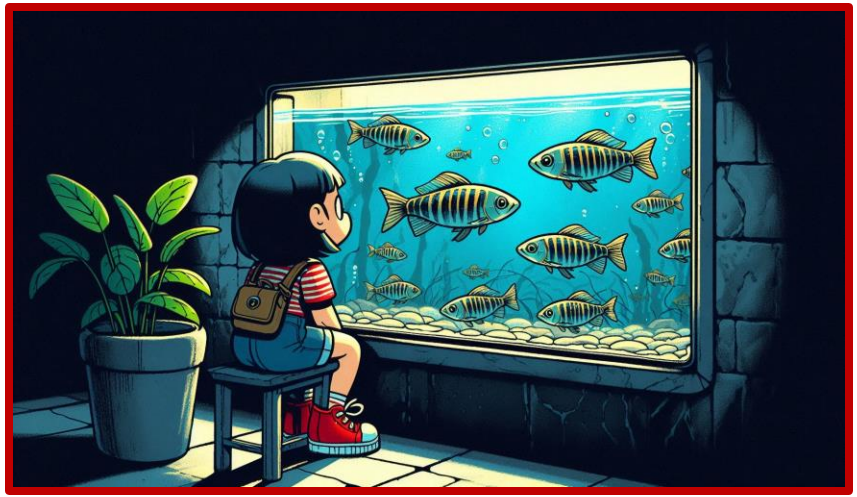
Cardiovascular Disease In a Retrospective Cohort of Adults with Fetal Alcohol Spectrum Disorders



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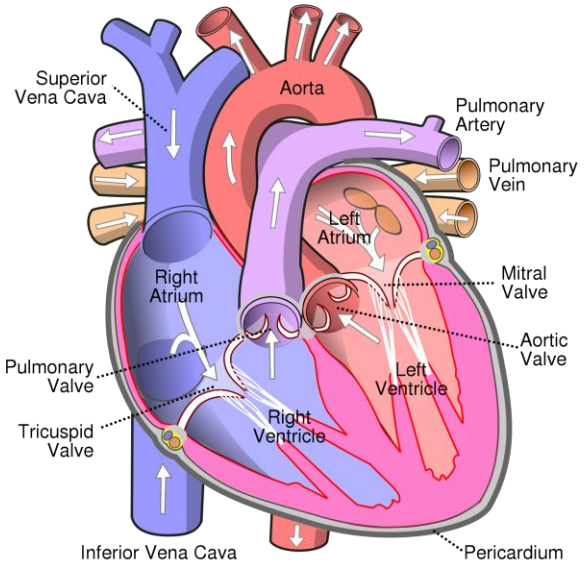
Cardiovascular Health In Individuals With FASDs



- We have a limited understanding of cardiovascular health across the lifespan in individuals with FASDs
- Past literature suggests that children with FASDs have higher rates of congenital heart defects (CHDs) than the general population; however, reported prevalence is variable (~3% vs. >30%)
- Cardiovascular problems have been described as enriched in adults with FASDs (Attell et al., 2025), but comprehensive, systematic studies on CVD burden are needed
- Adult cardiovascular diseases (CVDs), including **cardiomyopathy** and **heart failure**, are poorly documented in FASD patient populations despite their association with CHDs

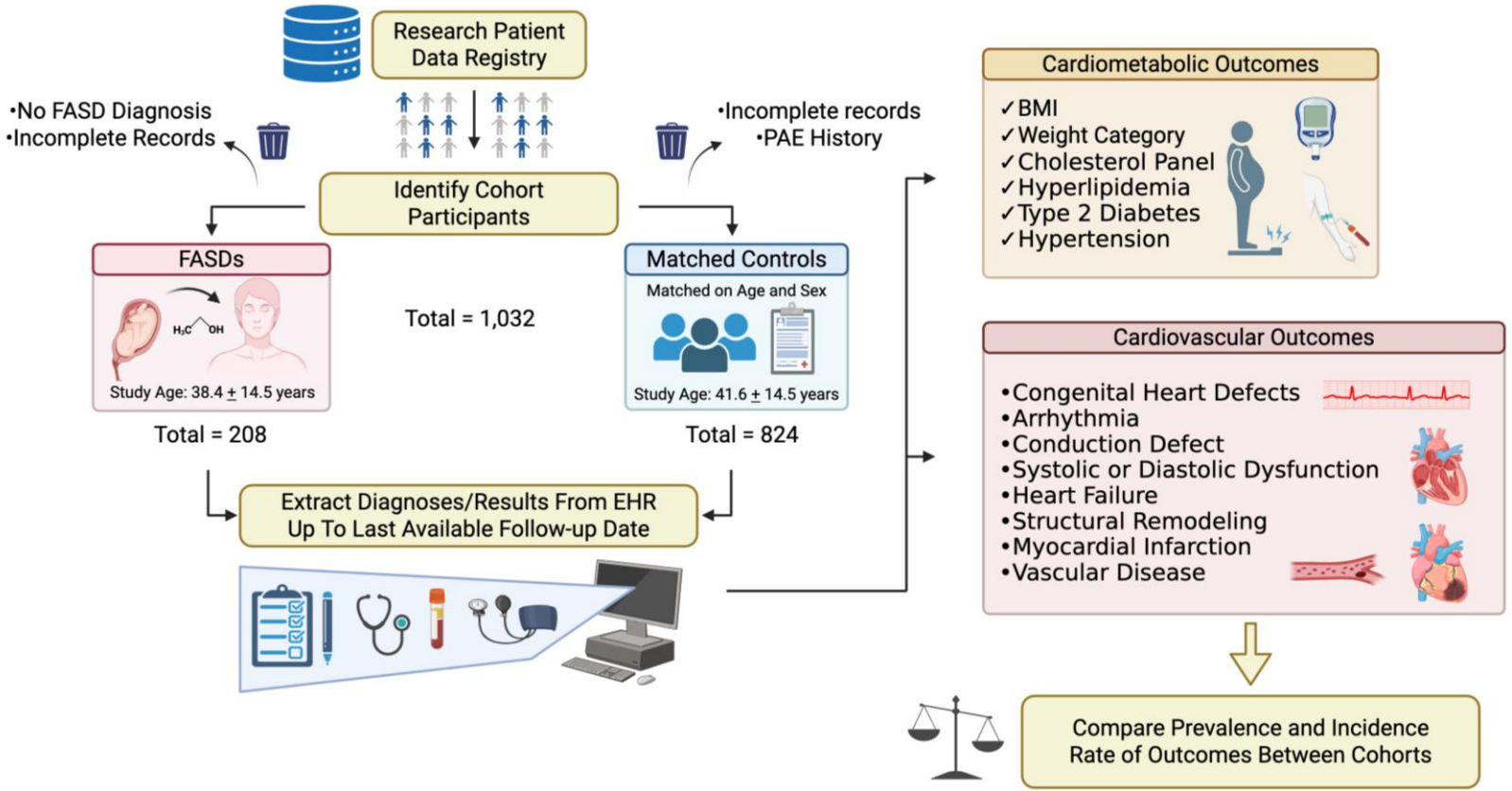
PROJECT GOALS

1. *To **determine the prevalence** of cardiometabolic risk factors, congenital heart defects, and adult cardiovascular disease in a current FASD cohort.*

