How Patient Preference Information is Used by the Center for Devices and Radiological Health

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Delivered by Sara Eggers
in Dr. Gebben's absence

OUTLINE

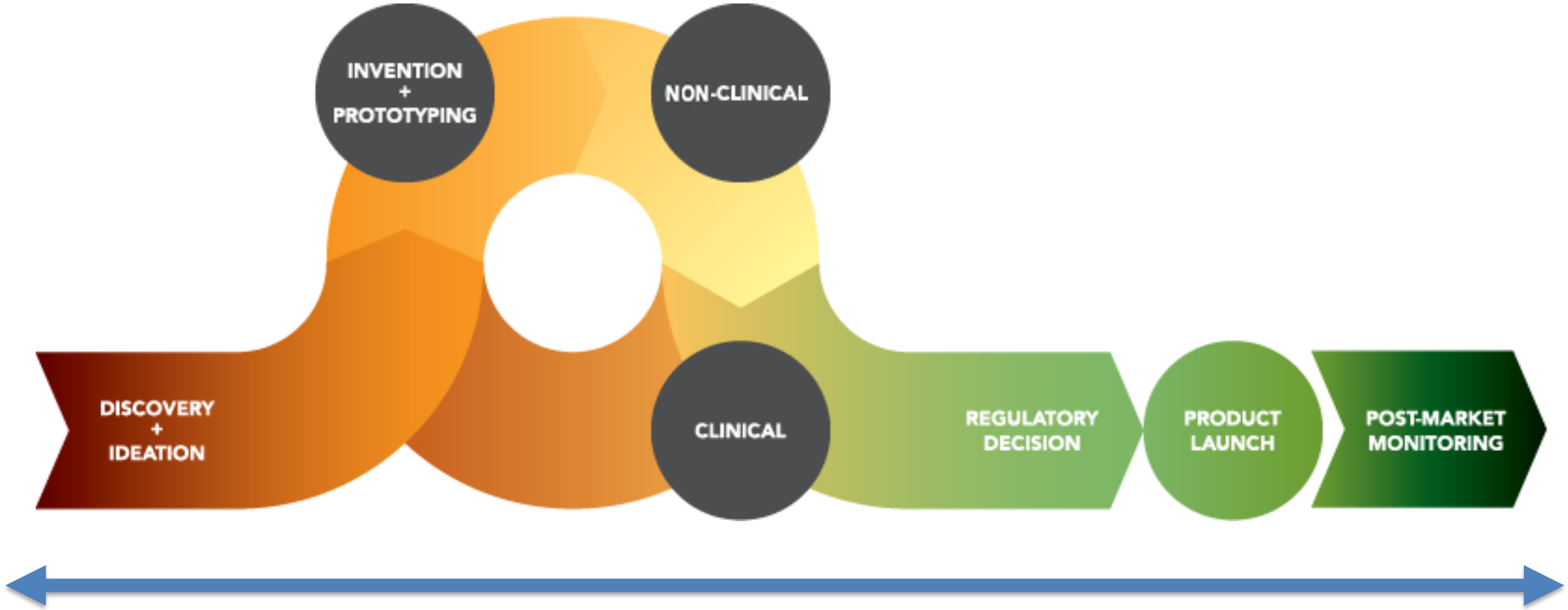
- PPI background
- Case example of PPI across the total product life cycle
- PPI in the regulatory context
- Experience & challenges with PPI study samples

This talk is presented in the context of medical device review, in line with the specific statutes the govern medical device regulation. With that said, the principles and practices in this talk broadly overlap with FDA's drugs and biologics regulatory review.

