The Illusions and Innovations of Heart Failure Therapy in Children

Paul F. Kantor MBBCh, MSc. FRCPC
Professor and Division Chief
Pediatric Cardiology

Children's Hospital LOS ANGELES®

USC University of Southern California

Disclosure

Relationship with Industry:

Novartis (consultant/ scientific advisory)

Off label use of medical therapy for children with heart failure

Objectives

- Understand the challenges we face in treating heart failure in children.
- Review some common illusions of success in heart failure treatment
- Highlight some innovative approaches and why they may prove effective.
- I will not discuss improvements in devices,or cardiac transplantation today.

Imagine the conversation….

Mother: Doctor what has happened to my child ?

You: He has heart failure, due to a problem with the heart muscle.

Mother: What is the actual problem with the heart muscle ?

You: We don't really know

Mother: Well, can you tell me what caused it ?

You Actually, it's hard to say…it may have been any one of a number of things, that he was born with or acquired. We don't really know.

Children's Hospital LOS ANGELES | USC University of Southern California

Imagine the conversation….

Mother: What do we do now ?

You : Well, we have a number of tests to run, and then we have a number of treatments for heart failure, which we can try.…

Mother: Do you know if they will help ?

You: No, we don't really know- maybe, but not for sure.

Mother: Well, will he get better ?

You: I'm afraid we don't know.

Children's Hospital LOS ANGELES | USC University of Southern California

Children's Hospital LOS ANGELES

USC University of Southern California

Challenges we face

- Disease presents at an advanced stage, with indistinct symptoms
- There are many causes and great variation in the underlying etiology.
- Medical treatments are largely unproven, in children: with uncertainty as to
  - Indications
  - Dosing
  - When to discern treament failure.

CASE SCENARIO 1

The case of EB

- Female age 4 days
- Unremarkable pregnancy. NSVD at 36 $^{6/7}$
- Weight 3.3 kg
- Apgars 9 / 9.
- Discharged from birthing hospital at 72 hrs after phototherapy

CASE SCENARIO 1

- Presents to ER, drowsy, not feeding well.
- BP 65/45, HR 150, Femoral pulses normal.
- Afebrile
- WBC 23,000/mm^3 , no left shift.
- Admitted to NICU for empirical antibiotics (rule out sepsis).
- Mother: Fever in the last week, upper respiratory symptoms.

ROOM	TIME	FAST TRACK	ACCOMPANIED BY	NOTIFICATION OF KIN	EMERGENCY PHYSICIAN
opth	1955	☐	Parents ☐ UNACCOMPANIED	☐ YES ☐ NO WHOM	[illegible signature]

TEMP.	PULSE	RESP.	B.P.	SAO2	O2 rate	PEAK FLOW	VA RT	VA LT	LEFT PUPIL SIZE / REACT	RIGHT PUPIL SIZE / REACT	WT.	HT.	LNMP	LAST TETANUS
36.4	168	40	/								3.2K			

MEDICATIONS ☒ NONE

MODE OF ADMISSION ☐ WALK ☐ W/C ☒ CARRIED ☐ STRETCHER ☐ AMBULANCE

ALLERGIES/ REACTIONS ☒ NONE

Born at 36wks ē 6 days vaginally. Jaundiced. Had phototherapy on Wednesday and Thursday for same. Today, decreased PO intake. Drowsy. Normal diapers. Air entry clear. Abd. soft. Bowel sounds present. Mucous membranes moist. Appears + jaundice. Rouses for short brief periods. Warm, dry. [signature]

ORDERS

☐ CBC ☐ TBIL ☐ CARDIAC ENZYMES
☐ ELEC. ☐ LIPASE ☐ ABG
☐ GLUCOSE ☐ ALT ☐ ECG
☐ UREA ☐ ALP ☐ U/A ☐ CXR
☐ CREAT ☐ LD ☐ PREG ☐ OC

Neonatal bili | ED15
glucose
CBC

Neonatal consult

TIME	HISTORY, FINDING, TREATMENT
20:00	Neonatal bili 364 — 288
	9/19
	• Photo Tx Wed - Thurs Expressed b-milk feeds 40-45 now 20-25ml q3h Regular BM's 4-5
	⊖ vomiting ⊖ fever G2
	Maternal fever — induced.
	O/E: alert fontanelle —
	⊖ hepat D,D2 —
	Resp
	21:35 Bili 366
	NICU →
	lethargic - Jaundice. Rea Cpre
	- admit to NICU. - as Team
	Hyperbili - suspect sepsis Elsharkawy

INSTRUCTION FOR FOLLOW UP

MEDICAL RECORDS EMERGENCY

Cardiology consult

- Fellow called 5pm next day (Saturday), because ectopic beats noted on monitor in the NICU.
- Patient examined.

  Afebrile.

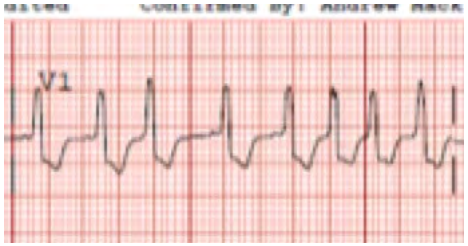
  BP 55/35mmHg

  SaO2 96% on RA.

  RR 50 HR 176

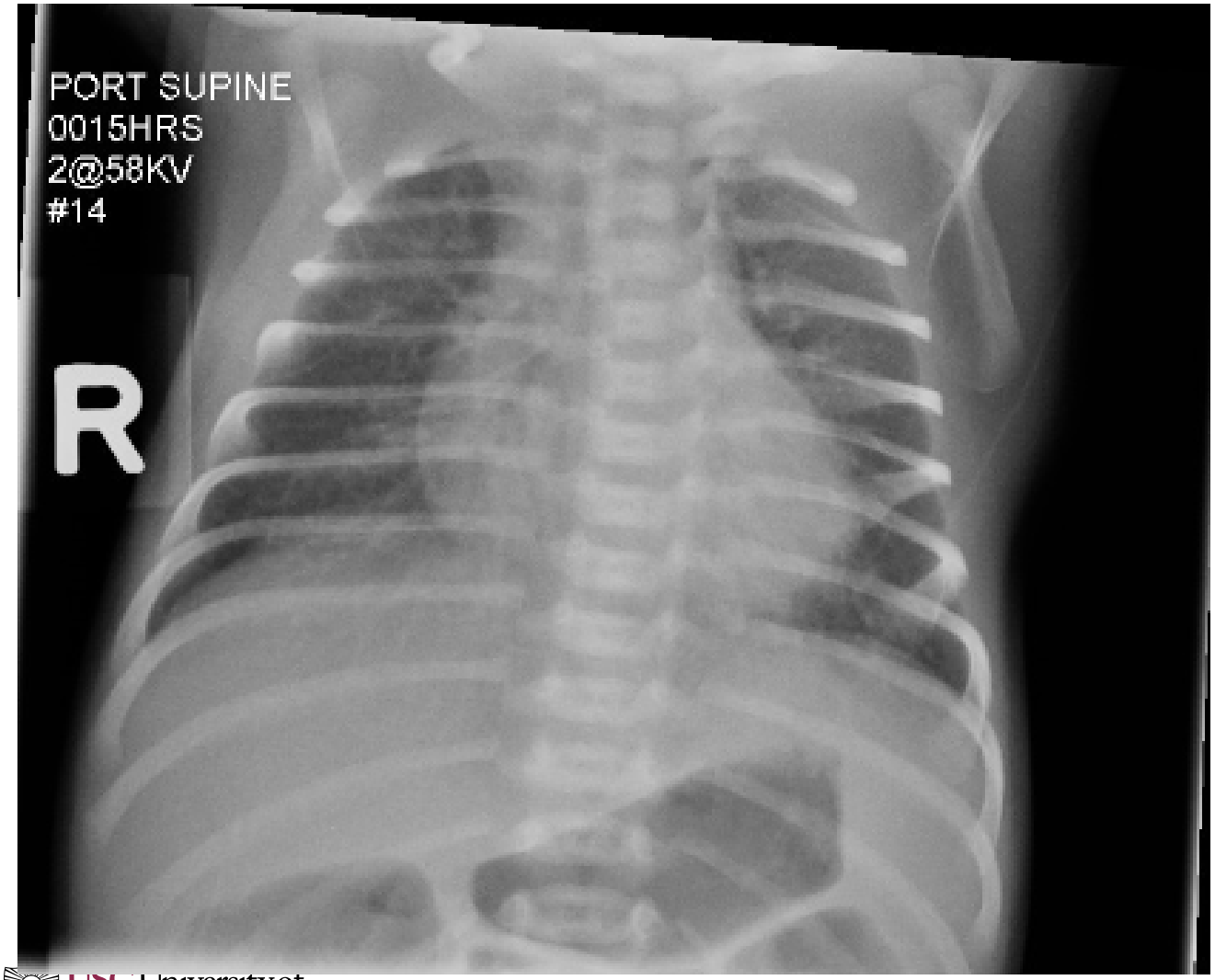
  ? Diminished pulses

"Occasional wide complex beats"

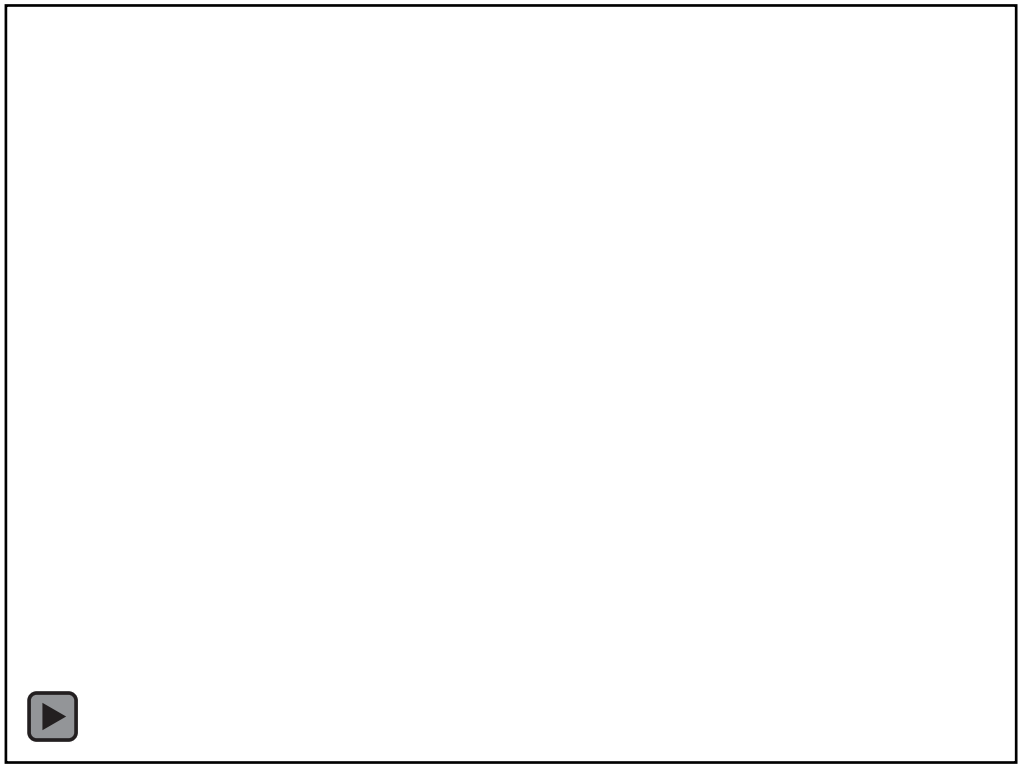


Children's Hospital LOS ANGELES | USC University of Southern California

Chest X-Ray



Diagnosis: Acute Fulminant Myocarditis



- Persistent lactate of 3-4
- Bradycardic at 8pm
- CPR for 30 minutes- cannulated onto ECMO
- Troponin T = 9.8

Treatment of Acute Fulminant Myocarditis.

