Impact of Disruptions in the Tc-99m Supply Chain on Cardiac Testing

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Disclosures

- Consulting/Speaking Honoraria:
  - INVIA Medical Imaging Solutions
  - Ionetix
  - Bracco Diagnostics
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  - Society of Nuclear Medicine & Molecular Imaging
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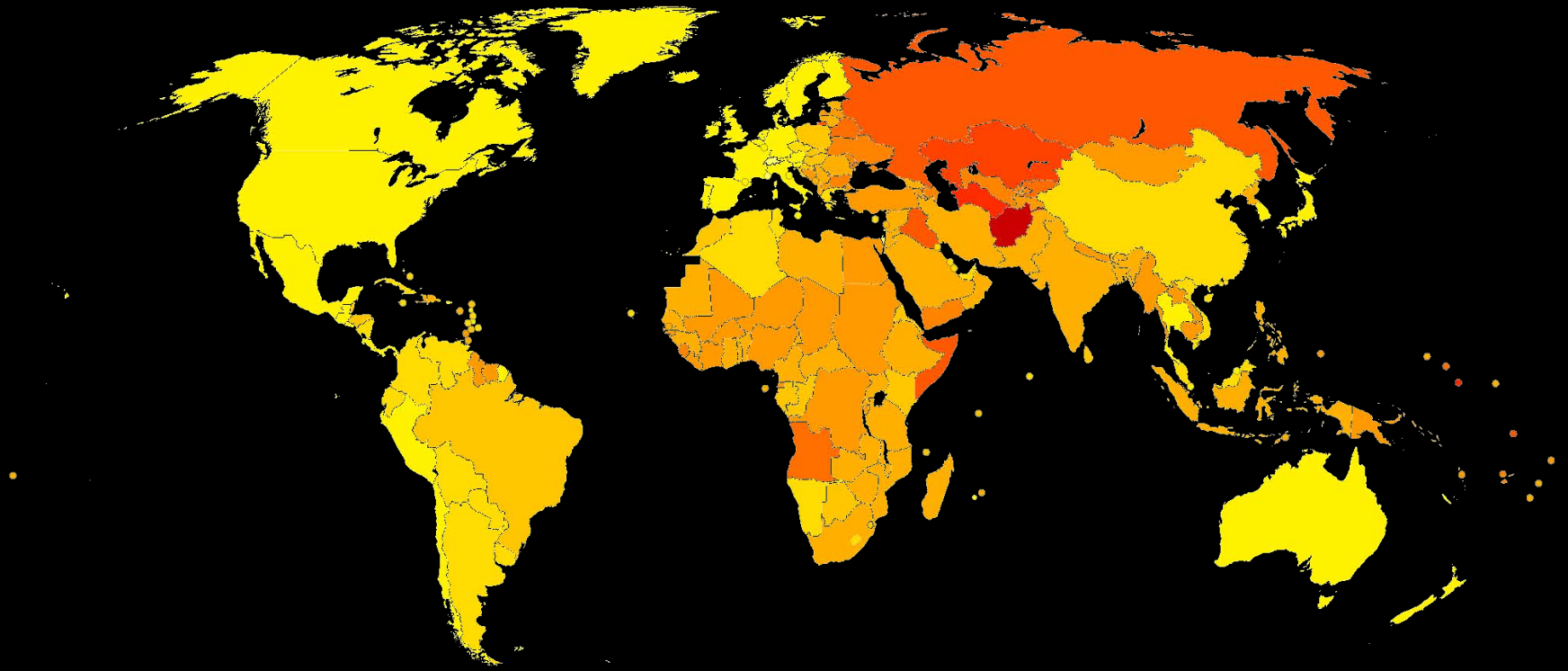
Cardiovascular Disease Worldwide



Disability Adjusted Life-Years Lost due to Cardiovascular Disease per 100,000

<900	2300-3000	4400-5100	6500-7200
900-1650	3000-3700	5100-5800	7200-7900
1650-2300	3700-4400	5800-6500	>7900

