Summary Statements

Hypertension in High Risk Adult

(pages 17-25 of handout – background information)

Question 1: What blood pressure measurement techniques should be used to diagnose hypertension? *(page 25 - 29 of handout)*

According to the 2018 Hypertension Canada Guidelines[1]

- Automated office blood pressure (AOBP) measurements are the preferred in-office technique for diagnosing hypertension as compared to non-automated office blood pressure (non-AOBP) measurements (Grade D).[1]
- The use of both office blood pressure measurements, along with either ambulatory blood pressure monitoring (ABPM) or home blood pressure monitoring (HBPM), should be used for diagnosing hypertension (Grade C).[1]

Question 1a: What is the evidence for the diagnostic accuracy of different blood pressure measurements? *(pages 25 - 27 of handout)*

- ABPM is considered the reference standard in diagnosing hypertension since observational trials suggest that elevated ABPM is associated with an increased risk of CV events (independent of office blood pressure).[2]
- HBPM is considered an alternative to ABPM in diagnosing hypertension since observational trials suggest that elevated HBPM is also associated with increased risk of CV events (independent of office blood pressure). HBPM has fewer studies to support its use compared to ABPM.[2]
- A systematic evidence-based review found that office based measurements (both AOBP and non-AOBP) have lower diagnostic accuracy when compared to ABPM as the reference standard.[2]

Question 1b: How do office-based measurements, AOBP and non-AOBP, compare for diagnosing hypertension? *(pages 27- 28 of handout)*

- AOBP measurements are often promoted as more accurate since they may minimize many non-AOBP measurement errors, including those related to provider hearing deficits, terminal digit preference and rapid deflation.
- AOBP devices use proprietary algorithms to calculate systolic blood pressure (SBP) and diastolic blood pressure (DBP); therefore, it is important to use AOBP devices that have been validated for accuracy. *(page 12 of handout - Useful Links - Dabl Education Trust)*

- One particular method of office blood pressure measurement has not been **consistently** found to be more accurate than another in clinical trials; neither when compared directly with each other nor when compared with ABPM.
  - Trials have found slight variations in mean BP measurements when using different office blood pressure techniques (i.e. AOBP vs. non-AOBP).[2,3,4]
  - Trials have also found differences in mean BP measurements when comparing different AOBP devices.[5,6]
  - **These variations do not occur in a consistent pattern.** For example, some studies have reported lower mean BP while other trials have reported either higher or similar mean BP levels when an AOBP device is compared to a mercury sphygmomanometer.[2,3,4]

Question 1c: Is there evidence for improving the diagnostic accuracy of non-AOBP measurements? *(pages 28 – 29 of handout)*

- Using standardized techniques improves the accuracy of non-AOBP measurements including taking multiple measurements (i.e. three readings and taking an average of reading 2 and 3). Using standardized techniques bring non-AOBP measurements more in line with ABPM.[7,8]
- Multiple BP measurements over time (i.e. serial office visits) have better positive predictive value for hypertension than a single measurement using non-AOBP measurements.[2]

Question 2: What is the evidence to treat to a target SBP < 120 mmHg in adults with high risk of cardiovascular disease? *(pages 30 – 34 of handout)*

- According to the 2018 Hypertension Canada Guidelines[1]
  - Intensive management is promoted for high risk patients and the BP targets in this high-risk group is a systolic BP < 120 mmHg based on AOBP measurements (Grade B).
    - The definition of high-risk patients used in the guidelines are the same as the patient population included in the SPRINT trial.
  - Starting therapy at a SBP ≥ 130 mmHg (using AOBP measurements) is recommended (Grade B).
- The SPRINT trial was a large open label RCT that compared a BP target < 120 mmHg to a standard target of < 140 mmHg in a population > 50 years of age **with** high CV risk (Framingham risk > 15%) but **without** diabetes, stroke, HF, or ESRD. [9]
- Patients in the SPRINT trial were a treated population (> 90% already treated with antihypertensives), with a mean BP of 140/78 mmHg at the start of the trial, and a Framingham risk of ~20%.[9]
  - The primary outcome of fatal and non-fatal CV events (MI, other ACS, stroke, HF or death from CV cause) occurred at a significantly lower rate in the intensive treatment arm compared to the standard treatment arm resulting in a NNT of 63 over 3.3 years.[9]