In addition to supportive care

- Antiviral therapy ? (which agent)
- Steroids ?
- IVIG ?
- Azathioprine/Cyclosporine ?

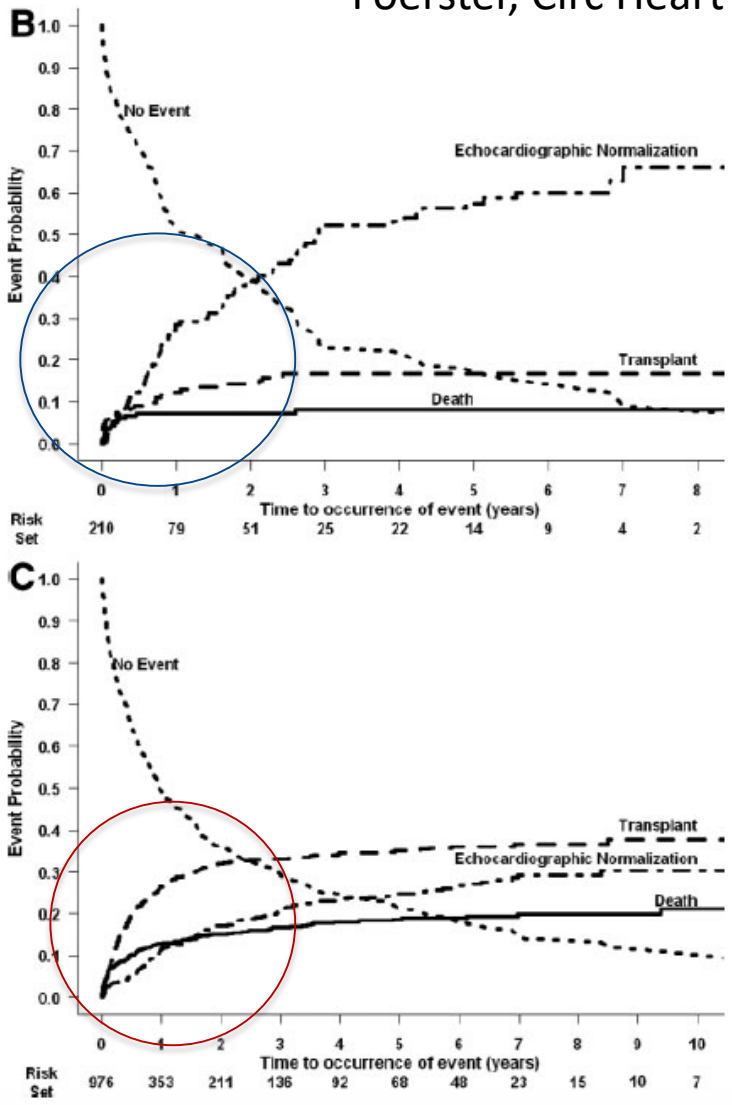
- The role of Biopsy:

Conventional Wisdom

Foerster, Circ Heart Fail. 2010;3:689-697

Myocarditis

Idiopathic dilated cardiomyopathy



Children's Hospital LOS ANGELES

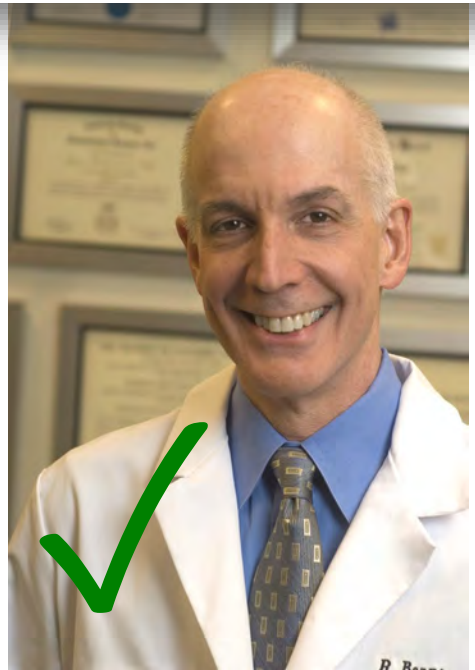
USC University of Southern California

Don’t worry- We have the best doctors !

Hair Transplant Pioneer Named "Best Doctor" in New York Magazine for 10th Consecutive Year

Like Share

Dr. Robert M. Bernstein, the only hair transplant physician to be included in New York Magazine's 2009 Best Doctors edition for ten consecutive years, was selected as one of the top 1,107 physicians by a peer-review survey of 12,000 New York City area medical professionals.



Children's Hospital LOS ANGELES

Illusion 1:

Knowing the possible outcome does not mean we understand the disease, or that we able to treat it effectively

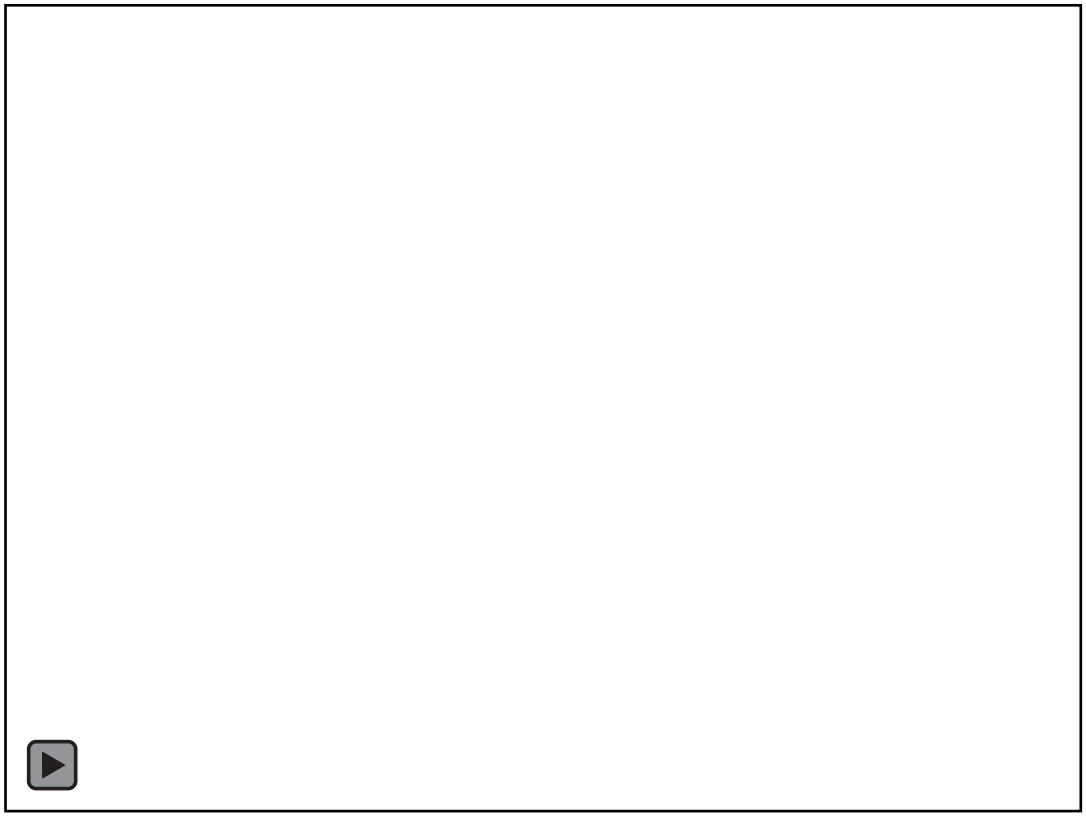
Enterovirus in blood

Extensive lateral wall infarction

Centrimag

Transplant

Died (Renal Failure)



Children's Hospital LOS ANGELES | USC University of Southern California

Illusion 2:

Immune supression (or immune modulation) is effective treatment

Table 6 Controlled immusuppression trials in myocarditis and dilated cardiomyopathy

Trial	Year	Type	Pts (*n*)	Diagnosis	Primary endpoint	Results	Author[ref]
Prednisone trial for DCM	1989	Randomized controlled trial (RCT): prednisone (PDN)	102	'Reactive' DCM ($n = 60$) 'Nonreactive DCM)' ($n = 42$)	Either higher LV ejection fraction (LVEF) at 3 months or lower LV end-diastolic dimension and better exercise tolerance	Favourable	Parrillo[176]
MTT	1995	RCT: PDN and cyclosporine or azathioprine	111	Acute biopsy-proven myocarditis (unknown aetiology)	LVEF at 6 months	Neutral	Mason[6]
Giant cell myocarditis treatment trial	2008	Prospective: PDN and cyclosporine	11	Giant cell myocarditis (autoimmune)	Survival at 1 year	Favourable	Cooper[99]
	2003	Prospective: PDN and azathioprine	41	Active myocarditis and chronic heart failure (aetiology known in retrospect)	LVEF at 1 year	Favourable in virus-negative aabs-positive autoimmune forms	Frustaci[100]
	2001	RCT: PDN and azathioprine	84	Inflammatory DCM (unknown aetiology, increased HLA espression on EMB)	LVEF at 3 months, sustained at 2 years	Favourable	Wojnicz[103]
TIMIC	2009	RCT: PDN and azathioprine	85	Inflammatory virus-negative DCM	LVEF at 6 months	Favourable	Frustaci[101]

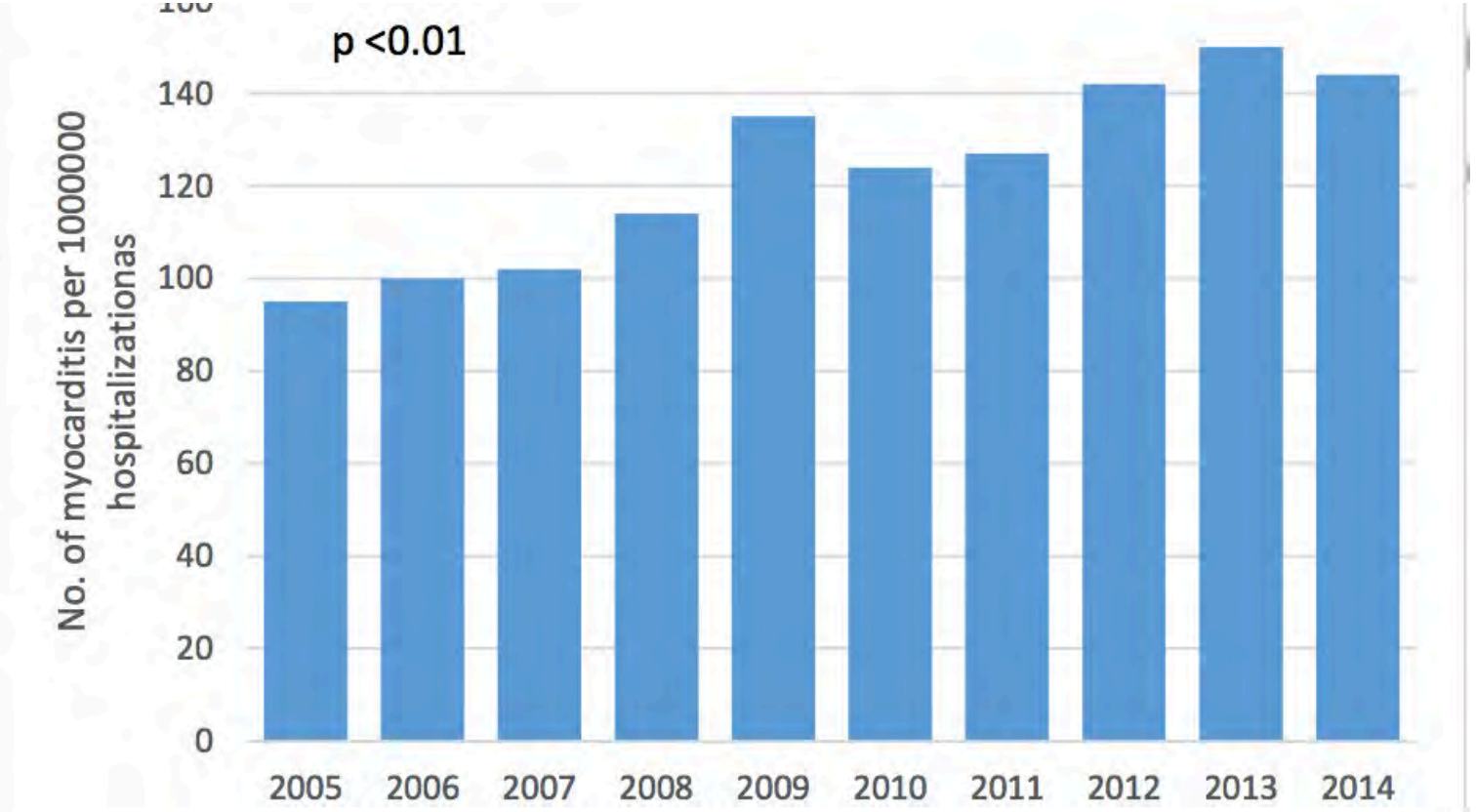
Children's Hospital LOS ANGELES | USC University of Southern California

What have we done ?

