Pregnancy in Women with a Fontan Circulation – is there an effect on maternal outcomes post partum?

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Presenting on behalf of my co-authors: Ms Emily Moroney, Ms Diana Zannino and Prof Yves d'Udekem

The Royal Melbourne Hospital THE UNIVERSITY OF MELBOURNE Murdoch Childrens Research Institute
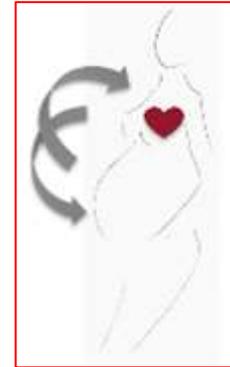
Background – 1
Pregnancy is a challenge for the heart

- Pregnancy is a challenge for the normal heart
  - Global longitudinal strain (GLS)
    - Decline by term (Zentner, Preg HPT 2012; (Cong, CVS US 2015)
    - Lower post partum (w/in 48 h) cf non pregnant controls; lower still in historical PPCM (Khan, PLOS One 2016)

- Delayed 'pregnancy effect' in other cardiac conditions
  - Systemic RV - TGA with an atrial baffle (Zentner, HLC 2015)
  - Congenital AS (Tzemos, Am HJ 2009)
  - DCM (Grewal, JACC 2009)

- Later cardiac events more common if cardiac event occurred in pregnancy (mix diagnoses, 5 y f/up) (Balint, Heart 2010)

Background – 2
Pregnancy is a <u>bigger</u> challenge for the Fontan circulation

- Fontan physiology:
  - Abnormal single ventricle mechanics and ventricular filling
  - Reduced capacity to increase CO
  - Reduced HR reserve
  - Venous HPT
  - Mild hypoxia
  - Reduced exercise capacity
    - lung volumes
    - reduced skeletal muscle mass and aerobic capacity

(Whitehead, Circ 2007; Veldtman 2017; Gewillig Heart 2016; Senzaki, JACC 2006; Cordina, Heart 2013; Ohuchi, J Cardiol 2016; Navaratnam, Am J Cardiol 2016; Goldstein, Am J Cardiol 2010; De Haas, US Obstet Gynecol 2017; Macklin, BJOG 1997; Turquetto, Ped Cardiol 2017)

- Known increased incidence of maternal and fetal complications in ***pregnancy***

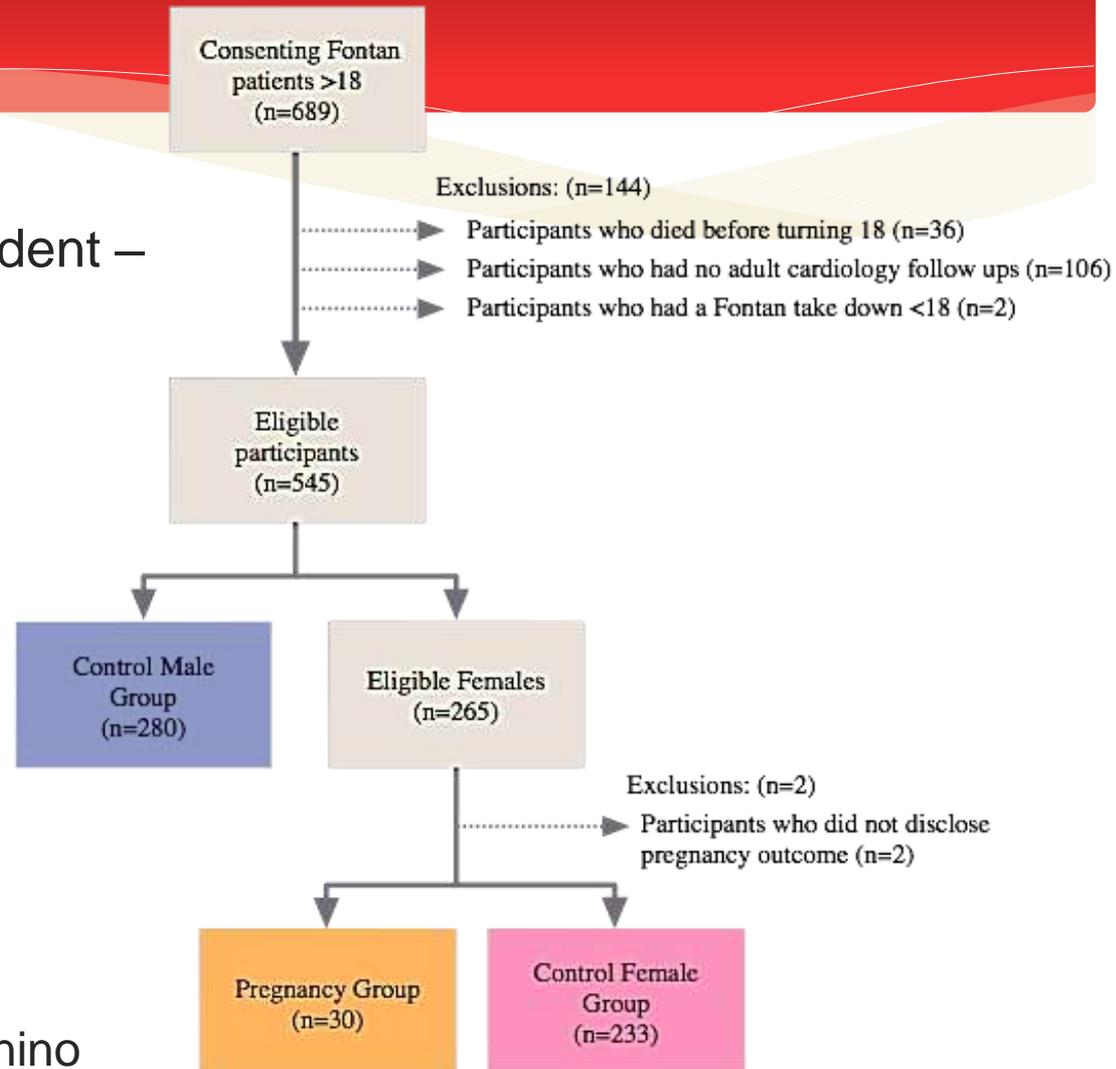(Ropero, RoosHesselink, Girnius, Zentner, Swan, Brown, Ladouceur, Baskar, Veldtman, Systematic Review – under review)

