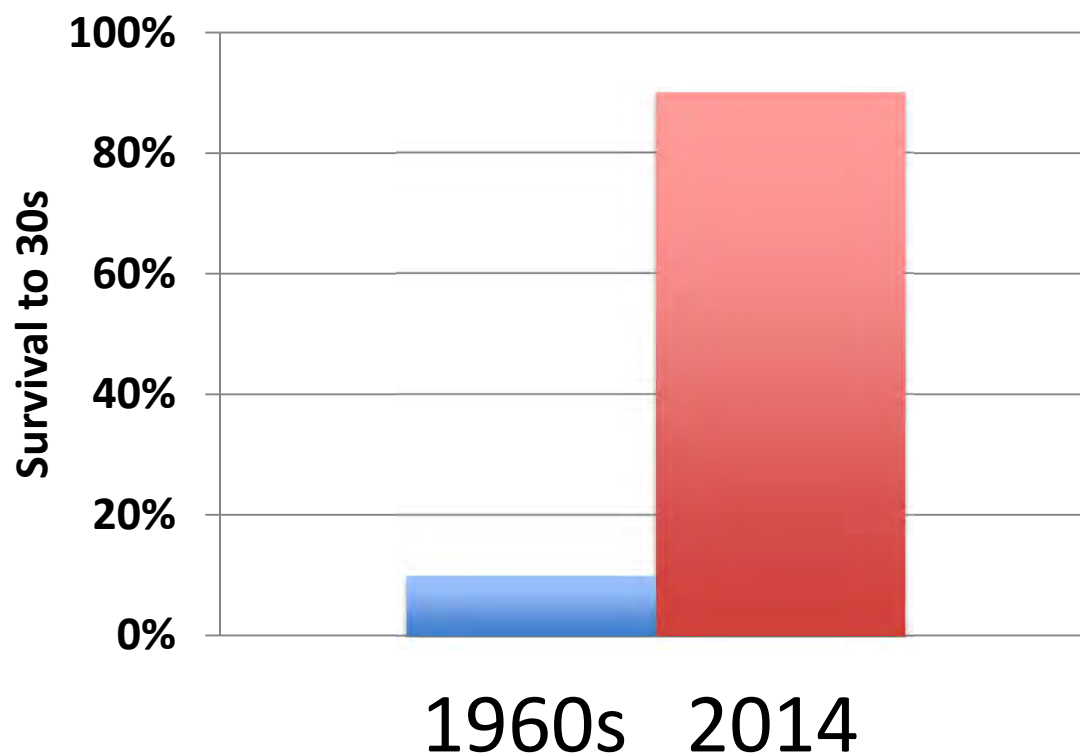


# Transitional Urology: Optimizing Care for Adolescents and Adults with Pediatric-Onset Urologic Conditions

Michael Hsieh, MD, PhD



# Spina Bifida Survival: a Medical Triumph





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# It's Not Just Spina Bifida



# (Most) Adults are Not Big Children



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# Who Will Take Care of Jenny As She Gets Older?



Born with spina bifida  
VP shunt  
Spina bifida closure

Shunt revisions  
Bladder  
augmentation  
Mitrofanoff

Needs cancer  
surveillance  
Mitrofanoff  
stenosis  
Needs C-section  
for pregnancy



*The Department of*  
**Urology**

# Pediatric and “Adult” Urologists



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# Challenges of Transitional Care

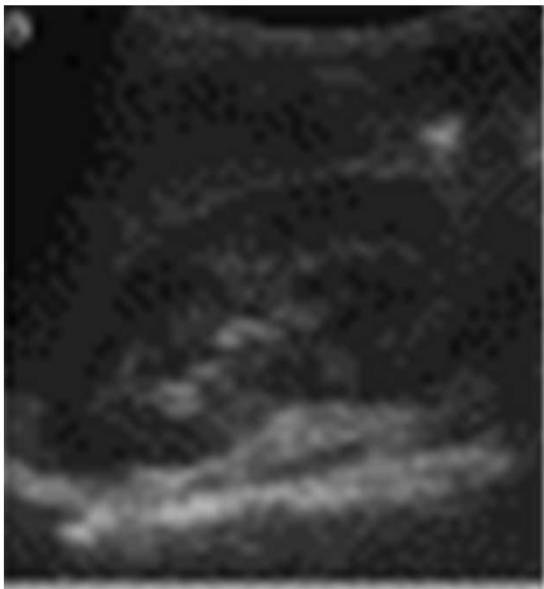


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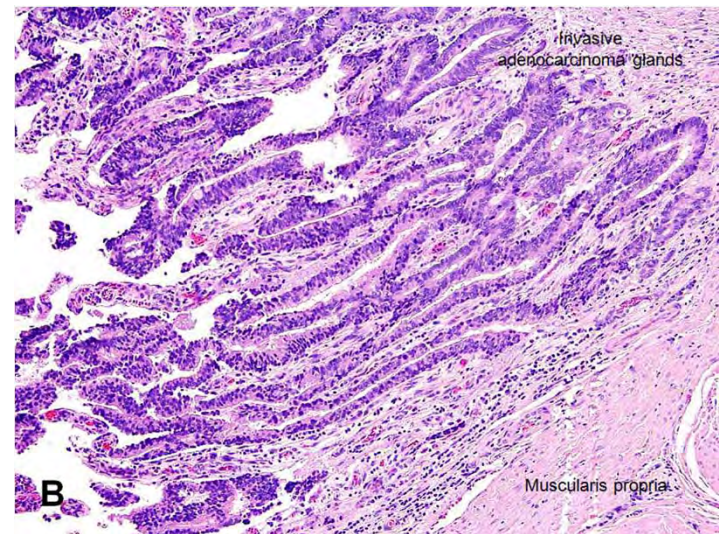
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# Urology-Specific Challenges of Transitional Care



# Urology-Specific Challenges of Transitional Care



# This is an Ongoing, National-Level Discussion

## Research Needs for Effective Transition in Lifelong Care of Congenital Genitourinary Conditions

February 2, 2015



NIH

National Institute of  
Diabetes and Digestive  
and Kidney Diseases

atcher Conference Center  
Conference Rooms E1 & E2  
NIH Building 45  
Bethesda, MD



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# *Lifelong Urologic Care- Conceptual Framework*