- Put out guidelines
- 2004
- 2013
- 2015

- Published textbooks
- Many many review articles
- Held symposia
- Funded grants
- Increased advocacy

We are making the diagnosis of myocarditis more often (not by biopsy)

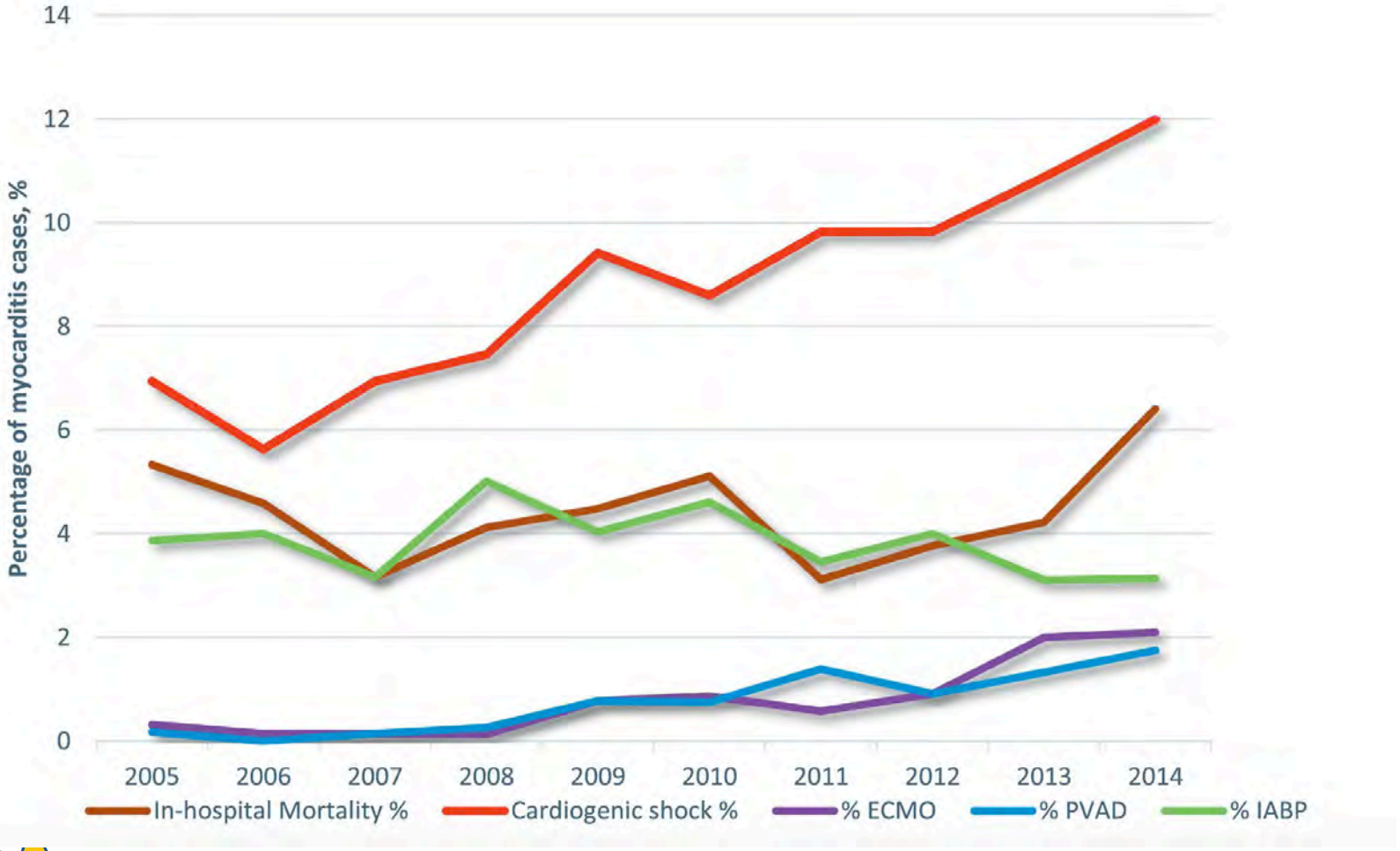


Trends in the Incidence of In-Hospital mortality, Cardiogenic Shock and Utilization of Mechanical Circulatory Support Devices in Myocarditis (Analysis of National Inpatient Sample Data, 2005-2014)

Children's Hospital LOS ANGELES | USC University of Southern California

J Card Fail. 2019 Apr 26

We are using mechanical support devices more commonly



Children's Hospital LOS ANGELES | USC University of Southern California

J Card Fail. 2019 Apr 26

Illusion 3:

Myocarditis is entirely an acquired cardiomyopathy

	Gene Status		
	Positive n=49	**Negative n=117**	**VUS n=113**
Myocarditis			
Yes n=32	4 (13%)	15 (47%)	13 (41%)
No n= 247	45 (18%)	102 (41%)	100 (41%)

Myocarditis did not exclude the presence of a gene mutation.

Children's Hospital LOS ANGELES | USC University of Southern California

Innovation

Myocarditis may be a coincident event in a patient with an underlying cardiomyopathy – related gene anomaly

Autosomal Recessive Cardiomyopathy Presenting as Acute Myocarditis

Serkan Belkaya, PhD,[a] Amy R. Kontorovich, MD, PhD,[b,c] Minji Byun, PhD,[a] Sonia Mulero-Navarro, PhD,[b] Fanny Bajolle, MD, PhD,[d] Aurelie Cobat, MD, PhD,[e] Rebecca Josowitz, MD, PhD,[b] Yuval Itan, PhD,[a] Raphaelle Quint, MSc,[a] Lazaro Lorenzo, MSc,[e] Soraya Boucherit, MD,[e,f] Cecile Stoven, MD,[g] Sylvie Di Filippo, MD, PhD,[h] Laurent Abel, MD, PhD,[a,e,f] Shen-Ying Zhang, MD, PhD,[a,e,f] Damien Bonnet, MD, PhD,[d] Bruce D. Gelb, MD,[b] Jean-Laurent Casanova, MD, PhD[a,e,f,i,j]

J Am Coll Cardiol. 2017 Apr 4; 69(13): 1653–1665.

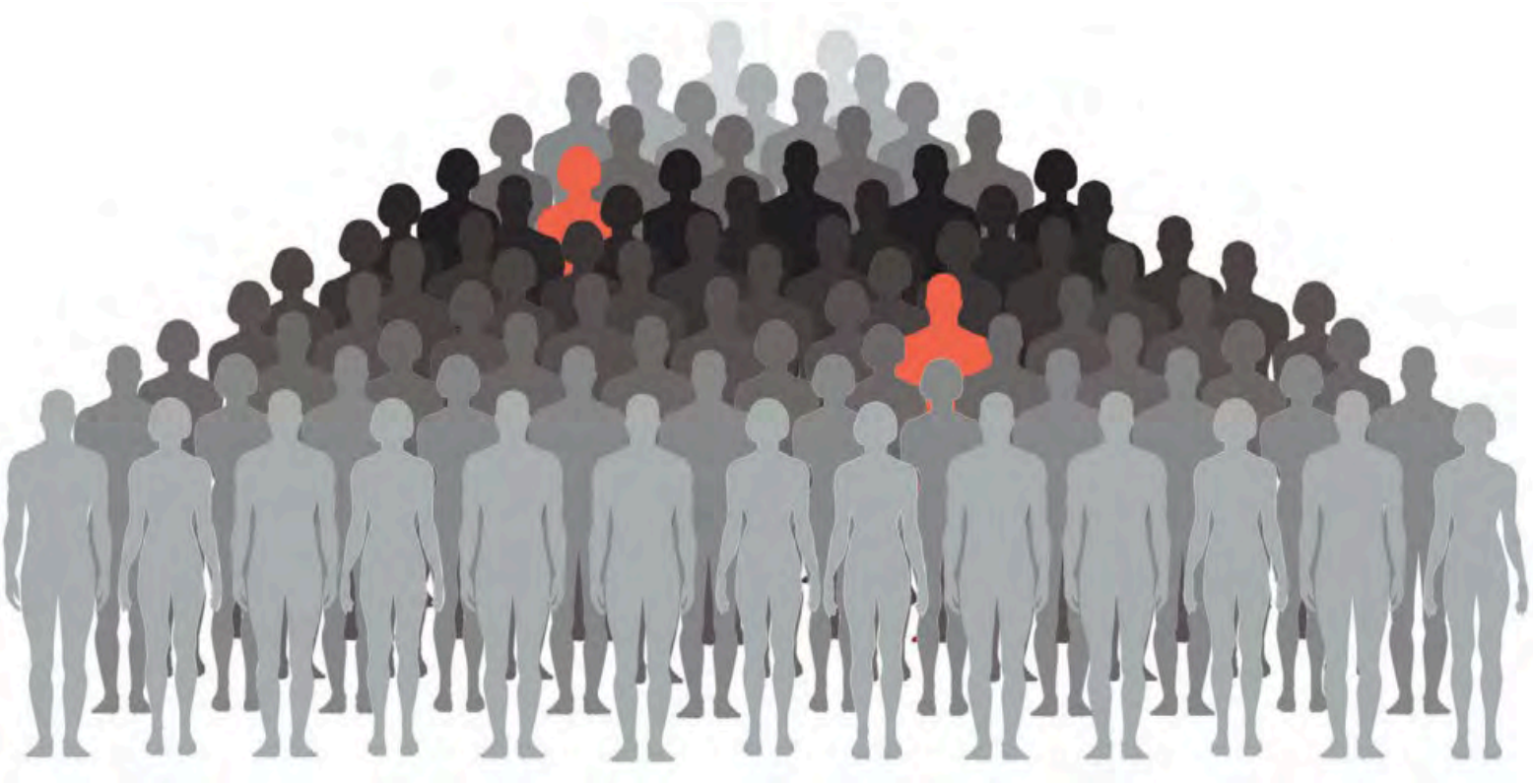
Children's Hospital LOS ANGELES | USC University of Southern California