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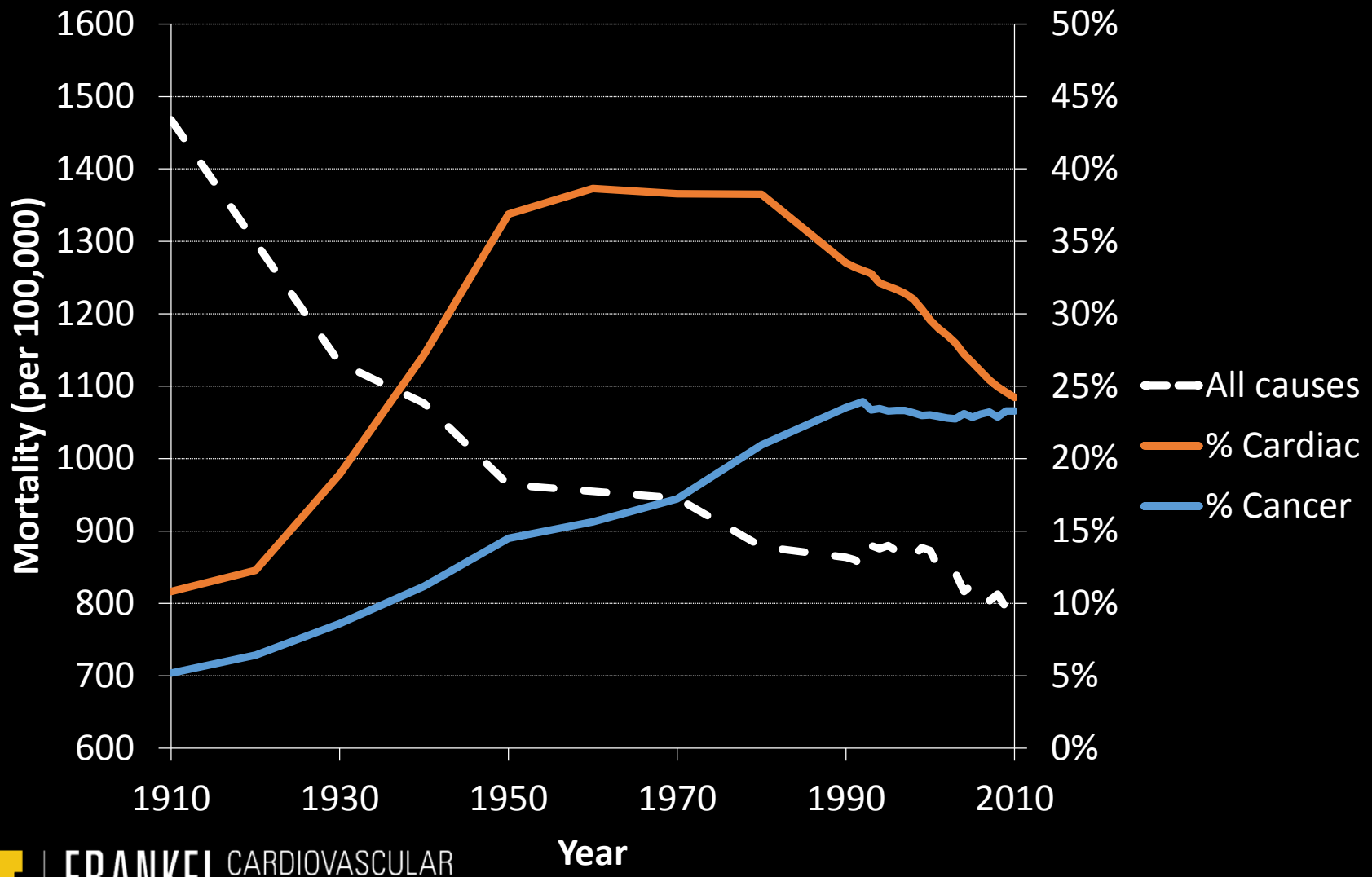
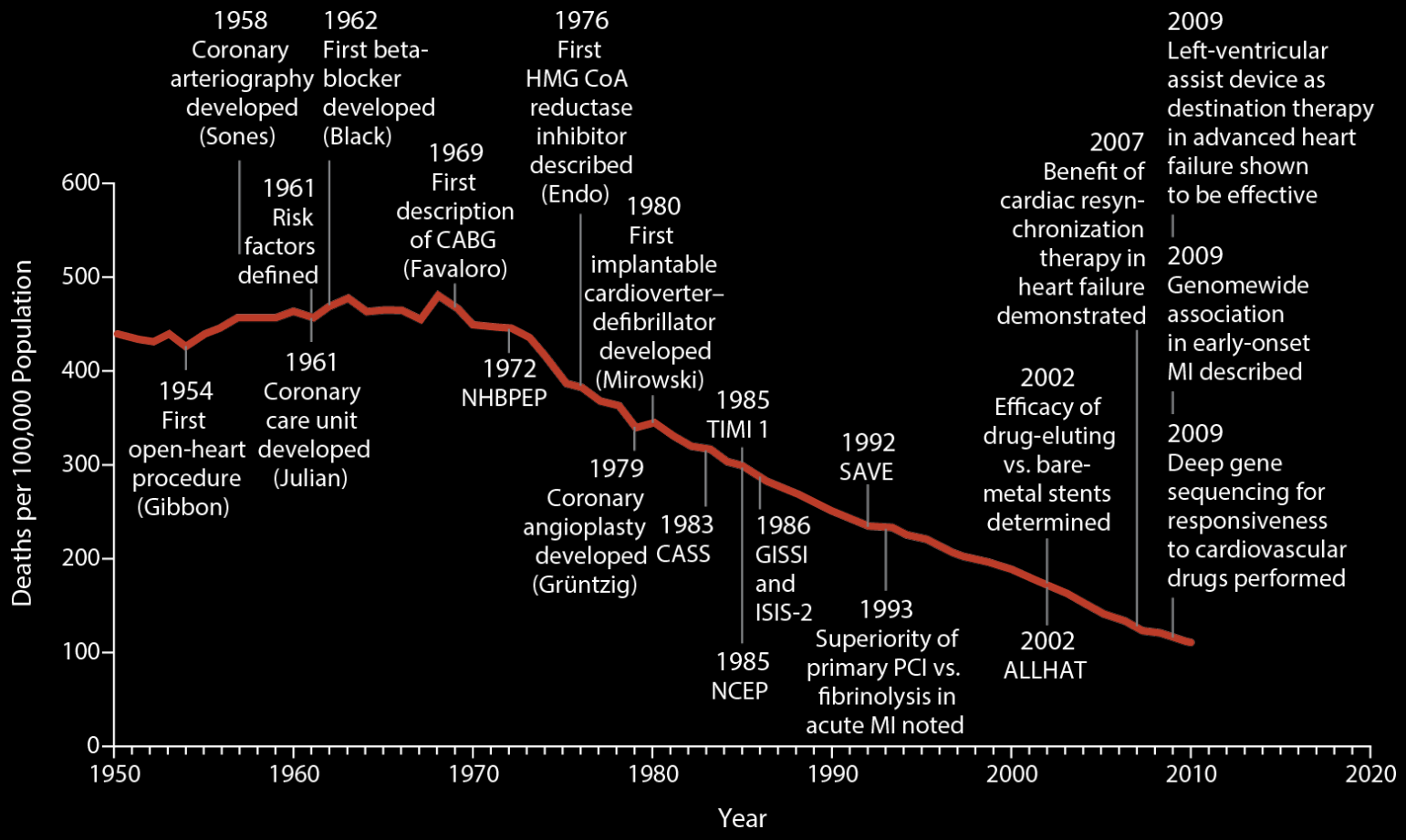
WHO Disease and injury country estimates 2004. World Health Organization.