- Serious AE related to treatment with antihypertensives occurred at significantly higher rates in the intensive treatment arm compared to the standard treatment arm over the same time frame resulting in a NNH of 46 over 3.3 years.[9]

SPRINT Bottom Line

- A target SBP of < 120 mmHg vs. a target SBP < 140 mmHg results in a trade-off between benefit and harm.
  - For every 50 people treated to a target SBP < 120 mmHg for 3.3 years instead of a SBP < 140 mmHg there will be approximately one less CV event (mostly HF or death) BUT there will be approximately one more treatment related serious adverse event (mostly acute kidney injury).
- The risks and benefits for each individual patient need to be assessed.
  - Patients similar to the population in SPRINT with a Framingham risk > 15% with relatively few comorbidities may be considered to be treated to a target SBP < 120 mmHg.
- It is important to remember that lower targets will potentially increase the number of antihypertensive medications, drug interactions, risk of serious side effects, need for monitoring, and costs.
- Also, a SBP < 120 mmHg was a target in the trial; a sizeable portion of patients in the study **did not** reach this target.

Question 2a: What is the evidence for lower BP targets in patients with established CV disease? *(pages 34 – 35 of handout)*

- A 2018 Cochrane Review compared lower targets (< 135/85 mmHg) to standard targets (≤ 140 - 160/90 -100 mmHg) in patients with established CV disease. There were no differences in total mortality, total CV events, CV mortality or serious AE.[10]

Question 2b: Is there evidence for the < 120 mmHg blood pressure target in patients with diabetes, history of previous stroke, or the very frail elderly? *(pages 36 – 38 of handout)*

- The results of SPRINT are not generalizable to all hypertensive patients with elevated CV risk.
  - Two recent Cochrane Reviews have evaluated lower BP targets in patients with diabetes or prior stroke. Results of the meta-analyses found that lower BP targets are not associated with better outcomes compared with standard BP targets (SBP < 140 mmHg).[11,12]
  - The strength of evidence for frail elderly is insufficient to draw any conclusions for treatment targets in this population.[13,14,15]

Antihypertensive Drug Therapy Tidbit: Thiazide-Type vs. Thiazide-Like Diuretics

(pages 40 - 43 of handout, pages 108 - 110 - Appendix 1 - Drug Tables)

- No RCT has directly compared TT and TL diuretics for CV outcomes and currently available evidence has several important limitations.[1]
- As for safety, a 2014 Cochrane Review found chlorthalidone had a greater reduction in serum potassium than hydrochlorothiazide or indapamide.[2]
  - Monitor electrolytes, especially in the first 2 weeks after starting TT or TL diuretics and after dose changes.[3]
- The observational evidence investigating the possible association between hydrochlorothiazide use and increased risk of non-melanoma skin cancer (NMSC) has several significant limitations.[4,5]
- Hydrochlorothiazide is **not** the only antihypertensive agent associated with photosensitivity reactions.[4]
  - Well-designed studies are needed to investigate hydrochlorothiazide, other diuretics, and other antihypertensive drugs and possible associations with NMSC.
- Patients should be educated on sun safety and be advised to regularly check their skin for new or changing marks or growths, especially patients taking medications associated with photosensitivity, such as hydrochlorothiazide.[6]
- The Veterans Affairs Cooperative Study #597 Diuretic Comparison Project to be published in 2023, may provide more guidance on diuretic preference.[7]

Hypertensive Disorders of Pregnancy

(pages 50 – 56 of handout – background information)