Autosomal Recessive Cardiomyopathy Presenting as Acute Myocarditis

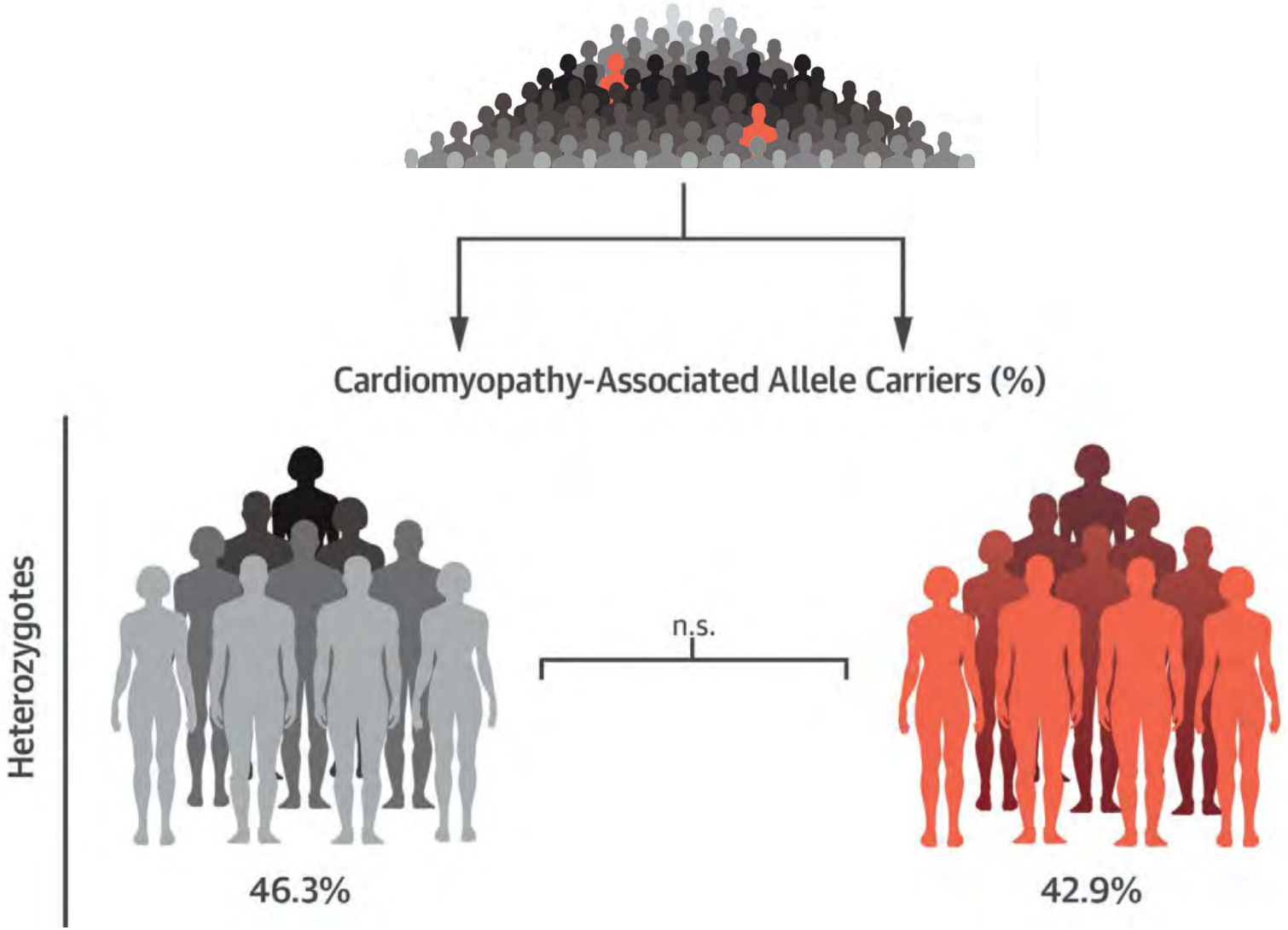
Serkan Belkaya, PhD,[a] Amy R. Kontorovich, MD, PhD,[b,c] Minji Byun, PhD,[a] Sonia Mulero-Navarro, PhD,[b] Fanny Bajolle, MD, PhD,[d] Aurelie Cobat, MD, PhD,[e] Rebecca Josowitz, MD, PhD,[b] Yuval Itan, PhD,[a] Raphaelle Quint, MSc,[a] Lazaro Lorenzo, MSc,[e] Soraya Boucherit, MD,[e,f] Cecile Stoven, MD,[g] Sylvie Di Filippo, MD, PhD,[h] Laurent Abel, MD, PhD,[a,e,f] Shen-Ying Zhang, MD, PhD,[a,e,f] Damien Bonnet, MD, PhD,[d] Bruce D. Gelb, MD,[b] Jean-Laurent Casanova, MD, PhD[a,e,f,i,j]

- whole-exome sequencing of 42 unrelated children with acute myocarditis some with proven viral causes.

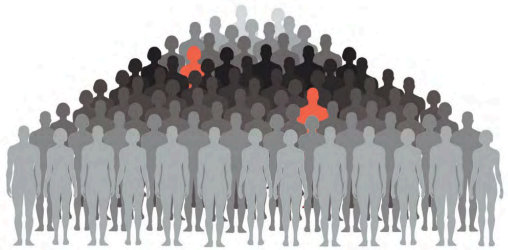
Population of individuals who carry a gene variant in a cardiomyopathy associated gene

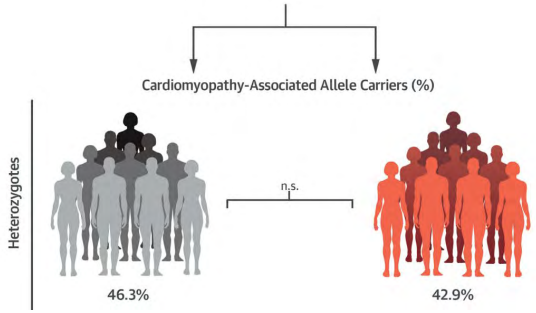


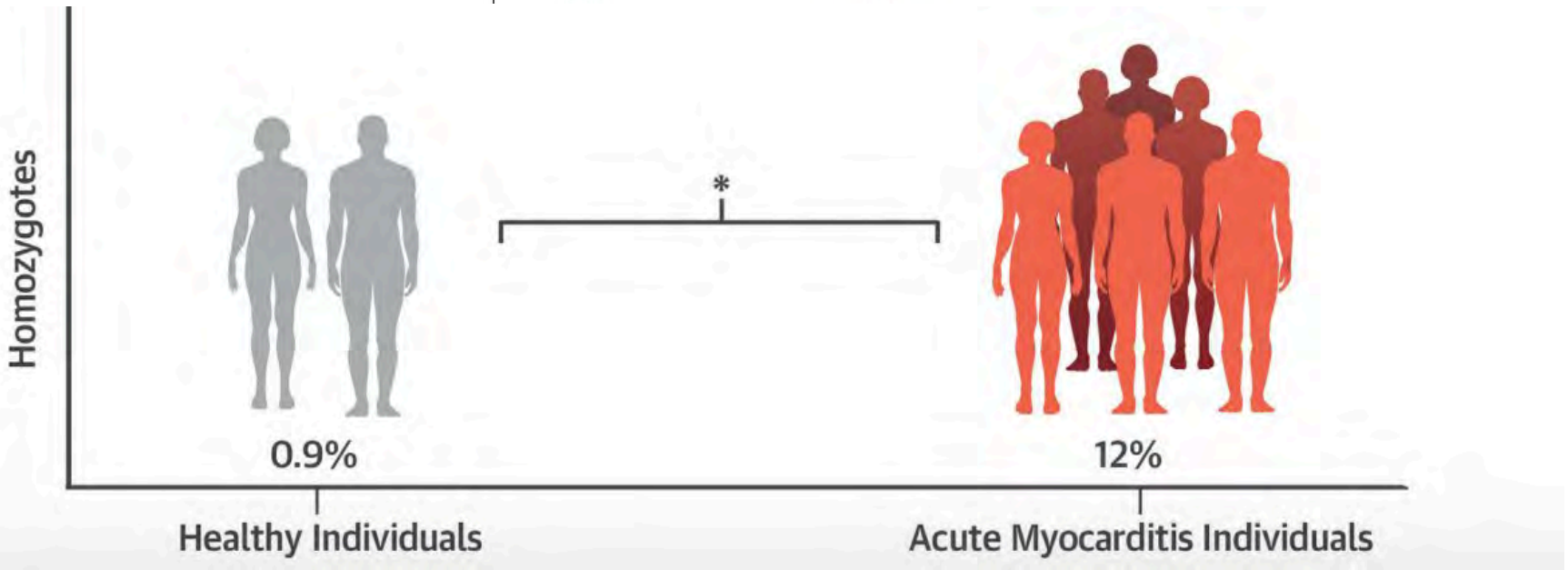
Children's Hospital LOS ANGELES | USC University of Southern California



Children's Hospital LOS ANGELES | USC University of Southern California







Hospital LOS ANGELES | University of Southern California

Findings

- No enrichment of TLR or IL-α/ß genes
- No enrichment of heterozygous rare variants
- Massive enrichment of homozygous rare variants, and some compound heterozygous rare variants

What does this mean ?

- Many people get a virus, but vanishingly few get myocarditis.
- Still fewer, will die from the disease
- We can likely predict which those people will be by having exome sequence information available
- What can we do about it ?

Case 2

14 year old with increasing SOB on effort.

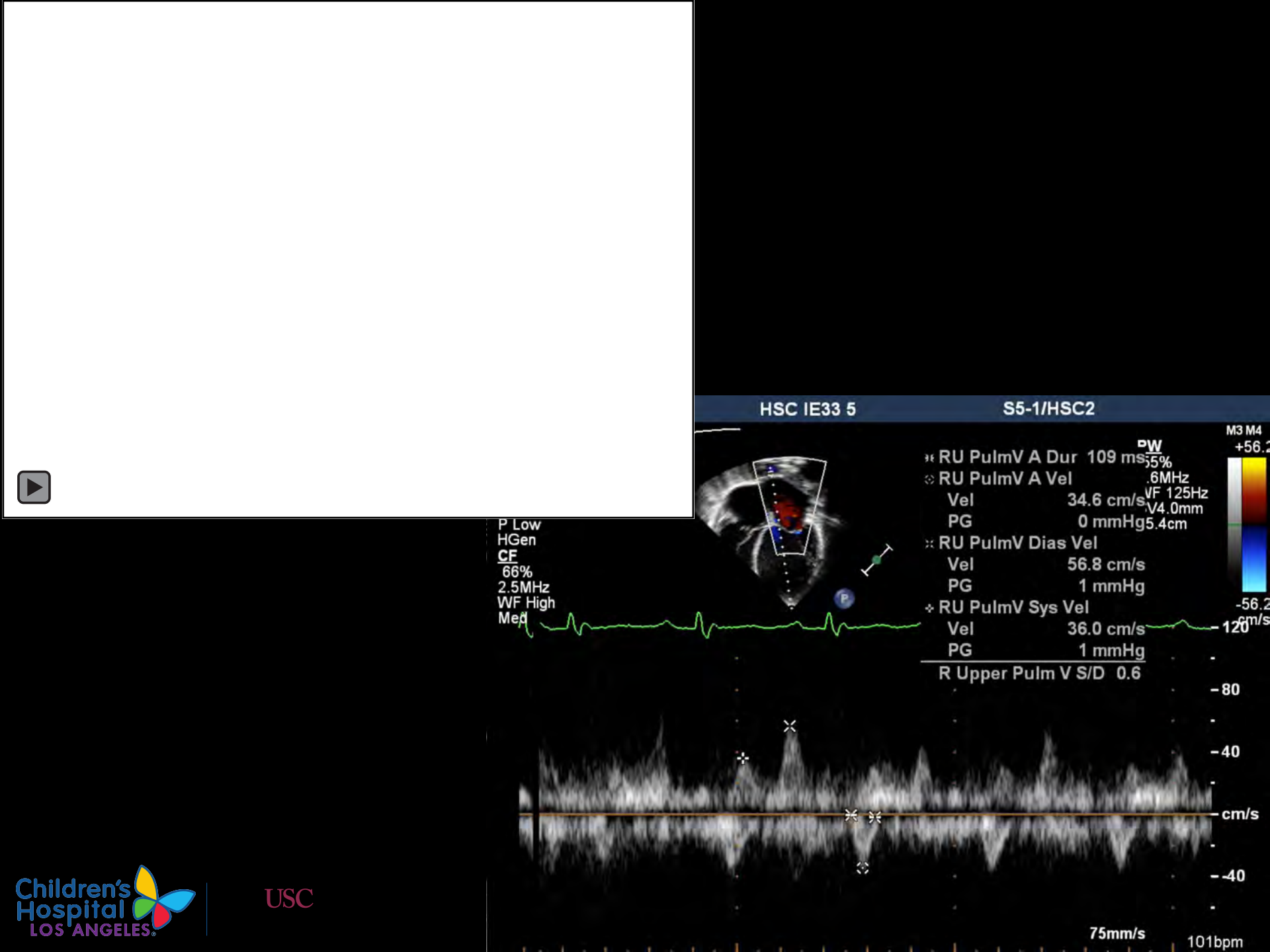
- Only child, South Asian descent.
- No sports, “works in mushrooms”

