

# **Analyze That: Ongoing Policy Efforts for Deceased Donor Intervention**



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**ASTS WINTER SYMPOSIUM**  
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**NO CONFLICTS TO DISCLOSE**



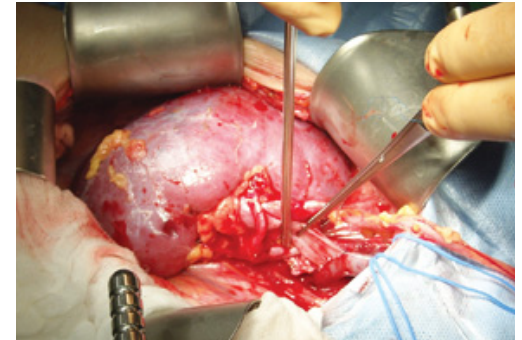
**NO DISCUSSION OF  
OFF-LABEL USE OF  
ANY MEDICATIONS**

# The Problem



- Demographics of the U.S. population project
  - Increased demand for transplantable organs
  - Decreased quality and low to modest increase of organs suitable for transplantation

# The Rationale



- Brain death is physiologic, cellular, and molecular catastrophe that compromises organ viability and function
- The injury sustained in the donor is compounded by cold storage followed by ischemia / reperfusion injury in the recipient
- Organs procured from older, less healthy (diabetes, hypertension, obese) donors are especially vulnerable.

# Conceptualizing Research to Improve Organ Quality



**Brain death**

**Reperfusion**

**Donor**

**Organ**

**Recipient**

Mitigate injury  
?Repair injury

Mitigate injury  
?Repair injury

Accelerate recovery  
from injury

## Examples of randomized trials in kidney transplantation

- Dopamine
- Hypothermia
- Machine Perfusion
- Furosemide
- IGF-1
- $\alpha$ -ICAM-1
- Erythropoietin
- Pentoxifylline
- YPSL (rPSGL-Ig)
- Thymoglobulin

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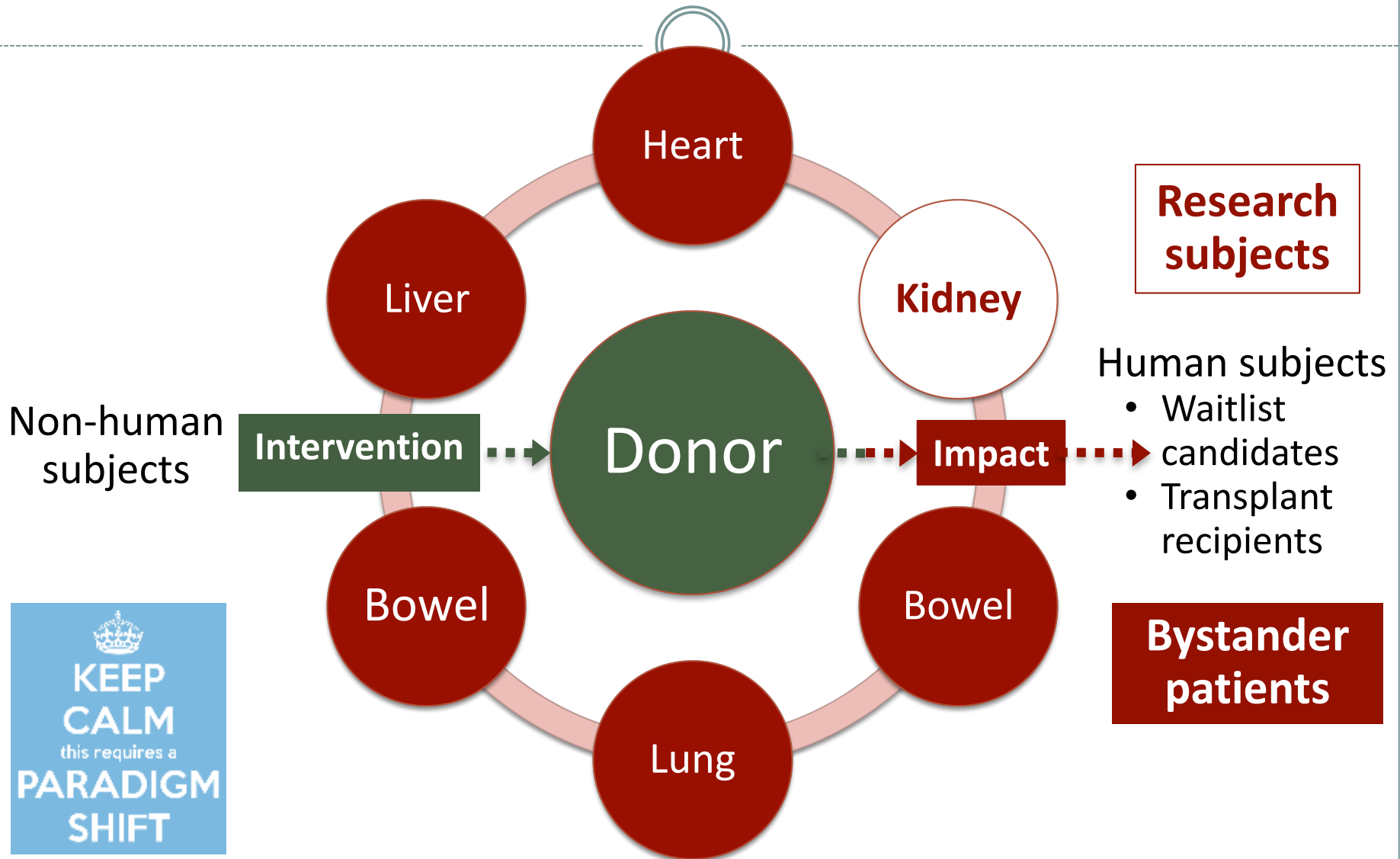
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# Research in Deceased Donors: A Paradigm Shift