## Congenital

Spina  
Bifida

Ureteral/  
Urethral  
Abnormalities

Epispadias/  
Exstrophy

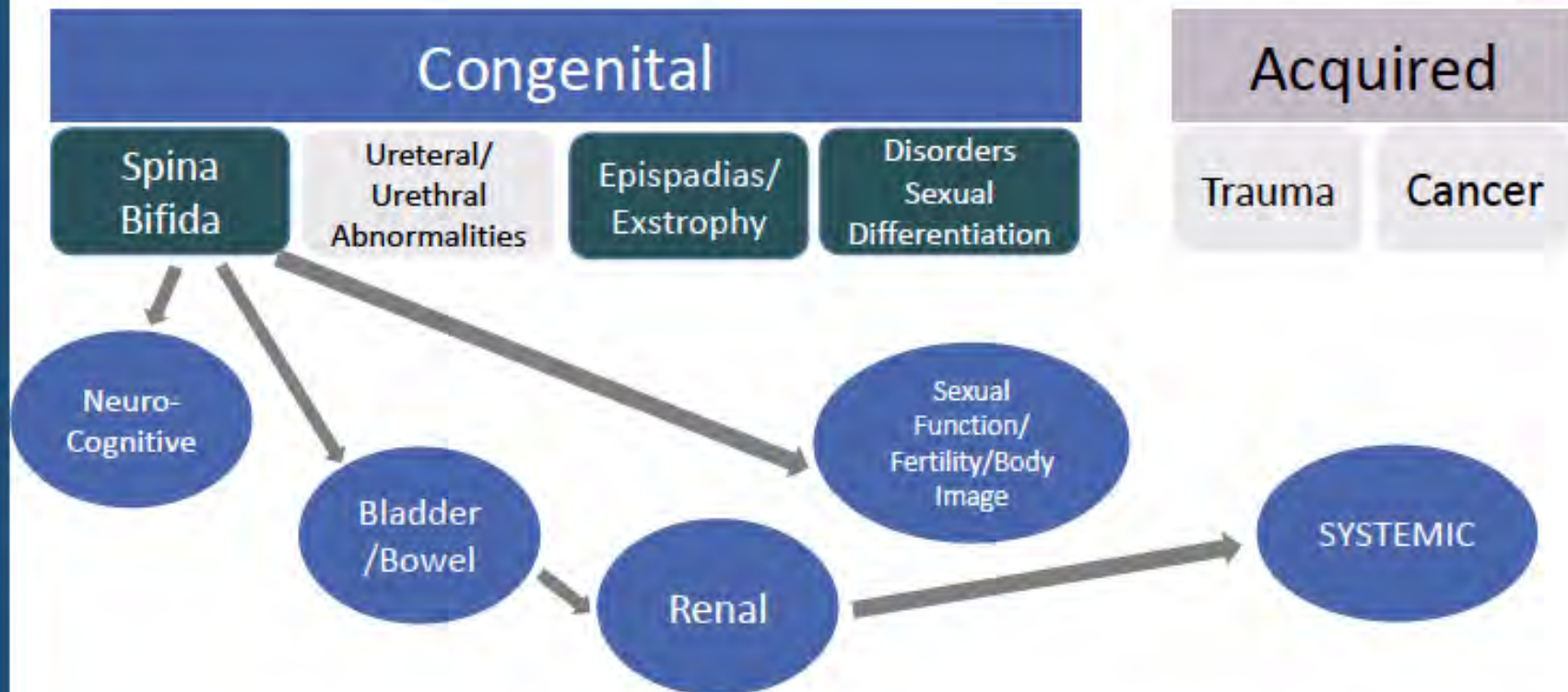
Disorders  
Sexual  
Differentiation

## Acquired

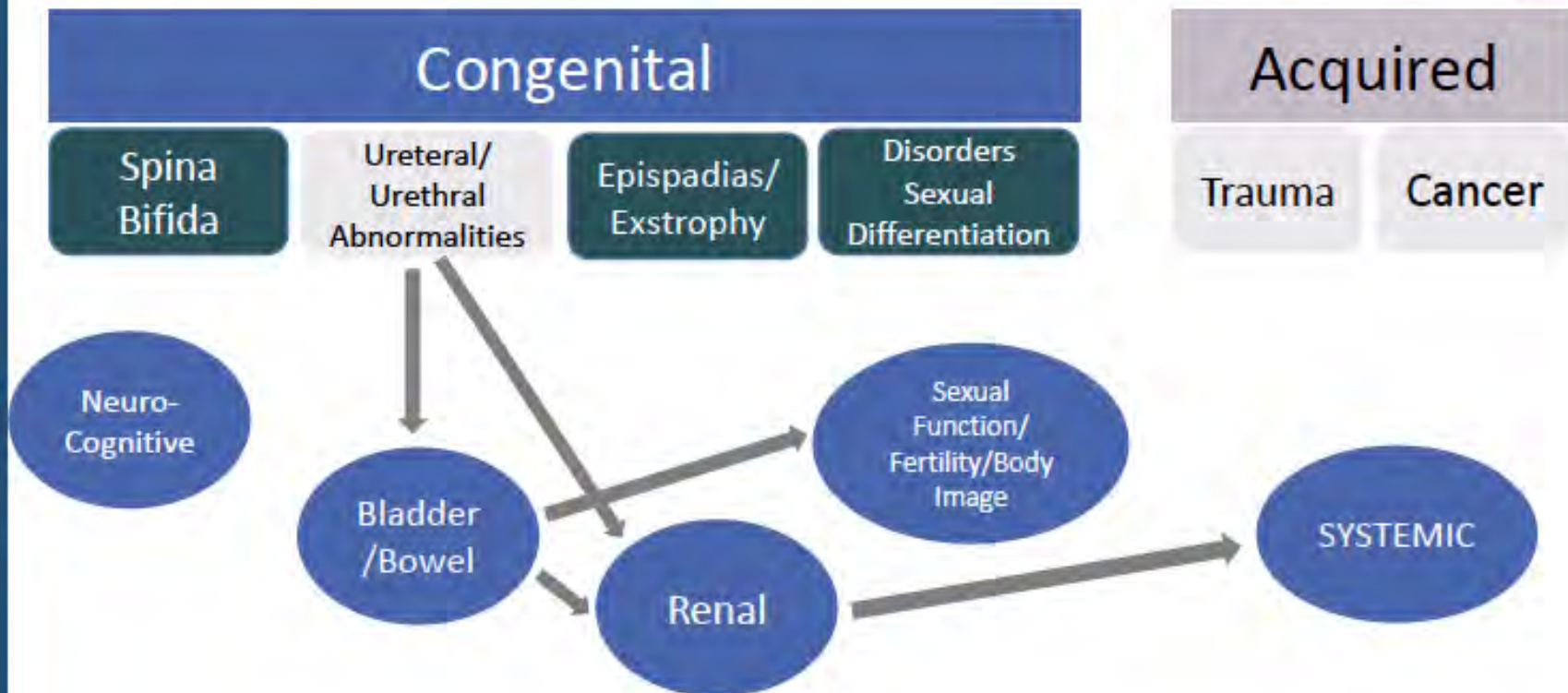
Trauma

Cancer

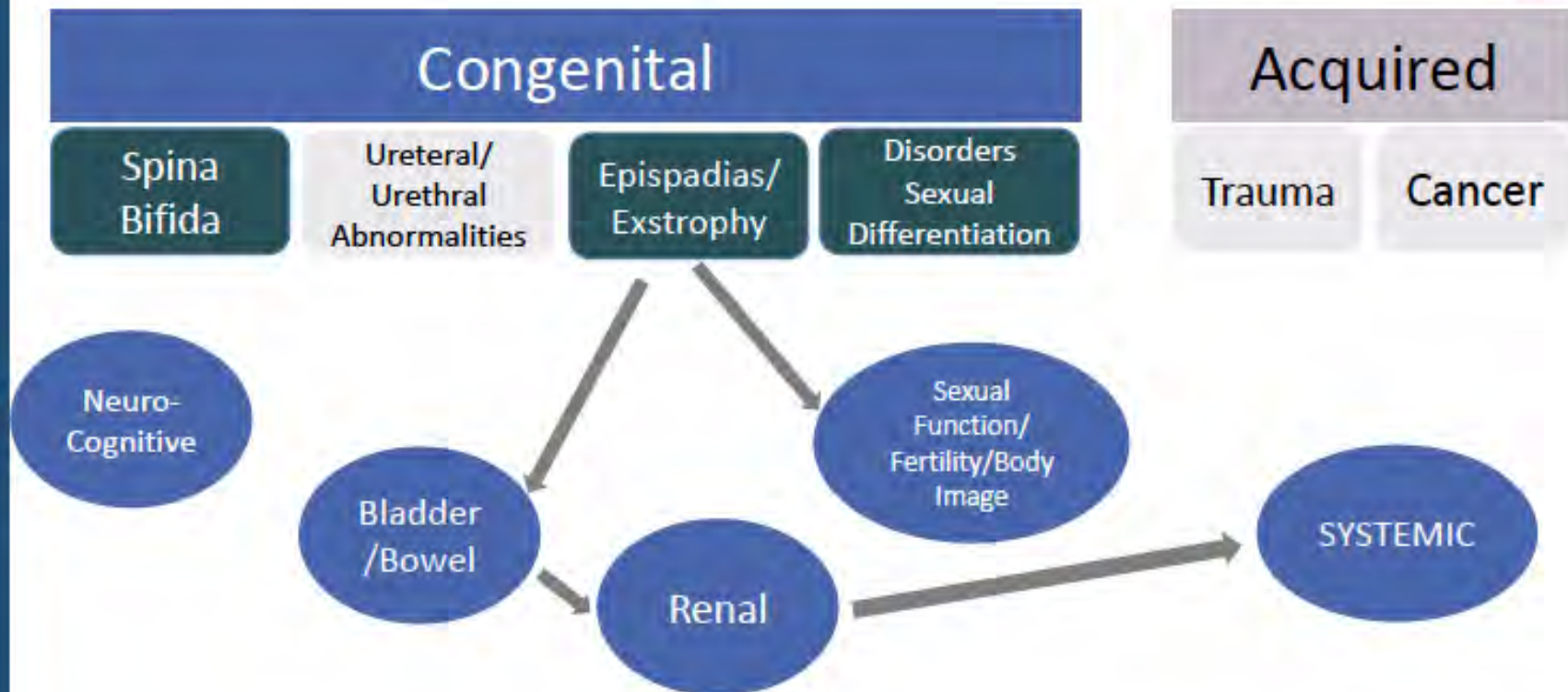
# Lifelong Urologic Care- Conceptual Framework