PATIENTS ARE AT THE HEART OF ALL WE DO

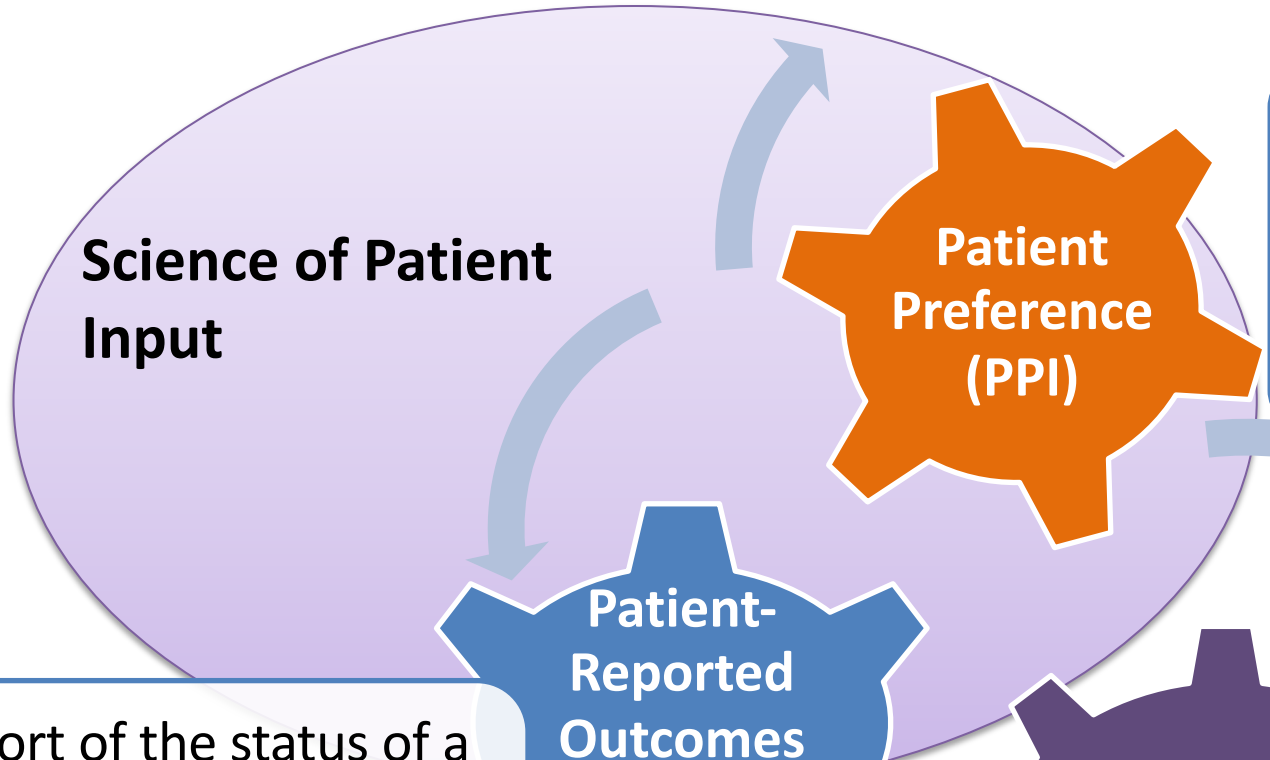
Inspired by Patients, Driven by Science

PATIENT EXPERIENCE DATA ACROSS THE TOTAL PRODUCT LIFECYCLE



This in the context of medical devices, though principles broadly overlap with drugs and biologic regulatory review.

PATIENT INPUT IN REGULATORY EFFORTS



- qualitative or quantitative assessments of the relative desirability or acceptability of attributes that differ among alternative diagnostic or therapeutic strategies

- any report of the status of a patient's health condition that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else