Plasma volume expansion

Pregnancy is a physiologically dynamic state

Dilated veins and reduced vein flow velocity

Baby and placenta – ultimate end organ requiring adequate perfusion

Post partum?
Methods - 1

- ANZ Fontan Registry
  - Biomedicine Honours student – Emily Moroney

  - Data extraction
    - Age
    - Fontan type
    - Follow up duration
    - Pregnancies reported
    - Endpoints of
      - morbidity and
      - mortality

  - Data analysis
    - with thanks to Diana Zannino

Consenting Fontan patients >18 (n=689)

Exclusions: (n=144)
- Participants who died before turning 18 (n=36)
- Participants who had no adult cardiology follow ups (n=106)
- Participants who had a Fontan take down <18 (n=2)

Eligible participants (n=545)

Control Male Group (n=280)

Eligible Females (n=265)

Exclusions: (n=2)
- Participants who did not disclose pregnancy outcome (n=2)

Pregnancy Group (n=30)

Control Female Group (n=233)

Results – 1
Mortality

Characteristic	Pregnancy group (n=30)	Women controls (n=233)	Male controls (n=280)	Statistical comparison
Age at last follow up, median (IQR), y	32.9 (26.6-37.3)	25.0 (20.5-29.3)	24.2 (20.8-29.5)	p= 0.002[a]
Post-operative follow-up time, median (IQR), y	22.7 (20.5-26.6)	19.5 (15.1-23.9)	19.3 (15.0-23.5)	p= 0.001[a]
Type of Fontan, n (%)				p= 0.172[b]
Atriopulmonary	14 (46.7)	77 (33.0)	87 (31.1)	
Lateral Tunnel	13(43.3)	88 (37.8)	106 (37.9)	
Extra Cardiac Conduit	3(10.0)	68 (29.2)	87 (31.1)	
Predominant Ventricle, n (%)				p= 0.270[b]
Right	4 (13.3)	48 (20.6)	75 (26.8)	
Left	24 (80.0)	161 (69.1)	180 (64.3)	
Indeterminate/ Biventricular	2 (6.7)	24 (10.3)	25 (8.9)	

[a] Calculated using non-parametric comparison, median test
[b] Calculated using Pearson's chi square test

- Women reporting pregnancy are older and therefore have more 'follow up' time

- Despite this, no difference in mortality, Fontan conversion or heart transplant

Results – 2
Morbidity

- Morbidity: arrhythmias, cardioversions and thromboembolic (TE) events
  - The only difference was seen in TE
  - HR (95% CI): 4.84 (1.08-21.6), p=0.04 – history of pregnancy
- Challenges in interpretation
  - Limited follow up time post partum: 2.89 y (0.72-7.2) and
  - Potential for 'healthier' women to be those that have pregnancy…..so is this even more significant?