2. *To **assess the relationship** between adverse cardiac events and cardiometabolic risk factors in individuals with FASDs.*

3. *To **validate cardiac findings** in an animal model where environmental factors are controlled.*

Retrospective Cohort Study of Adults With FASDs



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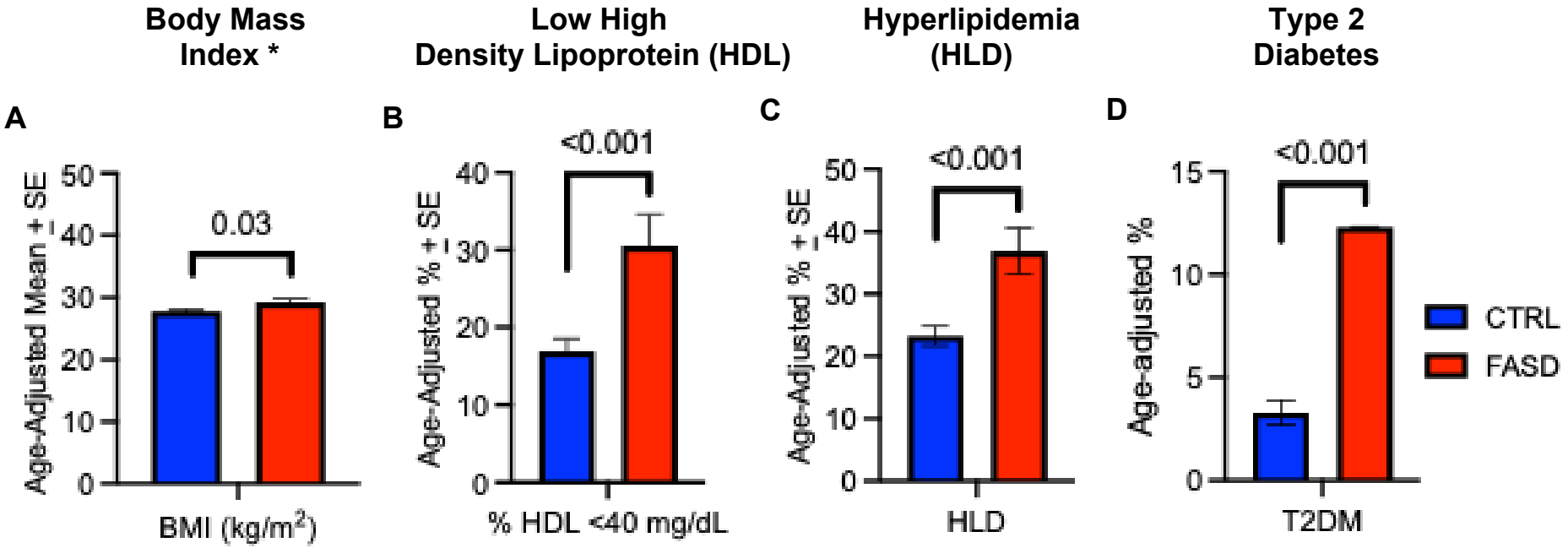
Cardiometabolic Risk Factors For Heart and Vascular Disease

Created with ChatGPT-5.3

Cardiometabolic risk factors are a cluster of interconnected metabolic and cardiovascular abnormalities that significantly increase the likelihood of developing heart disease and stroke.

Increased Cardiometabolic Disease In Adults With FASDs



Adults with FASDs had a **higher age-adjusted BMI, lower HDL, higher triglycerides, more T2DM,** and a **greater probability of having multiple metabolic abnormalities.**

*Sex-by-diagnosis interaction: Females with FASDs were more likely to have overweight/obesity than controls.

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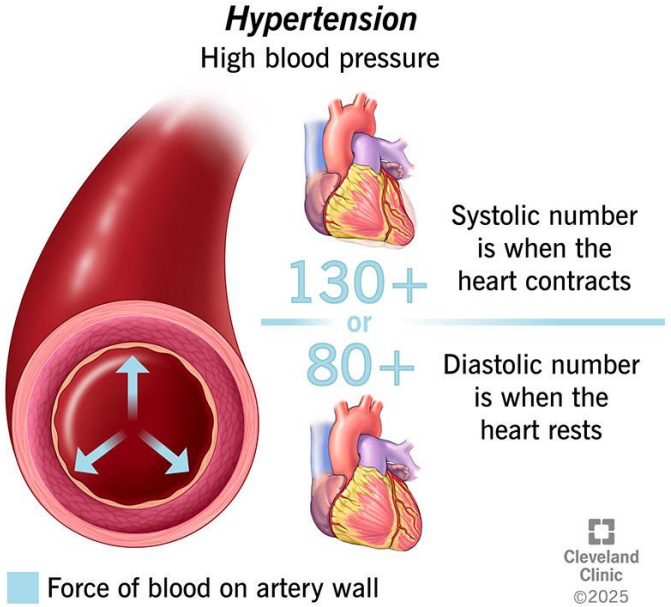
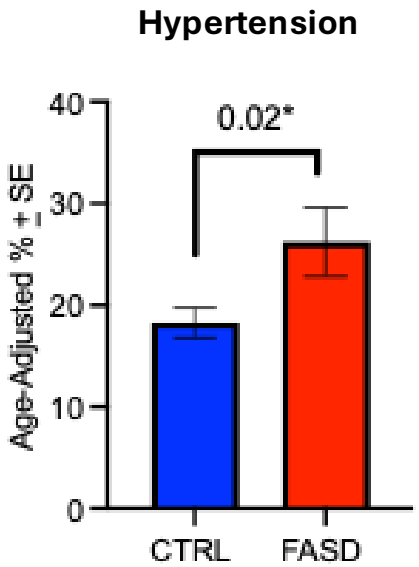
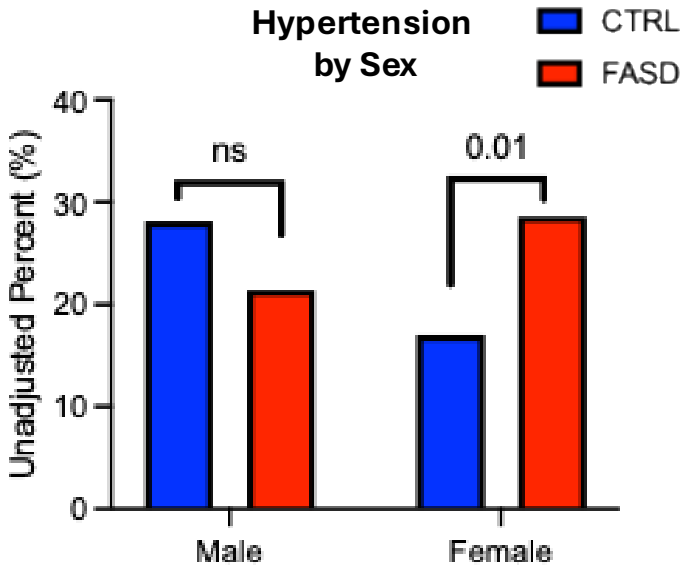
Hypertension Is More Common In Females With FASDs Than Controls



