

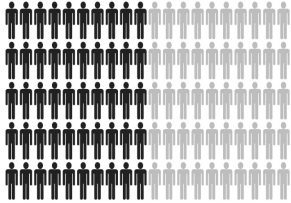
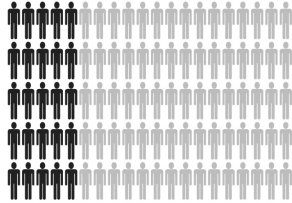
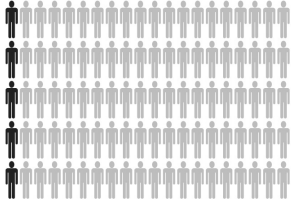
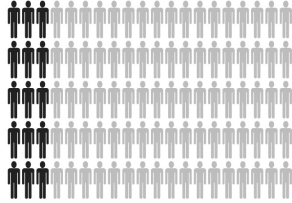
ONLINE APENDIX – SUPPLEMENTAL FIGURES

Figure S.1. Example Benefits-Harms Choice Question (First Set)

		Outcomes A	Outcomes B
Symptoms in a Typical Week	Improvement in positive symptoms	Much improved (50% reduction)	No improvement (<10% reduction)
	Improvement in negative symptoms	Minimally improved (25% reduction)	Very much improved (80% reduction)
	Social functioning	Moderate problems	Severe problems
Side Effects within the First Year	Weight gain	None	7%
	EPS	No	Yes
	Hyperprolactinemia	No	Yes
	Hyperglycemia	Yes	No
		Outcomes A	Outcomes B
Which set of outcomes is better for the patient?		<input type="radio"/>	<input checked="" type="radio"/>

EPS = extrapyramidal symptoms.

Figure S.2. Example Formulation Choice Question With Follow-up Adherence Information (Second Set)

	Medication A (Trial data)	Medication B (Trial data)
Mode of administration	Injection once every 3 months	Pill once a day
Percent of patients with at least minimally improved ($\geq 25\%$ reduction) in positive symptoms in a typical week, compared to initial presentation	50 out of 100 (50%) 	25 out of 100 (25%) 
Percent of patients with EPS within the first year	5 out of 100 (5%) 	15 out of 100 (15%) 

	Medication A	Medication B
Which treatment is better for the patient?	<input checked="" type="radio"/>	<input type="radio"/>

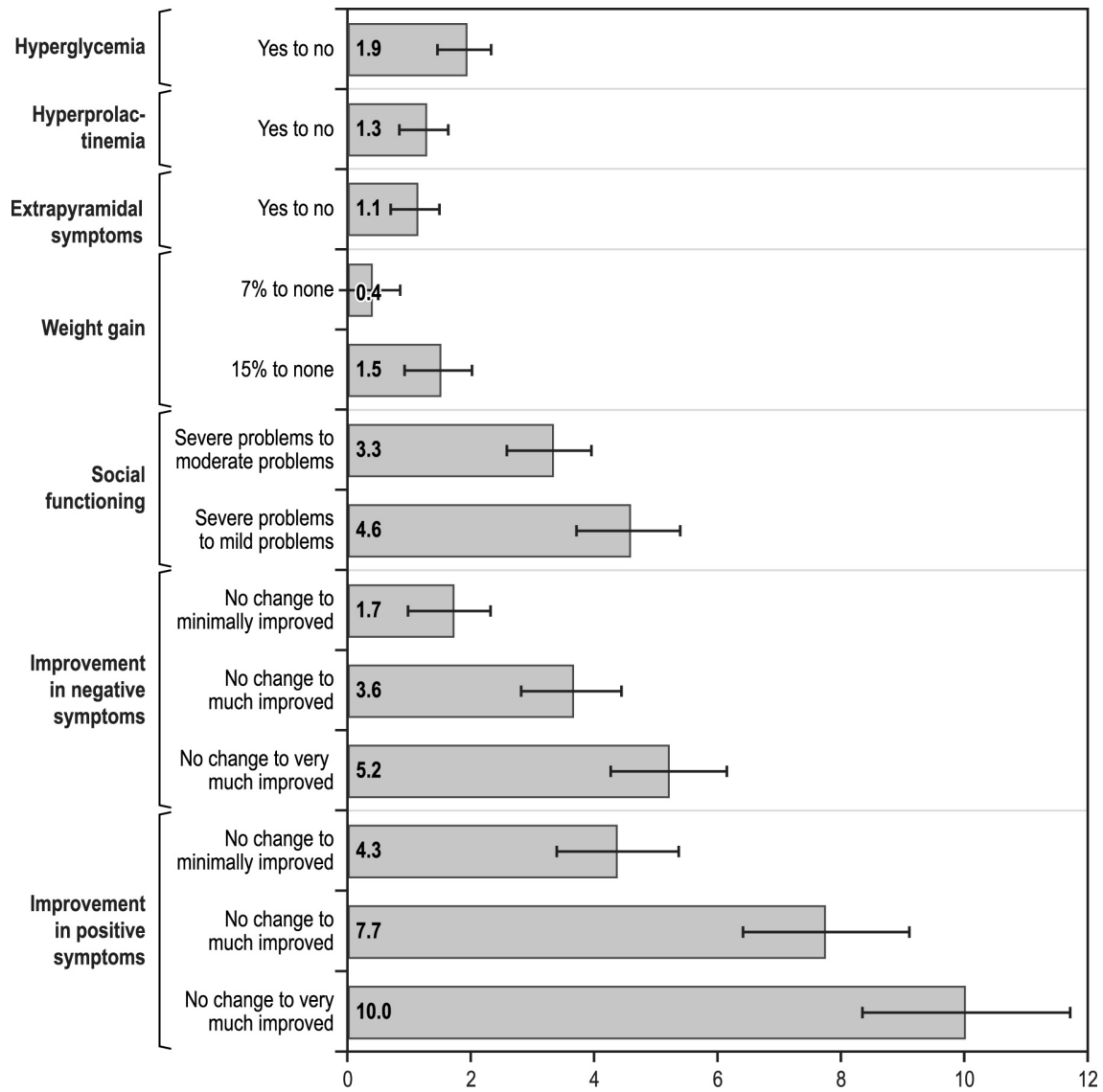
New information: The patient has missed or skipped 20% of his doses or oral medication in the past.

