

CPA DOSSIER CONTENTS- Dr Rachel Wald

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Introduction

As an adult congenital and pediatric cardiologist with a special interest in advanced cardiac imaging, I have had the unique opportunity to explore the impact of imaging techniques on the clinical care of adults, children, and pregnant women with congenital heart disease. With a primary appointment in the Department of Pediatrics and cross-appointments to the Departments of Medicine, Medical Imaging and Obstetrics/Gynecology I am fortunate to be uniquely positioned at the University of Toronto for completion of research studies across the spectrum of life.

My participation in a vibrant, multi-faceted, forward thinking Division of Cardiology has afforded me unparalleled opportunities to immerse myself in a wide array of complementary clinical activities. Following completion of pediatric cardiology training at SickKids, a non-invasive imaging fellowship at Boston Children's Hospital and an Adult Congenital Heart Disease fellowship at the UHN, I joined the Division of Cardiology at the University Health Network as an adult congenital cardiologist in 2008, and became the first pediatric cardiologist to work full-time within the Department of Medicine. Shortly thereafter, I became the first cardiologist to join the cardiac imaging group in the Joint Department of Medical Imaging to independently interpret cardiovascular magnetic resonance imaging studies within the established group of radiologists. Finally, I joined the maternal cardiac disease in pregnancy group to care for mothers with congenital and acquired forms of heart disease. I currently participate in the ambulatory clinics at the Toronto General Hospital (adults with congenital heart disease), Mount Sinai Hospital (pregnant women with heart disease), cardiac imaging at the University Health Network (cardiovascular magnetic resonance imaging) and echocardiography at SickKids.

My areas of active research are intertwined with my clinical interests. My perspectives on clinical research are further strengthened by my ability to regularly interact, not only with clinical researchers within the Peter Munk Cardiac Centre at the University Health Network, but with a wide array of dynamic researchers across Toronto (within the Divisions of Pediatric Cardiology and Cardiovascular Surgery at SickKids Hospital, the Lunenfeld Research Institute at Mount Sinai Hospital and clinician scientists with research interests in fibrosis within the Department of Medicine at St. Michael's Hospital [Divisions of Cardiology, Nephrology and Endocrinology]), across Canada (in pediatric and ACHD programs in Nova Scotia, Quebec, Alberta and British Columbia as part of the Canadian Institutes of Health Research outcome studies) and around the world (with collaborative studies ongoing with colleagues in Boston, Hong Kong, Leuven, Melbourne, and Rome).

Since my promotion to Associate Professor in 2015, much of my research has focused on a single form of congenital heart disease (tetralogy of Fallot) and a single imaging modality (cardiovascular magnetic resonance imaging). Benchmarks of my contributions to the field of congenital cardiology since my appointment to Associate Professor in 2015 have included:

- my role as nominated principal investigator on two multi-centre Canadian Institutes of Health Research (CIHR) grants:
 - "the CORRELATE study" – or Comprehensive Outcomes Registry Late After Tetralogy of Fallot repair [awarded \$621,000 over 3 years] was completed in March 2019

- “Right Ventricular Fibrosis Study from Bench to Bedside [awarded \$617,000 over 3 years] is set to commence in August 2019.
- More than 40 articles published in peer-reviewed journals
- More than 30 invitations to participate in international conferences or academic meetings
- Invitations to serve on National and International Committee on Guidelines for management of children and adults with congenital heart disease (American Thoracic Society and Canadian Cardiovascular Society) and advanced cardiovascular imaging (Canadian Cardiovascular Society)
- International recognition for a cardiovascular magnetic resonance imaging core lab (excellence in congenital heart disease imaging with a focus on tetralogy of Fallot, housed at the University Health Network)
- National recognition for a large and expanding biobank for tetralogy of Fallot heart muscle samples (stored at the University Health Network)

This dossier will expand upon professional innovation, development of professional practice and exemplary professional practice as these relate to the following themes pertaining to my current academic accomplishments and future career aspirations:

- 1. Multi-centre and multinational networks to advance care in complex congenital heart disease: tetralogy of Fallot (TOF) and hypoplastic left heart syndrome (HLHS)**
- 2. New Frontiers for Advanced Cardiovascular Imaging: Expanding Applications for Cardiovascular magnetic resonance imaging (CMR)**