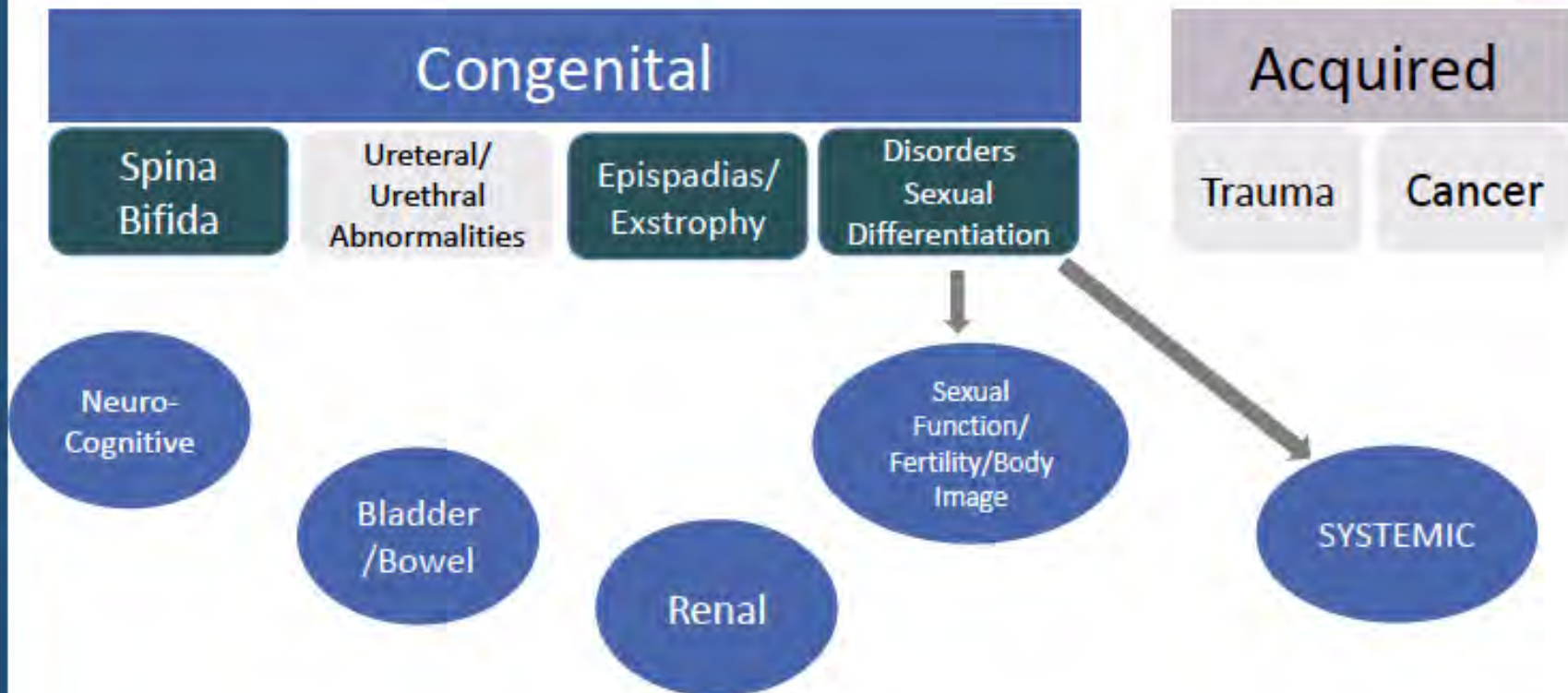
# Lifelong Urologic Care- Conceptual Framework



# Lifelong Urologic Care- Conceptual Framework

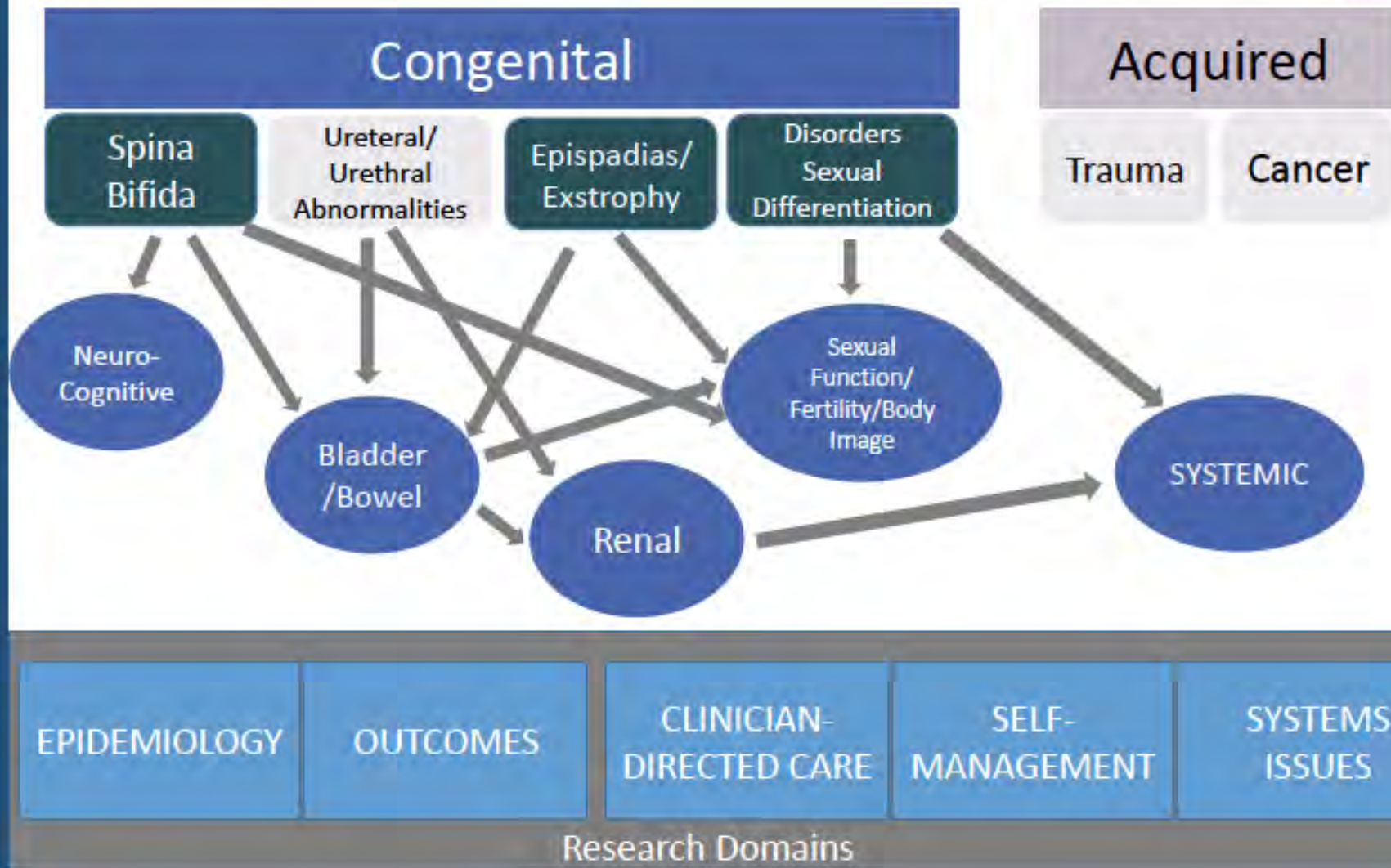


# Lifelong Urologic Care- Conceptual Framework





# Lifelong Urologic Care- Conceptual Framework



# What Should We Be Doing to “Transition” Our Patients?

## Recommended Health Care Transition Timeline

AGE:	12	14	16	18	18-22	23-26
	Make youth and family aware of transition policy	Initiate health care transition planning	Prepare youth and parents for adult model of care and discuss transfer	Transition to adult model of care	Transfer care to adult medical home and/or specialists with transfer package	Integrate young adults into adult care

[Gottransition.org](http://Gottransition.org)



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# Transitional Urology: a Joint Children's-GW Venture

## The Clinic for Adolescent and Adult Pediatric Urology (CAPITUL)



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# CAPITUL

- First dedicated transitional urology program in the mid-Atlantic region
- Will also see adults with pediatric onset urologic disorders
- Interface closely with other regional medical centers and practices (think Maryland!)

