ANEMIA AND HEAVY MENSTRUAL BLEEDING

MENAKA PAI, BSC, MSC, MD, FRCPC

Associate Professor, Dept Of Medicine, McMaster University

Associate Member, Dept Of Pathology & Molecular Medicine, McMaster University

Consultant Laboratory Hematologist, Hamilton Regional Laboratory Medicine Program

Site Head – Hematology, Hamilton General Hospital

PRESENTER DISCLOSURE

- **Faculty:** Menaka Pai

- **Relationships with commercial interests:**
  - **Grants/Research Support:** International Society on Thrombosis and Haemostasis
  - **Speakers Bureau/Honoraria:** Novartis, Bayer
  - **Consulting Fees:** None
  - **Other:** Employee of Hamilton Health Sciences, McMaster University

OBJECTIVES FOR TODAY

- Recognize women at risk for iron deficiency anemia
- Identify the role of menstrual suppression in the management of anemia secondary to heavy menstrual bleeding
- Identify the role of iron replacement in the management of anemia secondary to heavy menstrual bleeding

RECOGNIZE WOMEN AT RISK FOR IRON DEFICIENCY ANEMIA

What is HMB? What is iron deficiency?

Why should we care about either?

How do we make the diagnosis?

TWO BASIC DEFINITIONS

Heavy menstrual bleeding

- Excessive menstrual blood loss which interferes with a woman's physical, emotional, social, and overall quality of life

Ferritin <15–30 ug/L
TSAT < 20%
Low Hb

Iron deficiency

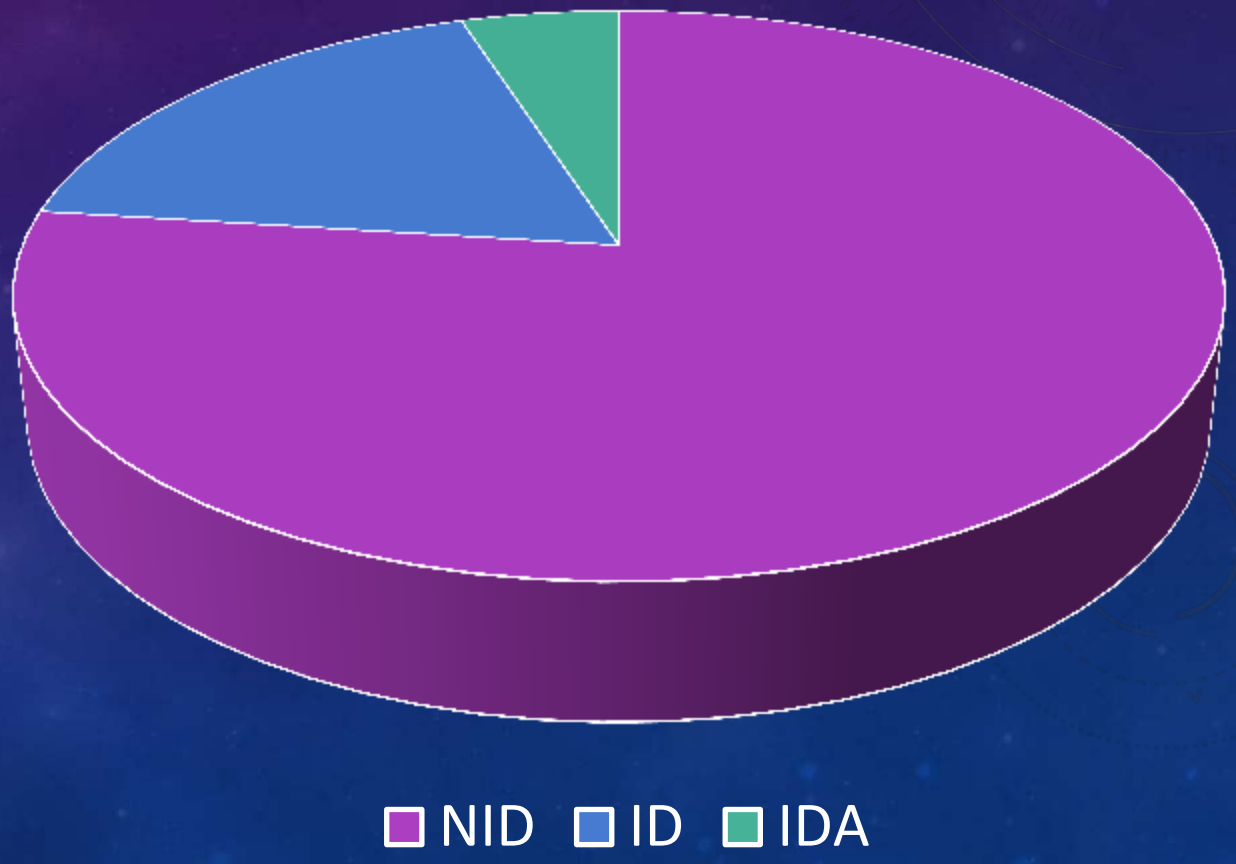
- Abnormally low serum ferritin, transferrin saturation, or free erythrocyte protoporphyrin
- If present with a low hemoglobin value – **iron deficiency anemia**