	Medication A	Medication B
Which treatment is better for the patient?	<input type="radio"/>	<input type="radio"/>

EPS = extrapyramidal symptoms.

Figure S.3. Mean Relative Importance Weights of Changes in Outcome Levels

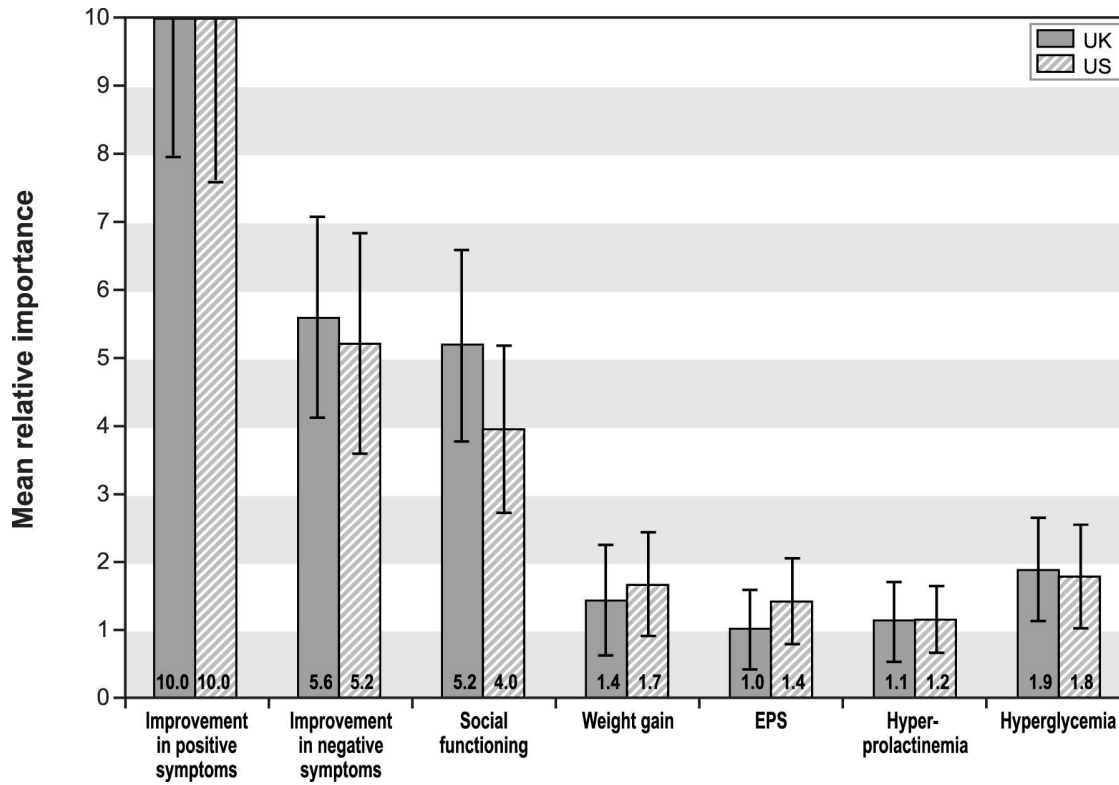
(N = 394)



EPS = extrapyramidal symptoms.