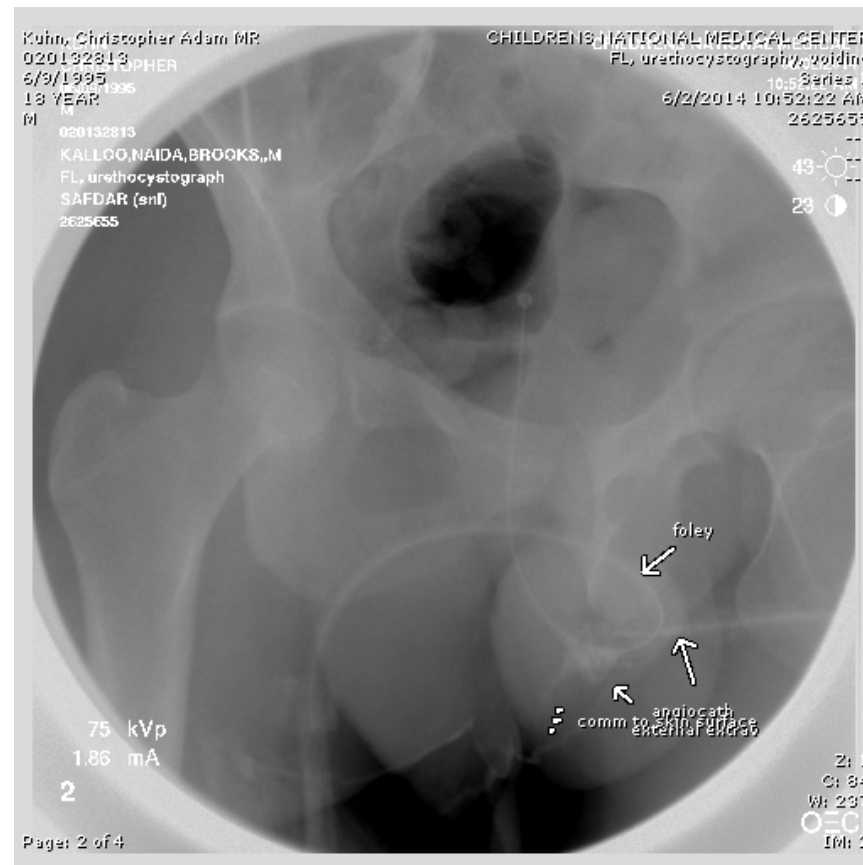


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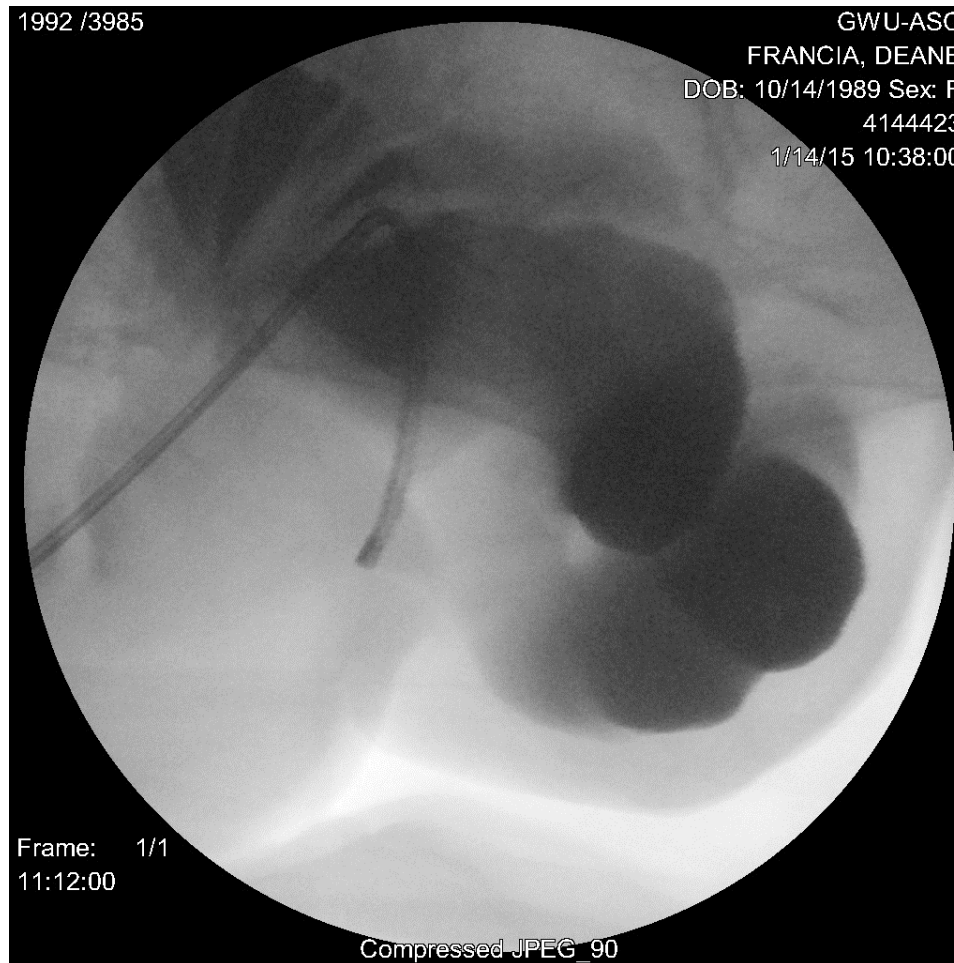