National Institute for Health and Care Excellence. Heavy menstrual bleeding: assessment and management. London, 2007.

IRON DEFICIENCY IS COMMON IN WOMEN

- **Up to 20%** of reproductive age women in North America are iron deficient
- **Up to 5%** of reproductive age women in North America have iron deficiency anemia

- At greatest risk…
  - Women of colour
  - Women experiencing food insecurity
  - Adolescents



MMWR October 11, 2002 / 51(40);897899

THE SYMPTOMS OF IRON DEFICIENCY ARE MYRIAD

- Fatigue
- Lack of motivation
- Mood lability
- Irritability
- Difficulty concentrating
- Poor school performance
- Pica
- Restless legs
- Cold intolerance
- Hair loss
- Maternal and infant effects*

Percy L, Mansour D, Fraser I. Iron deficiency and iron deficiency anaemia in women. Best Practice & Research Clinical Obstetrics & Gynaecology. 40:55-67, April 2017.

HEAVY MENSTRUAL BLEEDING (HMB) IS THE KEY TO IRON DEFICIENCY IN WOMEN

- Every year, 5% to 15% of reproductive aged women seek medical care for HMB
- Far more have symptoms, and never seek care!
- **63% of women with HMB have confirmed iron deficiency**

Percy L, Mansour D, Fraser I. Iron deficiency and iron deficiency anaemia in women. Best Practice & Research Clinical Obstetrics & Gynaecology. 40:55-67, April 2017.

WHY SHOULD WE CARE ABOUT IRON DEFICIENCY AND HMB?

