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Patient Preferences for First-Line Maintenance Treatments for Ovarian Cancer

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Disclosures and Disclaimers

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Background

- Ovarian cancer is the fifth most common cancer among women in the United States (US)
- ~70% of women are diagnosed when the disease is advanced
- Two primary options are available for patients who do not progress after first-line therapy:
  - "Watch and wait," with no additional therapy
  - Maintenance therapy
- Up to 80% of women who respond to first line maintenance therapy will experience a recurrence
- Havrilesky et al. (2014) studied preferences for chemotherapy to treat ovarian cancer; there are no published studies on patients' benefit-risk preferences for maintenance treatments in ovarian cancer

Havrilesky LJ, Alvarez Secord A, Ehrisman JA, Berchuck A, Valea FA, Lee PS, Gaillard SL, Samsa GP, Cella D, Weinfurt KP, Abernethy AP, Reed SD. Patient preferences in advanced or recurrent ovarian cancer. Cancer. 2014 Dec 1;120(23):3651-9.

Objective

- Elicit patient benefit-risk trade-off preferences for outcomes associated with selected first-line maintenance therapies for advanced ovarian cancer among patients with ovarian cancer eligible for maintenance treatment
  - Estimate relative preferences for a set of treatment-related benefits and toxicities
  - Calculate progression-free survival (PFS) equivalences for improvements in other treatment-related attribute levels (also called minimum acceptable benefit [MAB])

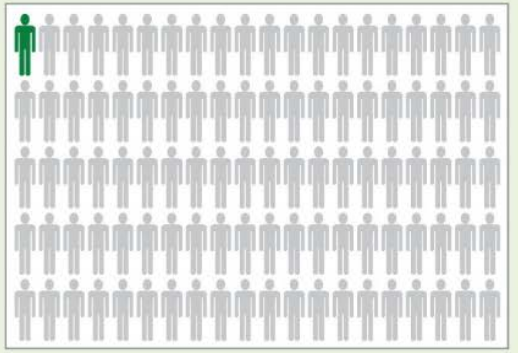
Study Design: Discrete-Choice Experiment

- Web-enabled discrete-choice experiment (DCE)
  - DCEs are designed to provide information about individuals' willingness to accept tradeoffs among features of multiattribute products
- Respondents were asked to decide between hypothetical maintenance medicines for ovarian cancer
- Each hypothetical treatment was defined by a set of attributes (features) with varying levels determined by an experimental design
- Choices for treatments revealed respondents' willingness to accept tradeoffs among treatment attributes

Study Design: Attributes and Levels

Attribute	
1. How long until the cancer comes back	• 19 months (7 additional months) • 16 months (4 additional months) • 14 months (2 additional months)
2. Feeling weak or tired	• None • Mild-to-moderate • Severe
3. Diarrhea	• None • Mild-to-moderate • Severe
4. Nausea and vomiting	• None • Mild • Moderate
5. High blood pressure	• None • Manageable increase
6. Risk of developing a hole in your gastrointestinal (GI) tract	• None • 1 out of 100 (1%) • 5 out of 100 (5%)

Study Design: Example Question

Medication Feature	Medication A	Medication B
How long until the cancer comes back	16 months (4 additional months)	19 months (7 additional months)
Feeling week or tired	Severe	Mild-to-moderate
Diarrhea	None	Severe
Nausea and vomiting	None	Moderate
High blood pressure	Manageable increase	None
Risk of developing a hole in your gastrointestinal (GI) tract	None	 1 out of 100 (1%)
Which would you choose?	○	○

Study Design: Survey Structure

- Contents of final patient survey
  - Questions about disease experience, including time since diagnosis, stage, treatment experience, toxicity experience, and selected comorbidities
  - Introduction to attributes and levels included in the DCE questions, with a complete description
  - 9 DCE questions
  - Demographic questions
- Attributes for DCE selected with input from literature and clinicians
- Survey pretested with face-to-face and webcam interviews for comprehension, relevance to patients, and question wording

Inclusion Criteria and Recruitment

- Inclusion criteria
  - Aged 18 years or older
  - Self-reported physician diagnosis of ovarian cancer, any stage
  - Eligible for maintenance treatment, defined as follows:
    - Patient completed surgery to remove all or part of the ovarian cancer tumor
    - Patient received chemotherapy to treat ovarian cancer
    - Cancer has not returned after completing surgery and chemotherapy
- Recruitment
  - Study approved by RTI International's institutional review board
    - All respondents provided online informed consent
  - US respondents recruited by Nielsen through its panel, clinics, and patient support groups
- Final sample size: 200