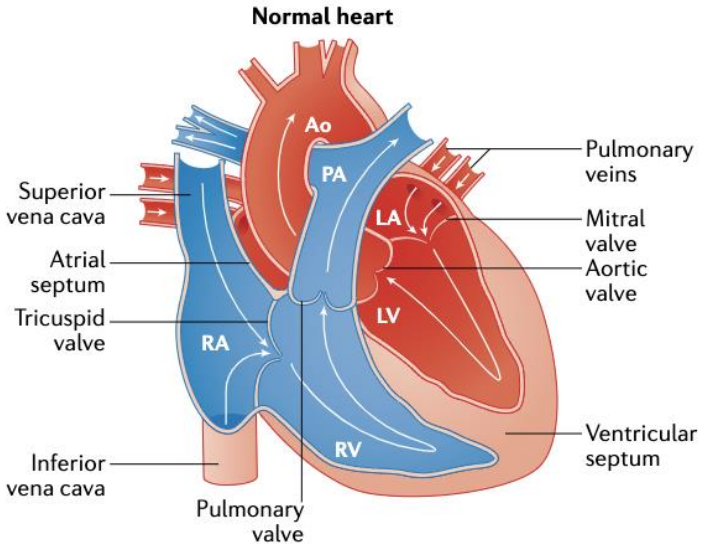


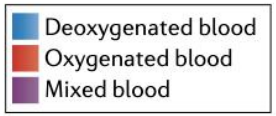


* Not significant by Poisson analysis (incidence rate), only by logistic regression (prevalence). However, sex-by-diagnosis interaction is significant.

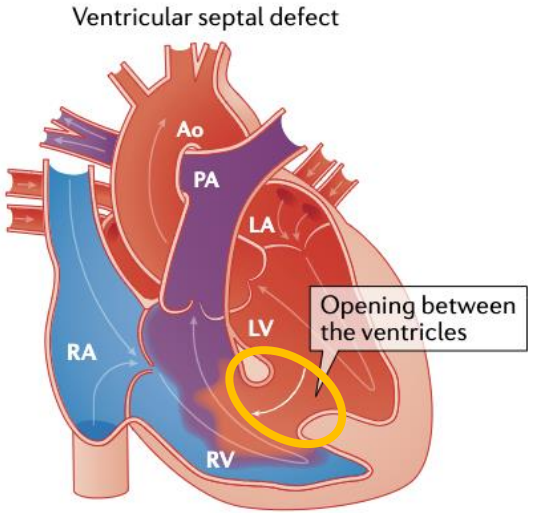
Congenital Heart Defects: Developmentally-Derived Structural Problems

- Congenital heart defects (CHDs) occur when the heart is not built properly during development
- There are many types of CHDs with varying degrees severity



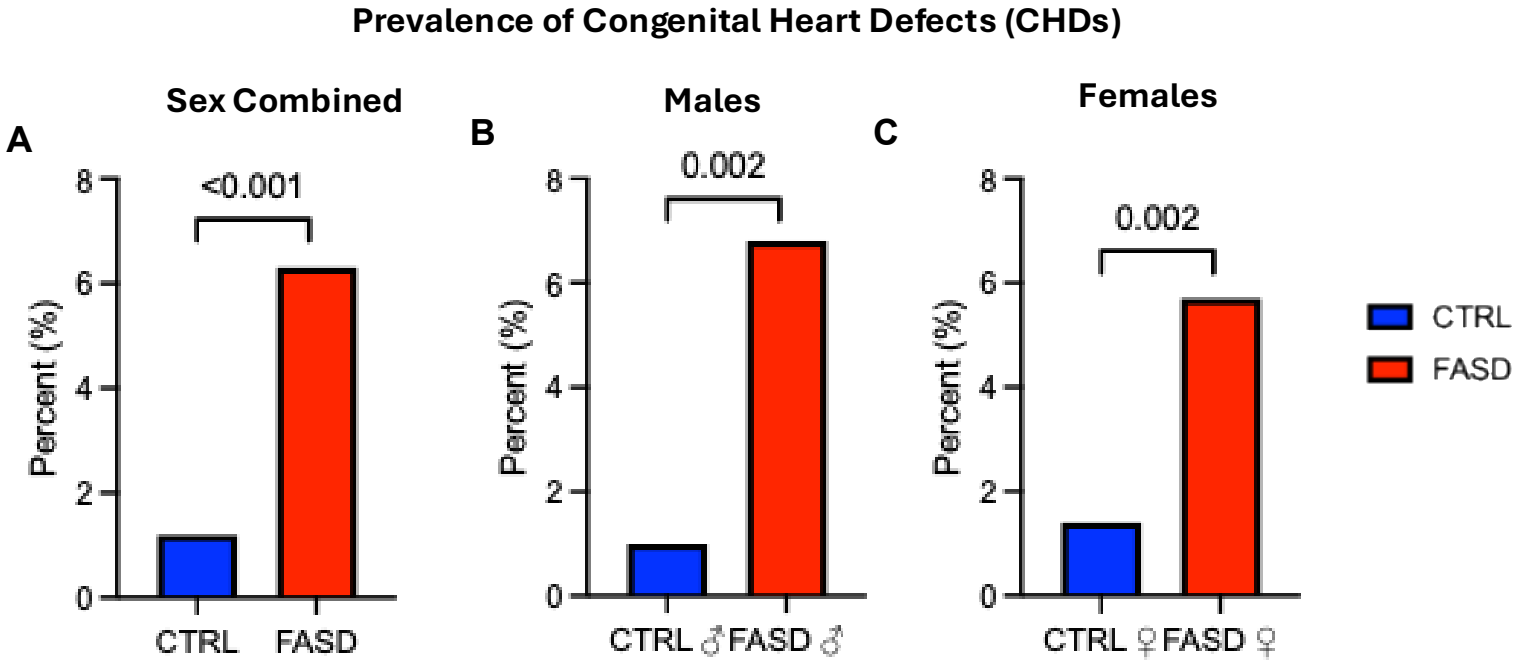


Example: "Hole In the Wall"



Morton et al, 2022.