# Ethical and oversight constructs



## Deceased Donors

**VOLUNTARINESS  
AND  
TRANSPARENCY**

**DIGNITY**

**MAXIMIZING  
THE GIFT**

**Authorization  
???**

## Living Human Subjects

**AUTONOMY**

**BENEFIENCE**

**JUSTICE**

**Informed Consent  
IRBs**



Courtesy of A. Glazier



# Authorization / Consent Issues, by Stage

## Intervention

- **Authorization for research**
  - Scientific merit
  - Risk assessment
  - Ethical treatment of the donor

## Transplant

- **Informed consent to accept organ**

*Is this a consent for clinical care or for research?*

*Is the transplant itself research?*

## Outcomes

- **Informed consent to participate in research**
  - Data submission
  - Specimen collection
  - Other study procedures

# Stakeholders

**THE  
PUBLIC**

JCAHO  
CMS

**Donors**  
**Donor Families**  
**Donor Hospitals**  
**OPOs**

Prof  
Societies

**Waitlisted  
Candidates**

UNOS/  
OPTN  
CMS

**Transplant  
Physicians and  
Centers**

NIH  
FDA

**Organ  
Recipients**  
**Targeted /  
Bystander**

HRSA  
OHRP

## Minireview

# Donor Intervention and Organ Preservation: Where Is the Science and What Are the Obstacles?

S. Feng

The organ shortage is widely acknowledged as the most critical factor hindering the full realization of success for solid organ transplantation. Innovation in the areas of donor management and organ preservation offers the most realistic hope to improve both the quality and size of the current organ supply. Although the basic science dissecting the complex processes of brain death and ischemia/reperfusion injury is replete with exciting discoveries, the clinical science investigating donor management and organ preservation is sparse in contrast. This review will survey the current landscape of trials to mitigate organ injury through interventions administered to donors *in vivo* or organs *ex vivo*. Consideration will then be given to the scientific, logistical and ethical obstacles that impede the transformation of laboratory breakthroughs into innovative treatments that simultaneously improve organ quality and supply.