- Fatigue and weakness

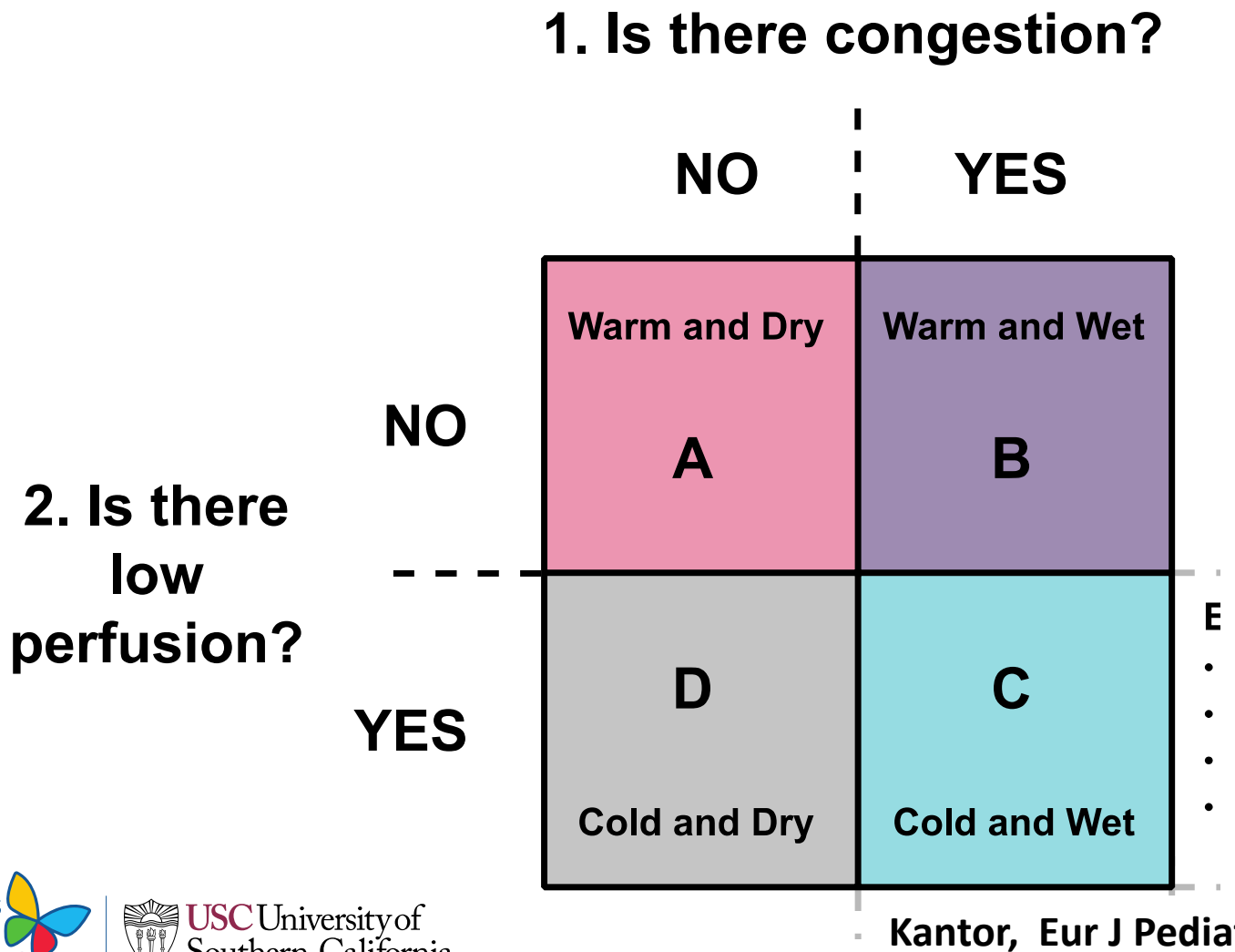
Background

- No Family History. Non-consanguineous
- No toxin exposure (mushrooms ?)

- Examination: mild dyspnea at rest
- No muscle weakness/ wasting.
- BP 80/55, HR 115. Pulses reduced. Liver 3cm. JVP 6 cm. Gallop rhythm. Soft blowing systolic murmur


HSC IE33 5
S5-1/HSC2
RU PulmV A Dur 109 ms
RU PulmV A Vel
Vel 34.6 cm/s
PG 0 mmHg
RU PulmV Dias Vel
Vel 56.8 cm/s
PG 1 mmHg
RU PulmV Sys Vel
Vel 36.0 cm/s
PG 1 mmHg
R Upper Pulm V S/D 0.6
P Low
HGen
CF
66%
2.5MHz
WF High
Med
PW
55%
6MHz
VF 125Hz
V4.0mm
5.4cm
M3 M4
+56.2
-56.2
cm/s
120
80
40
cm/s
-40
75mm/s
101bpm