Congenital Heart Defect Burden Is Increased In FASDs



Given that 2 - 5% of the U.S. population is estimated to have a FASD, and that up to 5 - 7% of individuals with FASD may have a CHD, PAE and/or gene-alcohol interactions could account for a meaningful fraction of total CHDs (up to 10%).

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Congenital Heart Defect Burden Is Increased In FASDs

	Combined		
Defect	**FASD**	**Control**	***P* value**
N	208	824	
Any CHD diagnosis	13 (6.3%)	10 (1.2%)	**<0.001**
Patent Foramen Ovale (PFO)	3 (1.4%)	4 (0.5%)	0.15
Atrial septal defect (ASD)	4 (1.9%)	4 (0.5%)	0.06
Bicuspid aortic valve	1 (0.5%)	4 (0.5%)	1.00
Ventricular septal defect (VSD)	2 (1.0%)	1 (0.1%)	0.11
Coarctation of the aorta	0 (0%)	2 (0.2%)	1.00
Tetralogy of Fallot (TOF)	2 (1.0%)	0 (0%)	**0.04**
Patent ductus arteriosus (PDA)	1 (0.5%)	0 (0%)	0.20
Transposition of the great arteries (TGA)	1 (0.5%)	0 (0%)	0.20
Aortic stenosis	0 (0%)	2 (0.2%)	1.00
Heart Murmur	11 (5.3%)	22 (2.7%)	0.07

The prevalence of any one subtype of congenital heart defect was low; however, there is a suggestion that atrial septal defect (p = 0.06), ventricular septal defect (p = 0.11), and **Tetralogy of Fallot (TOF) (p = 0.04) are more common in the FASD cohort**.

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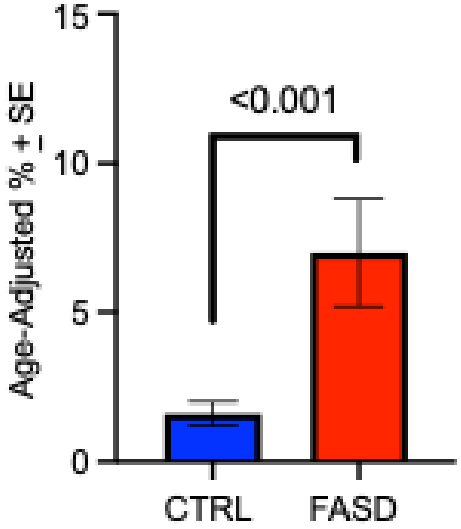
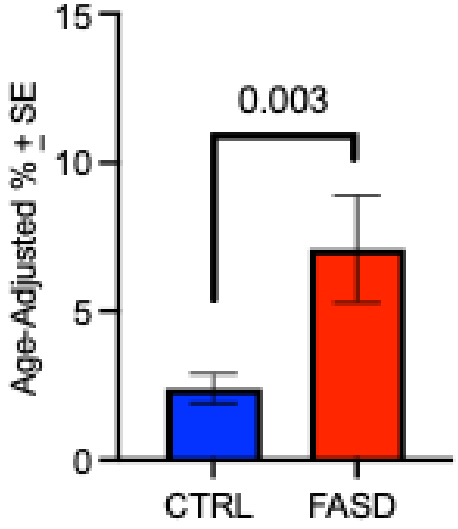
Conduction Defect And Arrhythmia Burden In FASDs: Problems With Electrical Signaling or Rhythm of the Heart