Note: The horizontal bars surrounding each mean relative importance estimate denote the 95% confidence interval about the point estimate.

Figure S.4. Mean Relative Importance Weights for Indicated Outcomes for US (n = 197) and UK (n = 197) Respondents



EPS = extrapyramidal symptoms; UK = United Kingdom; US = United States.

Notes: The vertical bars surrounding each mean importance estimate denote the 95% confidence interval about the point estimate.

The mean relative importance score for each attribute is estimated as an improvement from the worst level to the best level. For example, for improvement in positive symptoms, it is an improvement from no improvement to very much improved.

Schizophrenia Treatment Preference Survey

[Consent Screen 1]

This research study is being conducted by Research Triangle Institute (RTI) on behalf of a pharmaceutical company. RTI is a not-for-profit research organization in Research Triangle Park, North Carolina, United States. RTI has contracted with Kantar Health (KH) to collect data.

You are one of about 200 psychiatrists in the United States and 200 psychiatrists in the United Kingdom who are being asked to take a survey to help us understand how physicians make treatment decisions for patients with schizophrenia.

KH will protect your responses under its Privacy Policy. RTI and the pharmaceutical company will only receive your survey responses, no personal identifiers.

The survey will take around 20 minutes to complete.

Your responses will be used by us and the sponsoring pharmaceutical company for market research only. All information included is for research only and not to promote the product discussed.

Your responses will be collated with other respondents and presented to the sponsor in aggregated or de-identified form. Your responses will be confidential and will not be used for any other purposes or disclosed to any third party without your approval.

Please confirm that you have read and understood this information.

YES [\[CONTINUE\]](#)

NO [\[INELIGIBLE, END SURVEY\]](#)

[Consent Screen 2]

You are about to enter a market research interview. We are now being asked to pass on to our client details of adverse events and/or product complaints that are raised during the course of market research interviews. Although this is an on-line market research interview and how you respond will, of course, be treated in confidence, should you raise an adverse event and/or product complaint, we will need to report this, even if it has already been reported by you directly to the company or the regulatory authorities using the MHRA's 'Yellow Card' system. In such a situation you will be contacted to ask whether or not you are willing to waive the confidentiality given to you under the market research codes of conduct specifically in relation to that adverse event and/or product complaint. Everything else you contribute during the course of the interview will continue to remain confidential.

Are you happy to proceed with the interview on this basis?

- I would like to proceed and protect my anonymity. [\[CONTINUE\]](#)
- I would like to proceed and give permission for my contact details to be passed on to the Drug Safety department of the company if an adverse event is mentioned by me during the survey. [\[CONTINUE\]](#)
- I don't want to proceed and end the interview here. [\[INELIGIBLE, END SURVEY\]](#)

If you have any problems or concerns about this survey, please e-mail Ateesha Mohamed at amohamed@rti.org. Messages will be answered within 24 hours of their receipt.

First, please answer some questions about your situation to confirm that you are eligible to participate in the survey.

[Screening Questions]

S1. Are you currently a practicing, board certified (or eligible) psychiatrist involved in treating patients with schizophrenia?

- YES [\[CONTINUE\]](#)
- NO [\[INELIGIBLE, END SURVEY\]](#)

S2. Are you currently treating 5 or more patients with schizophrenia per month?

- YES [\[CONTINUE\]](#)
- NO [\[INELIGIBLE, END SURVEY\]](#)

S3. Have you participated in a market research study within the past three months?

- YES [\[INELIGIBLE, END SURVEY\]](#)
- NO [\[CONTINUE\]](#)

Eligible if answer “yes” to S1, S2, and S3.

[If ineligible to participate]

Thank you for your consideration, but you are not eligible to participate in this survey.

[Consent Screen 3]

If you have read the previous screens and agree to participate, please click the **Yes** button, if not, click the **No** button.

- Yes, I agree to participate. [\[Continue with next section\]](#)
- No, I do not agree to participate. [\[Go to next question\]](#)

Are you sure you don't want to participate? Your opinions are important to us. Please select the **Yes** button to continue this survey; if not, select the **No** button to exit.