Temporal Trends in US Mortality



National Vital Statistics System. Centers for Disease Control

Steady Advancements in Cardiovascular Care



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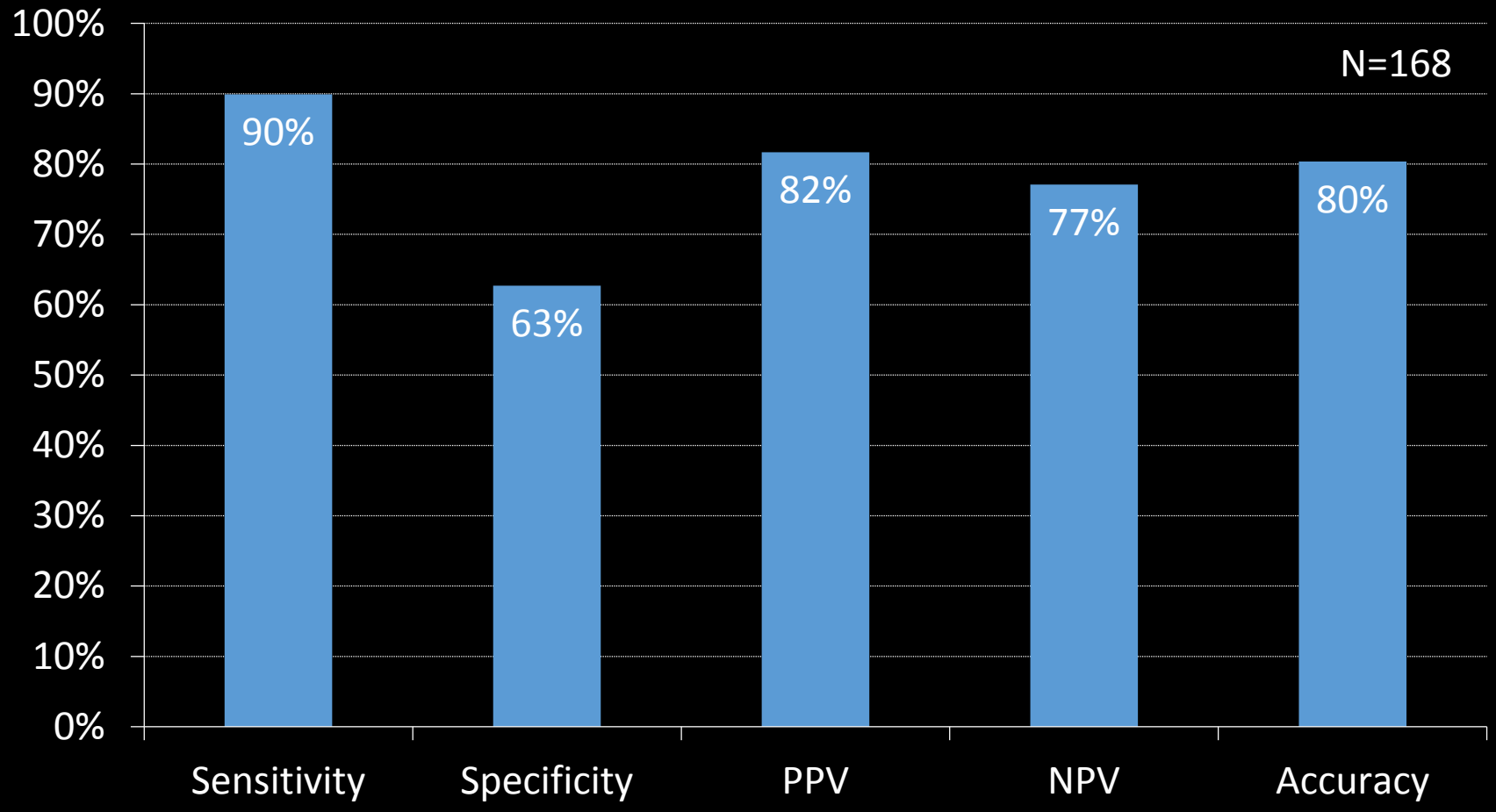
Braunwald, *et al*. N Engl J Med 366:54-63(2012)

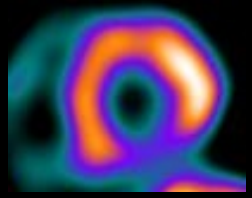
History and Physical Exam are Limited



Pryor DB, *et al*. Ann Intern Med 118:81-90 (1993)

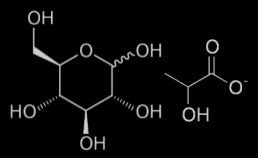
Stress Testing

ISCHEMIA



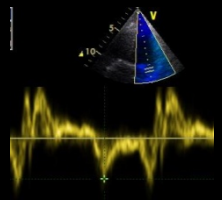
Perfusion Defect

Mild stenoses may result in perfusion defects without any other abnormalities. These can be detected by a variety of imaging modalities, although nuclear methods (shown) are most common.



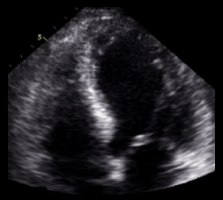
Metabolic Changes

Shift from oxidative metabolism results in increased glucose utilization and lactate production. Increased adenosine levels may lead to adaptive responses. These are only detectible using invasive methods or with investigational imaging methods such as magnetic resonance spectroscopy.



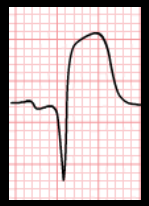
Relaxation Abnormalities

Impairments in diastolic relaxation occur before systolic dysfunction and can be detected with echocardiography (shown) and cardiac MRI. The use of these tools in stress testing remains investigational.



Systolic Dysfunction

Regional and global systolic abnormalities can be detected with a variety of techniques including echocardiography (shown), nuclear methods and cardiac MRI

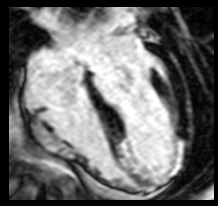


EKG Changes

EKG monitoring may reveal ST-segment depression or elevation depending on the severity of ischemia. This is a routine part of most stress testing modalities.

Symptoms

Symptoms are a relatively late finding in the ischemic cascade. The occurrence of chest pain during stress testing may be a helpful adjunct, but is neither sensitive nor specific on its own.



Myocardial Infarction

Untreated ischemia may lead to myocardial infarction shown here as an area of late gadolinium enhancement on cardiac MRI.