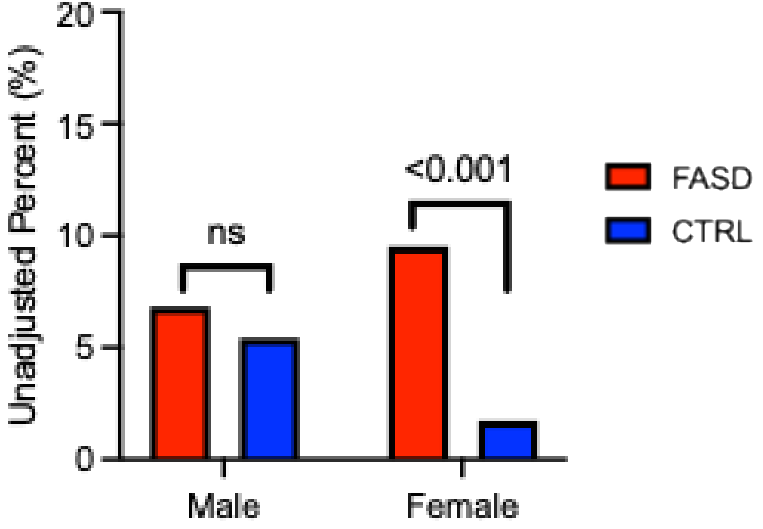
A **Conduction Defect**



B **Arrhythmia***



C **Arrhythmia by Sex**



*Sex-by-diagnosis interaction

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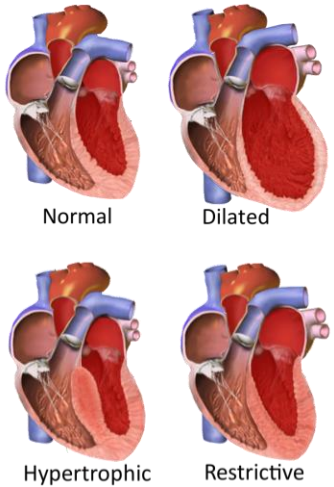
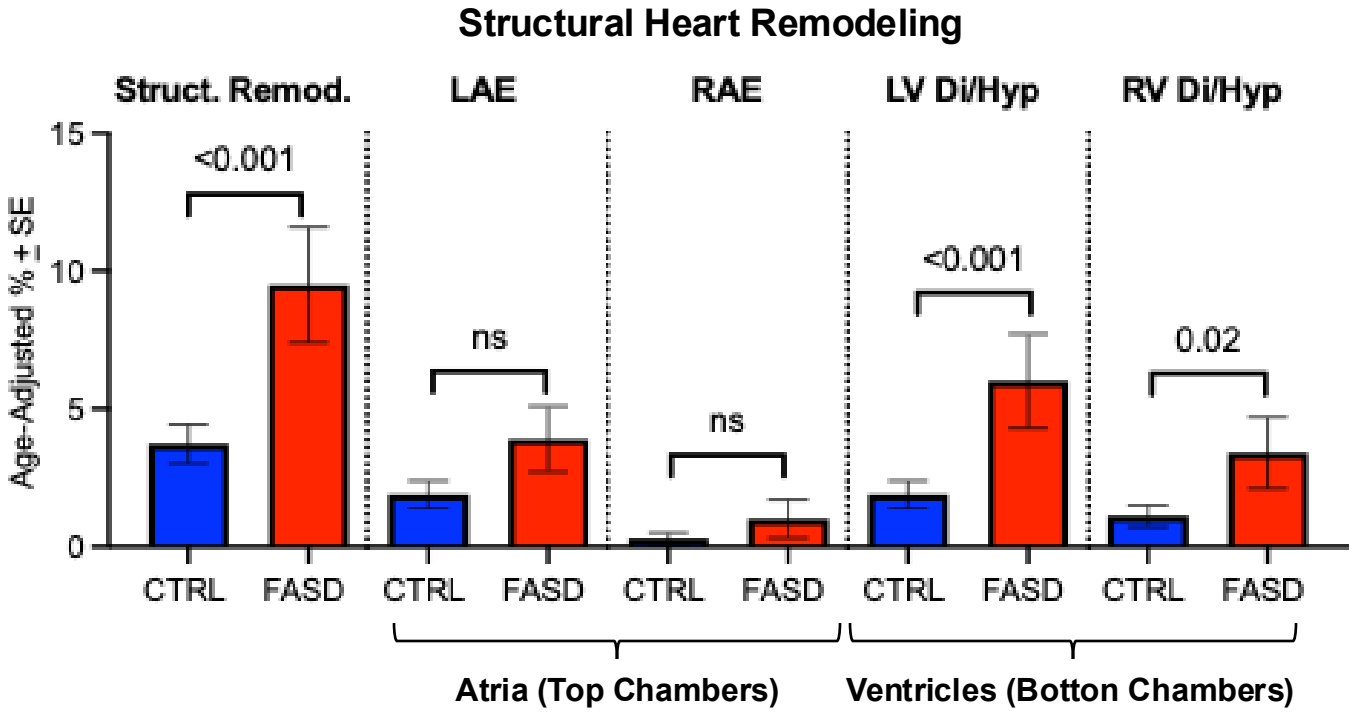
Structural Heart Remodeling Is Increased in Adults With FASDs

LV Remodeling:





RAE = right atrial enlargement
LAE = left atrial enlargement
LV Di/Hyper = left ventricular dilation or hypertrophy
RV Di/Hyper = right ventricular dilation or hypertrophy

Adults with FASD had **more cardiac remodeling of the ventricles** than controls.
There was no sex-by-diagnosis interaction.

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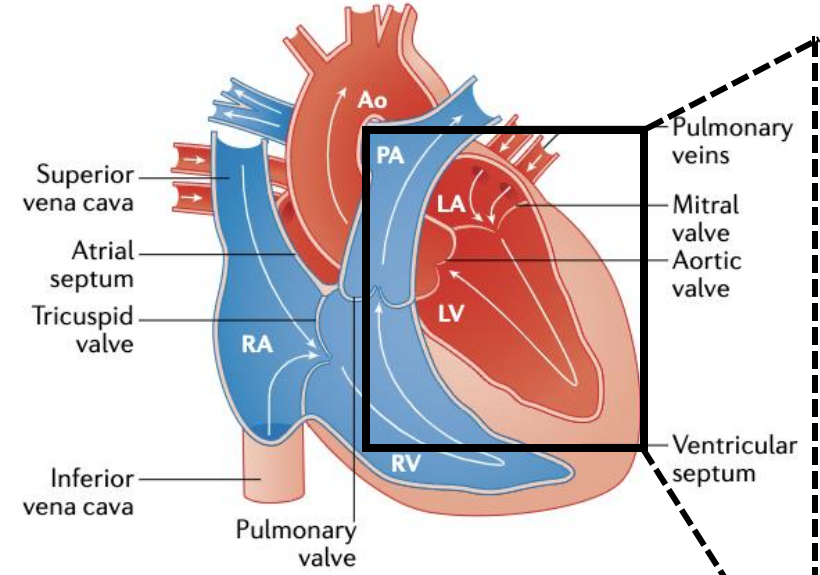
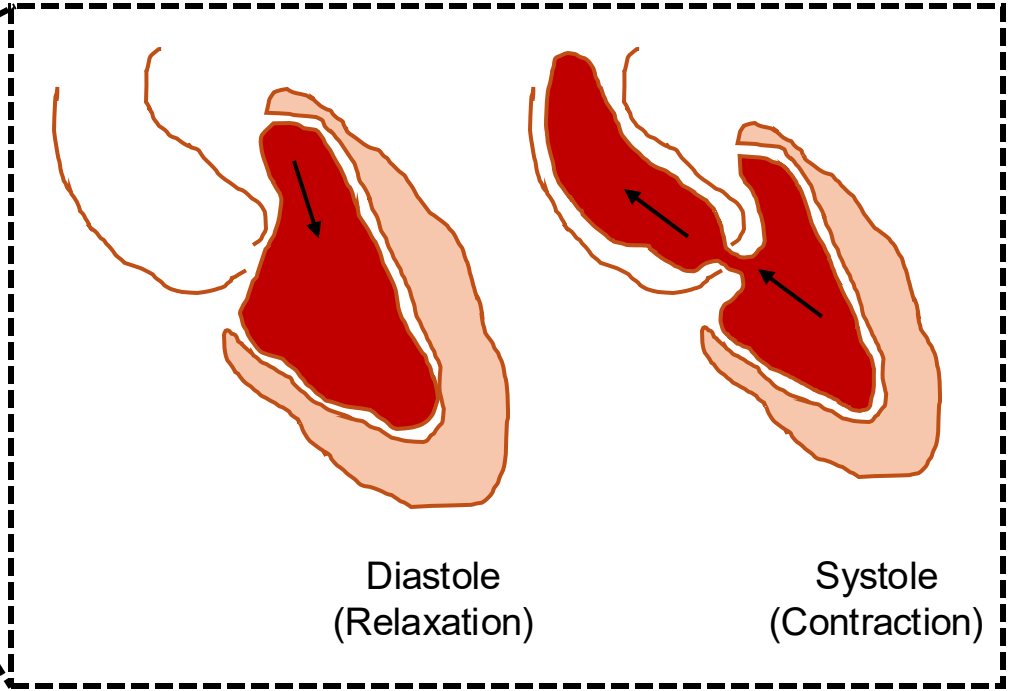
Left Ventricular Systolic Function



Morton et al, 2022.