- Yes, I agree to participate. [\[Continue with next section\]](#)
- No, I do not agree to participate [\[End survey\]](#).

[If they do not agree to participate]

Thank you for your consideration. You have exited the survey.

Background Questions

B1. What is your gender?

Male

Female

B2. How many years have you been in practice since completing your medical training (i.e. after residency and/or fellowship)?

Less than 1 year

1—3 years

4—6 years

7—9 years

10—15 years

16—20 years

21—25 years

More than 25 years

B3. On average, how many patients with schizophrenia do you treat each month?

Less than 5 patients

5—20 patients

21—50 patients

51—100 patients

More than 100 patients

B4. Which of the following describes your practice? (*Please check all that apply*)

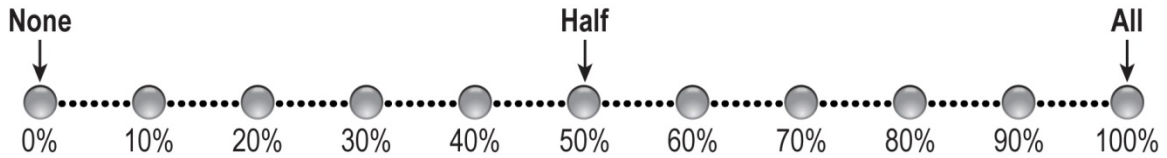
- Office-based private practice
- Academic hospital-based practice
- In-patient setting in a psychiatric hospital
- In-patient setting in a general hospital
- Out-patient community mental health center or equivalent
- Emergency room
- Other (*please specify*) _____

B5. On average, how many hours do you work per week in direct patient care?

- 5 hours or less
- 6—10 hours
- 11—20 hours
- 21—30 hours
- 31—40 hours
- More than 40 hours

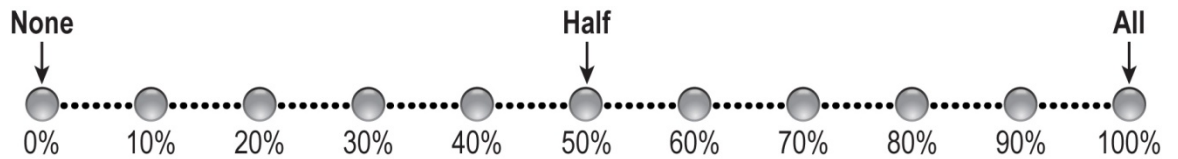
On the scales below indicate the point describing the following:

B6. What is the percent of patients with schizophrenia in your practice to whom you prescribe antipsychotic medications?

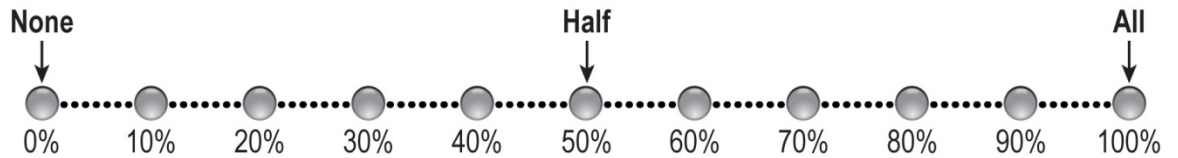


B7-8. Considering patients with schizophrenia in your practice whom you prescribe antipsychotic medications (referenced in the prior question)

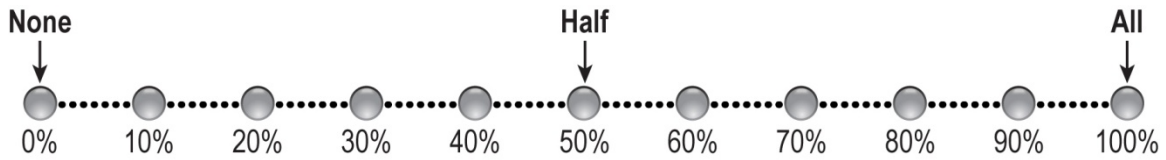
B7. What is the percent who are treated with **oral** antipsychotic medications?



B8. What is the percent who are treated with **long acting injectable** antipsychotic medications?



B9. Considering typical patients with schizophrenia in your practice whom you treat with **oral** antipsychotic medications, what is the percent of doses you believe they actually took as prescribed in the past month?



B10. Are you familiar with the scoring procedure for the Positive and Negative Syndrome Scale (PANSS) instrument for rating of symptoms of schizophrenia?