1. Multi-centre, multinational and multi-disciplinary networks to advance care in complex congenital heart disease

1.1 Tetralogy of Fallot

Preamble: Tetralogy of Fallot (TOF) represents the most common cyanotic congenital heart defect at birth. In the current era, virtually all children born with TOF in Western countries undergo timely repair and prognosis is considered to be good. Despite successful repair, chronic pulmonary valve regurgitation is ubiquitous and has been associated with late development of heart failure, malignant arrhythmia and death. However, when to implant a prosthetic pulmonary valve to mitigate the effect of chronic regurgitation continues to be one of the most controversial questions in contemporary congenital cardiology. Furthermore, the presence and prognostic relevance of right heart scarring is being increasingly recognised and yet therapies to ameliorate or prevent fibrosis in the right heart remain undefined. With the objective of advancing care for adults late after TOF repair I am actively involved in 3 large multi-centre studies, as described below.

Multi-centre, multinational outcome studies:

The prospective CORRELATE (principal investigator):

- The Comprehensive Outcomes Registry Late After Tetralogy of Fallot (CORRELATE) began as a Canadian Institutes of Health Research (CIHR) funded pan-Canadian prospective registry of high-risk children and adults late after tetralogy of Fallot repair to document major adverse outcomes and to determine how timing of pulmonary valve intervention may impact on clinical status and clinical outcomes. We are now a global study and have currently enrolled more than 700 patients in Canada, Europe and Asia with cardiovascular magnetic resonance imaging studies at baseline and follow-up. **IMPACT: When completed, CORRELATE will contribute evidence to one of the most pervasive, but as yet unanswered questions in ACHD – optimal timing of pulmonary valve replacement to address significant pulmonary regurgitation.**
- **CPA type: Creative and Professional Excellence.** Through CORRELATE I have assembled the largest prospective registry of a high-risk cohort of patients with significant pulmonary regurgitation in the world. **Exemplary Professional Practice.** Under the auspices of the CORRELATE study I have set-up an internationally recognized cardiovascular magnetic resonance imaging core lab and a large biobank for TOF heart muscle samples.
- **Selected Documentation:**
 - Grants:**
 - 2012 Oct - 2019 Mar. **Principal Investigator.** CORRELATE study: Canadian Outcomes Registry Late After Tetralogy of Fallot Repair. Canadian Institutes of Health Research (CIHR). **621,931 CAD.**
 - 2016 Jul – 2018. Jun **Co-Investigator.** Impact of pulmonary valve replacement in children with repaired tetralogy of Fallot: meeting the knowledge gap. Canadian

Institute of Health Research (**CIHR**). Subvention Project. PI: Dallaire, Frederic. **129,966 CAD**.

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Publications:

- Van De Bruaene A, Horlick E, Benson L, **Wald RM**. Characterization of the Surgically Modified Right Ventricular Outflow Tract Using Magnetic Resonance Angiography in Adults Late After Tetralogy of Fallot Repair. *Journal of American College of Cardiology: Cardiovascular Imaging*. 2019 Mar. Impact Factor 10.247. **Senior Responsible Author**.
- **Wald RM** on behalf of the CORRELATE investigators. **Principal Author**. Patient-Reported Outcomes in Tetralogy of Fallot: Baseline Results From a Prospective, International, Multi-Site Study. *Circulation* 2017; 136:A20897.
- **Wald RM** on behalf of the CORRELATE investigators. **Principal Author**. Baseline Cardiovascular Magnetic Resonance Imaging Measurements Are Associated With Clinical Outcomes at Three Years of Follow-Up: Results From a Prospective, International, Multi-Site Study of Patients With Significant Pulmonary Regurgitation Late After Tetralogy of Fallot Repair. *Circulation* 2017;136:A21055.
- Bhagra C, Hickey E, Van De Bruaene A, Roche L, Horlick E, **Wald RM**. Pulmonary valve procedures late after repair of tetralogy of Fallot: Current perspectives and contemporary approaches to management. *Can J Cardiology*. 2017 Sep;33(9):1138-1149. Impact Factor 3.71. **Senior Responsible Author**.
- Dallaire F, **Wald RM**, Marelli A. The role of cardiopulmonary exercise testing in the decision making in patients with repaired tetralogy of Fallot. *Pediatric Cardiology*. 2017 Aug;38(6):1097-1105. Impact Factor 1.452. **Coauthor or Collaborator**.
- Tretter JT, Friedberg M, **Wald RM**, McElhinney DB. Defining and refining indications for transcatheter pulmonary valve replacement in patients with repaired tetralogy of Fallot: Contributions from anatomical and functional imaging. *International J of Cardiology*. 2016 Oct 15;15(21):916-925. Impact Factor 4.034. **Coauthor or Collaborator**.
- **Wald RM**, Valente AM, Marelli A. Heart failure in adult congenital heart disease: Emerging concepts with a focus on tetralogy of Fallot. *Trends in Cardiovascular Medicine*. 2015 Jul 1;25(5):422-432. Impact Factor 2.91. **Principal Author**.

