PREDICTORS OF INTENTIONAL AND UNINTENTIONAL NON-ADHERENCE, AND ASSOCIATED HEALTH UTILITIES, AMONG WOMEN RECEIVING ORAL TREATMENTS FOR BREAST CANCER

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BACKGROUND
Introduction

• As breast cancer (BC) survivorship increases, maintenance treatment with adjuvant endocrine therapy (ET) is critical to improved long-term survival and recurrence prevention.¹-⁶

• Suboptimal adherence is seen in clinical practice: 12-59% (tamoxifen, a selective estrogen receptor modulator [SERM]) and 9-50% (aromatase inhibitors [AIs]) non-adherence, plus high non-persistence after 5 years.⁷

• Factors associated with non-adherence to tamoxifen and AIs:⁸
  – Patient-related (race, age, fear of adverse events [AEs], forgetfulness, smoking)
  – Tx-related (duration, additional Rx, side effects)
  – Healthcare system (patient-provider relationship)
  – Socioeconomic (Rx costs, marital status)
  – Disease-related (comorbidities, BC stage)

¹. From Cancer Patient to Cancer Survivor: Lost in Transition. Institute of Medicine; 2005
². Burstein et al. J Clin Oncol. 2010
OBJECTIVE
Objective

- Examine potential predictors (demographic and lifestyle behaviors) of intentional (INA) and unintentional (UNA) non-adherence among women receiving oral treatments for BC using real-world data.
- Quantify health utilities (burden) associated with INA and UNA.
- These findings can help support development of targeted, effective interventions addressing underlying unhealthy behaviors to maximize the benefit of ET.
METHODS
Methods

Data Source

National Health and Wellness Survey (NHWS):

• Cross-sectional, Internet-based survey of adults (≥18 years)
• Stratified random sampling (by age, gender, and ethnicity) used to reflect Census distributions of the total US adult population
• 2010-2015 US NHWS data

$N=679$ females reporting diagnosis with BC and adjuvant/metastatic oral therapy (exclusive):

• AIs (n=457)
• SERMs (n=222)
Methods

Measures

• Demographics
  – Age
  – Race/ethnicity
  – Education
  – Employment
  – Income
  – Marital status
  – Health insurance

• Health Outcome
  – SF-6D health utilities\textsuperscript{11,12}

• Lifestyle Behaviors
  – Exercise
  – Alcohol
  – Cigarette smoking

• Health Characteristics
  – BMI (height/weight)
  – Charlson comorbidity index\textsuperscript{9,10}
  – BC stage at diagnosis
  – SERMs vs. AIs

\textsuperscript{9.} Charlson et al. \textit{J Chron Dis.} 1987; 40(5):373-83
\textsuperscript{10.} Quan et al. \textit{Am J Epidemiol.} 2011;173(6):676-82
\textsuperscript{11.} Brazier et al. \textit{J Health Econ.} 2002;21:271-92
Methods

Measures

• Adherence

  – Morisky Medication Adherence Scale (MMAS) equivalent items from MMAS-4\textsuperscript{13} and MMAS-8\textsuperscript{14} were summed to create scores for:
    • Intentional non-adherence (INA): stop taking medicine when feeling better/worse
    • Unintentional non-adherence (UNA): forget or miss taking medication
    • These were categorized: 0 = adherent; 1+ = non-adherent

Methods

Analyses

• Binary logistic regressions predicted INA or UNA from variables noted previously, plus UNA or INA, respectively.

• A normal generalized linear model predicted health utilities from INA and UNA, controlling for covariates.

RESULTS
Results

Sample

• Among 679 total respondents, 6.0% reported INA and 22.4% reported UNA; 3.2% reported both.
  – Mean age = 61.64 (SD=11.06)

<table>
<thead>
<tr>
<th>Descriptive Results</th>
<th>%</th>
<th>N</th>
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<tbody>
<tr>
<td>Non-adherence</td>
<td></td>
<td></td>
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<tr>
<td>Adherent</td>
<td>74.8%</td>
<td>508</td>
</tr>
<tr>
<td>Non-adherent</td>
<td>25.2%</td>
<td>171</td>
</tr>
<tr>
<td>Oral ET</td>
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<tr>
<td>AIs</td>
<td>67.3%</td>
<td>457</td>
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<tr>
<td>SERMs</td>
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<tr>
<td>Employment status</td>
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<tr>
<td>Employed FT/PT/Self</td>
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<tr>
<td>Disabled</td>
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<td>Unemployed</td>
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<tr>
<td>Yes</td>
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<tr>
<td>Smoke cigarettes</td>
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<tr>
<td>No</td>
<td>87.2%</td>
<td>592</td>
</tr>
<tr>
<td>Yes</td>
<td>12.8%</td>
<td>87</td>
</tr>
</tbody>
</table>
Results

Multivariable Results

- Significant predictors of INA included UNA (OR=4.17), age (OR=0.96), income <$25K (OR=5.28), non-overweight BMI (OR=3.90), and non-obesity (OR=4.17).
- Significant predictors of UNA included INA (OR=4.13), age (OR=0.97), non-white ethnicity (OR=1.70), obesity (OR=1.77), infrequent exercise (OR=1.60), and smoking (OR=2.14).
Results

Multivariable Results

• Adjusting for covariates (age, ethnicity, employment, marital status, BMI, health insurance, income, etc.):
  – INA and UNA were each associated with significantly lower health utilities ($b_{INA}=-0.071$, $p=0.001$; $b_{UNA}=-0.023$, $p=0.048$)
CONCLUSIONS
Conclusions

• Self-reported non-adherence to oral ET in women with BC was common (25.2%).
  – Similar to previously reported rates of 23.7%-32.2%15,16

• Both INA and UNA were associated with significantly poorer health status; INA had a greater impact (>minimally important difference [MID]).12
  – Non-adherence and decreased health-related quality of life (HRQoL) findings mirror previous NHWS research in BC and other conditions17

• Younger age was associated with both INA and UNA.
  – Previous research found 1-year age increments were associated with better adherence16

• Lower income and non-overweight/obese respondents were at greater risk of INA.

Conclusions

• Given relatively high UNA prevalence in BC, targeted interventions may help reduce UNA especially, to improve outcomes among at-risk populations (e.g., younger adults, non-whites, obese or sedentary patients, and smokers) predisposed to non-adherence.

• Given recommendations of 10 years of adjuvant therapy and evidence of decreased survival when this is interrupted, improved adherence is key in delaying disease progression, thereby leading to better outcomes.

• Targeted interventions should be less complex and less toxic, as previous research found that forgetfulness and AEs are the most common reasons for non-adherence.17

Limitations

- Causal conclusions cannot be drawn from cross-sectional data.
- Self-report measures associated with recall and other biases.
- Generalizability is limited to those with access, motivation, and ability to participate in online surveys.
- Majority of patients were non-Hispanic white.
Implications

Given increasing use of oral ET in BC, suboptimal adherence levels, and detrimental effects of non-adherence, interventions in those at highest risk should be developed and tested.

For UNA:
- Develop tools to aid adherence (e.g., reminders; get family/caretaker involved)
- Refills on time

For INA:
- Increase patient education
- Address costs