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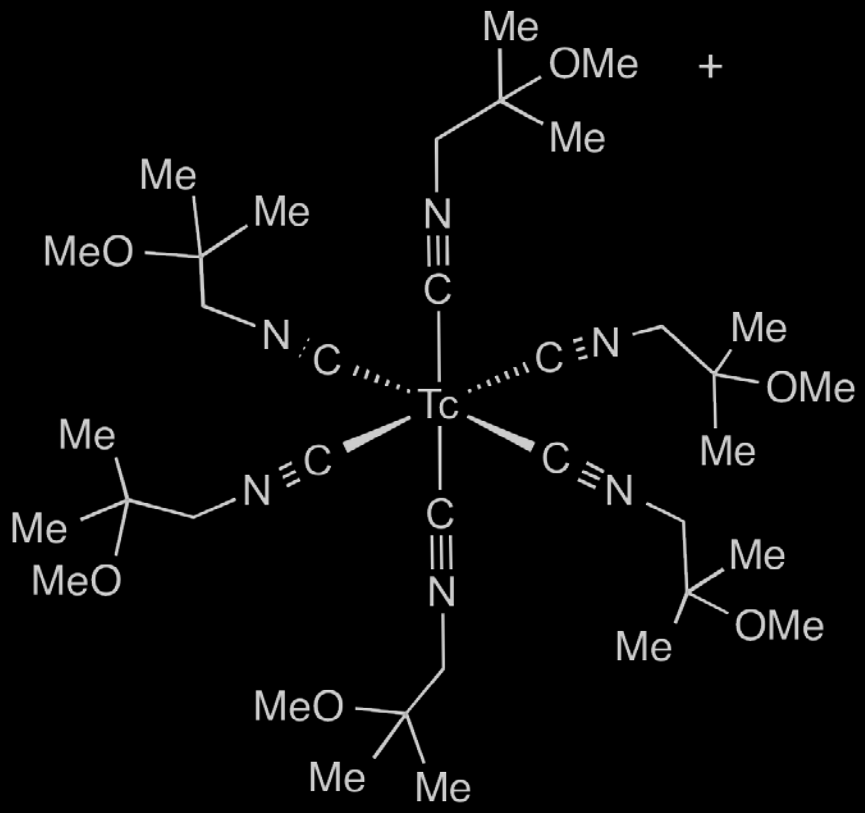
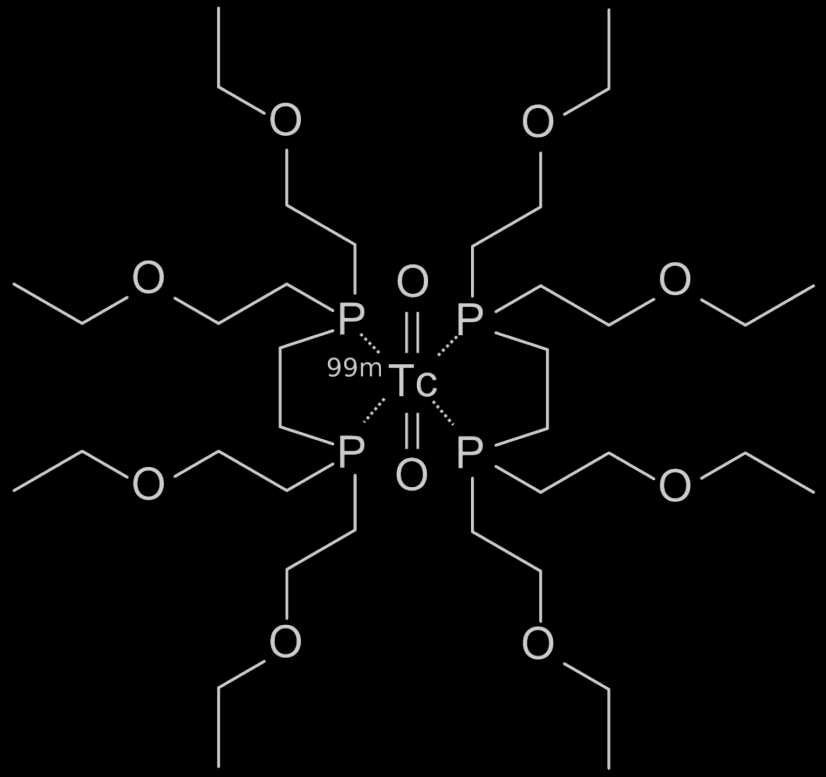
Farhad H and Murthy VL. Pharmacol Ther. 2013 140:121-32