International Invitations/Presentations:

- 2019 May 4. **Invited Speaker**. Outcomes in congenital heart disease - tetralogy of Fallot. European Association of Cardiovascular Imaging (EACVI) - EuroCMR 2019. **Venice, Italy**.
- 2019 Feb 8. **Invited Speaker**. CMR Characteristics of Asymptomatic and Symptomatic Patients Referred for PVR Late after TOF Repair - Global Practice Patterns. SCMR 22nd Annual Scientific Sessions. **Seattle, Washington, United States**.
- 2018 Feb 26. **Invited Speaker**. Tetralogy of Fallot - past, present and future. Update on Tetralogy of Fallot, Bambino Gesù Hospital. **Rome, Italy**.
- 2018 Feb 1. **Invited Speaker**. What Cardiovascular magnetic resonance adds in congenital heart disease Euro CMR and Society for Cardiovascular Magnetic Resonance (SCMR). **Barcelona, Spain**.

- 2017 Nov. **Podium presentation.** Risk-benefit Ratio May Not Justify A Further Decrease in Threshold For Pulmonary Valve Replacement Late After Tetralogy of Fallot Repair: An Experience with 2579 Patients. American Heart Association. **Anaheim, California**, United States. Authors: Hickey E, Roche S, Silversides C, Oechslin E, Crean A, Colman J, Heggie J, Pham-Hung E, Van Arsdell G, Caldarone C, Honjo O, **Wald RM. Senior Responsible Author.**

Guidelines:

- 2017 Apr – present. **Panel Member**, Adult Congenital Heart Disease **Primary Panel** – Guideline Development for the Management of the Adult with Congenital Heart Disease, Canada. ****only pediatric cardiologist on this panel***
- 2015 Feb – 2017 Feb. **Panel Member**, American Association for Thoracic Surgery Guidelines Committee, Beverly, Massachusetts, United States. ****only Canadian cardiologist on this panel***

Awards:

- ***Winner of the best abstract award at EuroEcho 2017*** Characterization of the Surgically Modified Right Ventricular Outflow Tract Using Magnetic Resonance Angiography in Adults Late After Tetralogy of Fallot Repair. Van De Bruaene A, Horlick E, Benson L, **Wald RM. Senior Responsible Author.**

The retrospective INDICATOR (co-investigator and site principal investigator):

- **International Multicenter Tetralogy of Fallot registry** is a highly successful, retrospective collaboration between adult congenital heart disease centres with large CMR programs in North America (Boston, Toronto) and Europe (London, Netherlands) has resulted in multiple publications which have helped to shape clinical ACHD practice today. One of the largest patient cohorts in the INDICATOR study is from Toronto and I have been personally responsible for collecting data and updating outcomes for close to 400 patients. **IMPACT: Through linkage of large databases spanning thousands of patient years of follow-up, statistical power will be adequate to finally understand the impact of pulmonary valve replacement on longer term clinical outcomes.**
- **CPA type: Development of Professional Practice.** Following a study of 507 patients with 2 or more CMR studies, we were able to determine the optimal frequency for surveillance CMR to determine which patients may require pulmonary valve replacement. Following publication of our results, the optimal surveillance frequency that we identified has since been incorporated into adult congenital heart disease management guidelines in the United States and Canada.
- **Selected Documentation:**
Publications:

- Geva T, Mulder B, Gauvreau K, Gatzoulis M, Babu-Narayan S, Powell A, **Wald RM**, Valente AM. Preoperative predictors of death and sustained ventricular tachycardia after pulmonary valve replacement in patients with repaired tetralogy of Fallot enrolled in the INDICATOR cohort. *Circulation*. 2018 Nov;138(19):2106-2115. Impact Factor 19.309. **Coauthor or Collaborator**.
- Bokma J, Geva T, Sleeper L, Babu-Narayan S, **Wald RM**, Hickey K, Jansen K, Wassall R, Minmin L, Gatzoulis M, Mulder B, Valente A. A propensity score-adjusted analysis of clinical outcomes after pulmonary valve replacement in tetralogy of Fallot. *Heart*. 2018 May;104(9):738-744. Impact Factor 5.6. **Coauthor or Collaborator**.
- **Wald RM**, Valente AM, Gauvreau K, Babu-Narayan SV, Assenza GE, Schreier J, Gatzoulis MA, Kilner PJ, Koyak Z, Mulder B, Powell AJ, Geva T. Cardiac magnetic resonance markers of progressive right ventricular dilation and dysfunction after tetralogy of Fallot repair. *Heart*. 2015 Nov 1;101(21):1724-30. Impact Factor 5.6. **Principal Author**.

Guidelines:

- Findings from our research into optimal CMR surveillance strategies in TOF have been incorporated into the Guidelines for Multimodality Imaging in TOF published by the American Society of Echocardiography by Valente et al in 2015.

Multi-disciplinary studies:

Right Ventricular Fibrosis from Bench to Bedside – a Fibrosis Translation Platform (principal investigator):

- I have assembled a network of fibrosis researchers (including investigators from the University Health Network, SickKids, Mount Sinai Hospital and St. Michael’s Hospital spanning cardiology, nephrology and endocrinology). The proposed fibrosis research platform is comprised of distinct yet inter-related research cores of diagnosis, therapy and discovery. Under my leadership this team is focused on answering the following critical questions related to heart failure:
(1) Can diagnostic tools be improved to non-invasively quantify ventricular fibrotic burden, and to identify those at risk of functional deterioration secondary to fibrosis?
(2) Can novel drug targets be identified to interrupt/reverse ventricular fibrosis?
(3) Can new pro-fibrotic pathways be elucidated that will result in diagnostic and/or therapeutic breakthroughs? **IMPACT: This is a “first of its kind” fibrosis research network in Canada which will leverage the skill sets of multiple highly successful teams with complimentary studies in patients with tetralogy of Fallot (serum and imaging biomarkers of adverse outcomes related to fibrosis), related animal models of and gene discovery. This unique consortium of individuals with the potential to transform management of fibrosis in patients with right heart disease was recently recognized with a Canadian Institutes of Health Research project grant.**
- **CPA type: Professional innovation and creative excellence.** The establishment of this unique fibrosis network highlights innovation as it is a novel amalgamation of scientists with multiple interests spanning a variety of disciplines with the common goal of furthering therapies in fibrosis. Our assembled multi-disciplinary team bridges basic science

and clinical medicine by going a step beyond the traditional “organ-based” silos for the study of fibrosis.

- **Selected Documentation:**

Grants:

- 2019 Apr - 2022 Mar **Principal Investigator**. “Right Ventricular Myocardial Fibrosis from Bench-to-Bedside: Implications for Care”. Canadian Institutes for Health Research **CIHR**. Project Grant. **627,301 CAD**.