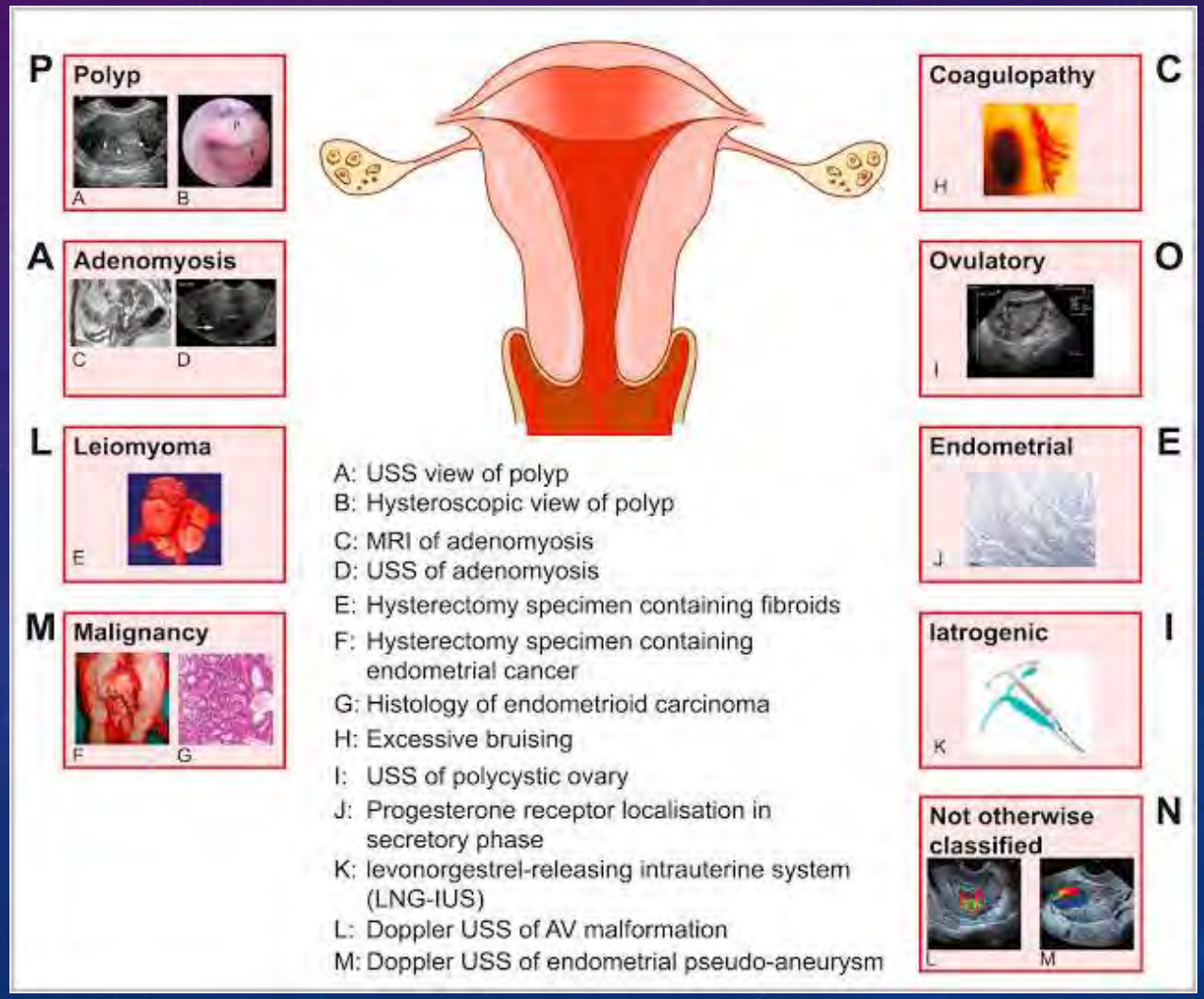
- **In 2011, the global prevalence of anemia in women was 528 million women**
- **Tremendous personal and societal impact**

- Annual direct costs associated with HMB = $1 billion USD
- Annual indirect costs associated with HMB = $12 billion USD

WHO. The global prevalence of anaemia in 2011. Geneva: World Health Organization; 2015

A QUICK DIFFERENTIAL OF HMB: PALM-COEIN

- **PALM = structural causes**
  - Polyp
  - Adenomyosis
  - Leimyoma
  - Malignancy and hyperplasia
- **COEIN = functional causes**
  - Coagulopathy
  - Ovulatory dysfunction
  - Endometrial
  - Iatrogenic
  - Not yet classified