Approaches to Stress Testing

Single Photon Perfusion Tracers



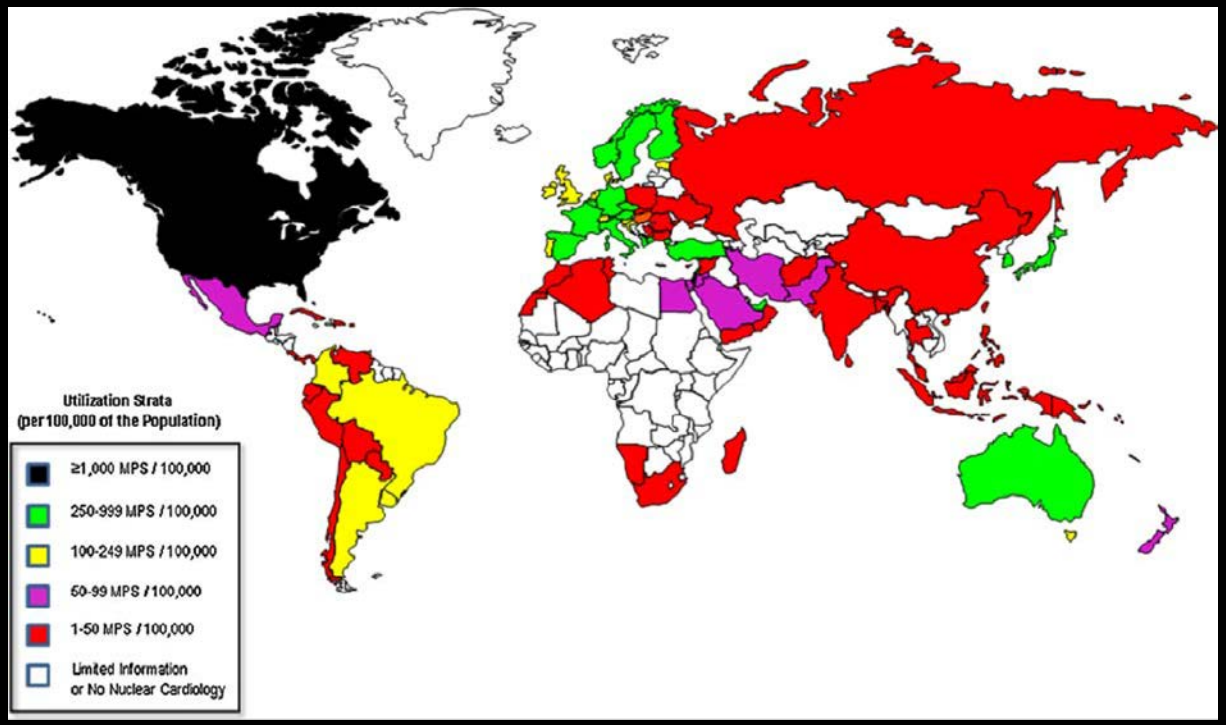
^{99m}Tc-Sestamibi



^{99m}Tc-Tetrofosmin

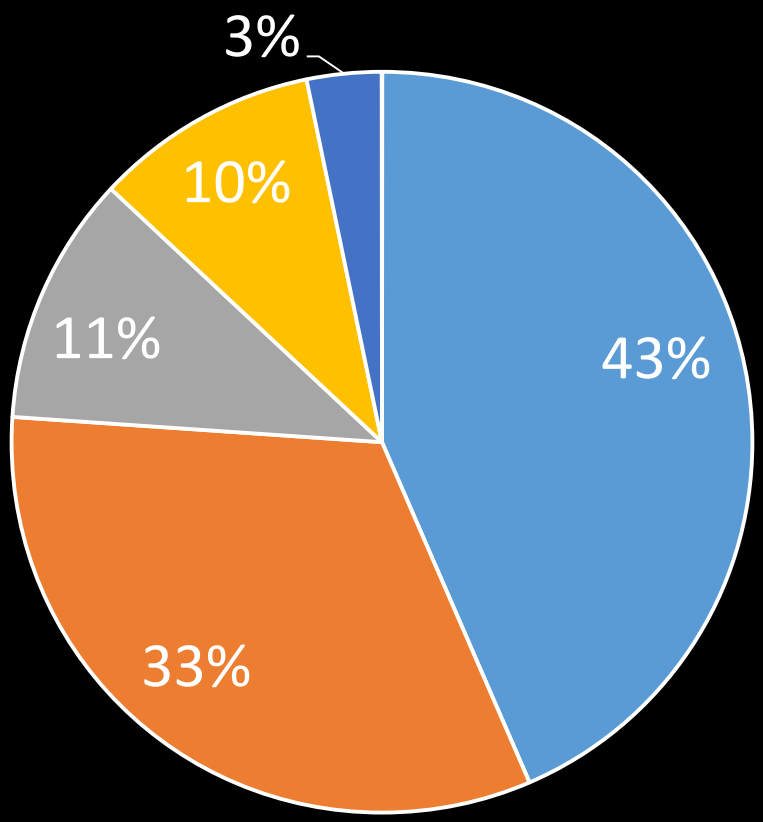
Utilization of SPECT Myocardial Perfusion Imaging

- 11 million MPI procedures annually in 2007
- More than 50% of US nuclear medicine procedures



Delbeke & Segall. J Nuc Med 2011 52(S2):245-85

Supply of Mo-99



Thomas & Maddahi. J Nucl Cardiol 2010 17:993-8

Strategies to Cope with Supply Disruption

- Avoid unnecessary testing
- Use alternative SPECT radiotracers – Thallium-201
- Reduce activity administered
  - Stress only/stress first imaging
  - Advanced reconstructions/cameras
- Alternative testing
  - PET
  - CT
  - Echo
  - MRI

2009 Supply Disruption… What to Do?

Myocardial Perfusion Imaging with ^{201}Tl*

Robert A. Pagnanelli, BSRT(R)(N), CNMT, NCT[1], and Danny A. Basso, CNMT, NCT, FSNMTS[2]

[1]*Duke University Hospital, Durham, North Carolina; and* [2]*Cardiac Imaging of Augusta, Augusta, Georgia*

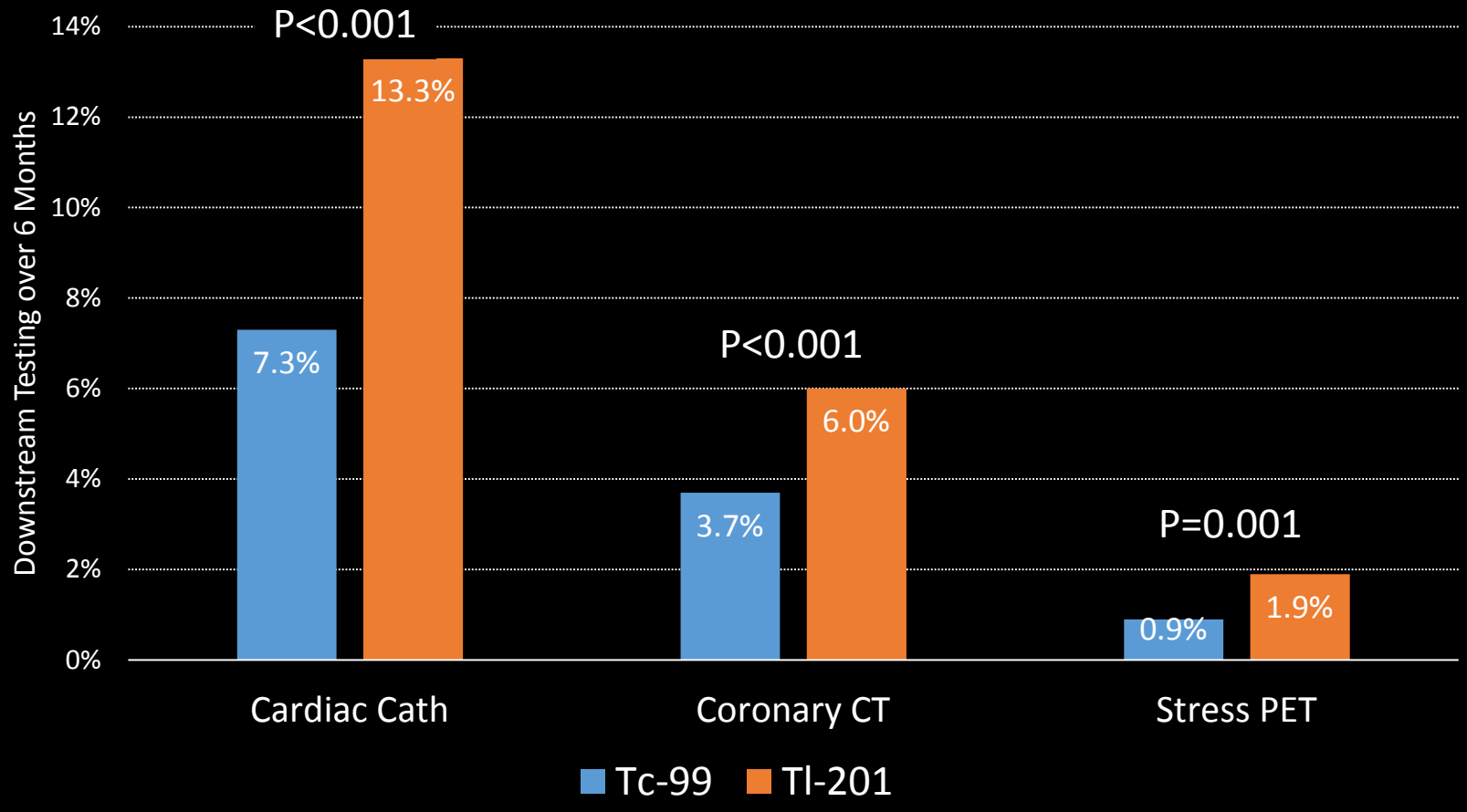
J Nucl Med Technol 2010; 38:1–3
DOI: 10.2967/jnmt.109.068593