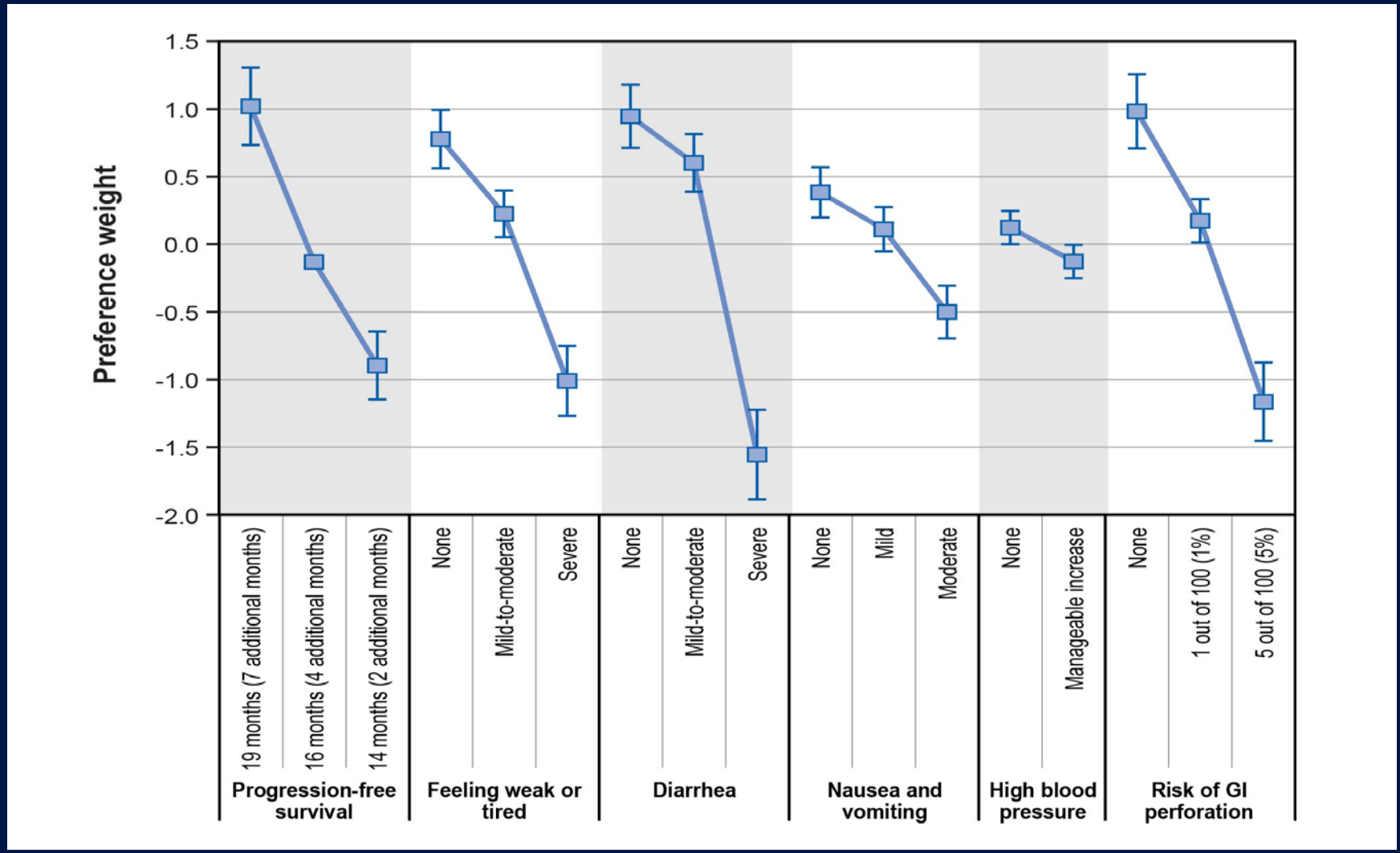
Results: Patient Characteristics

Characteristic	Respondents (N = 200)
Median age, years	49
Stage I or II at diagnosis	73%
Stage III or IV at diagnosis	26%
Diagnosed within the last 2 years	44%
Diagnosed more than 2 years ago	56%
Currently on treatment	17%

Study Methods: Analysis of Preference Results

- Random-parameters logit (RPL) model
  - Estimates a preference weight for each attribute level
  - Accounts for the panel nature of the data
  - Accounts for unobserved differences in preferences across respondents (taste heterogeneity)
- Variable coding
  - All attribute levels except PFS were included as categorical variables and were effects-coded
    - Effects coding estimates each preference parameter relative to the mean effect
    - Effects coding produces parameter estimates for all attribute levels
  - PFS was modeled as a continuous variable

Results: Preference Weights



Note: The vertical bars surrounding each mean relative importance weight denote the 95% confidence interval (CI) about the point estimate. All levels are different from each other within attributes at the 5% level except “none” and “mild” nausea and vomiting (P = 0.07).