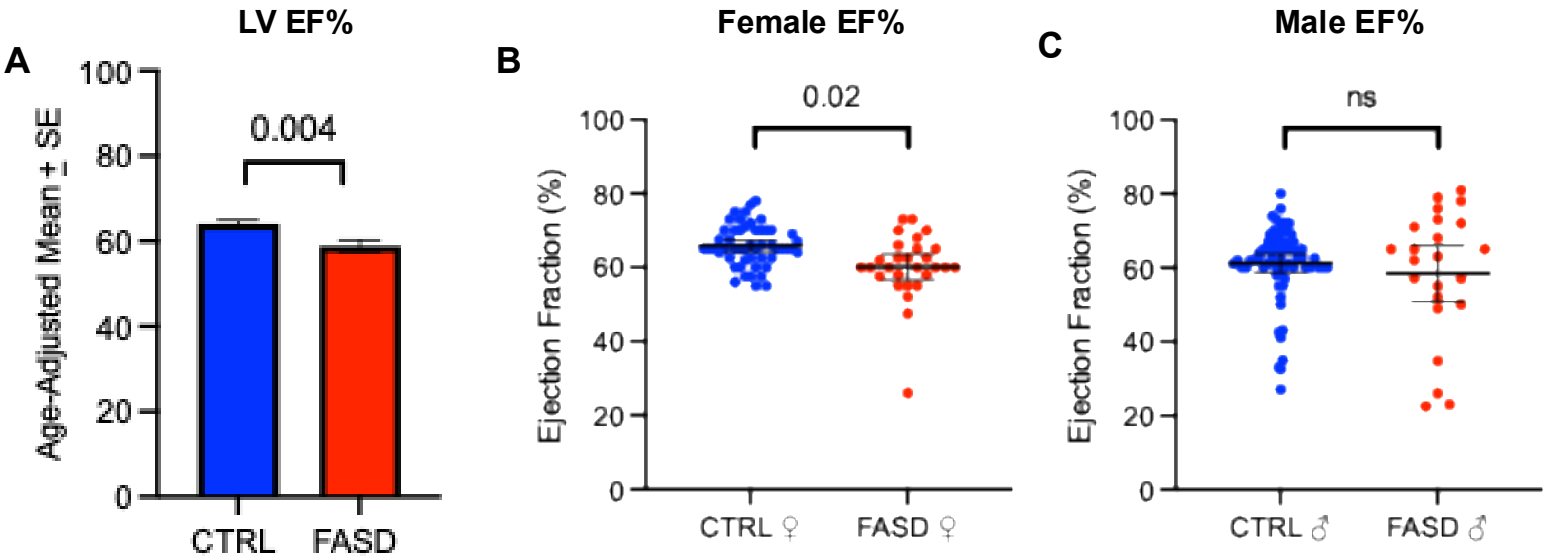
Systolic function relates to how well the left ventricle contracts. If the ventricle can contract well and pump a normal amount of blood, systolic function is generally normal. If contraction is impaired [often causing too little blood to be pumped out with contraction], there is **systolic dysfunction.**

Adults With FASDs Have Reduced Heart Function

Ejection fraction is a measure of the percent of blood the left ventricle pumps out during each contraction. When ejection fraction is too low, a patient is diagnosed with **systolic dysfunction** or **heart failure**.

$$\text{Left ventricular (LV) ejection fraction (\%)} = \frac{\text{Stroke volume (SV)}}{\text{End-diastolic volume (EDV)}} \times 100$$

Normal: 50 – 70%



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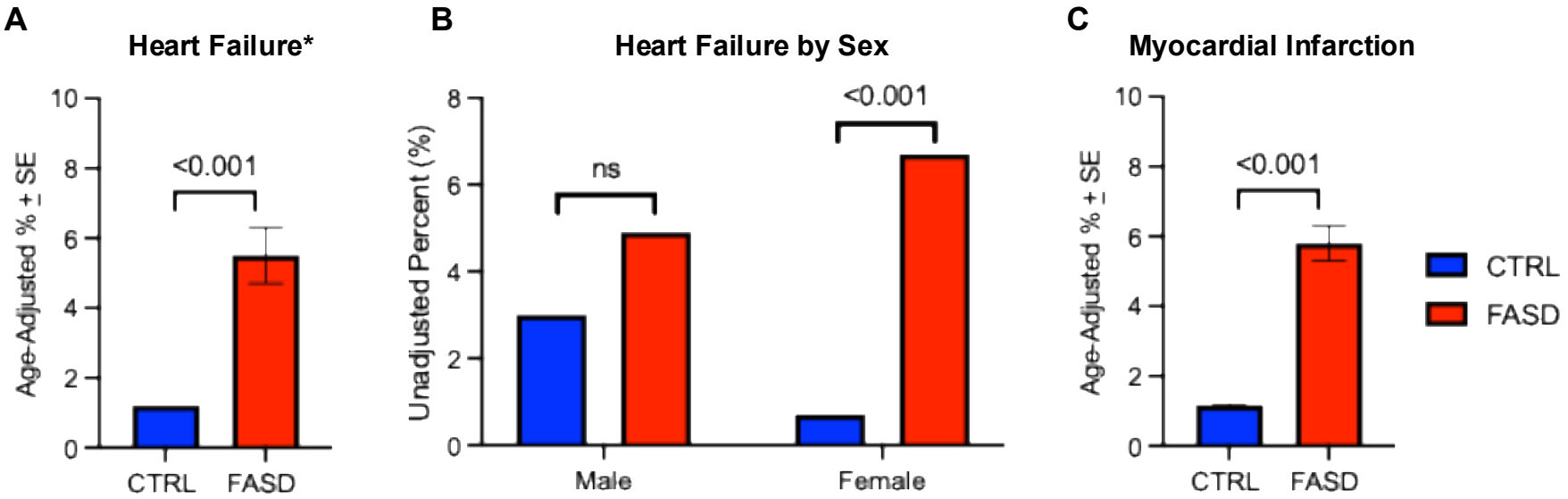
Heart Failure and Heart Attack Are Increased in Adults with FASDs



Adults with FASD had **higher prevalence of heart failure and heart attack/myocardial infarction (MI).**

*A sex-by-diagnosis interaction was observed for heart failure.