- Hypertensive disorders of pregnancy (HDP) occur in about 7% of pregnancies in Canada and 10% of pregnancies worldwide.[1,2]
- HDP encompass a range of conditions: chronic hypertension (detected prior to pregnancy or at <20 weeks gestation), gestational hypertension (detected at ≥20 weeks gestation), preeclampsia and other hypertensive effects, which can cause fetal, newborn, and maternal complications.[1,3]
- Hypertension in pregnancy is defined as a systolic blood pressure (SBP) ≥140 mmHg and/or a diastolic blood pressure (DBP) ≥90 mmHg (average of at least 2 measurements taken at least 15 minutes apart).[1]
- Hypertension can be further classified as severe or non-severe hypertension.
  - Non-severe hypertension:
    - Blood pressure (BP) between 140/90 mmHg and <160/110 mmHg.[1,3]
  - Severe hypertension:
    - SBP of ≥160 mmHg or a DBP of ≥110 mmHg.[1,3]

- This threshold has been established based on its association with increased risk of maternal stroke.[1]

- BP measurement devices that have been validated for use in pregnancy and preeclampsia should be used to measure BP in pregnant women.[3]
- The SOGC have most recently published guidelines on the diagnosis, evaluation and management of HDP in 2014, and Hypertension Canada in partnership with the SOGC published their first guideline for the management of hypertension in pregnancy in 2018.[1,3]
- The Reproductive Care Program of Nova Scotia is currently updating the Nova Scotia Prenatal Record, and the Nova Scotia Prenatal Record Companion Document.[4]
- Unfortunately, many Nova Scotians do not have a family doctor. Pregnant women without a family doctor can call their local Prenatal Clinic to make an appointment. A list of available clinics across Nova Scotia is available here: http://www.nshealth.ca/service-details/Prenatal%20Clinics.

Question 1: Which antihypertensive medications should be avoided in pregnancy? *(pages 57 – 61 of handout, pages 60 – 61 – Table 8 – pregnancy and lactation drug information resources)*

- Consideration should be given to the risk of teratogenicity when prescribing antihypertensive medications to women of child-bearing age, since 50% of pregnancies are not planned.[2,3]
- ACEi, ARBs, direct renin inhibitors, atenolol, and spironolactone should be avoided in pregnancy.[3,5]

Question 2: What is the role of ASA in preventing preeclampsia? *(pages 62 – 69 of handout)*

- A 2018 meta-analysis by Roberge et al. found a significant reduction in the risk of preterm preeclampsia in high risk patients who started ASA therapy compared to placebo at ≤16 weeks gestation and at a daily dose of ≥100 mg.[6]
  - There was no significant difference between ASA and placebo groups when ASA was started at >16 weeks gestation or at a daily dose of <100 mg.[6]
- The largest trial assessing ASA at a daily dose of ≥100 mg initiated at ≤16 weeks gestation was the ASPRE trial. ASPRE found that ASA 150 mg once daily at night started at 11-14 weeks gestation and continued until 36 weeks gestation reduced the risk of preterm preeclampsia compared to placebo in women at high risk (NNT = 38, 95% CI 23-101).[7]
- The Reproductive Care Program of Nova Scotia Recommends: [8,9]
  In pregnant women at high risk for developing pre-eclampsia (see Table 10 in the handout document), initiating ASA 150 mg (or in its absence, 2 x 81 mg tablets = 162 mg) once daily at bedtime reduces the risk of preeclampsia.
  - ASA should be:
    - initiated between 11-16 weeks gestation (ideally between 11-14 weeks), and
    - continued until 36 weeks gestation.

Question 3: What is the role of calcium supplementation in preventing preeclampsia? *(pages 70 - 73 of handout)*

- A 2018 Cochrane Review identified that supplementation with ≥1 g/day of elemental calcium in pregnant women with low dietary calcium intake (<600 mg/day) reduces the risk of preeclampsia.[10]
- The Reproductive Care Program of Nova Scotia Recommends: [8]
  Calcium supplementation with ≥ 1 g of elemental calcium/day in those with low calcium intake to prevent preeclampsia.

Question 4: How should antihypertensive agents be managed in HDP? *(pages 74 – 83 of handout)*

The management of some of the HDP are outside of the scope of this review, the focus of this section is treatment of non-severe hypertension in pregnancy without comorbid conditions.