have reverted to ^{201}Tl – the radiopl
replaced by ^{99}Tc^{m} agents 15–20 years ago. Tl is produced by cyclotron and so its availability is not affected by reactor shutdowns. The quality of ^{201}Tl images has improved owing to advances in gamma-camera design and performance, but there is a generation of nuclear medicine consultants who have never worked with ^{201}Tl. They will require training in the use of this radiopharmaceutical and its image interpretation.

Ottawa Heart Institute: Shortage Worsened Accuracy

Small, *et al*. Circ Cardiovasc Imaging 2013 6:683-91

Ottawa Heart Institute: Increased Downstream Testing

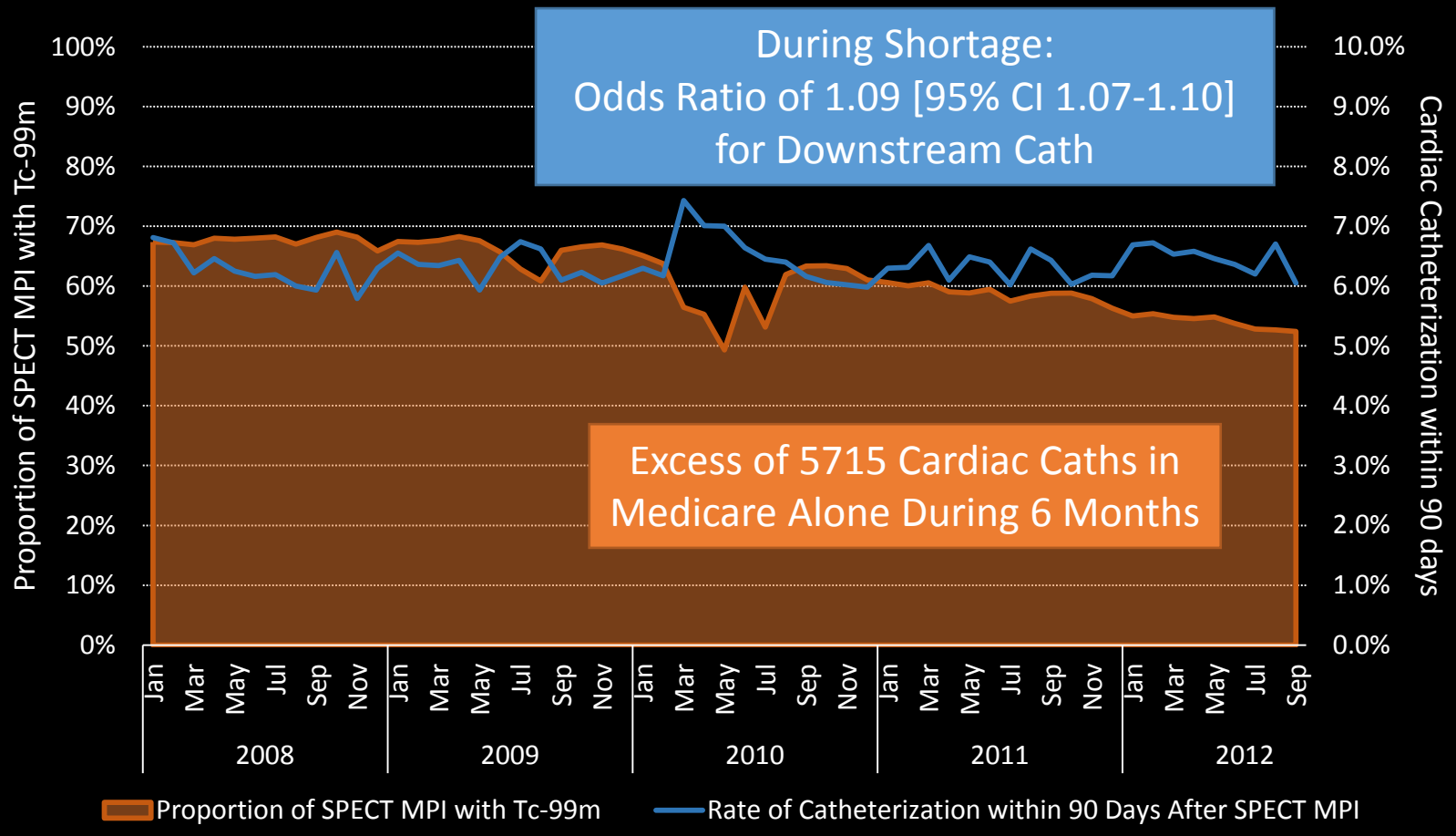


Small, *et al*. Circ Cardiovasc Imaging 2013 6:683-91

What Happened in the US?