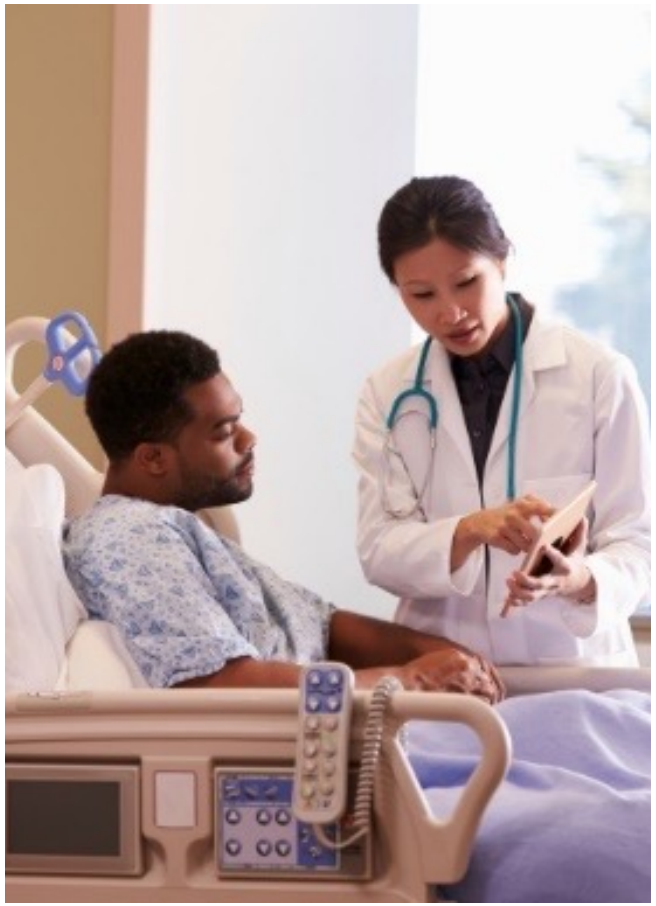
- intentional, meaningful interactions with patients that provide opportunities for mutual learning and effective collaborations across the total product life cycle

WHAT IS PATIENT PREFERENCE INFORMATION (PPI)?

- PPI is defined by CDRH as:
  - Qualitative or quantitative assessments of the relative desirability or acceptability to patients of specified alternatives or choices among outcomes or other attributes that differ among alternative health interventions
- Relevant preferences of care-partners (e.g., parents) and health care professionals may also be considered as appropriate
  - While it is always preferable to hear the preferences directly from patients, there are conditions where patients are not able to express or provide their preferences in a structured way
  - In those select cases, the preferences of care partners or caregivers may be solicited
  - May apply to patients who are non-verbal or cognitively unable to perform the preference exercises, such as young children or patients with advanced dementia

HOW IS PRO DIFFERENT FROM PPI?

- ***Patient-reported outcomes (PRO) and PPI are not the same.***
- **PRO** is any report of the status of a patient's health condition that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else.
  - PRO measures a patient's perceptions of how they feel and function and can be administered before, during, and after treatment
  - Example: grading pain as 6 out of 10 on a numerical rating scale)
  - Comparisons within patients and between patient groups
- **PPI** measures a patient's relative value of a therapy's benefit-risk profile (or attributes) compared to the other given options.
  - Example: minimally invasive heart valve replacement vs standard heart valve replacement in elderly patients



PPI AND STATED PREFERENCE

- PPI is generated using survey-based techniques that establish valuations of attributes that define a medical product from the patient perspective
  - Techniques/tools from a domain in economics called Stated Preference (contingent valuation)

- Stated preferences have been used since the 1960s in various contexts
  - Marketing, transportation economics, engineering
  - Grounded in economics - microeconomic theory
  - Increasingly used in health care/regulatory settings in the last decade

- Axioms that apply in preference research:
  - People can make choices about what they prefer
  - People can make decisions under constraints
  - People can be educated about relevant options

TYPICAL OUTCOMES OF A PPI STUDY

- PPI data can provide valuable information in quantitative format about:
  - Importance scores/rankings for treatment outcomes
    - What treatment outcomes/attributes (benefits, risks, convenience factors etc.) are most important to affected patients
  - Tradeoffs
    - What benefit-risk (B/R) tradeoffs are acceptable from the patient perspective
    - Maximum acceptable risk of a side effect
  - Proportion of patients that would accept a treatment
  - Subgroup preferences
    - Are there clinically-relevant subgroups of patients that would accept a particular benefit-risk profile and/or choose one treatment option over other alternatives?
    - How do treatment priorities for men and women compare?