Results: Preference Weights

- Preferences were ordered as expected, with respondents preferring greater efficacy, lower risks, and less severe side effect

- Differences between the highest and lowest weights indicate the overall importance of attributes over the ranges included in the study
  - Diarrhea, risk of a GI perforation, and PFS were the most important attributes in this set of attributes and for these attribute ranges
  - High blood pressure was the least important attribute

- Differences between all adjacent levels were statistically significant ($P < 0.05$) except “none” and “mild” nausea and vomiting ($P = 0.07$)

Results: Minimum Acceptable Benefit for Changes in Treatment Profiles

- Minimum acceptable benefit is defined as the minimum incremental amount of PFS needed to compensate respondents for changes in toxicity levels

Results: Highest Minimum Acceptable Benefit for Changes in Toxicities (Additional months of PFS)

Attribute	Change in Level	Mean MAB in Additional Months of PFS (95% CI)
Feeling weak or tired	**None to severe**	**4.7 (3.5-6.5)**
	Mild-to-moderate to severe	3.2 (2.4-4.4)
	None to mild-to-moderate	1.4 (0.7-2.5)
Diarrhea	**None to severe**	**6.5 (5.2-7.9)**
	Mild-to-moderate to severe	**5.6 (4.4-7.0)**
	None to mild-to-moderate	0.9 (0.2-1.7)
Nausea and vomiting	None to moderate	2.3 (1.4-3.2)
	Mild to moderate	1.6 (0.8-2.4)
	None to mild	0.7 (–0.1-1.4)
High blood pressure	None to manageable	0.7 (0.0-1.3)
Risk of GI perforation	**None to 5%**	**5.6 (4.2-7.1)**
	1% to 5%	3.5 (2.5-4.4)
	None to 1%	2.1 (1.2-3.0)

Results: Lowest Minimum Acceptable Benefit for Changes in Toxicities (Additional months of PFS)

Attribute	Change in Level	Mean MAB in Additional Months of PFS (95% CI)
Feeling weak or tired	None to severe	4.7 (3.5-6.5)
	Mild-to-moderate to severe	3.2 (2.4-4.4)
	None to mild-to-moderate	**1.4 (0.7-2.5)**
Diarrhea	None to severe	6.5 (5.2-7.9)
	Mild-to-moderate to severe	5.6 (4.4-7.0)
	None to mild-to-moderate	**0.9 (0.2-1.7)**
Nausea and vomiting	None to moderate	2.3 (1.4-3.2)
	Mild to moderate	1.6 (0.8-2.4)
	None to mild	**0.7 (–0.1-1.4)**
High blood pressure	None to manageable	**0.7 (0.0-1.3)**
Risk of GI perforation	None to 5%	5.6 (4.2-7.1)
	1% to 5%	3.5 (2.5-4.4)
	None to 1%	2.1 (1.2-3.0)

Results: Subgroup Analysis

- Estimated separate RPL models for several mutually exclusive subgroups and tested for differences in preferences

- Considered three different subgroup pairs
  - Stage I/II vs. stage III/IV ovarian cancer
  - Diagnosed < 2 years ago vs. diagnosed ≥ 2 years ago
  - Aged ≤ 49 years vs. ≥ 50 years

- Found no statistically significant differences between overall preferences for any of the subgroup pairs ($P > 0.05$)

CONCLUSIONS AND DISCUSSION

- Women with ovarian cancer who responded to this survey demonstrated distinct preferences for treatment attributes and were willing to trade efficacy (PFS) for improvements in side effect severity and risk
- The lack of differences across subgroups suggest consistent preferences across the attributes within our sample
- Studies such as this will make the following contributions to patient care:
  - Help physicians and policy makers better understand patient preferences and the trade-offs patients are willing to make between risks and benefits
  - Improve treatment to reflect the preferences of individual patients