(Zentner, IJC 2016)

Advice	Pregnancy (n = 27)	No pregnancy (n = 70)
No advice	1 (3.7%)	5 (5.2%)
Ok/ ok to increased risk	3 (11.1%)	9 (12.9%)
Increased risk	15 (55.6%)	27 (38.6%)
Increased risk to inadvisable	2 (7.4%)	10 (14.3%)
Inadvisable	6 (22.2%)	19 (27.1%)

70% / 30% (Pregnancy) — 59% / 41% (No pregnancy)

Results – 3
Explore 'pregnancy effect' further…...
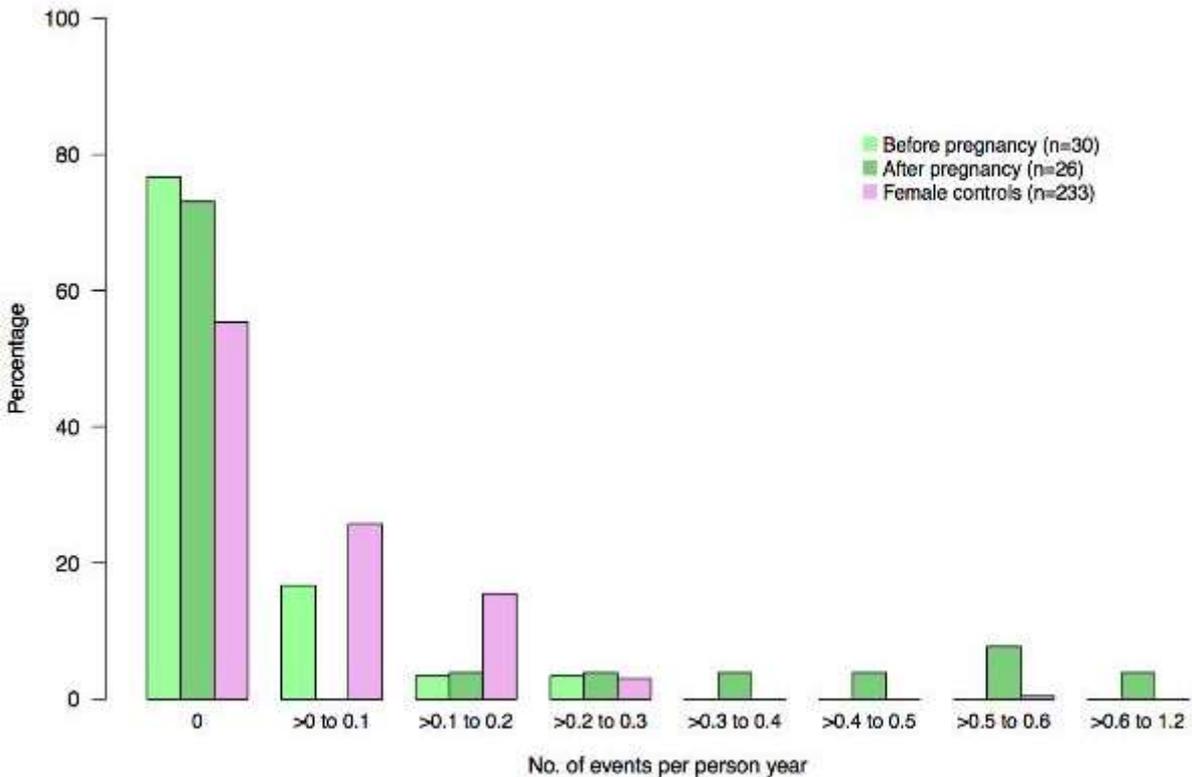
Number of adverse cardiac events per person year
Events refers to arrhythmias, cardioversions, thromboembolic events, pacemaker insertion, heart transplant, Fontan conversion and death.

- Appears that women having pregnancy are healthier, before
  - Adequate counseling ✓
- Pregnancy may convey an effect on maternal outcomes

Conclusions -1

1. Pregnancy in the Fontan circulation may increase TE risk
   - Pregnancy and PP: known increased risk for TE events in ALL women
   - However, events in this cohort occurred beyond the puerperium time period *(? related to cessation of thromboprophylaxis?)*

2. The answer to the question of long term maternal sequelae remains incomplete

3. Limitations:
   - We lack outcome data that is both *matched* and *long term*
   - We do not know whether pregnancies have a cumulative effect
   - Realistically, this is on the background of limited knowledge about the whole of life experience and outcomes for these individuals (remembering that mortality concerns apply to both men and women)

Conclusions – 2
Where to now?

- PROFAT (PRegnancy Outcomes in Fontans with Anticoagulation Therapy; funded by ISACHD, PI G Veldtman, Cincinatti USA – reveal role of thromboprophylaxis

- Fontan Pregnancy Outcomes Registry
  - proposed at I-FIG meeting 2017

Ethics
✓
(last week!)

Retrospective
- Differences between women who have and have not had a pregnancy?
- Clinical risk factors ?
- Do EST parameters differ?

Pregnancy Registry
- Match women with ≥ 1 pregnancy to ≥ 1 never pregnant control (same centre of care/ country)
- Match: Fontan type, age at Fontan, systemic ventricle morphology
- (Matched to ≥ 1 to allow cross over to pregnancy and matched to country to account for potential regional variation in care)

5 year prospective data collection
- Do cardiac morbidity and mortality events differ between the groups?
- Are multiple gestations higher risk?

Thank you

Please email me if you would like to join the

Fontan Pregnancy Outcomes Registry
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