Question 4a: What is the evidence for treating non-severe hypertension in pregnancy without comorbidities? *(pages 76 – 77 of handout)*

Question 4b: Is one drug or class of drug better than another for treating non-severe hypertension in pregnancy without comorbid conditions? *(pages 76 - 77 of handout)*

- A 2018 Cochrane Review found that use of antihypertensive drug therapy in women with mild to moderate hypertension in pregnancy, without co-morbidities (e.g., diabetes or renal disease), significantly reduced the risk of severe hypertension compared to no antihypertensive drug therapy (NNT = 10, 95% CI 8-13).[11]
  - *B*-blockers or calcium channel blockers were more effective than methyldopa in avoiding an episode of severe hypertension.
    - RR = 0.70 (95% CI, 0.56-0.88)
- According to local clinical reviewer opinion, the preferred first line antihypertensive agents in this patient population are oral labetalol or nifedipine XL.[8,12]

Question 4c: What is the evidence for the 2018 Hypertension Canada treatment target of a "DBP of 85 mmHg for pregnant women receiving antihypertensive therapy with chronic hypertension or gestational hypertension"? *(pages 78 - 82 of handout)*

- The SOGC 2014 guidelines recommend that antihypertensive drug therapy may be used to keep SBP at 130–155 mmHg and DBP at 80–105 mmHg (I-B; Low/Weak).[3]
- According to Hypertension Canada 2018 guidelines, a DBP of 85 mmHg should be targeted for pregnant women receiving antihypertensive therapy with chronic hypertension or gestational hypertension (Grade B). A similar target could be considered for pregnant women with preeclampsia (Grade D).[1]
- This difference in BP treatment targets is based on results of the CHIPS trial, a recent RCT:[13]
  - The CHIPS trial compared less-tight control [target DBP = 100 mmHg (100-104 mmHg)] vs. tight control [target DBP = 85 mmHg (81-85 mmHg)] of hypertension in pregnant

women with non-severe nonproteinuric pre-existing hypertension or gestational hypertension.[13]

- **Academic Detailing Note:**
  - **CHIPS compared the upper end vs the lower end of the SOGC target DBP range of 80-105 mmHg**.
- According to the trial protocol, CHIPS investigators hypothesized that less tight control may improve uteroplacental perfusion, fetal growth, and through these fetal/neonatal well-being.
- They actually found no significant difference in the risk of the composite outcome of pregnancy loss or high-level neonatal care for more than 48 hours (the primary outcome) between less-tight and tight control groups.[13]
- However, there was a significantly higher risk of developing severe hypertension in the less-tight control group (target DBP = 100 mmHg) compared to the tight control group (target DBP = 85 mmHg) (NNH = 8, 95% CI 5-14).[13]
- Study may have been underpowered and we must interpret results with caution.

➢ The CHIPS trial provides some reassurance that treating non-severe hypertension in pregnancy in patients without comorbid conditions to the lower end of the current SOGC target DBP range, may be safer than previously thought, and is associated with a lower risk of developing severe hypertension. However, caution must be exercised to ensure DBP does not fall to <80 mmHg as this may limit uteroplacental perfusion.

Question 5: According to guidelines and local clinical reviewers, which women at risk, or who have developed a HDP should obstetrics be consulted? *(page 84 of handout)*

➢ According to the Reproductive Care Program of Nova Scotia, consultation with an obstetrician should be considered:[8]
- For women with a history of previous preeclampsia or other strong clinical markers of increased risk, especially multifetal pregnancy, chronic hypertension, type 1 or 2 diabetes, renal disease, or autoimmune disease (antiphospholipid syndrome, systemic lupus erythematosus). Women with multiple other risk factors for preeclampsia should also be considered for consultation. See Table 10 and Appendix 3 in the handout document.
- For any pregnant woman **diagnosed with a HDP.**

Question 6: How should antihypertensive agents be managed postpartum? *(pages 85 – 87 of handout)*

➢ The time of peak BP postpartum is at 3 to 6 days after delivery, and BP should be monitored during this time.[3]