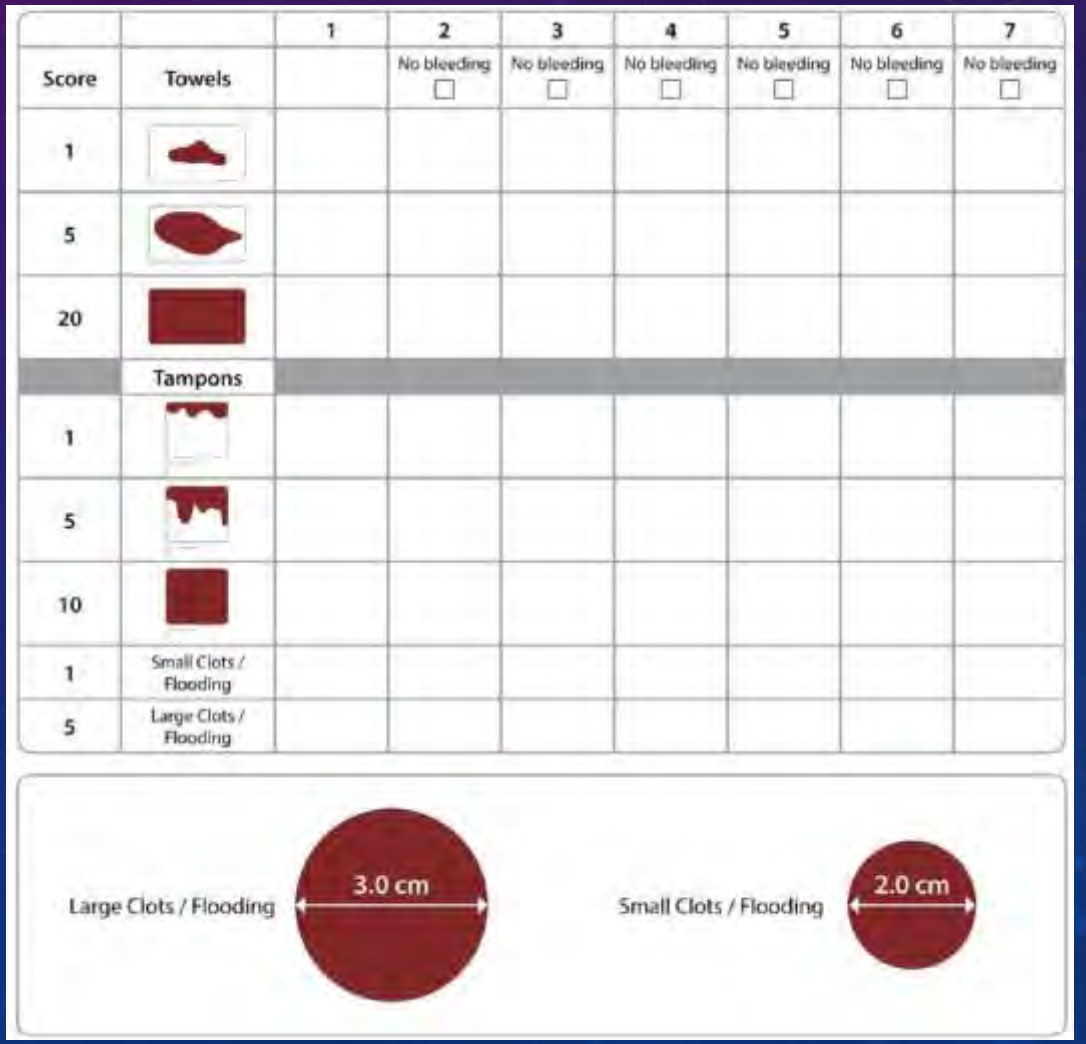


Fraser IS et al. Fertil Steril 2007;87:466–76.
Fraser IS et al. Hum Reprod 2007;22:635–43.

WHAT IS THE BEST WAY TO IDENTIFY WOMEN WITH HMB AND IRON DEFICIENCY?

- Risk-based screening questionnaires are not very effective
- Structured bleeding questionnaires have not been validated
- Pictorial assessment tools may not be practical in a busy clinic

- **Back to basics: focused history, physical, and lab testing**



Sekhar DL, Murray-Kolb LE, Schaefer EW, Paul IM. Risk-Based Questionnaires Fail to Detect Adolescent Iron Deficiency and Anemia. J Pediatr. 2017 Aug;187:194-199.e1

BACK TO BASICS HISTORY: WORKING UP HMB AND IRON DEFICIENCY

- Menstrual history
  - Clots? Flooding? Frequency of changing sanitary protection? Irregular or intermenstrual bleeding? Cycle length and duration of menses?
- Impact on QOL
- Other red flag bleeding symptoms
- Treatments tried to date
- What are the patients goals around fertility? What is the patient's insurance status? What symptoms concern her most?

BACK TO BASICS GYNE EVALUATION: WORKING UP HMB AND IRON DEFICIENCY

- Pelvic examination
- Transvaginal ultrasound
- Referral to gynaecology if structural problems, irregular menses, painful menses

BACK TO BASICS LAB INVESTIGATIONS: WORKING UP HMB AND IRON DEFICIENCY

- CBC
- Iron parameters – ferritin, transferrin saturation
- Full hemostasis evaluation?