# Patients to Date – Challenging!

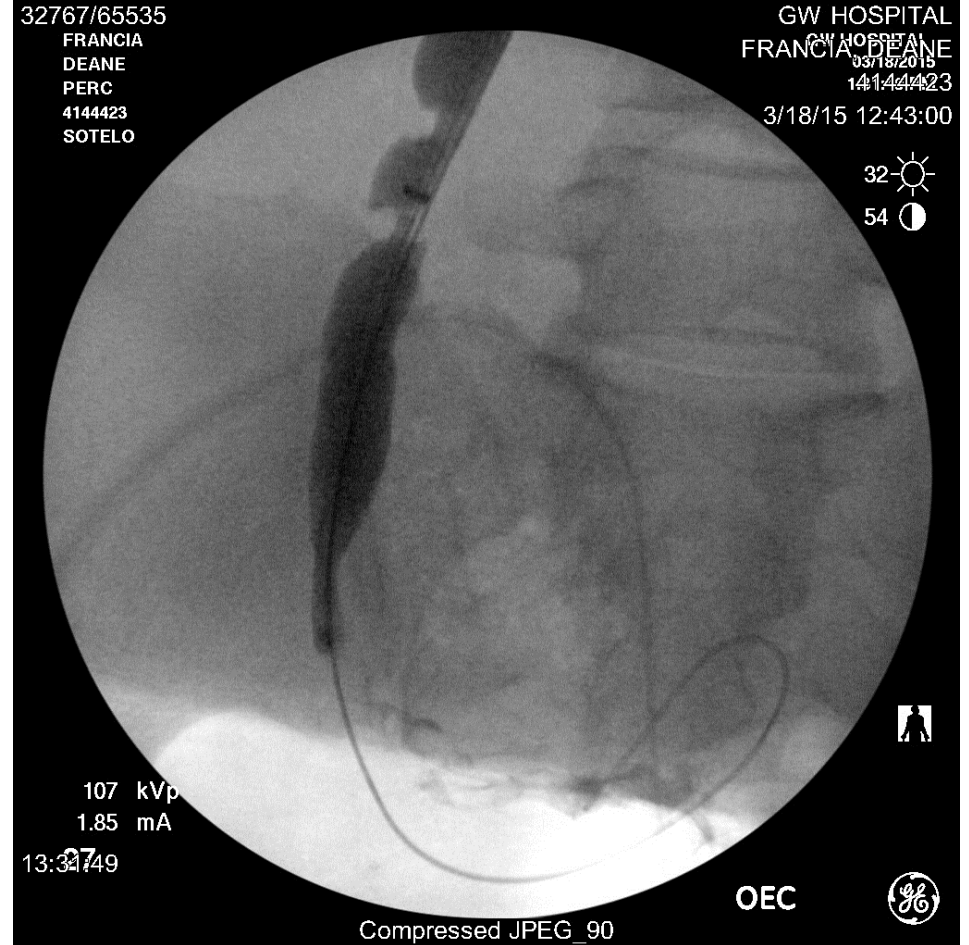
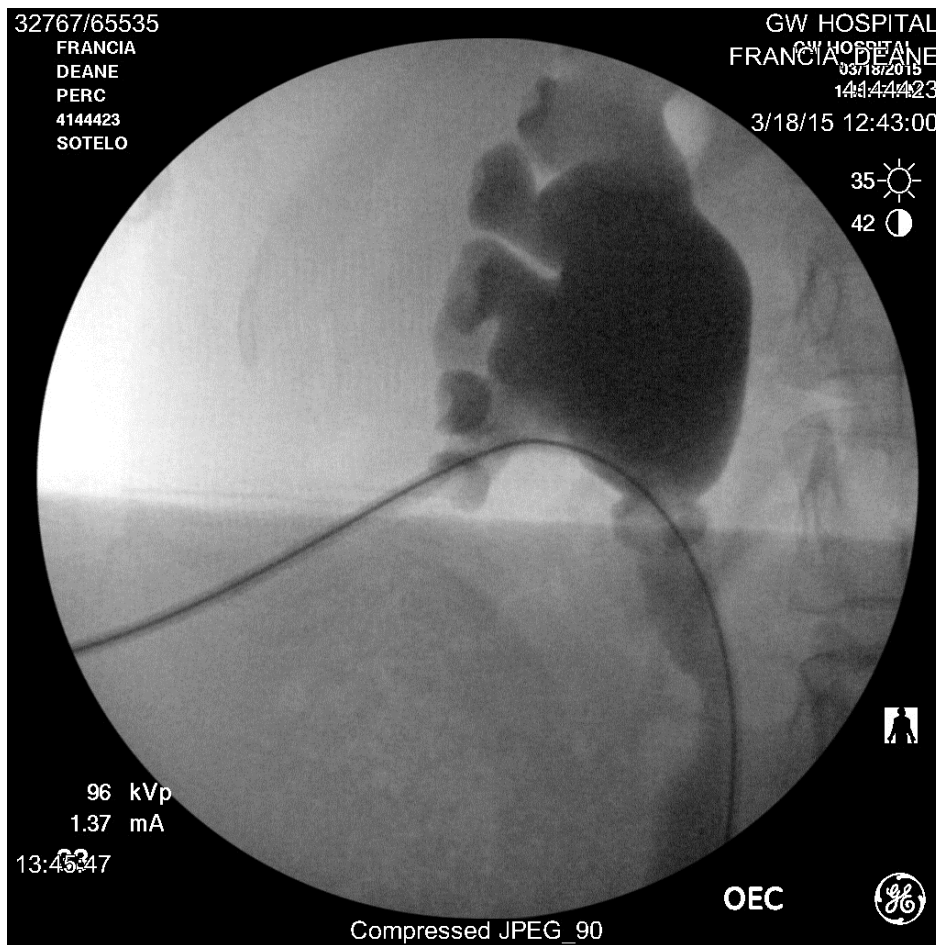
- 19 yo man with multiple urethrocutaneous fistulas after failed hypospadias repairs



# 25 yo woman with cloacal exstrophy and continent urinary diversion with UTI and stones



# 25 yo woman with cloacal exstrophy and continent urinary diversion with UTI and stones



# Challenging Patient #3

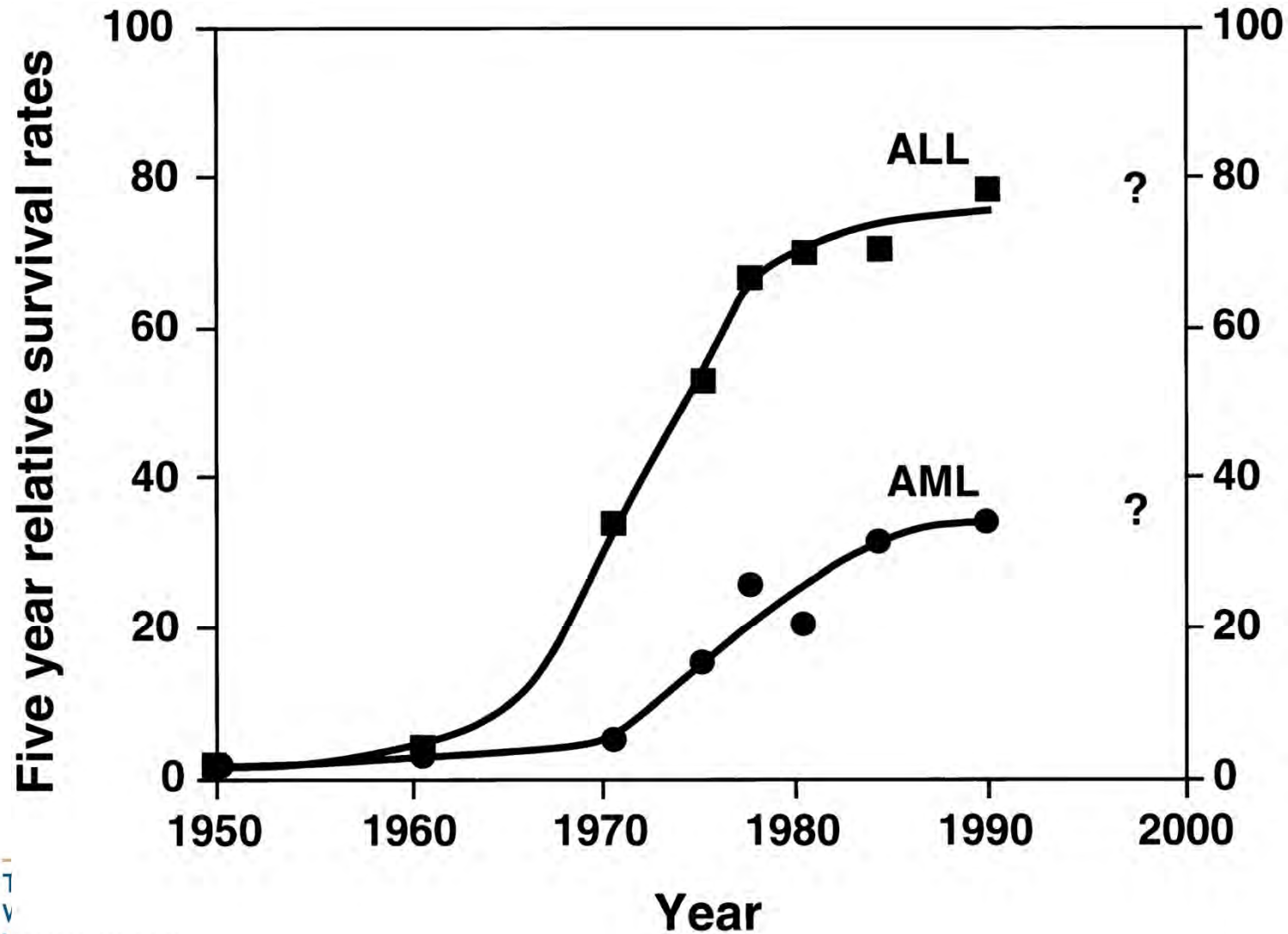
- 25 yo man with spina bifida with incontinence and urethral erosion from indwelling catheter



Appendicovesicostomy created and maximal anticholinergic rx – pt now continent!



# Cancer Survivorship



# Fertility Effects of BMT on Adolescent Boys

- 68 boys >12 yo (2003-2010)
- 6 tried sperm banking pre-rx
- 33 tried banking pre-BMT (39% azoospermic, 15% oligospermic)



Nahata et al., *Pediatr Blood Cancer* 2013



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# What Do Patients and Families Want?