- There is very limited evidence to guide the management of HDP postpartum. Authors of a recent systematic review of 39 studies (N = 2901) were unable to recommend a particular BP threshold, agent, or model of care.[14]
  - There is very little evidence to guide the management of antihypertensive drugs in the weeks after delivery.
- All medications should be assessed for safety in breastfeeding (see lactation drug information resources in Table 8 of the handout document).
- The SOGC 2014 guidelines suggest nifedipine XL, labetalol, methyldopa, captopril, and enalapril to be generally acceptable for use in breastfeeding.[3]
  - Although it is considered safe during breastfeeding, **methyldopa may increase risk of postpartum depression.** The National Institute for Health and Care Excellence (NICE) recommends to consider switching to an alternative therapy within 2 days of delivery.[3,15,16]

Hypertension in Children

(page 92 of handout – background information)

- The prevalence of hypertension in children is increasing.[1]
- Secondary hypertension is more common in children than adults.
  - Children who develop hypertension should have a focused history and physical examination and investigations for secondary causes.[1,2]
    - Common causes of secondary hypertension in children are renal, renovascular, endocrine, or cardiac disorders.[2] *(page 94 - Table 2 and 3)*
- In obese children and adolescents, primary hypertension is more common than secondary hypertension.[2]
- Hypertension Canada recommends that BP should be measured regularly in children 3 years of age and older by a health care professional using standardized pediatric techniques.[1] *(page 12 - Useful Links - YouTube video)*
- Unlike adults, a child's or adolescent's blood pressure is NOT compared to a single diagnostic threshold, instead, BP percentiles are used.[1]
  - BP readings should be compared with norms for age, sex, and height.[1] (*page 12 - Useful Links – link to CDC growth charts for height percentiles)*
    - Normative BP tables are available.[1] *(pages 114 - 117 - Appendix 4, pages 118 – 119 - Appendix 5 – Screening Chart and pages 97 – 100 of handout – Question 2)*
- Family physicians should be familiar with the criteria for diagnosis of hypertension in children and adolescents *(pages 101 - 103 of handout - Question 3).*

- Most children and adolescents with hypertension should be managed by an expert in pediatric hypertension *(pages 104 - 106 of handout - Question 4).*[1,3,4]

References:

Hypertension in High Risk Adults

1) Nerenberg KA, Zarnke KB, Leung AA, et al. Hypertension Canada's 2018 Guidelines for Diagnosis, Risk Assessment, Prevention, and Treatment of Hypertension in Adults and Children. Can J Cardiol 2018;34(5):506-25.
2) Piper MA, Evans CV, Burda Bu, et al. Screeing for high blood pressure in adults: a systematic evidence review for the U.S. Preventative Services Task Force. Evidence synthesis No. 121. AHRQ publication No. 13-05194-EF-1. Rockville, MD: Agency for Healthcare Research and Quality: 2014.
3) Pappaccogli M, Monaco S, Perlo E, et al. Comparison of automated office blood pressure with office and out-of-office measurement techniques a systematic review and meta-analysis. Hypertension 2019;73:481-490.
4) Roerecke M, Kaczorowski J, Myers M. Comparing automated office blood pressure readings with other methods of blood pressure measurement for identifying patients with possible hypertension a systematic review and meta-analysis. JAMA Internal Medicine 2019;179:351-362
5) Myers M, Valdivieso M, Kiss A, et al. Comparison of two automated sphygmomanometers for use in the office setting. Blood Pressure Monitoring 2009;14:45-47.
6) Rinfret F, Cloutier L, Wistaff R, et al. Comparison of different automated office blood pressure measurement devices: evidence of nonequivalence and clinical implications. Canadian Journal of Cariology 2017;33:1639-1644.
7) Handler J, Zhao Y, Egan B. Impact of the number of blood pressure measurements on blood pressure classification in US adults: NHANES 1999-2008. *J Clin Hypertens* (Greenwhich) 2001;14:751-759.
8) Campbell N, Culleton B, McKay D. Misclassification of blood pressure by usual measurement in ambulatory physician practices. American Journal of Hypertension 2005;18:1522-1527.
9) The SRINT Research Group. A randomized trial of intensive versus standard blood-pressure control. N Engl J Med 2015;373:2103-2116.
10) Saiz L, Gorricho J, Garjon J, et al. Blood pressure targets for the treatment of people with hypertension and cardiovascular disease. Cochrane Database of Systematic Reviews 2018, Issue 7. Art.No: CD10315.
11) Arguedsa J, Leiva V, Wright J. Blood pressure targets in people with diabetes mellitus. Cochrane Database of Systematic Reviews 2013, Issue 10.Art.No:Cd008277
12) Zonneveld T, Ricjard E, Vergouwen M, et al. Blood pressure-lowering treatment for preventing recurrent stroke, major vascular events, and dementia in patients with a history of stroke or transient ischemic attack. Cochrane Database of Systematic Reviews 2018, Issue 7 Art.No: CD007858
13) Weiss J, Freeman M, Low A, et al. Benefits and harms of intensive blood pressure treatment in adults aged 60 years or older a systematic review and meta-analysis. Ann Intern Med 2017;166:419-429.
14) Williamson J, Supiano M, Applegate W, et al. Intensive vs. standard blood pressure control and cardiovascular disease outcomes in adults aged ≥ 75 years: a randomized clinical trial. JAMA 2016;315:2673-2682.
15) Warwick J, Falaschetti E, Rockwood K, et al. No evidence that frailty modifies the positive impact of antihypertensive treatment in very elderly people: an investigation of the impact of frailty upon treatment effect in the hypertension in the very elderly trial (HYVET) study, a double-blind, placebo-controlled study of antihypertensives in people with hypertension aged 80 and over. BMC Medicine 2015;13