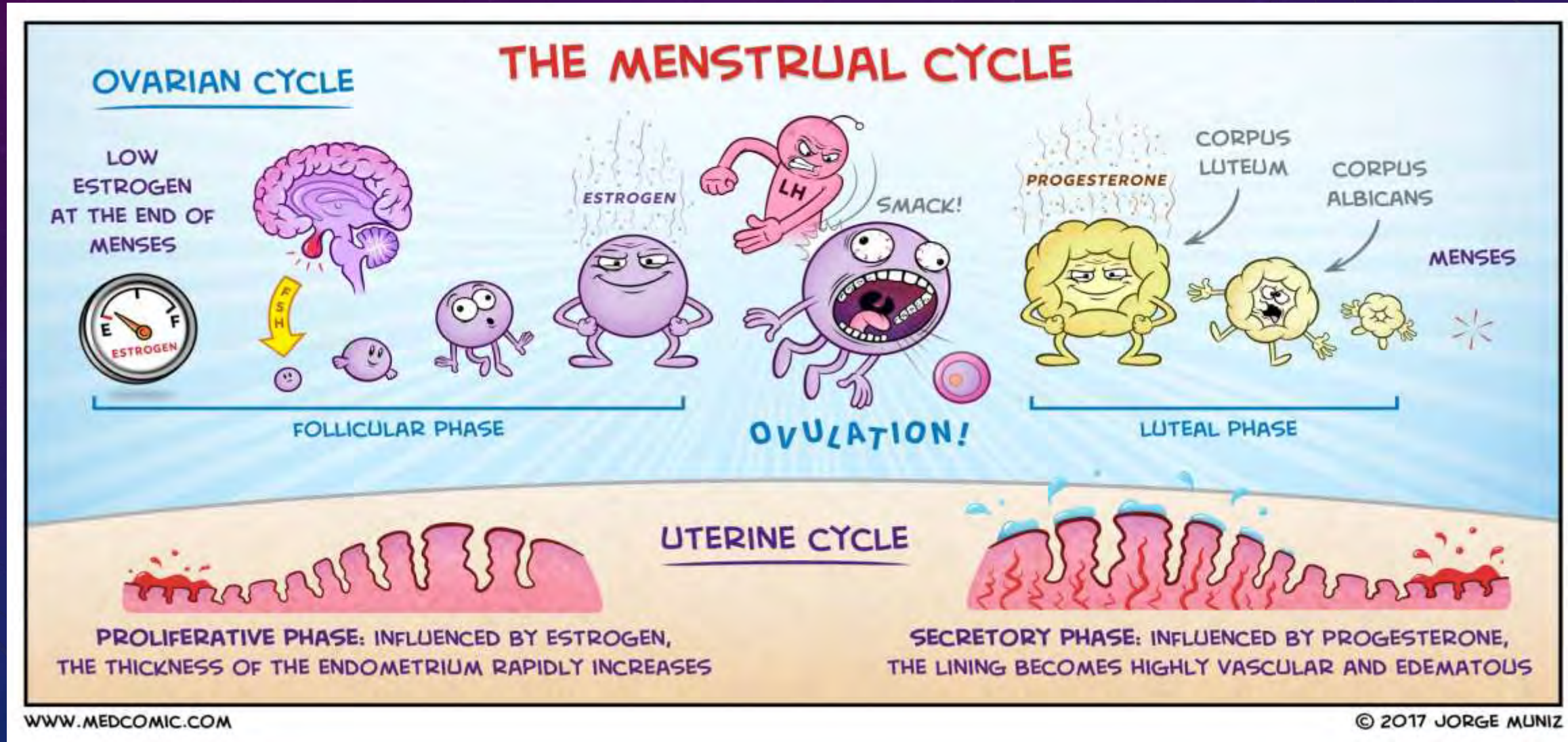
DISCUSS THE ROLE OF MENSTRUAL SUPPRESSION

A quick review of endocrinology (yikes!)