CDRH Guidance Documents

- Consideration of Uncertainty in Making Benefit-Risk Determinations in Medical Device Premarket Approvals, De Novo Classifications, and Humanitarian Device Exemptions

- Benefit-Risk Factors to Consider When Determining Substantial Equivalence in Premarket Notifications (510(k)) with Different Technological Characteristics

- Patient Preference Information - Voluntary Submission, Review in Premarket Approval Applications, Humanitarian Device Exemption Applications, and *De Novo* Requests, and Inclusion in Decision Summaries and Device Labeling

- Factors to Consider When Making Benefit-Risk Determinations in Medical Device Premarket Approval and *De Novo* Classifications

- Factors to Consider When Making Benefit-Risk Determinations for Medical Device Investigational Device Exemptions

- Factors to Consider Regarding Benefit-Risk in Medical Device Product Availability, Compliance, and Enforcement Decisions

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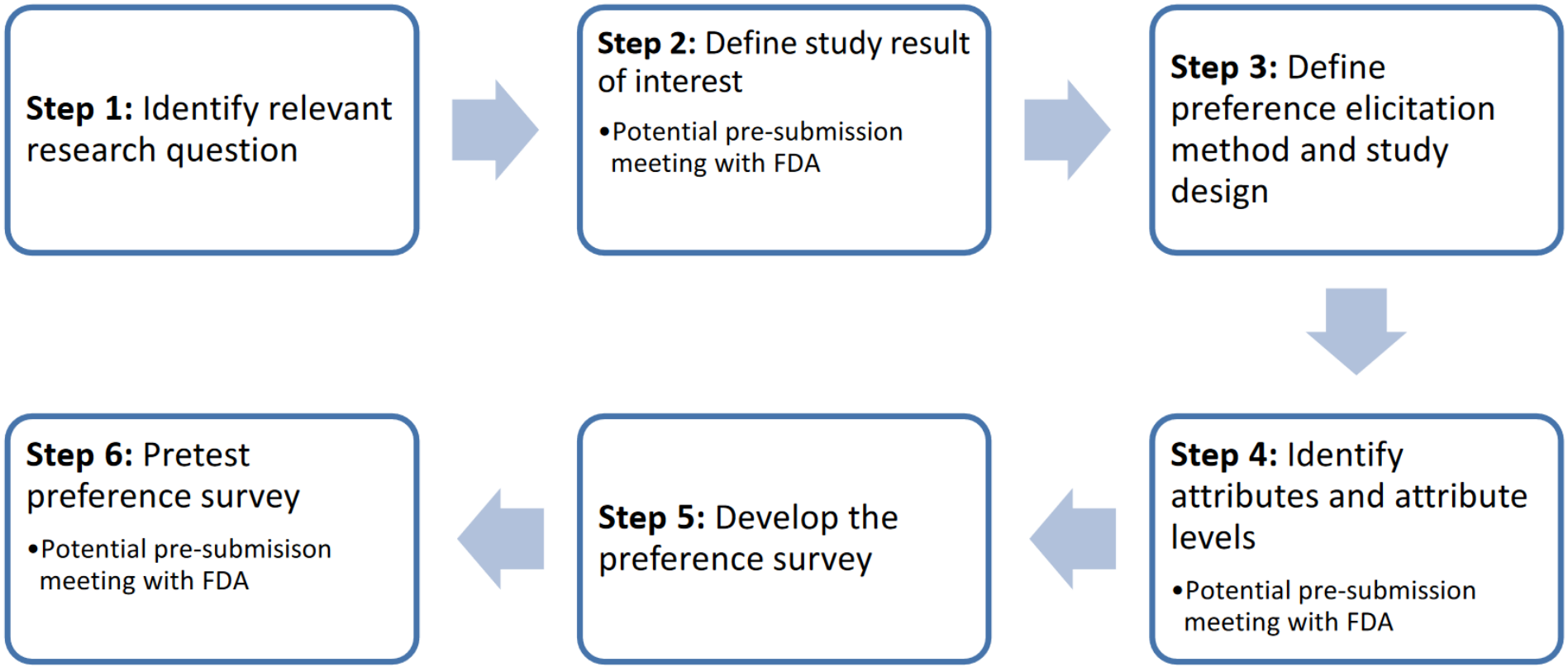
PPI Study Design Process



