson 20yr review (1962-1983)
- 666 patients with Hodgkin Lymphoma
- 46% developed HPV-related disease including anogenital & cervical cancers

Klosky J, Cancer, 2009

HPV-Cancers After Pelvic Irradiation
- Among women with prior pelvic irradiation: 49% with vaginal dysplastic lesions
- High-risk HPV types in 98% of lesions

Fujimura M, Cancer, 1991

HPV and Cancer Survivors
- ASCO & COG survivorship guidelines include education of HPV-disease risks and encouraging vaccination
- Uptake and Implementation of these guidelines unclear
- Our own review finds that AYA's who are survivors of childhood cancer are profoundly under-vaccinated, beyond the already lagging state vaccination rates

HPV Vaccination Among Childhood Cancer Survivors in South Texas

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HPV Vaccination in Cancer Survivors
- Current state vaccination programs do not target cancer survivors.
- Many survivors do not fully integrate back into regular primary care and vaccination schedules.
  - 3 years post-treatment, 61% of childhood cancer survivors not returned to vaccination schedules.

Texas Vaccination Resources
- Vaccine education programs: HHSC Healthy Texas Women, Family Planning, Primary Health Care, Texas Medicaid, CHIP.
- CPRIT supports vaccine education & access through grant awards.
- Collaborative partners: University of Texas MD Anderson Cancer Center, the Texas Pediatric Society, Texas Medical Association, and the Immunization Partnership.

Texas Vaccination Resources
- Texas Vaccines for Children (TVFC) Program:
  - Provides free HPV vaccine up to age 18.
- Adolescent Immunization Awareness Campaign:
  - Annual awareness targeting parents & providers.
- Provider Education HPV Vaccine Toolkit:
  - currently being developed.
  - clinician fact sheet.
  - strategies for counseling and recommending vaccines to patients.
  - TVFC program information.
  - Texas Immunization Registry (ImmTrac) materials.

Texas Screening Resources: BCCS
- Texas Breast and Cervical Cancer Services (BCCS) Program services include:
  - Breast exam & mammogram.
  - Pelvic exam & Pap test.
  - Confirmatory testing for pre-cancer or cancerous condition.
  - Treatment for cervical intraepithelial neoplasia (CIN) or pre-cancer including: conization and cryotherapy.
  - Individualized patient navigation and education.
  - Access to treatment via Medicaid for Breast and Cervical Cancer (MBCC).
Texas HPV Screening Resources
- Healthy Texas Women (HTW) and Family Planning Program (FPP)
  - HPV Immunization
  - Screening tests for cervical cancer
  - HTW serves women ages of 15 to 44 at or below 200%FPL, not pregnant
  - FPP serves women and men under age of 64 at or below 250%FPL
  - Services at little to no cost
  - www.HealthyTexasWomen.org

Texas HPV Screening Resources
- www.YourTexasBenefits.com
  - Texas Medicaid & CHIP
  - CHIP provides including HPV vaccines to uninsured children & youth in families with incomes up to 201%FPL.
- www.SomedayStartsNow.com
  - HHSC Primary Health Care Services Program (PHC)
  - Texas residents who do not qualify for other state or federal health care assistance programs

Conclusions
- HPV-related malignancies are prevalent across Texas and the financial and personal burdens of disease are high
- HPV exposure is nearly universal by adulthood
- HPV Vaccination PRIOR TO EXPOSURE is critical

Conclusions
- Lack of provider recommendation is the top barrier to HPV vaccination
- Cancer survivors are more susceptible to persistent infection following HPV exposure and HPV reactivation → increased risk for HPV-malignancies
- Cancer survivors are a high-risk subgroup and more likely to be under-vaccinated
Final Thoughts...

- Are you between the ages of 11-26? Do you know anyone who is?
- Have YOU completed the HPV vaccine series? Have your friends and family?
- If you are a provider, are you recommending HPV vaccination to your patients?
- Are you a cancer survivor and are you currently enrolled in a screening program?
- Get the word out!

Thank you!

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