# Step 2: Find Reinforcements



**HAPPINESS IS**



**...a partner  
in crime.**



# Timeline of Efforts

AJT 2/10



Engage Scientific Studies Committee

Form group to write paper with Ethics & Standards/ Quality Committees

Share and Revise Working Document  
AST, AOPO, SCCM, ASBH

AJT  
2/13

7/10

7/11

7/12

Discussions with Key Stakeholders

1<sup>st</sup> F2F Meeting  
ATC 2011  
ASTS, AOPO, ODRC

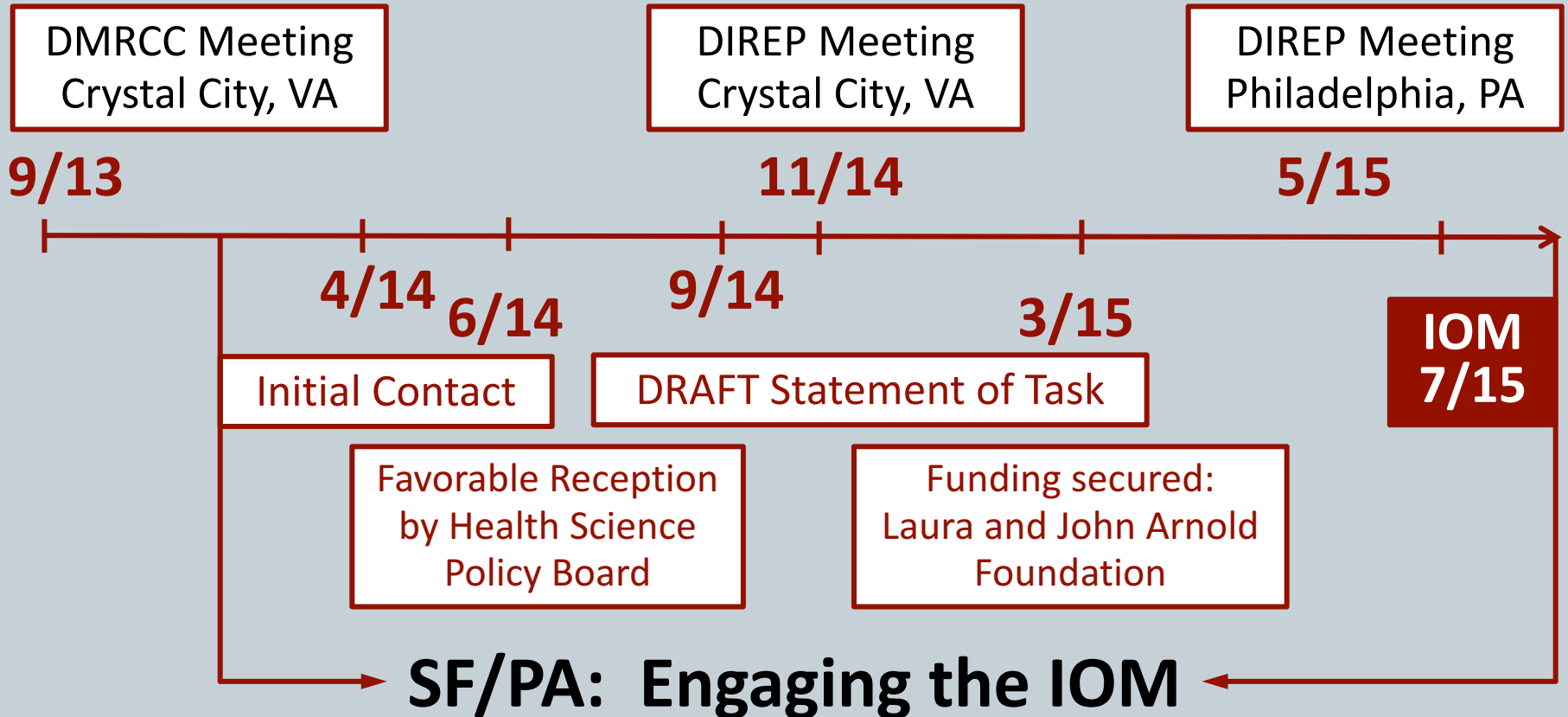
2<sup>nd</sup> F2F Meeting: ATC 2012  
ASTS, AST, AOPO, SCCM,  
ODRC, and HRSA ODTA

ACOT  
8/12

# More Recent Timeline



## HRSA / ODTA EFFORTS



# Why the IOM?



- IOM reports are respected by the public and healthcare professionals as independent, objective, and evidence-based.
  - Critically important, especially if issues involve ethics and controversy
- Prior IOM reports have had a proven transformative impact organ transplantation.
  - 1997: Non-Heart-Beating Organ Transplantation: Medical and Ethical Issues in Procurement
  - 2000: Non-Heart-Beating Organ Transplantation: Practice and Protocols
  - 2006: Organ Donation: Opportunities for Action



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Ensuring Independent, Objective Advice

## ENDURING INFLUENCE

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- National Research Council

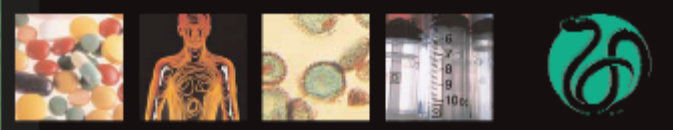
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## INSTITUTE OF MEDICINE

### ABOUT THE INSTITUTE OF MEDICINE

*Advising the Nation. Improving Health.*



INSTITUTE OF MEDICINE



## Activity

## Issues in

Type: Consensus S

Topics: Biomedical a

Board: Board on He

## Activity Descr

The Committee on Iss  
operational issues rele  
study, the concept exc  
cardiopulmonary criter  
opportunities for clinical  
donated organs availa  
and thus potentially af  
organ donor interventi  
organ donation proces

As of March 2016, the  
previously undertaken

For more information

### Upcoming Meetings for this Activity

#### Conference Call for the Committee on Issues in Organ Donor Intervention Research

January 31, 2017 (1:30 PM Eastern)

 OPEN MEETING

 AGENDA  REGISTER

#### Conference Call for the Committee on Issues in Organ Donor Intervention Research

February 13, 2017 (2:00 PM Eastern)

 OPEN MEETING

 AGENDA  REGISTER

### Previous Meetings for this Activity

#### Committee on Issues in Organ Donor Intervention Research: Public Workshop

December 14, 2016 (8:30 AM Eastern)

 VIEW AGENDA

#### First Meeting of the Committee on Issues in Organ Donor Intervention Research

September 29, 2016 (11:30 AM Eastern)

 VIEW AGENDA

# Summary



- Population demographics impose severe limits on both the quantity and quality of suitable organs for transplantation
- Research is the **ONLY** approach that can mitigate the injury that results from brain death and reperfusion
  - **Improve the function organs that are utilized**
  - **Recruit additional organs for transplantation**
- Heretofore, ethical, regulatory, and logistical challenges have stymied innovative in research deceased donors.
- Substantial efforts to resolve these quandaries by partnering with multiple stakeholders and engaging the IOM may yield the necessary guidance to advance discovery.

# Acknowledgments

- Peter Abt
- Alex Glazier
- Kate Heffernan
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- ASTS
- ACOT
- AST
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- AASLD
- HRSA
- NIAID/NIDDK/NHLBI
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- Institute of Medicine