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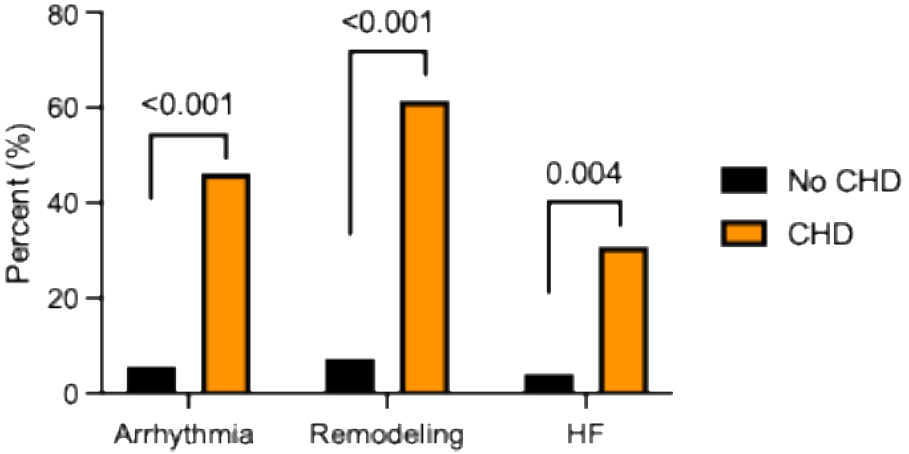
CHD Is A Risk Factor For Adult Cardiovascular Disease In FASDs

FASD Cohort	CHD		
Condition	**No**	**Yes**	***P value***
N	195	13	
Hypertension	48 (24.6%)	4 (30.8%)	0.74
Any cardiac condition (excluding HTN)	37 (19.0%)	13 (100%)	**<0.001**
Conduction defect	9 (4.6%)	6 (46.2%)	**<0.001**
Cardiac arrhythmia	11 (5.6%)	6 (46.2%)	**<0.001**
Atrial fibrillation	5 (2.6%)	3 (23.1%)	**0.009**
Structural heart remodeling	14 (7.2%)	8 (61.5%)	**<0.001**
Left atrial enlargement	8 (4.1%)	3 (23.1%)	**0.024**
Right atrial enlargement	2 (1.0%)	1 (7.7%)	0.18
LV dilation/hypertrophy	10 (5.1%)	6 (46.2%)	**<0.001**
RV dilation/hypertrophy	2 (1.0%)	5 (38.5%)	**<0.001**
Heart Failure (HF)	8 (4.1%)	4 (30.8%)	**0.004**
Systolic HF	7 (3.6%)	2 (15.4%)	0.10
Diastolic HF	5 (2.6%)	2 (15.450	0.06
Systolic or Diastolic Dysfunction	9 (4.6%)	4 (30.8%)	**0.005**
Myocardial infarction	10 (5.1%)	2 (15.4%)	0.17
Stroke/Cerebral Vascular Accident	6 (3.1%)	2 (15.4%)	0.08
Ischemic*	2 (1.0%)	1 (8.3%)	0.17
Hemorrhagic*	1 (0.5%)	0 (0%)	1.00
Thrombosis or embolism	9 (4.6%)	0 (0%)	1.00

CVD Outcomes In Individuals with FASDs



Note: In the general population, ~6.5% of individuals with CHDs (15% with complex CHDs) develop heart failure by 42. *31% of FASD adults in our cohort with a CHD developed heart failure.*

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Adult Cardiovascular Outcomes Stratified By Cardiometabolic Risk

- Cardiovascular disease risk is not explained by cardiometabolic risk factors alone.
- Covariate-adjusted models demonstrate that the FASD group is more likely to have a cardiovascular condition (excluding hypertension) or structural heart remodeling than controls, even after adjusting for cardiometabolic parameters.

% with Cardiovascular Condition (Excluding Hypertension)			
Condition	**FASD**	**Control**	**p-value**
Hyperlipidemia	23% (17/73)	19% (43/221)	0.50
No hyperlipidemia	24% (33/135)	8% (48/603)	<0.001
Multiple metabolic abnormalities*	27% (12/44)	24% (19/78)	0.83
No multiple metabolic abnormalities*	28% (23/82)	12% (36/312)	<0.001
% with Structural Heart Remodeling			
Condition	**FASD**	**Control**	**p-value**
Hyperlipidemia	11% (8/73)	10% (22/221)	0.82
No hyperlipidemia	10% (14/135)	3% (21/603)	0.002
Multiple metabolic abnormalities*	16% (7/44)	19% (15/78)	0.81
No multiple metabolic abnormalities*	11% (9/82)	3% (10/312)	0.008

*Includes 3 factors: overweight/obese; HDL cholesterol<40; type 2 diabetes mellitus

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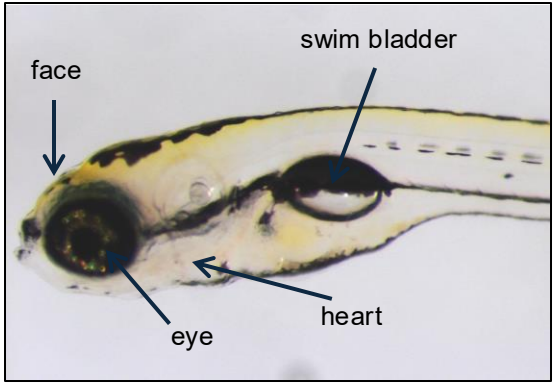
Zebrafish Recapitulate Key Features of FASDs

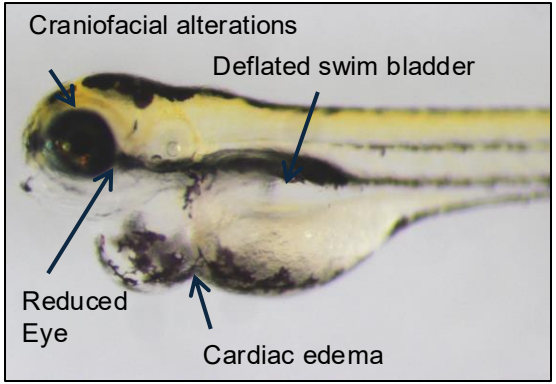
CHARACTERISTICS

- ✓ Short stature
- ✓ Cardiac defect
- ✓ Craniofacial anomalies
- ✓ Eye alterations
- ✓ Altered vasculature
- ✓ Hyperactivity
- ✓ Atypical behavior
- ✓ Altered kidney formation