- Very familiar with PANSS scoring procedure
- Familiar with PANSS instrument and can interpret the scores but not assess them for a patient
- Aware of the PANSS instrument but not familiar with the scoring procedure
- Not familiar with the PANSS instrument

B11. Are you familiar with the scoring procedure for the Clinical Global Impression (CGI) instrument for rating of symptoms of schizophrenia?

- Very familiar with CGI scoring procedure
- Familiar with CGI instrument and can interpret the scores but not assess them for a patient
- Aware of the CGI instrument but not familiar with the scoring procedure
- Not familiar with the CGI instrument

Schizophrenia patient profile

In this survey, we will ask you to think about medication choices for the following hypothetical patient.

A 40-year-old patient with a 20-year history of treated schizophrenia has just been released to your care from a hospital. He was previously stable on his antipsychotic medication but was brought to the hospital when he had an acute exacerbation in symptoms.

1. How typical is this hypothetical patient of NEW patients whom you treat?

- This profile describes **most** of my patients.
- This profile describes **some** of my patients.
- This profile describes **few** of my patients.
- This profile describes **none** of my patients.

Effects of Antipsychotic Medications

In this section, we will describe the effects of possible antipsychotic medications on various symptoms, as well as possible side effects when taking the medication.

The particular symptoms we would like you to consider include:

- Positive symptoms: Primarily delusions, hallucinations, conceptual disorganization and/or suspiciousness/persecution
- Negative symptoms: Blunted affect, emotional withdrawal, passive/apathetic social withdrawal, lack of spontaneity and/or flow of conversation
- Social functioning: Able to engage in socially useful activities, including work or study, and in personal and social relationships

The particular side effects we would like you to consider include:

- Weight gain (% increase from baseline) within the first year of starting treatment
- Extrapyramidal symptoms (EPS) — Parkinsonism (Parkinsonian tremor, rigidity, bradykinesia, abnormalities of gait and posture), dyskinesia, dystonia, and/or akathisia within the first year of starting treatment
- Hyperprolactinemia—greater than or equal to 2 times the upper limit of normal prolactin levels leading to clinical sequelae within the first year of starting treatment
- Hyperglycemia—fasting glucose \geq 100 mg/dL or 5.5 mmol/L within the first year of starting treatment in someone with normal baseline levels (i.e. <100 mg/dL) OR fasting glucose $>$ 125 mg/dL in a person with a baseline fasting glucose between 100-125 mg/dL

Improvement in positive symptoms

For the examples in the table below, consider the patient initially presenting with the positive symptom of severe hallucinations – being almost totally preoccupied with his hallucinations, which virtually dominate his thinking and behavior.

Improvement in Positive Symptoms	Description
No improvement	<10% reduction in positive symptoms compared to the patient's initial condition.
Minimally improved	25% reduction in positive symptoms compared to the patient's initial condition. <u>Example:</u> Although the patient is no longer totally preoccupied with his hallucinations, he continues to have hallucinations frequently or almost continuously. Patient responds to the hallucinations and may treat them as real perceptions.
Much improved	50% reduction in positive symptoms compared to the patient's initial condition. <u>Example:</u> Patient has hallucinations that occur frequently but not continuously, and the patient's thinking and behavior are affected only to a minor extent.
Very much improved	80% reduction in positive symptoms compared to the patient's initial condition. <u>Example:</u> Patient has minimally observable positive symptoms.

Improvement in negative symptoms

For the examples in the table below, consider the patient initially presenting with the negative symptom of severe emotional withdrawal – patient is almost totally withdrawn, uncommunicative, and neglecting personal needs as a result of lack of interest and emotional commitment.

Improvement in Negative Symptoms	Description
No improvement	<10% reduction in negative symptoms compared to the patient's initial condition.
Minimally improved	25% reduction in negative symptoms compared to the patient's initial condition. <u>Example:</u> Patient is no longer almost totally withdrawn, uncommunicative, and neglecting personal needs as a result of lack of interest and emotional commitment, but the patient continues to be clearly detached emotionally from persons and events and resists all efforts at engagement.
Much improved	50% reduction in negative symptoms compared to the patient's initial condition. <u>Example:</u> Patient is generally distanced emotionally from the milieu and its challenges but, with encouragement, can be engaged.
Very much improved	80% reduction in negative symptoms compared to the patient's initial condition. <u>Example:</u> Patient has minimally observable negative symptoms.