POTENTIAL USES OF PPI ACROSS THE TOTAL PRODUCT LIFE CYCLE (TPLC)

Device Development	Clinical Trial Design	Pre-Market Benefit-Risk Assessment	Post-Market Decisions
1. Identify unmet medical need 2. Understand what matters most to patients about their disease or treatment 3. Inform target product profiles	1. Inform endpoint selection 2. Inform performance goal 3. Inform effect size/meaningful changes 4. Weighting of composite endpoints	1. Analysis of condition 2. Current treatment options 3. Patient perspective on benefit-risk tradeoffs 4. Population subgroup considerations	1. Inform interpretation of new data affecting benefit-risk assessment 2. Inform studies of new/ expanded use populations 3. Communicate benefit-risk information to patients

CASE STUDY DEMONSTRATING APPLICATION OF PPI IN THE TPLC

Post-market Decision Making (label expansion)

This in the context of medical devices, though principles broadly overlap with drugs and biologic regulatory review.

CASE: PPI STUDY ON HOME HEMODIALYSIS[1]

Background

- Home Hemodialysis Device (HHD) approved for patients with end stage kidney disease for use in-clinic and at home with a care partner
- HHD has rare but serious adverse events so caregiver or trained partner must be present
- Risks include:
  - Dialysis-induced hypotension (approx. 1 in 20 treatments)
  - Needle dislodgment, leading to blood loss, loss of consciousness, or death (approx. 1 in 450 patients per year)
- A device (Solo HHD) was seeking a label expansion to remove requirement for presence of caregiver for HHD

1 https://www.accessdata.fda.gov/cdrh_docs/pdf17/k171331.pdf

PATIENT PREFERENCE STUDY DESIGN

- **Problem statement**: When considering a labeling expansion for a cleared device, is the reduced burden on patients worth the probable risks?

- A patient preference study can provide information about the **maximum acceptable risk** from patients' perspectives.

PPI STUDY DESIGN

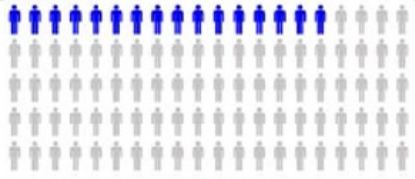
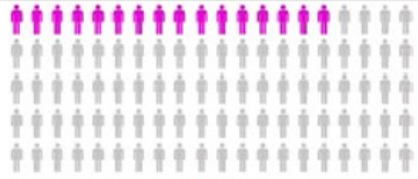
Primary Endpoints

1. Identify risk tolerance threshold of death for which experienced HHD/in-center self-care patients remain willing to choose to perform Solo HHD
2. Identify risk tolerance threshold of needle dislodgement for which experienced HHD/in-center self-care patients remain willing to choose to perform Solo HHD
3. Determine what percentage of the respondent group of current HHD/in-center self-care patients would choose to perform Solo HHD

PPI (TT) STUDY DESIGN

- Threshold technique (TT) is used to estimate how much patients are willing to tolerate higher risks of death and needle dislodgment of performing HD at home to avoid the more burdensome HD sessions in center or at home with care partners

- The B/R profile of solo HHD was presented side by side with a fixed profile of in-center HD to respondents who were asked which treatment option is best for people like you

Feature	In-Center Hemodialysis (Traditional Hemodialysis)	Solo Home Hemodialysis (Home without a Partner)
Number of treatments per week	3	From 3 to 7
Treatment schedule and flexibility	Scheduled by the clinic and only during clinic hours	You set your treatment schedule and you can treat any time of day
Diet and fluid restrictions	More	Less
Ability to travel without arranging dialysis treatments at your destination	No	Yes
Who inserts your needles for dialysis?	A dialysis center staff member	You
Who responds to problems that come up during treatment	A dialysis center staff member	You
On average, how long it takes to get back to normal activities after each treatment	8 hours	1 hour
Typical need for hypertension and phosphate medications	More	Less
Yearly chance of dying that is linked to the therapy option	 16% (16 out of 100 patients per year)	 16% (16 out of 100 patients per year)
Which dialysis option would you choose?	☐ In-Center Hemodialysis (Traditional Hemodialysis)	☐ Solo Home Hemodialysis (Home without a Partner)