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© Mary Ann Liebert, Inc.  
DOI: 10.1089/jayao.2014.0007

Original Article

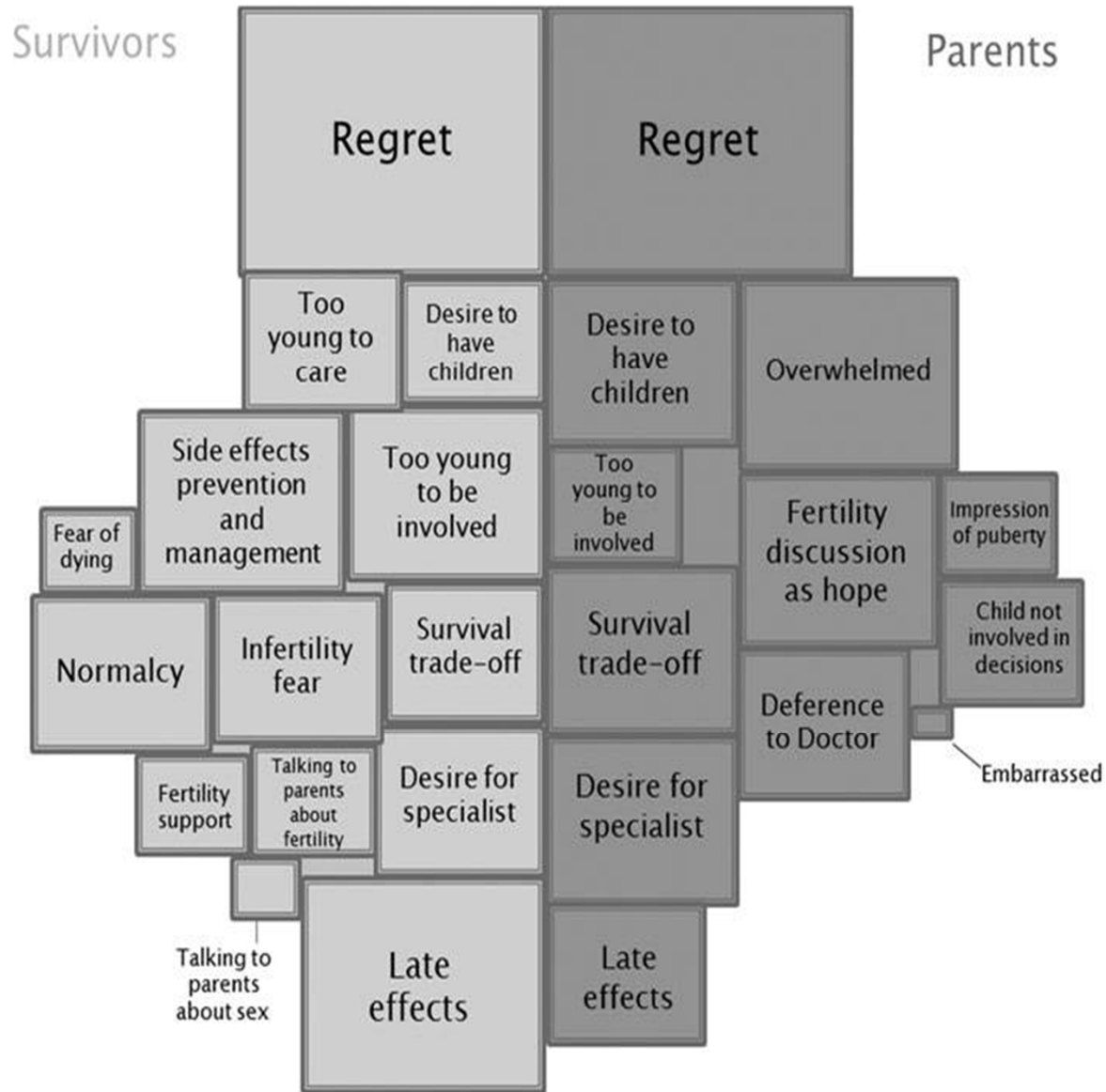
## Fertility Preservation Preferences and Perspectives Among Adult Male Survivors of Pediatric Cancer and Their Parents

Daniel M. Stein, MD, MHS,<sup>1,2</sup> David E. Victorson, PhD,<sup>2,3</sup> Jeremy T. Choy, MD,<sup>1</sup> Kate E. Waimey, PhD,<sup>4\*</sup>  
Timothy P. Pearman, PhD,<sup>2,3</sup> Kristin Smith,<sup>4</sup> Justin Dreyfuss,<sup>1</sup> Karen E. Kinahan, MS, RN,<sup>3</sup>  
Divya Sadhwani,<sup>5</sup> Teresa K. Woodruff, PhD,<sup>4</sup> and Robert E. Brannigan, MD<sup>1,4</sup>



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Special thanks to Shana Jacobs



# Critical Review of Clinical Practice Guidelines for Fertility Preservation in Teenagers and Young Adults with Cancer

Adam D. Jakes, MBBS, MSc,<sup>1</sup> Perrine Marec-Berard, MD,<sup>2</sup>  
Robert S. Phillips, MA (Cantab), BM BCh (Oxon), PhD,<sup>3</sup> and Daniel P. Stark, MB BChir, PhD<sup>1</sup>

Take home messages:

Guidelines vary widely in recommendations

All guidelines recommended sperm banking by postpubertal boys

**ASCO** 2013: if boys can't produce semen, epididymal/testicular aspiration/biopsy. Testicular shielding during XRT, testicular tissue preservation supported in trial setting. GnRH analogs mentioned but not supported

**AAP** 2008: in addition to above, electroejaculation & post-masturbation urine are options, testicular tissue preservation not recommended

Special thanks to Shana Jacobs

## male reproductive options

OPTION	Sperm Banking (Masturbation)	Sperm Banking (Alternative Collection Methods)	Radiation Shielding of Gonads
MEDICAL STATUS	Standard	Experimental	Standard
DEFINITION	Sperm is obtained through masturbation, then frozen	Sperm obtained through testicular extraction or electroejaculation under sedation	Use of shielding to reduce the dose of radiation delivered to the testes
PUBERTAL STATUS	After puberty	After puberty	Before and after puberty
TIME REQUIREMENT	Outpatient procedure	Outpatient procedures	In conjunction with radiation treatments
SUCCESS RATES	Generally high The most established technique for men	If sperm is obtained, similar to standard sperm banking	Possible with select radiation fields and anatomy
COST	Approx. \$1,500 for 3 samples; storage fees average \$500/year	Varies greatly based on collection method	Generally included in the cost of radiation treatments
TIMING	Before treatment	Before treatment	During treatment
SPECIAL CONSIDERATIONS	Deposits can be made every 24 hours	Can be considered if male cannot ejaculate	Expertise required; does not protect against effects of chemotherapy



## male reproductive options

Testicular Tissue Freezing	Testicular Sperm Extraction	Donor Sperm	Adoption
Experimental	Standard	Standard	Standard
Tissue obtained through biopsy and frozen for future use	Use of biopsy to obtain individual sperm from testicular tissue	Sperm donated by a man for artificial insemination or IVF	Process that creates a legal parent-child relationship
Before and after puberty	After puberty	After puberty	After puberty
Outpatient procedure	Outpatient procedure	Readily available for purchase	Varies depending on the type of adoption
No available human success rates	30-70% in post-pubescent patients	50-80%	N/A
\$500-\$2,500 for surgery; \$300-\$1,000 for freezing; \$500/year for storage	\$4,000-\$16,000 (in addition to costs for IVF)	\$200-\$500 per vial (in addition to costs for IUI or IVF)	\$2,500-\$35,000
Before treatment	Before or after treatment	After treatment	After treatment
May be only option for pre-pubescent boys	Center should be able to freeze sperm found at time of biopsy	Can choose donor based on wide range of characteristics	Medical history often a factor