Publications:

- Yamamura K, Yuen D, Hickey E, He X, Chaturvedi R, Friedberg M, Hanneman K, Billia F, Farkouh M, **Wald RM**. Right ventricular fibrosis is associated with cardiac remodeling after pulmonary valve replacement. *Heart*. 2019 Jun; 105(11): 855-863. Impact Factor 5.6. **Senior Responsible Author**
- Hanneman K, Wintersperger B, Crean A, Thavendiranathan D, Kayedpour C, Nguyen E, Silversides C, Farkouh M, **Wald RM**. The relationship between cardiovascular magnetic resonance imaging measurement of extracellular volume fraction and clinical outcomes in adults with repaired tetralogy of Fallot. *European Heart Journal Cardiovascular Imaging*. 2018 Jul 1;19(7):777-784. Impact Factor 5.99. **Senior Responsible Author**.

1.2 Hypoplastic left heart syndrome

Preamble: Of all patients with single ventricle physiology, those with hypoplastic left heart syndrome (HLHS) have the worst survival in childhood, and yet this is the most common anatomic lesion resulting in a Fontan palliation for a dominant right ventricle in pediatric life. Despite increasing numbers of survivors into adulthood, late outcomes were not elucidated in HLHS despite the recognition that this is a particularly high-risk cohort in the adult congenital heart disease population.

Multi-centre multinational outcome studies:

Hypoplastic Left Heart Syndrome (HLHS) Multi-Centre Outcomes (principal investigator):

- I assembled a network of Fontan palliation experts at large centres around the world. Collectively we documented a high adverse outcome rate in 59 adults at 7 centres (Toronto, Boston, Edmonton, Vancouver, Melbourne, Newcastle, Zurich). **IMPACT:** This study will allow for enhanced surveillance of an emerging, high risk population. Future directions will include a deeper understanding of the prognostic relevance of imaging predictors (right ventricular systolic function and severity of tricuspid regurgitation) with larger numbers and longer follow-up.
- **CPA type: Professional innovation and creative excellence.** The establishment of this global network is an example of innovation as this collaborative effort spanning North America, Europe and Australia is the first of its kind world-wide.

- **Selected Documentation:**

Publications:

- Wilson W, Valente A, Hickey E, Clift P, Burchill L, Emmanuel Y, Gibson P, Greutmann M, Grewal J, Grigg L, Gurvitz M, Hickey K, Khairy P, Mayer J, Teo E, Vonder Muhll I, Roche L, Silversides C, **Wald RM**. Outcomes of patients with hypoplastic left heart syndrome reaching adulthood after Fontan palliation: a multicenter study. *Circulation*. 2018 Jan;137:978-981. Impact Factor 14.43. **Senior Responsible Author**.
- **Wald RM**, Alonso R, Swan L. Transition to Adult Life. In: *Handbook on the Fontan Circulation*. New York: Springer, 2019. In progress. **Co-Principal Author**.

International Invitations:

- 2018 Aug 28. **Invited Speaker**. Long-term Outcome of the Hypoplastic Left Heart Syndrome. European Society of Cardiology (ESC) Congress. **Munich, Germany**.

2. New Frontiers for Advanced Cardiovascular Imaging: Expanding Applications for Cardiovascular Magnetic Resonance Imaging

Preamble: Cardiovascular magnetic resonance imaging (CMR) is an essential tool for contemporary surveillance of patients with congenital heart disease and is considered the reference standard for quantification of ventricular function, volumes and mass. Additional strengths of this robust imaging modality include non-invasive assessment of vasculature (anatomy and flows) as well as characterization of myocardial health (scar/fibrosis). Applications of CMR continue to expand and much of my research is dedicated to a better understanding of: (1) the clinical value of established and emerging CMR sequences in children and adults with congenital heart disease (2) the utility of CMR in novel patient populations, including pregnant women and their fetuses (3) the value of CMR measurements for evaluating the response to device therapy. Examples of projects highlighting each of these areas are detailed below.