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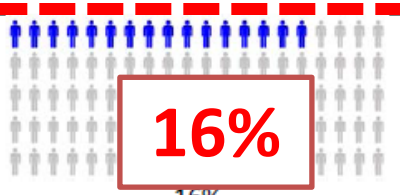
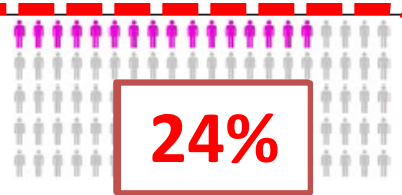
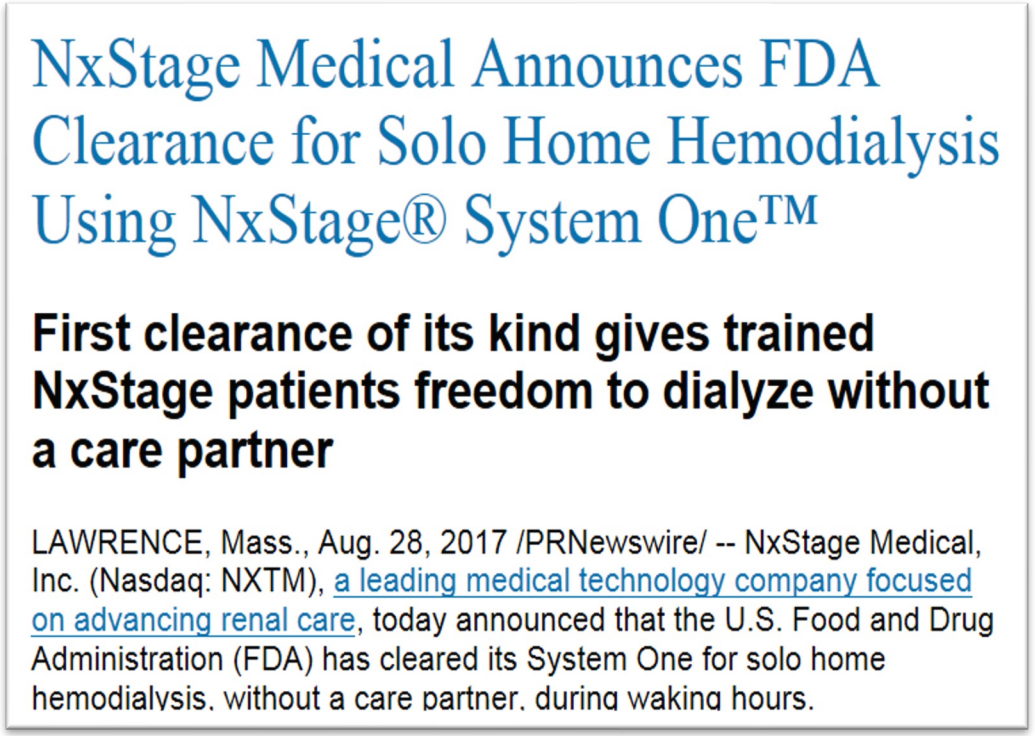
Yearly chance of dying that is linked to the therapy option	 16% 16% (16 out of 100 patients per year)	 24% 16% (16 out of 100 patients per year)
Which dialysis option would you choose?	In-Center Hemodialysis (Traditional Hemodialysis)	Solo Home Hemodialysis (Home without a Partner)

RESULTS & REGULATORY IMPLICATIONS

- Survey results provided demonstrable evidence of risk thresholds that patients are willing to tolerate
- As a result of PPI study, label expansion was approved as a therapy option