Antihypertensive Drug Therapy Tidbit: Thiazide-Type vs. Thiazide-Like Diuretics

1) Olde Engberink RH, Frenkel WJ, van den Bogaard B, et al. Effects of thiazide-type and thiazide-like diuretics on cardiovascular events and mortality: systematic review and meta-analysis. Hypertension 2015;65(5):1033-40.
2) Musini VM, Nazer M, Bassett K, et al. Blood pressure-lowering efficacy of monotherapy with thiazide diuretics for primary hypertension. Cochrane Database Syst Rev 2014;5:CD003824.
3) Mount DB. Causes of hypokalemia in adults. In: UpToDate [Internet]. Waltham, MA: UpToDate, updated 2017 Dec 18; cited 2019 May 24. Available from: https://www.uptodate.com/contents/causes-of-hypokalemia-in-adults.
4) Kreutz R, Algharably EAH, Douros A. Reviewing the effects of thiazide and thiazide-like diuretics as photosensitizing drugs on the risk of skin cancer [published online ahead of print 2019 June 5]. J Hypertens 2019. doi: 10.1097/HJH.0000000000002136.
5) Shin D, Lee ES, Kim J, et al. Association Between the Use of Thiazide Diuretics and the Risk of Skin Cancers: A Meta-Analysis of Observational Studies. J Clin Med Res 2019;11(4):247-55.

6) Health Canada. Summary Safety Review - Hydrochlorothiazide. Issued 2019 Jan 30; cited 2019 May 24. Available From: https://hpr-rps.hres.ca/reg-content/summary-safety-review-detail.php?lang=en&linkID=SSR00215#references.
7) US National Library of Medicine. ClinicalTrials.gov. Diuretic Comparison Project (DCP). Accessed Sept 2019. Available at: https://clinicaltrials.gov/ct2/show/NCT02185417