Thinking about schizophrenia treatments

A 40-year-old patient with a 20-year history of treated schizophrenia has just been released to your care from a hospital. He was previously stable on his antipsychotic medication but was brought to the hospital when he had an acute exacerbation in symptoms. In this exacerbation, he experienced both severe positive symptoms (e.g., hallucinations, delusions) and severe negative symptoms (e.g., emotional withdrawal, blunted affect). He no longer appears to respond to his current medication and you need to prescribe a new treatment. The patient has no other comorbidities.

The descriptions below show the outcomes the patient will experience **after one year of treatment**. In selecting the better set of outcomes, **please do not consider availability or cost** of the treatment to your practice or institution or to your patients.

Symptoms	Outcomes A	Outcomes B
Improvement in positive symptoms	Much improved (50% reduction)	Minimally improved (25% reduction)
Improvement in negative symptoms	Minimally improved (25% reduction)	Much improved (50% reduction)
Which set of outcomes is <u>better</u> for the patient?	<input type="checkbox"/>	<input type="checkbox"/>

Social functioning

Social functioning includes being able to engage in socially useful activities, including work or study, and in personal and social relationships.

Social functioning	Description
Mild problems	The impairments are known only to someone who is very familiar with the patient (e.g. spouse, relative, etc.).
Moderate problems	Marked difficulties that are clearly noticeable. The patient is still able to perform some functions without professional or social help but does so inadequately. If helped by someone, is able to reach a higher level of functioning.
Severe problems	The patient has severe difficulties in social functioning and is unable to perform socially useful activities, even if helped by someone.

Schizophrenia treatment choices

A 40-year-old patient with a 20-year history of treated schizophrenia has just been released to your care from a hospital. He was previously stable on his antipsychotic medication but was brought to the hospital when he had an acute exacerbation in symptoms. In this exacerbation, he experienced both severe positive symptoms (e.g., hallucinations, delusions) and severe negative symptoms (e.g., emotional withdrawal, blunted affect). He no longer appears to respond to his current medication and you need to prescribe a new treatment. The patient has no other comorbidities.

The descriptions you are going to see next show the outcomes the patient will experience **after one year of treatment**. Please assume all other side effects are the same for each set of outcomes. In selecting the better set of outcomes, **please do not consider availability or cost** of the treatment to your practice or institution or to your patients.

Some of the case scenarios that are presented may seem extremely unlikely, NEVERTHELESS, given your own process for making clinical judgments, how would you respond should you be presented with such a real life case. Assuming these were the actual outcomes observed, we will ask you which set of outcomes, in your professional opinion, is the better result for the patient.

Even if neither set of outcomes is optimal, please indicate which of the two sets of outcomes in your professional opinion would be the **better** result for the patient.

Notes to programmer: Include 8 choice questions based on the experimental design.

Choice Question 1

		Outcomes A	Outcomes B
Symptoms in a Typical Week	Improvement in positive symptoms	Very much improved (80% reduction)	No improvement (<10% reduction)
	Improvement in negative symptoms	No improvement (<10% reduction)	Very much improved (80% reduction)
	Social functioning	Mild problems	Moderate problems
Side Effects within the First Year	Weight gain	15%	7%
	EPS	Yes	Yes
	Hyperprolactinemia	No	Yes
	Hyperglycemia	Yes	No
Which set of outcomes is <u>better</u> for the patient?		<input type="checkbox"/>	<input type="checkbox"/>

Choice Question 2

		Outcomes A	Outcomes B
Symptoms in a Typical Week	Improvement in positive symptoms	Much improved (50% reduction)	Minimally improved (25% reduction)
	Improvement in negative symptoms	Very much improved (80% reduction)	No improvement (<10% reduction)
	Social functioning	Severe problems	No problems
Side Effects within the First Year	Weight gain	15%	15%
	EPS	No	Yes
	Hyperprolactinemia	Yes	Yes
	Hyperglycemia	Yes	No
Which set of outcomes is <u>better</u> for the patient?		<input type="checkbox"/>	<input type="checkbox"/>

Choice Question 3

		Outcomes A	Outcomes B
Symptoms in a Typical Week	Improvement in positive symptoms	No improvement (<10% reduction)	Very much improved (80% reduction)
	Improvement in negative symptoms	Minimally improved (25% reduction)	Minimally improved (25% reduction)
	Social functioning	No problems	Severe problems
Side Effects within the First Year	Weight gain	7%	None
	EPS	No	No
	Hyperprolactinemia	No	Yes
	Hyperglycemia	Yes	No
Which set of outcomes is <u>better</u> for the patient?		<input type="checkbox"/>	<input type="checkbox"/>