Patient assessment in acute decompensated heart failure

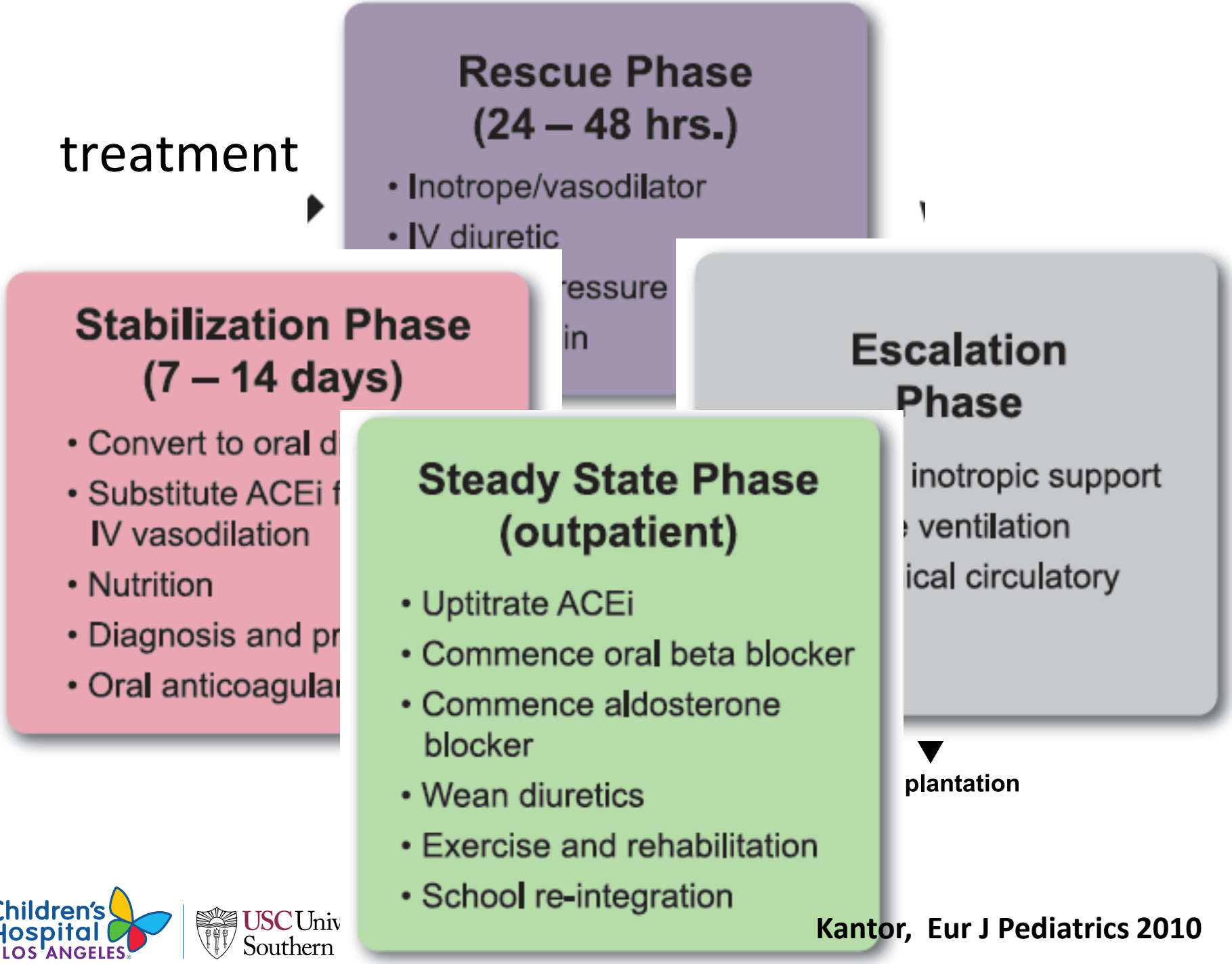


Kantor, Eur J Pediatrics 2010

Children's Hospital LOS ANGELES

USC University of Southern California

treatment



Kantor, Eur J Pediatrics 2010

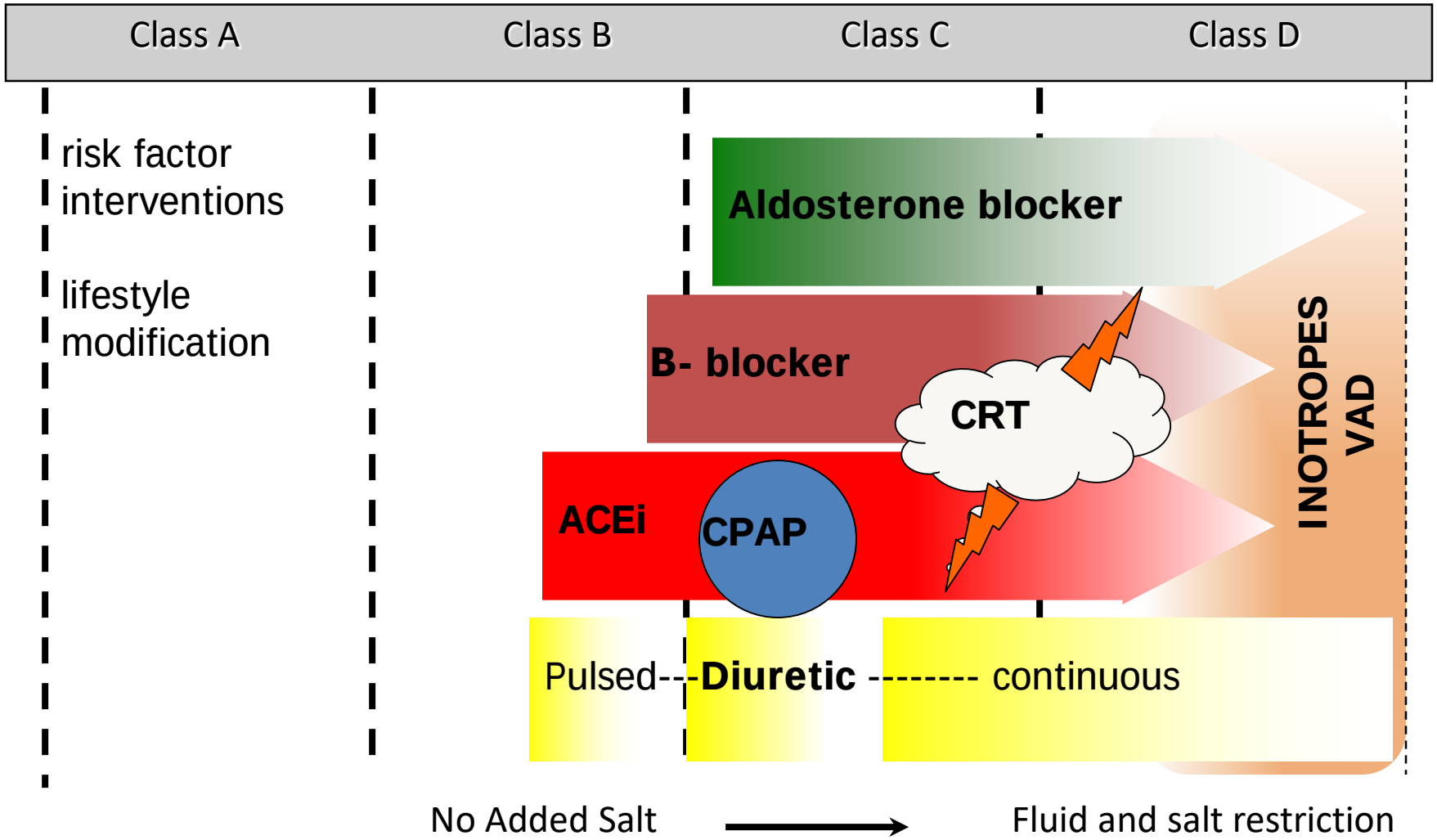
Table 3. Tests relevant to the evaluation of Cardiomyopathy.

Test	Important findings to note
ECG	Primary rhythm abnormality, evidence of ischemia, pre-excitation. Evidence of hypertrophy, T wave changes.
Echocardiogram	
- 2D	Morphologic pattern of cardiomyopathy.
- tissue Doppler	Assessment of diastolic function.
- colour Doppler, strain analysis	Evidence of mechanical dyssynchrony.
Urine	
- urine chemistry	Ketones (metabolic disorder), pH, concentrating defect.
- amino acids	Screening to exclude primary or secondary aminoacidurias.
- organic acids	Screening to exclude organic acidurias. Also abnormal in disorders of pyruvate and lactate metabolism, multiple carboxylase deficiency. 3-OH methyl glutaconic acid excretion in Barth syndrome.
- oligosaccharide screen	Disorders of carbohydrate metabolism.
- mucopolysaccharide screen	Screening to exclude genetic mucopolysaccharidoses (type I, II, III) mucolipoidosis.

Kantor, Eur J Pediatrics 2010

Blood chemistry	
- albumin	Nutritional status, protein losing states.
- amino acids	Exclusion of inborn errors of amino acid metabolism (e.g. oxalosis, alkaptonuria, homocysteinuria).
- ammonia	Presence of a hepatic disease, urea cycle abnormality or inborn error of metabolism.
- BNP or NT-proBNP	Evaluation of degree of heart failure severity.
- carnitine (total and free) including acylcarnitines	Screening for carnitine deficiency, fatty acid oxidation disorders (carnitine palmitoyl transferase IIt deficiency, long chain and very long chain acyl dehydrogenase deficiencies).
- calcium	Abnormal in vitamin D deficiency, renal disease.
- cholesterol	Abnormal in dyslipidemias, Wolman disease, Barth syndrome.
- copper, caeruloplasmin	Abnormal in Wilson's disease.
- glucose	Various acute metabolic disorders with abnormal hepatic function or carbohydrate metabolism.
- lactate	Mitochondrial disease, abnormal fatty acid oxidation, severe heart failure.
- liver enzymes	Abnormal in acute hepatic congestion, inborn errors of metabolism. Prothrombin time is useful function indicator.
- magnesium	Abnormal in renal tubular disease, relevant to cardiac rhythm management.
- pyruvate	Pyruvate dehydrogenase deficiency, mitochondrial OXPHOS abnormalities.
- selenium	Keshan disease, other trace element deficiency states.
- thyroid function tests	Hyperthyroidism, or hypothyroidism.
- venous pH	Determine anion gap in metabolic acidosis states.
- vitamin assays (D, B1, C)	Abnormal in Vitamin D deficiency (congenital or nutritional), Beri-beri, nutritional deficiencies.
Autoimmune disease markers	
- ANA	Screening test for systemic lupus (SLE).
- ASOT	Post streptococcal rneumatic heart disease.
- CRP	Marker of inflammatory dises, severity of cardiac faliure.
- ENA (Anti Ro/La)	Specific test for SLE.
- ESR	Indicates inflammatory disorder/infection.

Systolic Heart Failure general guide



Children's Hospital LOS ANGELES | USC University of Southern California

Polypharmacy in Heart Failure

1700s	1930s	1980s	1990s	2000s	2010s
Digoxin	Digoxin	Digoxin	Digoxin	Diuretic	Diuretic
	Diuretic	Diuretic	Diuretic	ACEi/ARB	ACEi/ARB
		ACEi	ACEi	Cardiosel. BB	Cardiosel. BB
		Nonsel. BB	MRA	MRA	MRA
			Nonsel. BB	Digoxin	Digoxin
			Nitrates	Nitro-dilator	Nitro-dilator
					K_{fi} inhibit.
					Secubitril

How is this interpreted ? 4 y/o Fontan

DISCHARGE MEDICATIONS:
1. Lansoprazole 15 mg G-tube b.i.d.
2. Azithromycin 100 mg G-tube b.i.d. on Monday, Wednesday, and Fridays.
3. Qvar 100 mcg/puffs MDI 2 puffs through an inhaler b.i.d.
4. PEG 3350 at 7 grams G-tube daily.
5. Vitamin D 2000 units G-tube daily.
6. Acetazolamide 100 mg G-tube b.i.d.
7. Amiloride 8 mg G-tube b.i.d.
8. Ethacrynic acid 25 mg G-tube b.i.d. with ethacrynic acid 10 mg IV every Tuesday and Friday.
9. Metolazone 4 mg G-tube daily.
10. Granisetron 3 mg G-tube b.i.d.
11. KCl 5 mmol per 100 mL of feed.
12. Sodium chloride 4 mmol per 100 mL of feed.
13. Aldactone 20 mg G-tube b.i.d.
14. Tadalafil 20 mg G-tube daily.
15. Metoclopramide 2 mg G-tube t.i.d.
16. Pedialyte 5 mL G-tube daily.

DISCHARGE RESPIRATORY MANAGEMENT:
BiPAP 130 over 6 cm of water overnight with 1.5 L/minute low-flow nasal cannula oxygen during the day.

DISCHARGE NUTRITION MANAGEMENT:
Feeds: 50% Pediatric complete over 50% Novoste source renal 2 kcal/oz formula with 2 scoops of Duocal and 5 mmol per 100 mL of KCL and 4 mmol per 100 mL of NACL to the daily formula volume.

4 Diuretics,
9 separate dose administrations per day

23 med administrations daily (not including feed supplements & anticoagulation).

No ACEi , Digoxin or Beta blocker therapy.

Problems with polypharmacy

Medication Initiation Burden Required to Comply With Heart Failure Guideline Recommendations and Hospital Quality Measures

Additive therapy is guideline driven

Allen L, Circulation 2015; 132:1347

"47% needed to start at least 1 NEW HF-related medication by discharge,
24% needed to start >1 medication,
14% needed to start ≥3 medications to be in compliance with HF guidelines"

Guidelines, polypharmacy, and drug-drug interactions in patients with multimorbidity

A cascade of failure

Open-ended guidelines drive drug interactions

Marengoni A, BMJ 11 March 2015

"How should doctors manage patients with multiple diseases to help to prevent a cascade of problems that starts with inadequate guidelines and moves through polypharmacy to an increased risk of drug-drug interactions?"

Recent Trials and Tribulations (AHF)

Drug	Trial	Result	Implication
Levosimendan (Ca^{2+} sensitizer)	REVIVE I and II (placebo) SURVIVE (Dobutamine)	No change in mortality ↑Arrhythmias Improved GAS	Not FDA approved. Some empirical use in Europe.
Nesiritide (natriuretuc analogue)	ASCEND-HF (placebo)	No change in symptoms, renal function readmission/ death	Limited role in Acute HF
Rolofylline (Adenosine A2 antagonist)	PROTECT (placebo)	No change in readmission renal failure	Not being marketed
Serelaxin (Human recombinant Relaxin -2 (pleiotropic effects)	RELAX –HF RELAX-2HF	Mildly improved Dyspnea. CV Death ?readmission same	EMA/FDA not fans. Pediatric Study suspended

PARADIGM-HF (2014) Valsartan-Sacubitril vs. Enalapril

N=8442

Background:

Age 69 (WM)