Hypertensive Disorders of Pregnancy

1) Butalia S, Audibert F, Cote AM, et al. Hypertension Canada's 2018 Guidelines for the Management of Hypertension in Pregnancy. Can J Cardiol 2018;34(5):526-31.
2) Magee LA, von Dadelszen P. State-of-the-Art Diagnosis and Treatment of Hypertension in Pregnancy. Mayo Clin Proc 2018;93(11):1664-77.
3) Magee LA, Pels A, Helewa M, et al. Diagnosis, evaluation, and management of the hypertensive disorders of pregnancy. Pregnancy Hypertens 2014;4(2):105-45.doi :https://doi.org/10.1016/j.preghy.2014.01.003. This article is published under the terms of the Creative Commons Attribution-NonCommercial-No Derivatives License (CC BY NC ND) https://creativecommons.org/licenses/by-nc-nd/4.0/.
4) Reproductive Care Program of Nova Scotia. Nova Scotia Prenatal Record. 2015. Available at: http://rcp.nshealth.ca/
5) Padwal R, Gibson P, Tsuyuki RT. Hypertension. In: RxTx [Internet]. Ottawa ON: Canadian Pharmacists Association; updated 2018 May; cited 2019 Feb 8. Available from: https://www.e-therapeutics.ca/.
6) Roberge S, Bujold E, Nicolaides KH. Aspirin for the prevention of preterm and term preeclampsia: systematic review and meta-analysis. Am J Obstet Gynecol 2018;218(3):287-93.
7) Rolnik DL, Wright D, Poon LC, et al. Aspirin versus Placebo in Pregnancies at High Risk for Preterm Preeclampsia. N Engl J Med 2017; 377(7):613-22.
8) Personal Communication: Dr. Heather Scott, Obstetrical Medical Advisor Reproductive Care Program of Nova Scotia and Maternal Fetal Medicine Specialist, Department of Obstetrics & Gynaecology, Faculty of Medicine, Dalhousie University.
9) Personal Communication: Dr. Chris Nash, Maternal Fetal Medicine Specialist, Department of Obstetrics & Gynaecology).
10) Hofmeyr GJ, Lawrie TA, Atallah AN, et al. Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems. Cochrane Database Syst Rev 2018,10:CD001059.
11) Abalos E, Duley L, Steyn DW, et al. Antihypertensive drug therapy for mild to moderate hypertension during pregnancy. Cochrane Database Syst Rev 2018;10:CD002252.
12) Personal Communication: Dr. Lynn Bussey, Chief of Family Medicine, Department of Family Medicine - Maternal Newborn Care, Dalhousie University.
13) Magee LA, von Dadelszen P, Rey E, et al. Less-Tight versus Tight Control of Hypertension in Pregnancy. N Engl J Med 2015;372(5):407-17.
14) Cairns AE, Pealing L, Duffy JMN et al. Postpartum management of hypertensive disorders of pregnancy: a systematic review. BMJ Open 2017;7(11):e018696.
15) National Institute for Health and Care Excellence. Hypertension in Pregnancy: Diagnosis and Management. 2019 NICE Guideline 133. Cited 2019 Sept 16. Available at: https://www.nice.org.uk/guidance/ng133/resources/hypertension-in-pregnancy-diagnosis-and-management-pdf-66141717671365
16) Kosar L. Peri-Pregnancy: Drug Treatment Considerations. In: RxFiles Drug Comparison Chart. 11th ed. Saskatoon, SK: Saskatoon Health Region; updated 2018 Aug, cited 2018 Dec 3. Available from: www.RxFiles.ca.

Hypertension in Children

1) Nerenberg KA, Zarnke KB, Leung AA, et al. Hypertension Canada's 2018 Guidelines for Diagnosis, Risk Assessment, Prevention, and Treatment of Hypertension in Adults and Children. Can J Cardiol 2018;34(5):506-25.
2) Harris KC, Benoit G, Dionne J, et al. Hypertension Canada's 2016 Canadian Hypertension Education Program Guidelines for Blood Pressure Measurement, Diagnosis, and Assessment of Risk of Pediatric Hypertension. Can J Cardiol 2016;32(5):589-97.
3) Dionne JM, Harris KC, Benoit G. Hypertension Canada's 2017 Guidelines for the Diagnosis, Assessment, Prevention, and Treatment of Pediatric Hypertension. Can J Cardiol 2017;33(5):577-85.
4) Personal Communication: Dr. Robyn McLaughlin, IWK Health Centre Pediatrician. 2019 Apr 2