Choice Question 4

		Outcomes A	Outcomes B
Symptoms in a Typical Week	Improvement in positive symptoms	Minimally improved (25% reduction)	Minimally improved (25% reduction)
	Improvement in negative symptoms	Very much improved (80% reduction)	Much improved (50% reduction)
	Social functioning	Severe problems	No problems
Side Effects within the First Year	Weight gain	15%	None
	EPS	Yes	Yes
	Hyperprolactinemia	Yes	No
	Hyperglycemia	No	No
Which set of outcomes is <u>better</u> for the patient?		<input type="checkbox"/>	<input type="checkbox"/>

Choice Question 5

		Outcomes A	Outcomes B
Symptoms in a Typical Week	Improvement in positive symptoms	No improvement (<10% reduction)	Minimally improved (25% reduction)
	Improvement in negative symptoms	Much improved (50% reduction)	Minimally improved (25% reduction)
	Social functioning	Mild problems	Mild problems
Side Effects within the First Year	Weight gain	15%	None
	EPS	Yes	No
	Hyperprolactinemia	No	No
	Hyperglycemia	Yes	Yes
Which set of outcomes is <u>better</u> for the patient?		<input type="checkbox"/>	<input type="checkbox"/>

Choice Question 6

		Outcomes A	Outcomes B
Symptoms in a Typical Week	Improvement in positive symptoms	Much improved (50% reduction)	Much improved (50% reduction)
	Improvement in negative symptoms	Very much improved (80% reduction)	No improvement (<10% reduction)
	Social functioning	Moderate problems	Mild problems
Side Effects within the First Year	Weight gain	7%	15%
	EPS	Yes	No
	Hyperprolactinemia	Yes	No
	Hyperglycemia	No	Yes
Which set of outcomes is <u>better</u> for the patient?		<input type="checkbox"/>	<input type="checkbox"/>

Choice Question 7

		Outcomes A	Outcomes B
Symptoms in a Typical Week	Improvement in positive symptoms	Very much improved (80% reduction)	Much improved (50% reduction)
	Improvement in negative symptoms	Much improved (50% reduction)	Much improved (50% reduction)
	Social functioning	Mild problems	No problems
Side Effects within the First Year	Weight gain	None	15%
	EPS	Yes	Yes
	Hyperprolactinemia	Yes	No
	Hyperglycemia	No	No
Which set of outcomes is <u>better</u> for the patient?		<input type="checkbox"/>	<input type="checkbox"/>

Choice Question 8

		Outcomes A	Outcomes B
Symptoms in a Typical Week	Improvement in positive symptoms	Very much improved (80% reduction)	No improvement (<10% reduction)
	Improvement in negative symptoms	Minimally improved (25% reduction)	Much improved (50% reduction)
	Social functioning	Moderate problems	Mild problems
Side Effects within the First Year	Weight gain	15%	None
	EPS	No	No
	Hyperprolactinemia	No	Yes
	Hyperglycemia	Yes	No
Which set of outcomes is <u>better</u> for the patient?		<input type="checkbox"/>	<input type="checkbox"/>

Mode of administration

We now will ask you to consider the following 3 hypothetical ways that a patient could take antipsychotic medications:

- Oral once a day
- Injection in the muscle once a month (administered by a health care professional in a clinic or at home by a visiting nurse)
- Injection in the muscle once every 3 months (administered by a health care professional in a clinic or at home)

The medications you are going to see next show the improvements in symptoms for the average patient who participated in clinical trials with patients taking their medication as prescribed in the trial. Please assume all other outcomes are the same for each medication.

We will ask you which medication, in your professional opinion, is the better result for the hypothetical patient described earlier.

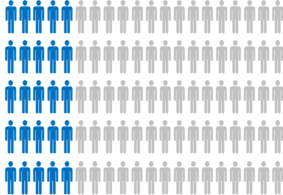

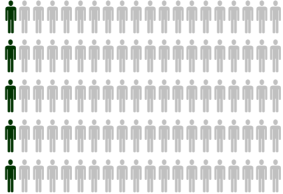
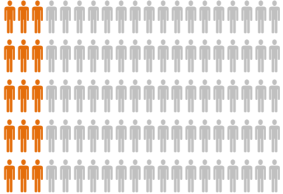
Notes to programmer: Include 4 mini-choice questions based on the experimental design.

Always include a “switching” question after the mini-choice question:

[If select option with “mode on Medicine A/B”] What percent of patients with at least minimally improved ($\geq 25\%$ reduction) in positive symptoms in a typical week, compared to initial presentation would make you switch to **[mode on Medicine A/B]**?