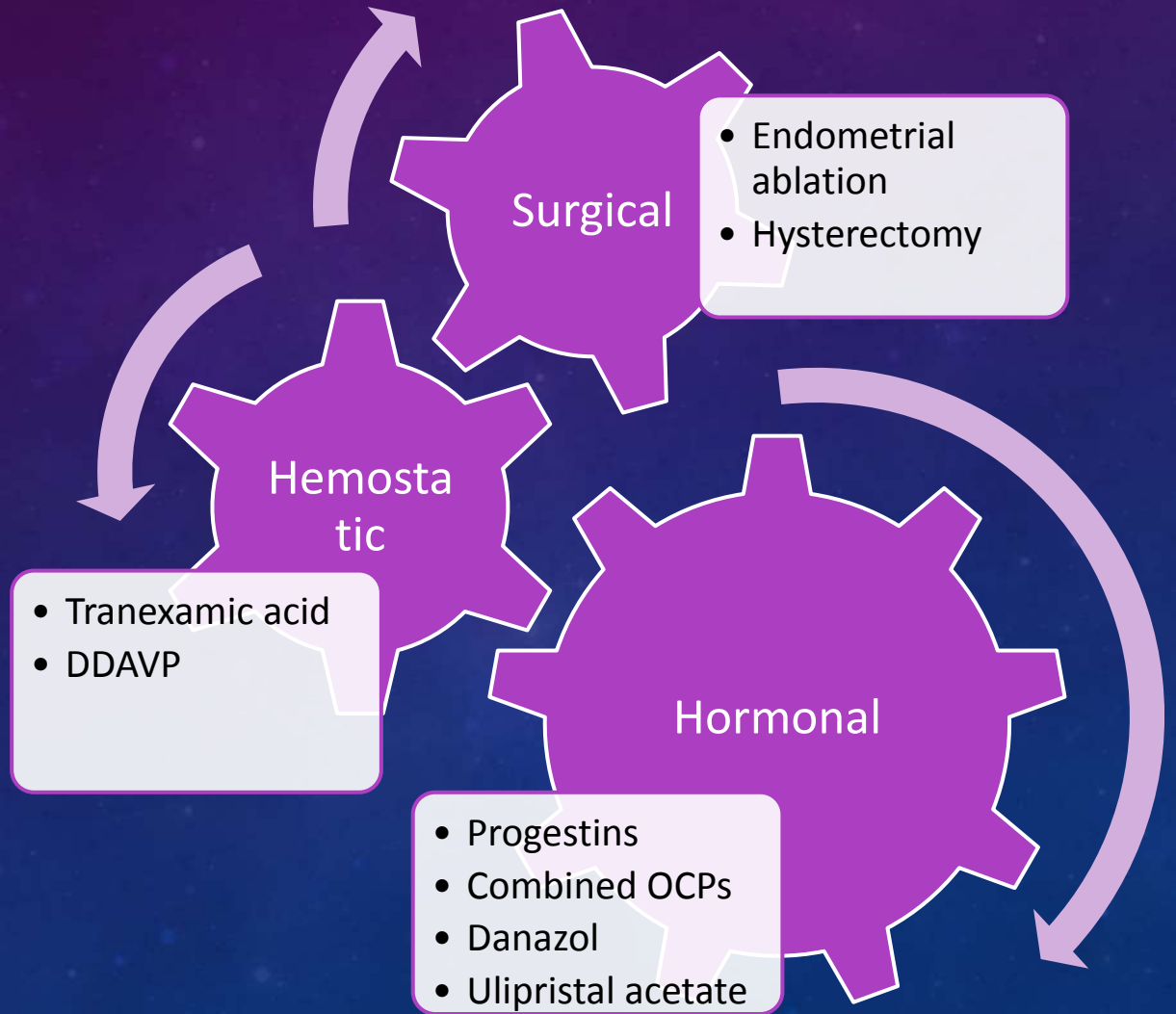
Hormonal interventions

Non-hormonal interventions

A QUICK ENDOCRINOLOGY REVIEW



THERE ARE MANY OPTIONS TO MINIMIZE HMB



HORMONAL OPTIONS

Intervention	Efficacy	Downsides
Progestin IUD	>70% reduction in blood loss (>80% when combined with OCP)	Progestogenic symptoms, expulsion, perforation, sepsis Costs $350 / 5 years
Combined OCP	>35% reduction in blood loss	Hormonal symptoms, VTE, stroke, breast cancer Costs $10-$30 / month
Cyclic oral progestogen	2% - 30% reduction in blood loss. (May be as high as 60% with long phase)	Progestogenic symptoms Costs $10-$30 / month
Injectable progestogen	50% achieve amenorrhea	Reduced bone density, fracture Costs $35 - $45 / 3 months
Danazol	>80% reduction in blood loss	Androgenic symptoms
Ulipristal acetate	70-90% reduction in blood loss	Headache, breast tenderness, *liver damage* Costs >$1000 – $2000 / 3 months