2.1 CMR for evaluation of diffuse fibrosis in the myocardium late after TOF repair – the TOF T1 study (principal investigator):

- I recently published a pilot project which confirmed the feasibility of measurement of fibrosis in the right heart in adults with repaired TOF and demonstrated that burden of diffuse fibrosis was associated with adverse cardiovascular outcomes. The results of this study led to a successful application to Canadian Institutes of Health Research to further establish the clinical utility of T1 mapping for assessment of diffuse myocardial fibrosis in adults with TOF. **IMPACT: Through this larger study we aim to validate novel non-invasive imaging biomarkers for prediction of adverse events in adults late after TOF repair.**
- **CPA type: *Professional innovation and creative excellence*.** This study is an example of innovation as a novel CMR technique is being applied to enhance risk stratification in a high-risk patient population.
- **Selected Documentation:**
 - Grants:**
 - 2019 Apr - 2022 Mar. **Principal Investigator.** “Right Ventricular Myocardial Fibrosis from Bench-to-Bedside: Implications for Care”. Canadian Institutes for Health Research **CIHR**. Project Grant. **627,301 CAD.**
 - Publications:**
 - Hanneman K, Wintersperger B, Crean A, Thavendiranathan D, Kayedpour C, Nguyen E, Silversides C, Farkouh M, **Wald RM.** The relationship between cardiovascular magnetic resonance imaging measurement of extracellular volume fraction and clinical outcomes in adults with repaired tetralogy of Fallot. *European Heart Journal Cardiovascular Imaging.* 2018 Jul 1;19(7):777-784. Impact Factor 5.99. **Senior Responsible Author.**

Guidelines:

- 2019 Jan – present. **Panel Member**. Safety for Cardiovascular Patients Undergoing Magnetic Resonance Imaging. Canadian Cardiovascular Society (CCS) and the Canadian Society of Cardiovascular Magnetic Resonance (CanSCMR). Ottawa, Ontario, Canada.

2.2 CMR for evaluation of cardio-hepatic interactions in patients with a Fontan palliation (principal investigator):

- The interactions between the diseased heart and the liver are increasingly being recognized and are a cause for concern, particularly in patients with Fontan physiology given the potential for development of hepatocellular carcinoma in the long term – a potentially lethal complication. Along with a Masters student in engineering, Elyar Bavil, we performed phase contrast flow studies to elucidate, for the first time, the pathophysiology of hepato-cardiac interactions using CMR. We documented a significant decrease in vascular flows exists at cardiac, hepatic and intestinal levels in patients with morphologic liver disease evident on CMR. **IMPACT: Our data suggest that a relationship between morphologic liver disease and vascular flows exists and we are the first to describe, in detail, hepatic and intestinal flow characteristics in adults late after Fontan palliation using CMR.**
- **CPA type: Professional innovation and creative excellence.** This study is an example of innovation as established CMR techniques are applied to further our understanding of the pathophysiology of failing Fontan physiology in terms of extra-cardiac disease, specifically this is the first description of liver and intestinal flows using CMR techniques.
- **Selected Documentation:**
Publications: Two manuscripts have been completed and submitted for publication in June 2019 in conjunction with an IMS Masters degree (Elyar Bavil):
 - *Bavil EA, Doyle MG, Debbaut C, Wald RM, Mertens L, Forbes TL, Amon, CH. Calibration of an electrical analog model of liver hemodynamics in Fontan patients. IEEE Transactions on Biomedical Engineering. 2019 Jun. Impact Factor 2.31. Co-Author.*
 - *Bavil E, Doyle M, Mertens L, Karur G, Yoo SJ, Bhagra C, Bhagra S, Ross H, Wald RM. Comparison of Cardiovascular and abdominal in adults with and without morphologic evidence of liver disease post Fontan palliation. EHJCVI. 2019 Jul. Impact Factor 5.6. Senior Responsible Author.*

2.3 CMR for evaluation of maternal-fetal interactions in moderate or severe forms of congenital or acquired heart disease – the MOMS HEARTS study (co-investigator along with Dr. Mike Seed):

- The increased hemodynamic demands of pregnancy are known to precipitate heart failure in women with structural or acquired heart disease. Although insufficient cardiac output has been implicated in poor maternal and fetal outcomes, no study to date has incorporated CMR for antenatal measurement of cardiovascular flows in the mother or delivery of oxygen/blood flow to the fetus. In the **MoMs HEARTs (cMr of Maternal Structural and Hemodynamic Effects in pregnancy with Residual cardiac pathology study)** we studied 20 pregnant women with moderate or severe heart disease and 20

healthy controls at SickKids during and after pregnancy with support from the Ted Rogers Centre for Heart Research. This work has formed the basis for a PhD degree for a student at the Institute for Medical Sciences, Brahmdeep Saini. **IMPACT: Cardiac output measurements during pregnancy may assist with early detection of heart failure in high risk women and an improved understanding of the impact of inadequate blood flow to the developing fetus. Future directions to arise from this feasibility study will include ongoing study of larger numbers of pregnant women with moderate or severe forms of heart disease.**