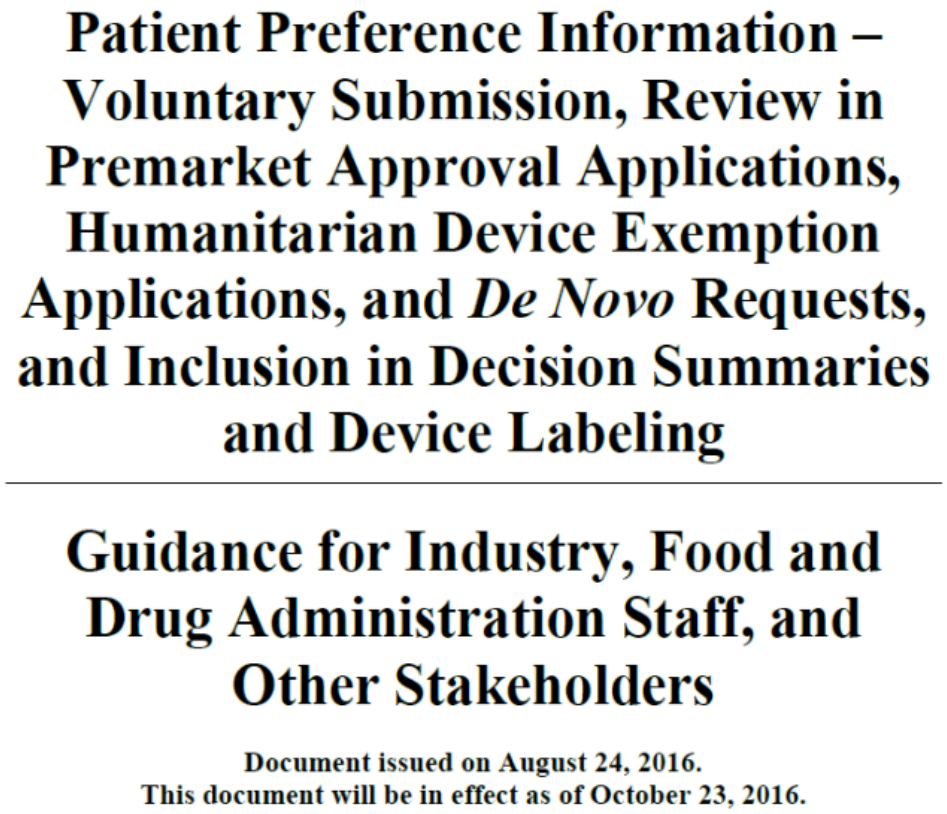
NxStage Medical Announces FDA Clearance for Solo Home Hemodialysis Using NxStage® System One™

First clearance of its kind gives trained NxStage patients freedom to dialyze without a care partner

LAWRENCE, Mass., Aug. 28, 2017 /PRNewswire/ -- NxStage Medical, Inc. (Nasdaq: NXTM), a leading medical technology company focused on advancing renal care, today announced that the U.S. Food and Drug Administration (FDA) has cleared its System One for solo home hemodialysis, without a care partner, during waking hours.

PPI AS VALID SCIENTIFIC EVIDENCE

- PPI does not change any review standards for safety or effectiveness
- Provides recommendations relating to the voluntary collection of PPI that may be submitted for consideration as valid scientific evidence as part of FDA's benefit-risk
- FDA may consider submitted PPI along with other evidence from clinical and nonclinical testing when making benefit-risk determinations



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Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders

Document issued on August 24, 2016.
This document will be in effect as of October 23, 2016.

PPI STUDY SAMPLES AND THE REGULATORY CONTEXT

- In summary PPI samples need to:
  - Identify and survey the right participants to be compatible with the regulatory context
  - Be representative (including under-represented populations) of the indication for use
  - Provide opportunities to capture heterogeneous patient preferences

FINAL CONSIDERATIONS

- PPI provides a systematic and scientific approach to integrating the patient voice into regulatory decisional frameworks
- Voluntary submission of PPI may be informative during benefit-risk determination
- PPI may also be informative earlier in device development (e.g., to inform clinical study parameters such as endpoint selection, performance goals, and effect size)
- We encourage early interactions with FDA review staff if planning to design a PPI study or to submit PPI
- Contact: CDRH-PPI@fda.hhs.gov

THANK YOU