NO ALCOHOL

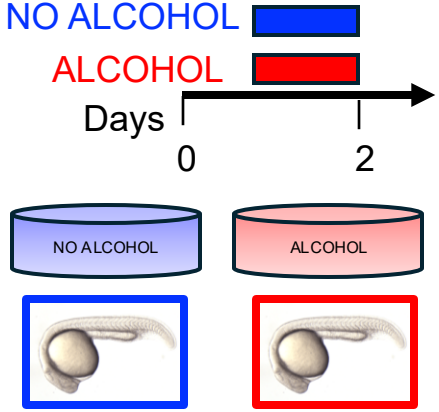


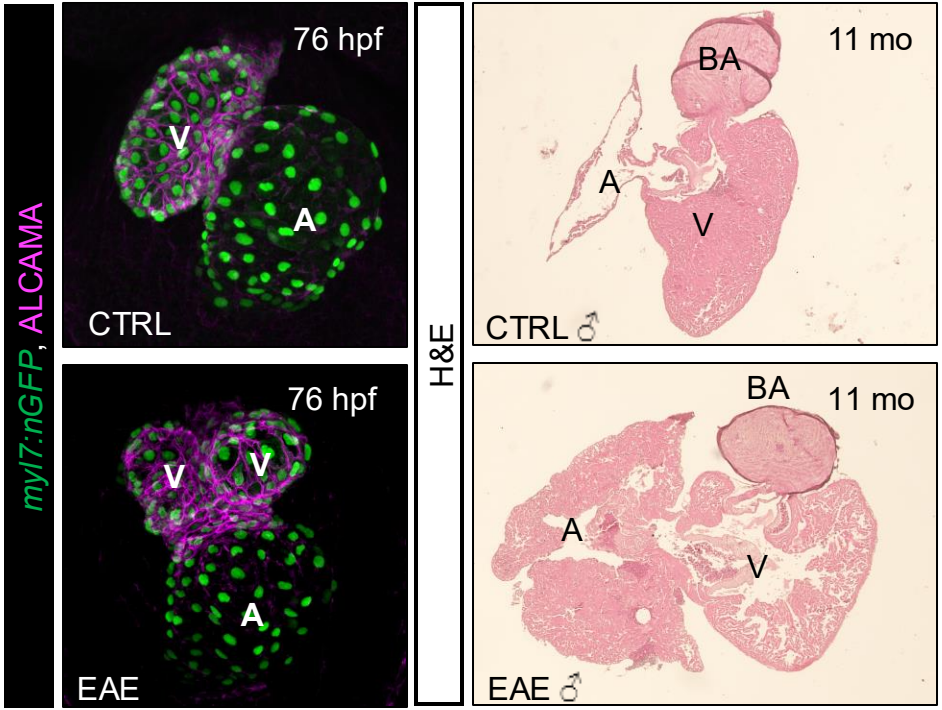
+ALCOHOL

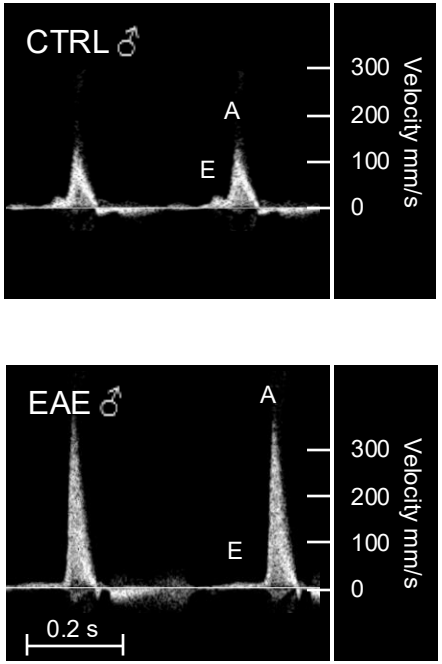


Bilotta et al., 2004; McCarthy et al., 2013; Marrs et al., 2010; Lovely, Fernandes, Eberhart, 2016; Loucks and Ahlgren, 2012; Li et al., 2016; Dlugos and Rabin, 2007; Swartz et al., 2014; Sheehan-Rooney et al., 2013. and more.

“FASD” Zebrafish Recapitulate Human Findings of CHDs and Cardiomyopathy







EAE = Embryonic Alcohol Exposure

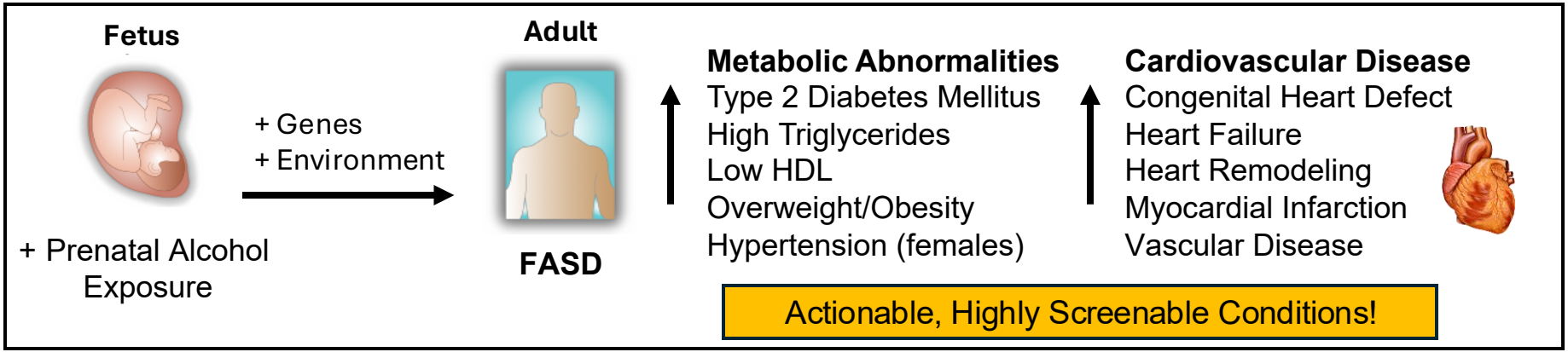
CONGENITAL HEART DEFECT

STRUCTURAL REMODELING

DIASTOLIC DYSFUNCTION

Weeks et al. 2024, CVR.

Conclusions and Implications



- Prenatal alcohol exposure (PAE) and FASDs are underrecognized risk factors for CHDs and adult CVD.
- Collecting information on PAE status as part of routine care may help identify individuals at risk for cardiac disease (less than 1% of individuals with FASD currently receive a diagnosis).
- Comprehensive longitudinal cardiovascular screening is not currently recommended for individuals with FASDs, but the clinical need for this should be re-evaluated.

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