- **CPA type: Professional innovation and creative excellence.** This study is an example of innovation as these established CMR flow techniques have never been applied to study the impact of significant heart disease on mothers and their fetuses.
- **Selected Documentation:**
 - Grants:**
 - 2016 Dec - 2017 Dec **Co-Investigator.** Heart failure management in pregnancy – the role of advanced MRI for maternal-fetal hemodynamic monitoring. **Ted Rogers Centre for Heart Research** Education Fund Awards 2016. PI: Marini, Davide. **40,000 CAD.**
 - 2016 Dec - 2017 Dec **Co-Investigator.** The effects of pregnancy on maternal cardiac function and materno-fetal hemodynamic interactions in women with pre-existing heart disease as assessed by cardiac magnetic resonance imaging. **Ted Rogers Centre for Heart** Research Education Fund Awards 2016. PI: Stochituiu, Ioana. **5,000 CAD.**
 - 2011 Jan - 2016 Jun **Co-Investigator.** Pregnancy and Cardiovascular Risk Factors in Women with Heart Disease. Canadian Institutes of Health Research (**CIHR**). PI: Siu, Samuel. **922,055 CAD.**

Publications:

- Ducas R, Nguyen ET, **Wald RM.** Contemporary considerations for the use of cardiovascular magnetic resonance imaging during pregnancy. *Obstetric Medicine.* 2019 Feb. **Senior Responsible Author**
- **Wald RM,** Silversides CK, Kingdom J, Toi A, Lau C, Mason J, Colman J, Sermer M, Samuel C, Siu SM. Maternal cardiac output and fetal doppler predict adverse neonatal outcomes in pregnant women with heart disease. *Journal Amer Heart Assoc.* 2015 Nov 23; 4:11. Impact Factor 4.306. **Principal Author.**

International Invitations:

- 2020 April. **Invited Speaker.** Cardiovascular magnetic resonance for assessment of the mother and baby in pregnancy. The 6th International Congress on Cardiac Problems in Pregnancy (CPP 2020). **Porto, Portugal.**
- 2018 Feb 23. **Invited Speaker.** Maternal Hemodynamics and Cardiovascular Magnetic Resonance Imaging- What Can We Learn About Women with Congenital Heart Disease? The 5th International Congress on Cardiac Problems in Pregnancy (CPP 2018). **Bologna, Italy.**
- 2018 Feb 23. **Invited Speaker.** Fetal Hemodynamics and Cardiovascular Magnetic Resonance Imaging- What Can We Learn About the Child with Congenital Heart

Disease? The 5th International Congress on Cardiac Problems in Pregnancy (CPP 2018). **Bologna, Italy.**

Advisory Board:

Cardiac Problems in Pregnancy International Congress Advisory Board:

- 2019 Apr – 2020 Apr **Member, Advisory Board and Faculty Member**, International Congress on Cardiac Problems in Pregnancy, **Porto, Portugal.**
- 2017 Apr – 2018 Apr **Member, Advisory Board and Faculty Member**, International Congress on Cardiac Problems in Pregnancy, **Bologna, Italy.**

2.4 CMR for evaluation of the impact of pulmonary valve replacement on pregnancy outcomes in women with TOF (co-investigator along with Dr. Anne Marie Valente, Children's Hospital Boston):