NYHA II

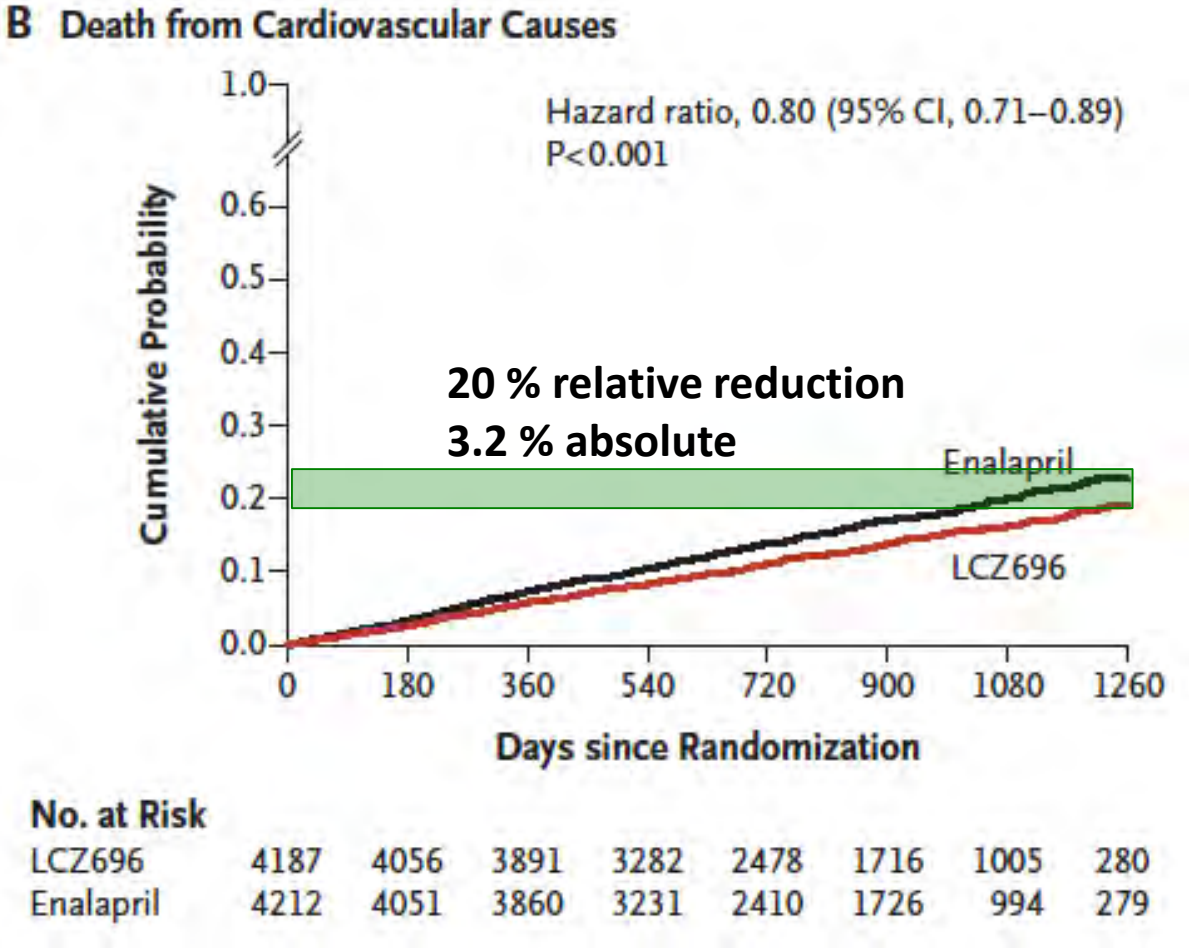
EF: 27 %

Therapy

Digoxin: 26 %

B-blockers: 93%

MRA: 54 %



Number needed to treat is 31

Children's Hospital LOS ANGELES | USC University of Southern California

How effective is all of this ?

Survival Without Cardiac Transplantation Among Children With Dilated Cardiomyopathy

Rakesh K. Singh, MD, MS,[a] Charles E. Canter, MD,[b] Ling Shi, PhD,[c] Steven D. Colan, MD,[d] Debra A. Dodd, MD,[e] Melanie D. Everitt, MD,[f] Daphne T. Hsu, MD,[g] John L. Jefferies, MD, MPH,[h] Paul F. Kantor, MBBCh,[i] Elfriede Pahl, MD,[j] Joseph W. Rossano, MD, MS,[k] Jeffrey A. Towbin, MD,[l] James D. Wilkinson, MD, MPH,[m] Steven E. Lipshultz, MD,[m] for the Pediatric Cardiomyopathy Registry Investigators

J Am Coll Cardiol 2017;70:2663–73

Children's Hospital LOS ANGELES | USC University of Southern California

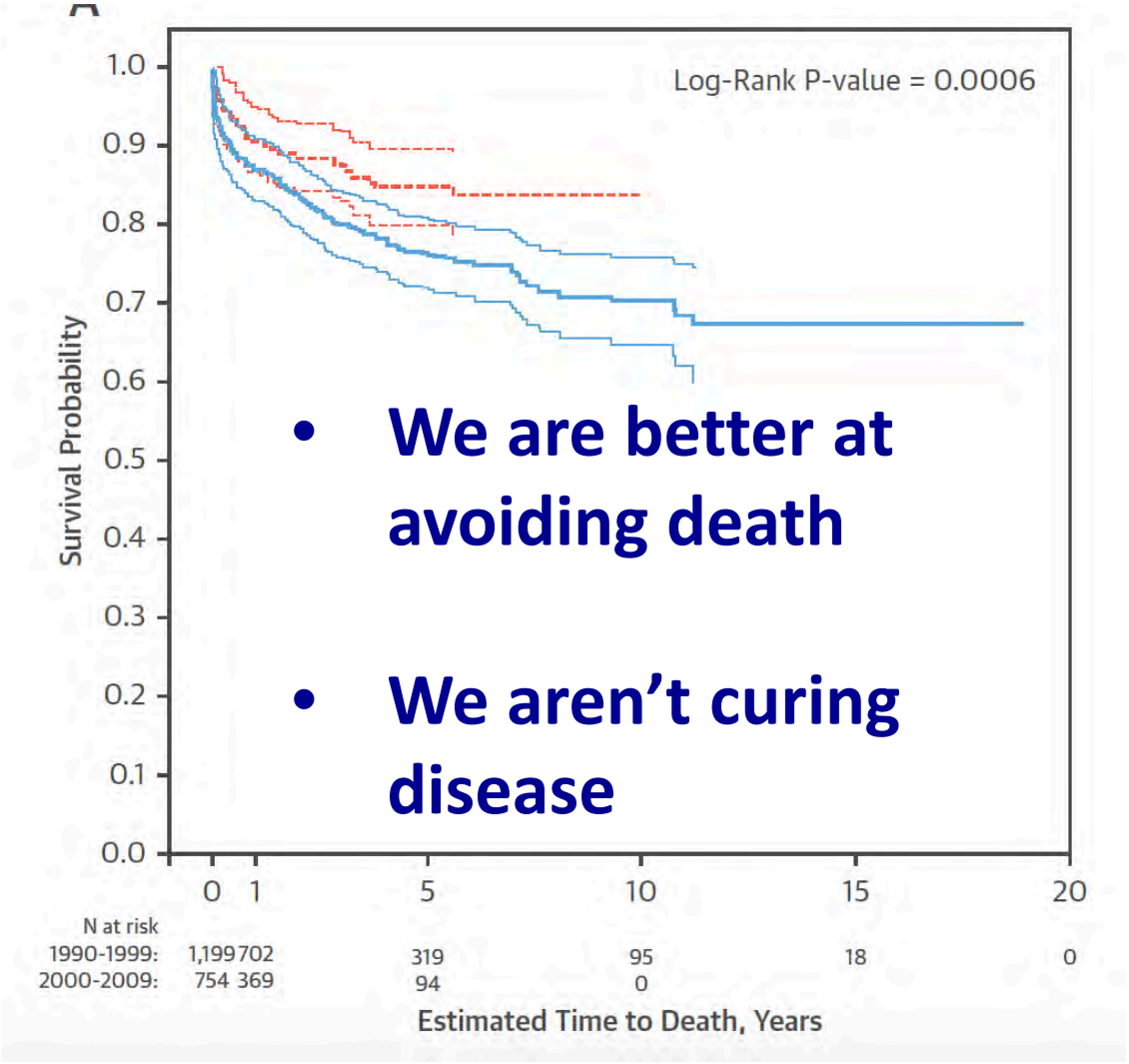
Illusion 4:

More medications = better outcomes

No difference in Transplant Rate

Difference in Mortality at 3 years

1990-1999 – 12%
2000-2009- 8%



- **We are better at avoiding death**
- **We aren't curing disease**

J Am Coll Cardiol 2017;70:2663–73

Children's Hospital LOS ANGELES | USC University of Southern California

Back to our patient

- Underwent a Transplant.
- Discharged home successfully.
- Still fatigued on effort with decreased effort tolerance.

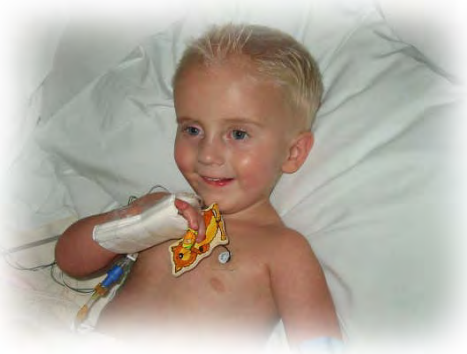
Illusion 5:

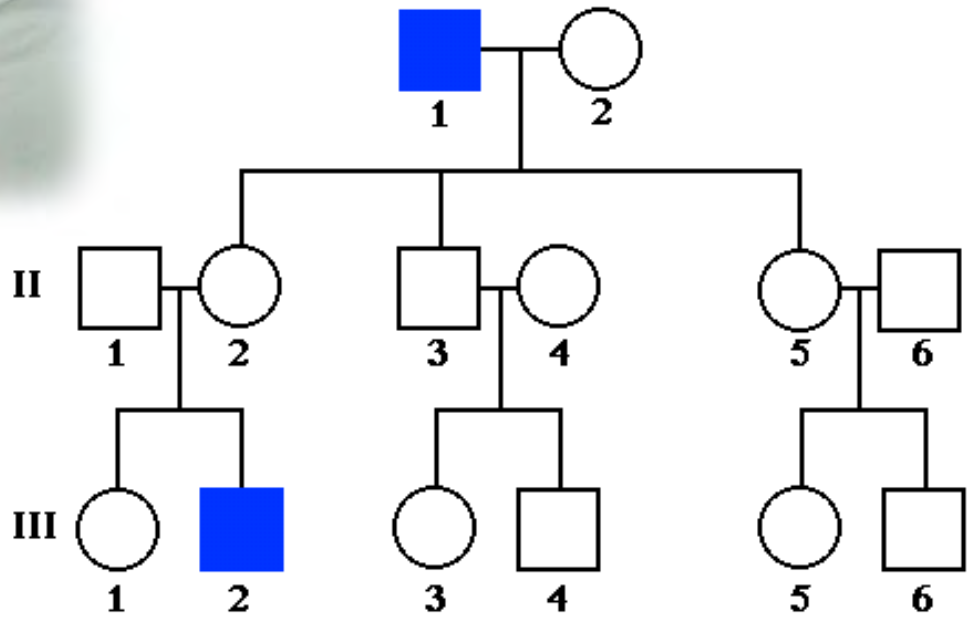
Transplantation cures the disease

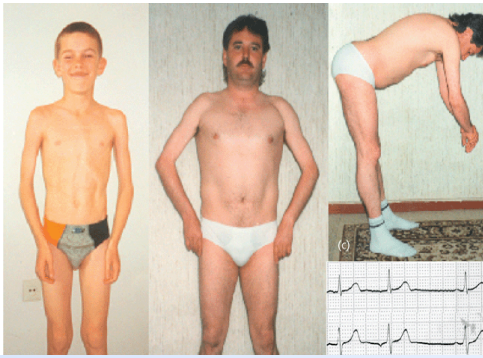
- CPK: 1200.
- Dystrophin Gene deletion= Becker Muscular dystrophy

What innovations are occuring in this area ?