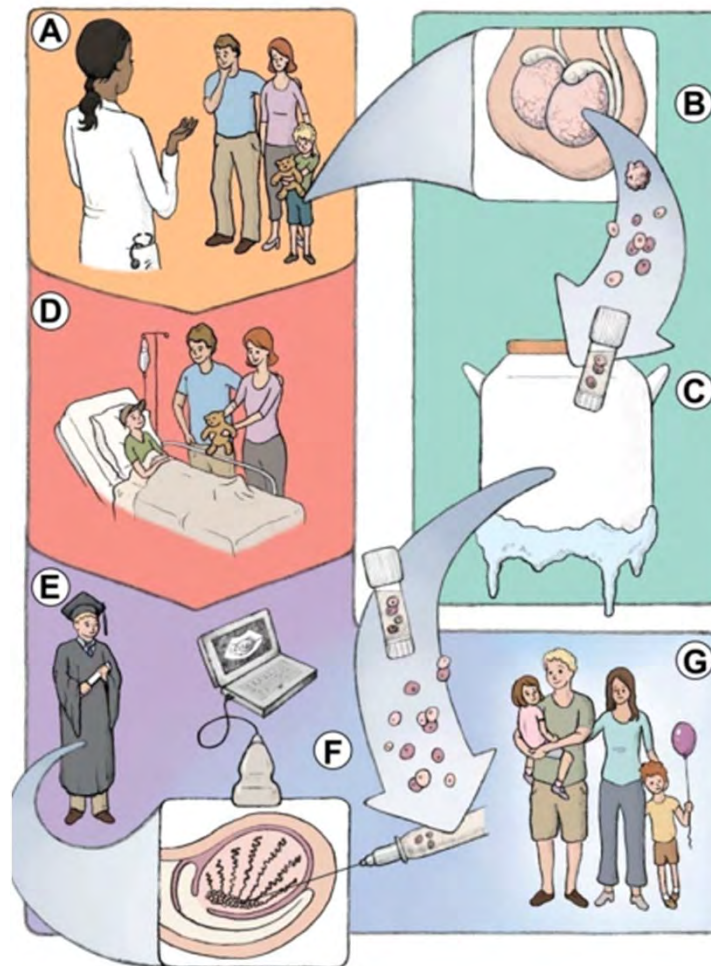


# Testicular Biopsy and Microsurgical Epididymal Sperm Aspiration (MESA)





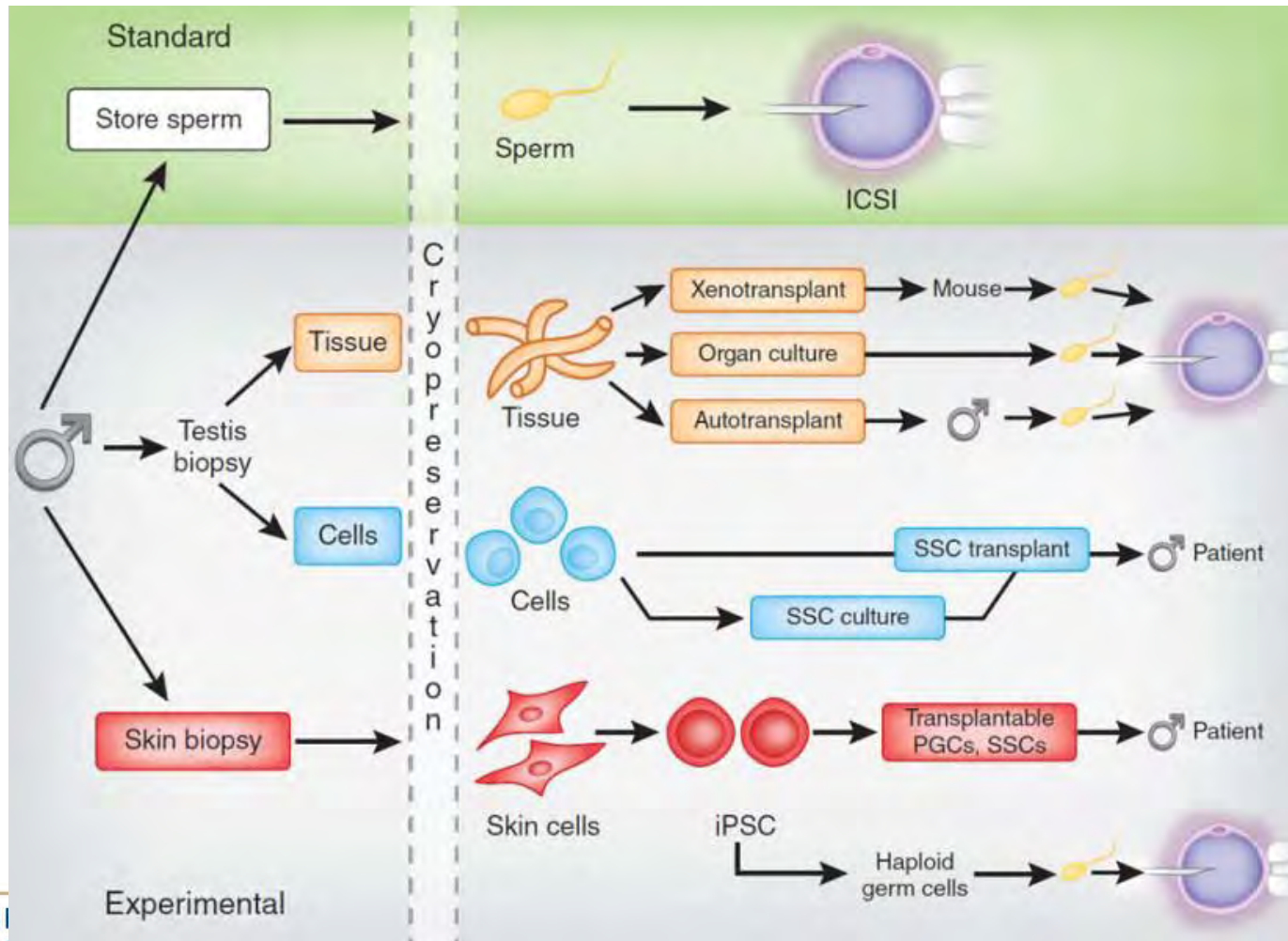
# Testicular Tissue Cryopreservation for Fertility Preservation in Patients Facing Infertility Causing Diseases or Treatment Regimens



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Hermann and Orwig (Eds) "Male Germline Stem Cells: Developmental and Regenerative Potential", Springer 2011

# Standard and Experimental Methods for the potential use of cryopreserved testicular tissue



# Challenges to SSC transplantation for cancer survivors

- **Majority of patients are not informed about fertility risks and options for preserving fertility**
  - Multidisciplinary discussions
- **Small biopsies from prepubertal patients may contain few stem cells**
- **Timing for reintroducing SSCs back into patients**
- **Malignant contamination in testicular biopsy**
- **Optimize cryopreservation**
  - Cell suspension versus tissue
  - Slow freeze versus vitrification



# Testicular Tissue Cryopreservation Study



## Study Aims (Abridged):

1. Optimize cryopreservation techniques for testicular cells from boys at risk of infertility
2. Assess and eliminate malignant cell contamination of harvest testicular tissue

## Eligibility:

-Male of any age scheduled for treatment with risk of causing permanent and complete loss of subsequent testicular function.

-For subjects  $\geq 18$  years old, eligibility is limited to high and intermediate risk patients

-For subjects  $< 18$  years old, eligibility is limited to high risk patients

“Piggyback” onto anesthesia given for bone marrow biopsies, line placement, etc.



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High Risk:  $\geq 80\%$  risk of prolonged azoospermia by Fertile Hope criteria  
Intermediate Risk: 21-79% risk

# Assessing Infertility Risk

Degree of Risk	Treatment	Common Usage
<b>High Risk</b> Prolonged azoospermia post-treatment	Total body irradiation (TBI)	Bone marrow transplant/stem cell transplant(BMT/SCT)
	Testicular radiation dose > 2.5 Gy in men	Testicular cancer, acute lymphoblastic leukemia (ALL), non-Hodgkin lymphoma (NHL)
	Testicular radiation dose $\geq$ 6 Gy in boys	ALL, NHL, sarcoma, germ cell tumors
	Protocols containing procarbazine: COPP, MOPP, MVPP, ChIVPP, ChIVPP/EVA, MOPP/ABVD, COPP/ABVD	Hodgkin lymphoma
	Alkylating chemotherapy for transplant conditioning (cyclophosphamide, busulfan, melphalan)	BMT/SCT
	Any alkylating agent (e.g., procarbazine, nitrogen mustard, cyclophosphamide) + TBI, pelvic radiation, or testicular radiation	Testicular cancer, BMT/SCT, ALL, NHL, sarcoma, neuroblastoma, Hodgkin lymphoma
	Cyclophosphamide >7.5 g/m <sup>2</sup> Cranial/brain radiation $\geq$ 40 Gy	Sarcoma, NHL, neuroblastoma, ALL Brain tumor