- While little evidence exists to support timing of pulmonary valve implantation in patients with chronic pulmonary regurgitation after TOF repair, and no evidence is available to support valve intervention prior to pregnancy, management guidelines continue to recommend that pulmonary valve replacement occur prior to pregnancy to decrease risk of adverse events related to pregnancy. We therefore sought to investigate the impact of valve intervention on pregnancy outcomes in pregnant women with repaired TOF followed in Toronto and Boston and we have recently received grant funding for this initiative from the American Adult Congenital Heart Association. Our findings show that pulmonary valve replacement prior to pregnancy results in preservation of right ventricular health as measured by right ventricular size and function (manuscript in preparation). **IMPACT: These data will provide evidence, for the first time, to support the expert opinion statement that pulmonary valve intervention should be considered prior to pregnancy.**
- **CPA type: Exemplary professional practice and Development of professional practice.** The core lab which I established at the Toronto General Hospital for TOF CMR studies was used for CMR analysis for this multi-centre study. Once published we anticipate that our data will be incorporated into guidelines for management of the adult with chronic PR late after TOF repair.
- **Selected Documentation:**
Grants:
 - 2019 Jul - 2021 Jun **Co-Investigator.** Improving Pregnancy Outcomes in Women with Tetralogy of Fallot (TOF). Adult Congenital Heart Association (**ACHA**). PI: Duarte, Valeria. 65,000 USD.

2.5 CMR for evaluation of response to novel ventilation therapies in patients with a Fontan palliation - the FONTAN CMR study (principal investigator):

- A strikingly high late complication rate has been recently recognized in adult Fontan survivors, which arises from failing Fontan physiology and results in multi organ dysfunction. In the fourth and fifth decades of life, nearly 70% of adult Fontan survivors will develop heart failure. Short of heart transplantation, which is only deemed suitable

for a small minority of Fontan patients, effective therapies are largely absent. A chronically low cardiac output state is the chief cause of complications and death late after Fontan surgery. With support from the Peter Munk Cardiac Centre Innovation Committee and the Labatt Family Heart Centre we have recently completed a feasibility study at SickKids to explore the effects of a novel, non-invasive, ambulatory treatment approach which provides external suction to the chest wall to increase cardiac output, called negative pressure ventilation (NPV) using a Cuirass® ventilator (Hayek Medical). **IMPACT: This pilot study which incorporates CMR measurement of cardiac output is a first-in-man application of an ambulatory negative pressure ventilation strategy for patients with congenital heart disease. Future directions to arise from this feasibility study will include application of the NPV ventilation strategy to children and adults with Fontan failure as a bridge to transplant or as destination therapy.**

- **CPA type: *Professional innovation and creative excellence*.** This study is an example of innovation as this is a first in man application of a ventilation strategy to augment cardiac output in the ambulatory setting using CMR measurements to calibrate response to therapy.

- **Selected Documentation:**

Grants:

- 2016 Dec - 2019 Nov. **Principal Investigator.** Feasibility and Efficacy of Biphasic Cuirass Ventilation in Fontan Patients (FBCV) - A Pilot Study. Peter Munk Cardiac Centre Innovation Committee. **PMCC Innovation Committee.** Collaborator(s): Co-investigators: Horlick E, Granton J, Honjo O. **130,224 CAD.**
- 2016 Dec – 2019 Nov. **Principal Investigator.** FONTAN-CMR: Feasibility and efficacy Of Negative Pressure Ventilation in The Ambulatory population -Cardiovascular flow assessment by Magnetic Resonance imaging. **Labatt Family Heart Centre. Innovation Fund.** Collaborator(s): Oechslin E, Granton J, Horlick E, Yoo S, Honjo O, Chaturvedi R. **23,766 CAD.**
- 2016 Jul - 2022 Mar. **Co-Investigator.** Congenital Heart Disease across the Lifespan: Improving Quality of Care with Health Services Interventions. Canadian Institute of Health Research (**CIHR**). Foundation Scheme. PI: Marelli, Ariane. **974,686 CAD.**

Awards:

- ***Winner of best abstract award at the Adult Congenital Heart Disease Symposium in 2018.*** Feasibility and Efficacy of Negative Pressure Ventilation in The Ambulatory Fontan population-(FONTAN-CMR)- A Global First Pilot Study. ACHD International Symposium. Toronto, Ontario, Canada. Authors: Charla P, Yoo S, Kaur G, Yamamura K, Granton J, Oechslin E, Shah A, **Wald RM. Senior Responsible Author.** Manuscript is complete and has been submitted for publication.