- 25%
- 30%
- 35%
- 40%
- 45%
- 50%
- 55%
- 60%
- 65%
- 70%
- 75%
- 80%
- 85%
- 90%
- 95%
- 100%

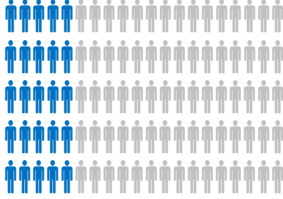



Question 1

	Medication A (Trial data)	Medication B (Trial data)
Mode of administration	Pill once a day	Injection once a month
Percent of patients with at least minimally improved ($\geq 25\%$ reduction) in positive symptoms in a typical week, compared to initial presentation	25 out of 100 (25%) 	50 out of 100 (50%) 
Percent of patients with EPS within the first year	5 out of 100 (5%) 	15 out of 100 (15%) 
Which treatment is <u>better</u> for the patient?	<input type="checkbox"/>	<input type="checkbox"/>

New information: The patient has missed or skipped 20% of his doses of oral medication in the past.

Which treatment is <u>better</u> for the patient?	<input type="checkbox"/>	<input type="checkbox"/>
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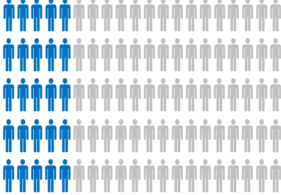
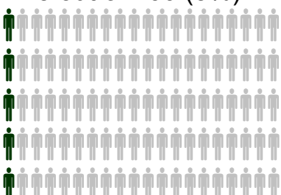
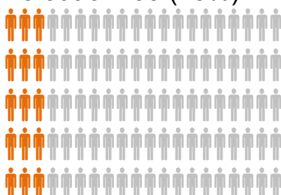
Question 2

	Medication A (Trial data)	Medication B (Trial data)
Mode of administration	Injection once every 3 months	Injection once a month
Percent of patients with at least minimally improved ($\geq 25\%$ reduction) in positive symptoms in a typical week, compared to initial presentation	25 out of 100 (25%) 	50 out of 100 (50%) 
Percent of patients with EPS within the first year	15 out of 100 (15%) 	5 out of 100 (5%) 
Which treatment is <u>better</u> for the patient?	<input type="checkbox"/>	<input type="checkbox"/>

New information: The patient has missed or skipped 50% of his doses of oral medication in the past.

Which treatment is <u>better</u> for the patient?	<input type="checkbox"/>	<input type="checkbox"/>
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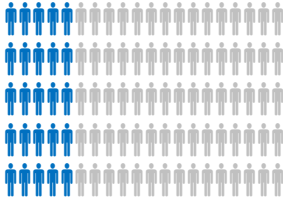

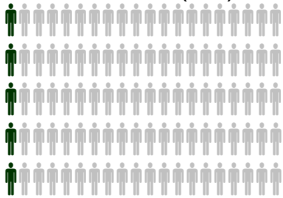
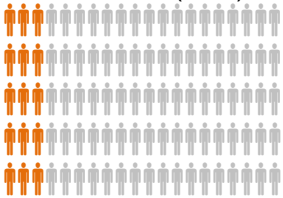
Question 3

	Medication A (Trial data)	Medication B (Trial data)
Mode of administration	Injection once every 3 months	Pill once a day
Percent of patients with at least minimally improved ($\geq 25\%$ reduction) in positive symptoms in a typical week, compared to initial presentation	50 out of 100 (50%) 	25 out of 100 (25%) 
Percent of patients with EPS within the first year	5 out of 100 (5%) 	15 out of 100 (15%) 
Which treatment is <u>better</u> for the patient?	<input type="checkbox"/>	<input type="checkbox"/>

New information: The patient has missed or skipped 20% of his doses of oral medication in the past.

Which treatment is <u>better</u> for the patient?	<input type="checkbox"/>	<input type="checkbox"/>
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Question 4

	Medication A (Trial data)	Medication B (Trial data)
Mode of administration	Pill once a day	Injection once a month
Percent of patients with at least minimally improved ($\geq 25\%$ reduction) in positive symptoms in a typical week, compared to initial presentation	25 out of 100 (25%) 	50 out of 100 (50%) 
Percent of patients with EPS within the first year	5 out of 100 (5%) 	15 out of 100 (15%) 
Which treatment is <u>better</u> for the patient?	<input type="checkbox"/>	<input type="checkbox"/>

New information: The patient has missed or skipped 20% of his doses of oral medication in the past.

Which treatment is <u>better</u> for the patient?	<input type="checkbox"/>	<input type="checkbox"/>
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