# Study Details

- **Inclusion Criteria:**
  - **Male of any age**
  - **Scheduled to undergo treatment for the treatment or prevention of a medical condition or malignancy with risk of causing permanent and complete loss of subsequent testicular function.**
  - **Newly diagnosed or recurrent disease**
- **Approved for wedge biopsy or orchiectomy**
- **Cryopreservation of testicular tissue pieces by slow freezing method (5% DMSO)**
- **A small portion of the tissue will be allocated to research (max. 25%) and stored at Magee-Womens Research Institute**
- **75% of the tissue for future patient use**
- **Long-term storage at Reprotech Ltd., Roseville, MN**



# TTC- Coordinating Center

## Recruitment Site

- ✓ Determine Eligibility
- ✓ Informed Consent
- ✓ Send blood and urine samples Memorial Blood Centers (MBC)
- ✓ Send paperwork and MBC lab results to Reprotect
- ✓ Send de-identified testicular tissue and plasma to CC



# Research Goals

- Optimize techniques for cryopreservation of testicular tissue
- Optimize methods for SSC transplantation
- Assess malignant cell contamination in harvested patient testicular tissue
- Develop methods for removing contaminating cancer cells in testicular tissue.
- Develop strategies to isolate/enrich the spermatogonial stem cell
- Establish culture conditions for *in vitro* expansion of human SSCs
- Testicular xenografting





# Financial Assistance

- **Insufficient insurance coverage**
- **Verna's purse in association with Reprotecth offers discounted storage fees**

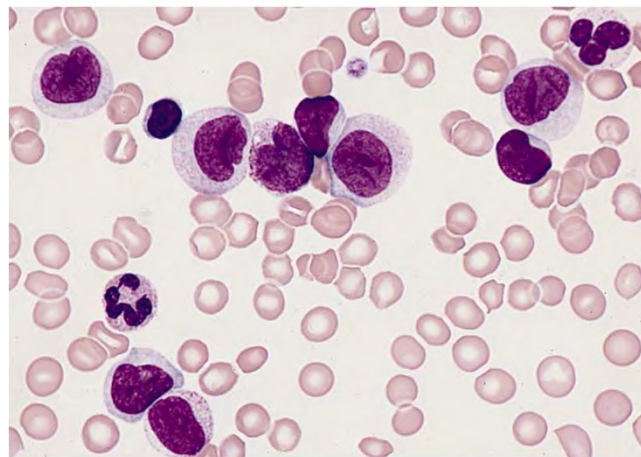


- **Participation in research studies to cover costs for tissue freezing and cryopreservation**



# Patients Already Being Recruited/Approached

- 17 yo boy with hepatosplenic T cell lymphoma about to undergo BMT – testicular tissue harvested



# Help is on the Way

- Kelly Chiles, GW andrologist



# Oncofertility Conclusions

- We are excited to offer the potential for fertility preservation to boys undergoing gonadotoxic therapy for cancer
- Thank you for your support of the program – you will help enable today's children to be tomorrow's parents!



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# The Broader Need

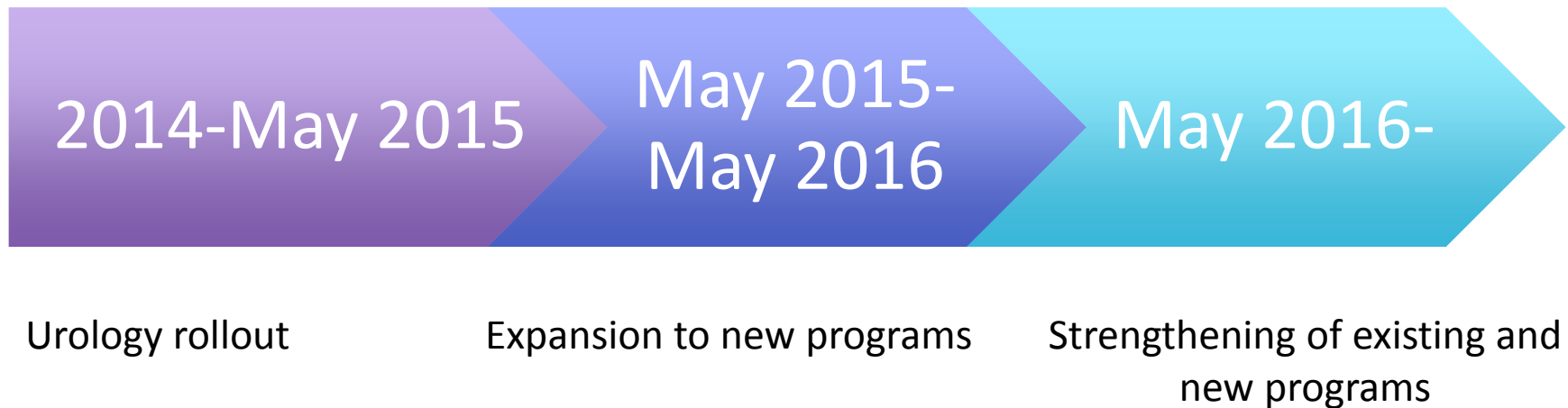
- Sally Evans – Spina bifida/PMR
- Jeff Dome - Oncology
- Jennifer Dean - Oncology
- Lisa Tuchmann – Adolescent Medicine
- April Barbour – Internal Medicine
- Tova Ronis - Rheumatology
- Barbara Speller-Brown – Sickle Cell
- Veronica Gomez-Lobo - Gynecology
- Judy Liu and Henry Kaminski - Neurology
- Christian Nagy - Cardiology
- Pam McClain

# The Solution

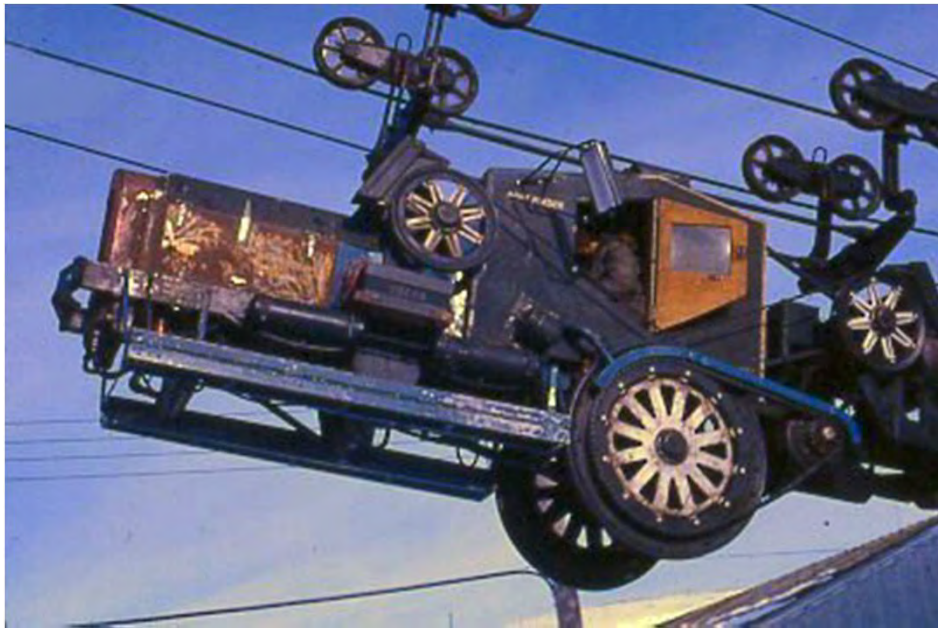
- Umbrella program with pool of dedicated:
  - **Social workers**
  - Nutritionists
  - Psychologists
  - Physical therapists
  - **Patient navigators**
  - Research coordinators
- Tremendous philanthropic potential
- Clearinghouse for transition policy guidelines, databases of adult regional caregivers
- Potential for transitional care fellowship
- Cost savings and increased clinical volume
- Higher quality patient care



# Implementation Timeline



# Transitional Medicine and Surgery (TRAMS) at GW



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# Acknowledgements

- Amanda Mahoney
- Kelsey Hilton
- Jeff Dome
- Alissa Mun
- Veronica Lobo-Gomez
- Gil Rushton
- David Jacobsohn
- Kathrin Gassei
- William Jerkins
- Catriona Mowbray
- Kyle Orwick
- Reuven Schore
- Allistair Abraham
- Cath Bollard