Children's Hospital LOS ANGELES | Southern California







X-LINKED

-Barth syndrome, mitochondriopathies

-Duchenne's, Becker's

- Emery Dreifuss

Becker Muscular Dystrophy

- "Milder" form of Duchenne's MD

- Variable presentation/clinical course
  - **Milder skeletal muscle disease**
  - **Only 10% are wheel chair bound by age 40 and none in childhood years**

Cardiac (DCM)

- Onset usually by 30 years
- 70% develop DCM
- Heart failure most common cause of death

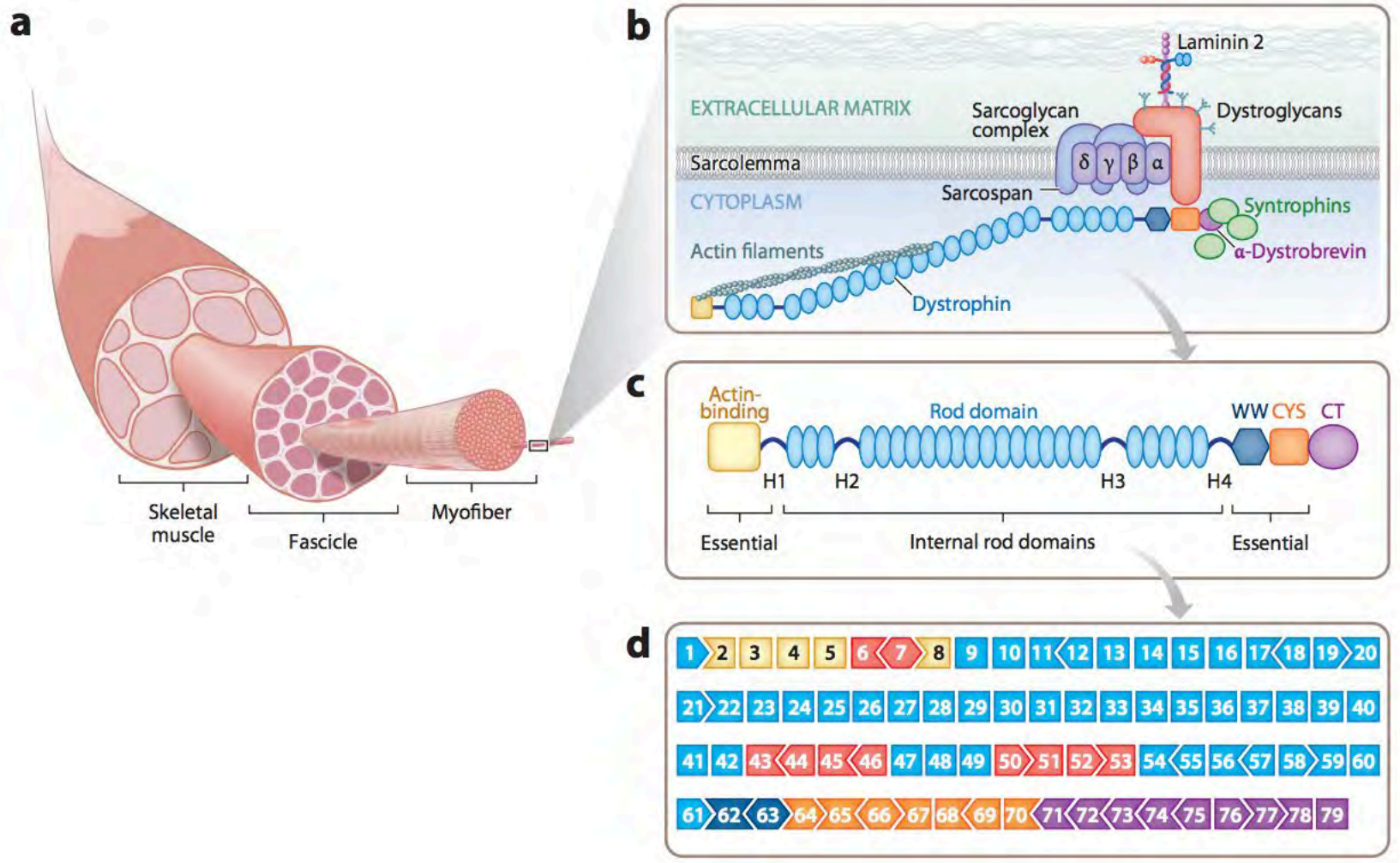
Cardiac surveillance and Rx in BMD

- First echo/ECG after 5 years
- q2 years till 10 years
- Annually thereafter (and within 12 mos prior to major surgery)

- cMRI not routinely recommended

- Treat LV dysfunction with ACE-I, beta blocker
- No pre-emptive therapy

Molecular basis of Duchenne-Becker

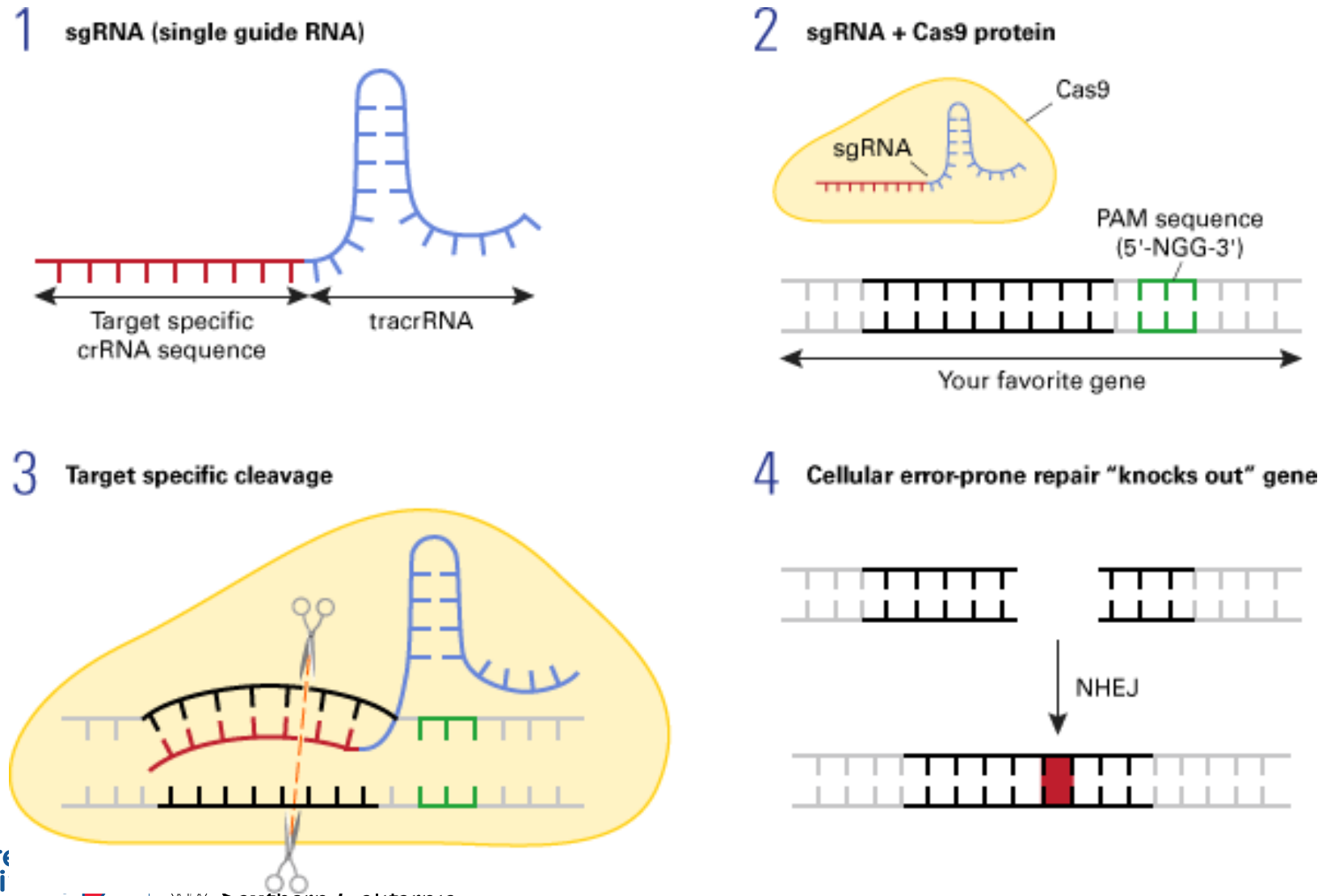


Innovation

Modifying gene expression by replacing cells, skipping exons, or editing the mutation

CAP-1002	**Cardiosphere derived cells (immunomodulatory, anti fibrotic) Improved exercise and respiratory capacity.**	**HOPE1 - intracoronary injection HOPE2 - IV injection in boys and young men**
Eteplirsen	**Anti-sense oligonucleotide (exon 51 skipping)**	**FDA approved**
Golodirsen	**Anti-sense oligonucleotide (exon 53 skipping)**	**Phase 1, 2**
Gene editing	**CRISPr/Cas9 dystrophin gene editing**	**Mouse models**

Gene correction

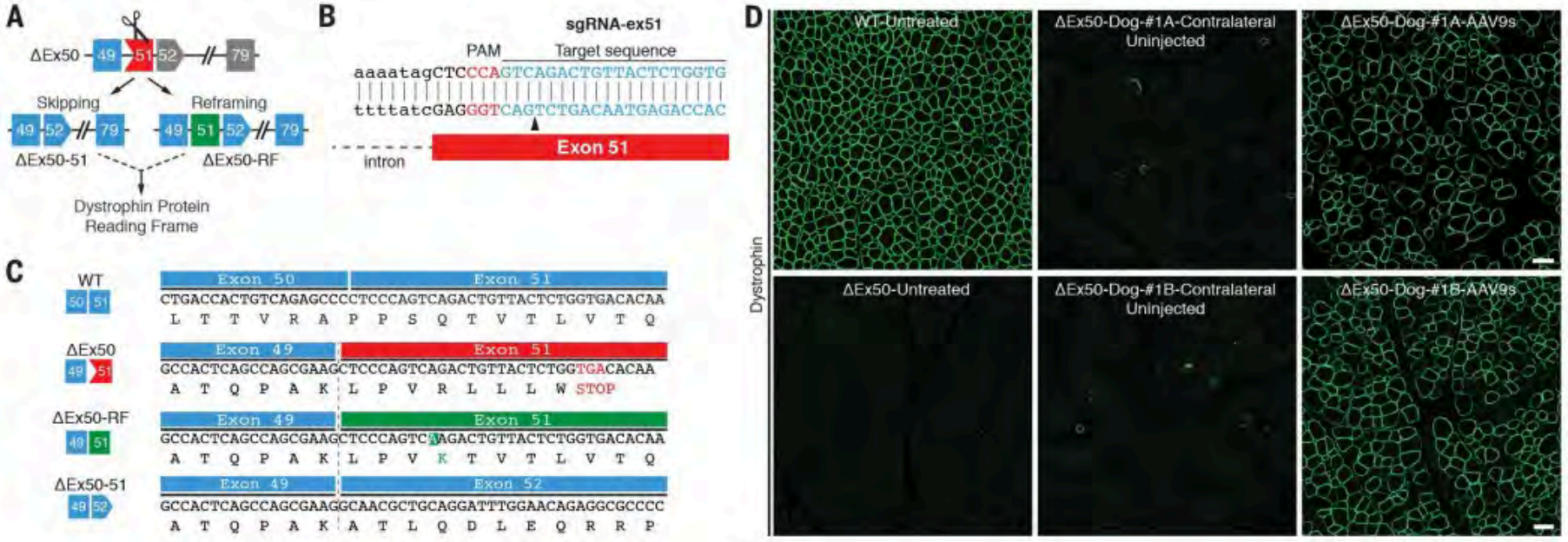


Children's Hospital LOS ANGELES | USC University of Southern California

Gene editing restores dystrophin expression in a canine model of Duchenne muscular dystrophy

Leonela Amoasii[1,2], John C. W. Hildyard[3], Hui Li[1], Efrain Sanchez-Ortiz[1], Alex Mireault[1], Daniel Caballero[1], Rachel Harron[3], Thaleia-Rengina Stathopoulou[4], Claire Massey[3], John M. Shelton[5], Rhonda Bassel-Duby[1], Richard J. Piercy[3], Eric N. Olson[1]*

Children's Hospital LOS ANGELES | USC University of Southern California



Amoasii et al., Science 362, 86–91 (2018)

Children's Hospital LOS ANGELES | USC University of Southern California

Conclusion

Illusion

There are many treatments for Heart Failure in Children that constitute the appearance of effectiveness, but in reality fall short

Innovation

Innovation is occurring and will almost certainly lead to molecular therapy for DCM

Challenge At this stage we have no basis for that treatment in more than 2/3 of cases. The cause remains indeterminate.

Children's Hospital LOS ANGELES®

USC University of Southern California

Thank You