- We studied data from Medicare claims 2008-2012
- 20% random sample of beneficiaries ≥65 years
- ~2 million stress tests with SPECT imaging
- Examined rates of downstream invasive coronary angiography within 90 days & alternative testing
- Compared March-August 2010 versus preceding and subsequent periods

Medicare Trends: Use of Tc-99 and Downstream Catheterization



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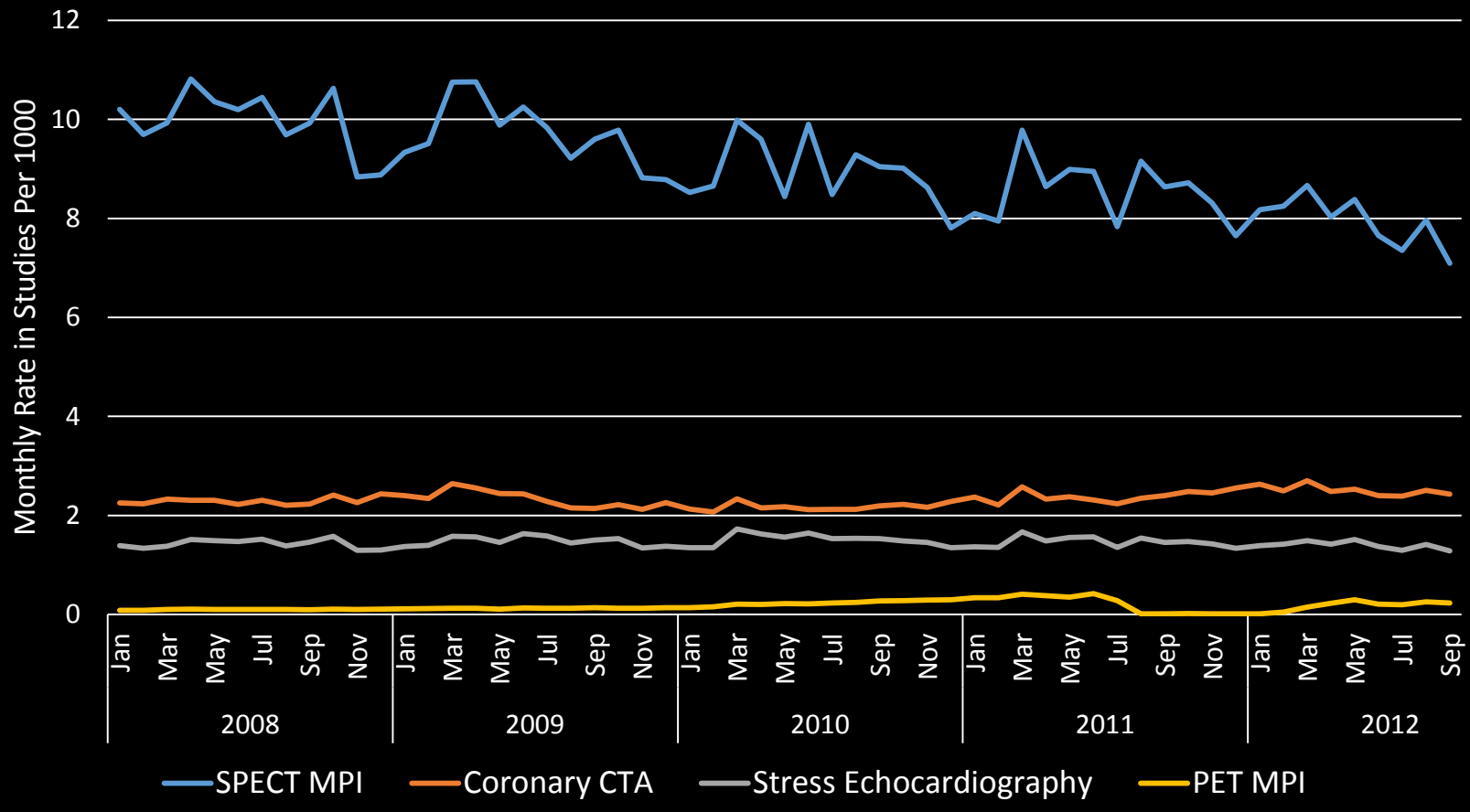
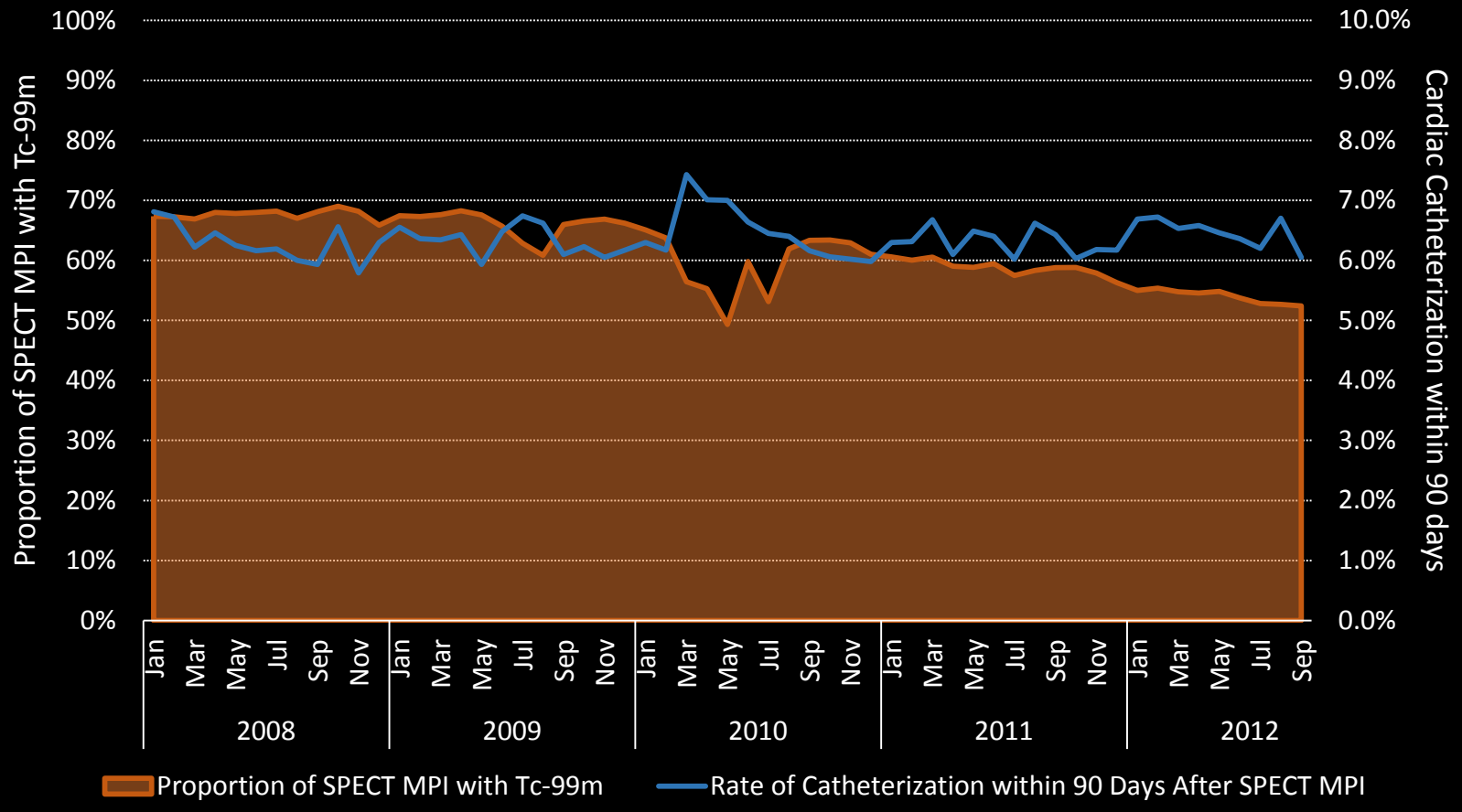
Medicare Trends: Alternative Testing



Concerning Pattern: Decreasing Rate of Technetium Use



Limitations

- Data are observational – causality is uncertain
- Medicare data may not generalize to private payers
- Formal analysis of costs, and projections for future shortages, not performed
  - Given average cost of cath likely to be $100s of millions/year

Implications

(c) Medical production license sunset
Effective 7 years after January 2, 2013, the Commission may not issue a license for the export of highly enriched uranium from the United States for the purposes of medical isotope production.

(g) Suspension of medical production license At any time after the restriction of export licenses provided for in subsection (c) becomes effective, if there is a critical shortage in the supply of molybdenum-99 available to satisfy the domestic United States medical isotope needs, the restriction of export licenses may be suspended for a period of no more than 12 months, if—

(1) the Secretary of Energy certifies to the Congress that the export of United States-origin highly enriched uranium for the purposes of medical isotope production is the only effective temporary means to increase the supply of molybdenum-99 necessary to meet United States medical isotope needs during that period; and

(2) the Congress enacts a Joint Resolution approving the temporary suspension of the restriction of export licenses.

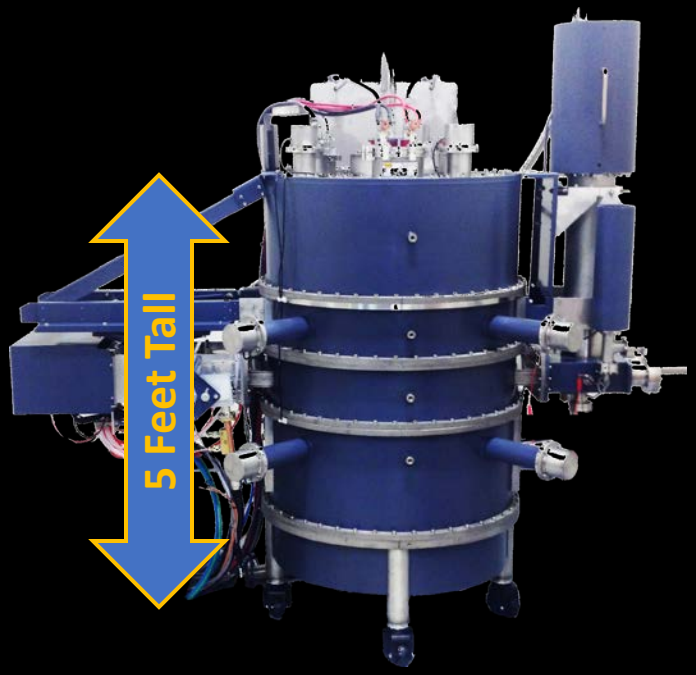
42 U.S. Code § 2160d

Issues Limiting Alternative Testing

- Stress echocardiography
  - Difficult to image patients with obesity or COPD
  - Requires skilled technologists
- CT coronary angiography
  - Not suitable for higher heart rates, renal disease, prior stents
  - May increase costs due to overestimation bias/lack of flow limitation assessment
- Stress MRI
  - Lack of widespread skillset
  - Complexity of managing complications in MR
  - Not suitable for renal disease, pacemakers and other devices
- Stress PET
  - High cost of cyclotron for production of N-13 ammonia or O-15 water
  - Limited supply and cost of Sr-82/Rb-82 generators

Possible Solution to the PET Tracer Problem: The Mini-Cyclotron

- 12 MeV, 10μA positive ion cyclotron
- 4.5 Tesla superconducting magnets enable compact form factor
- Standard power
- High temperature superconductor eliminates need for liquid nitrogen/helium
- Highly automated



ION-12^{SC} Validation Timeline at UMHS

Feb 1 2016	• Cyclotron Installed
Feb 16 2016	• Cyclotron Ramped to Full Field Strength
Feb 26 2016	• First Beam on Target
Feb 29 2016	• First ^{13}N-Ammonia Dose
Mar 7 2016	• Optimization Begins
Mar 23 2016	• 80 mCi Dose of ^{13}N-Ammonia
April 12 2016	• Full Clinical Workflow Simulation
Jul 11 2016	• Initial Cyclotron Magnet Tune
Aug 1 2016	• Final QA/QC Equipment Validation

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- Peter J.H. Scott, PhD

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SAVE THE DATE 7-9 May 2017, Vienna AUSTRIA

INTERNATIONAL CONFERENCE ON
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Call for abstracts & clinical cases
15 Sept – 21 Nov 2016

Early registration fee deadline
27 February 2017

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