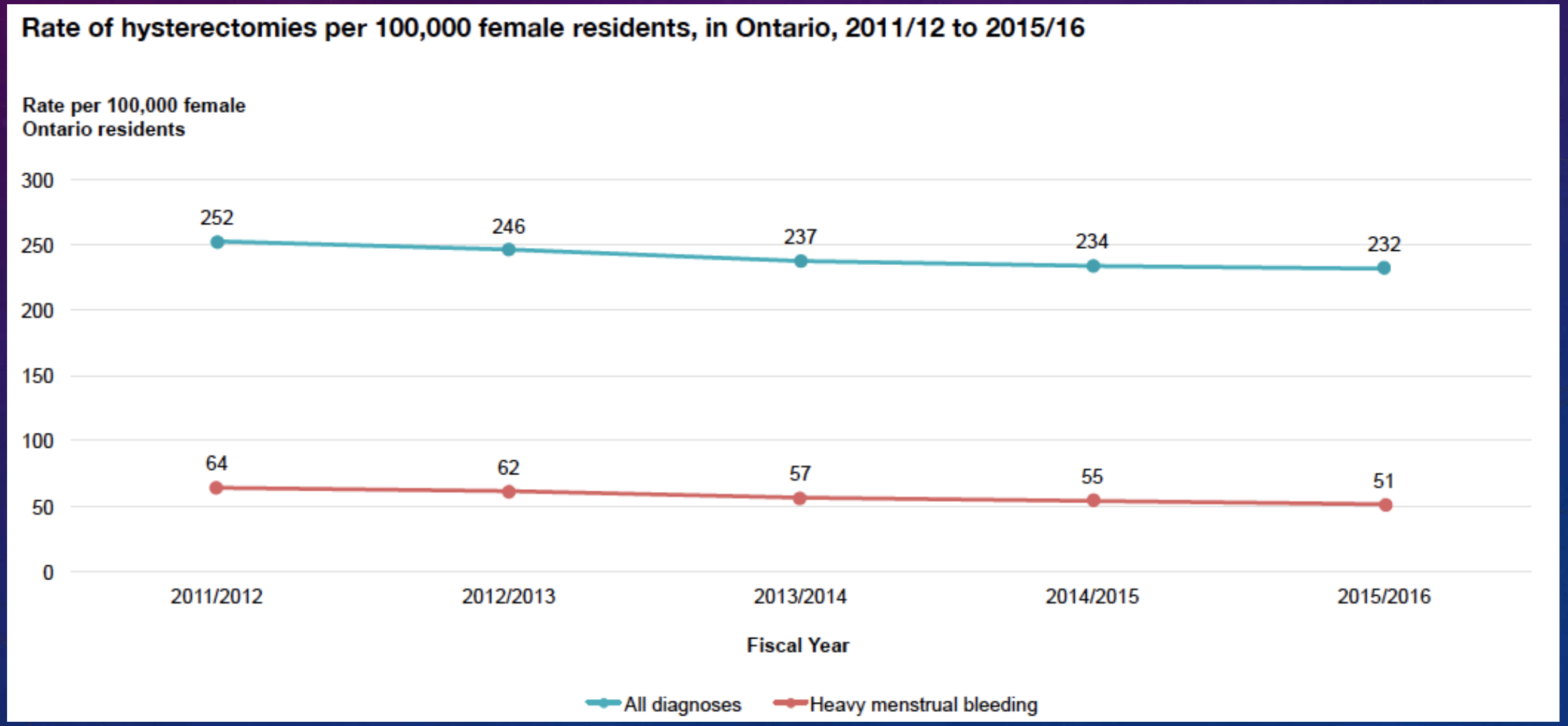
HEMOSTATIC OPTIONS

- DDAVP
- Tranexamic acid
- NSAIDs

SURGICAL OPTIONS

- Endometrial ablation
  - Minimally invasive
- Hysterectomy
  - Moderately – maximally invasive
  - 2016 data from Health Quality Ontario (HQO) has looked at local practice

IS HYSTERECTOMY OVERUSED IN ONTARIO?



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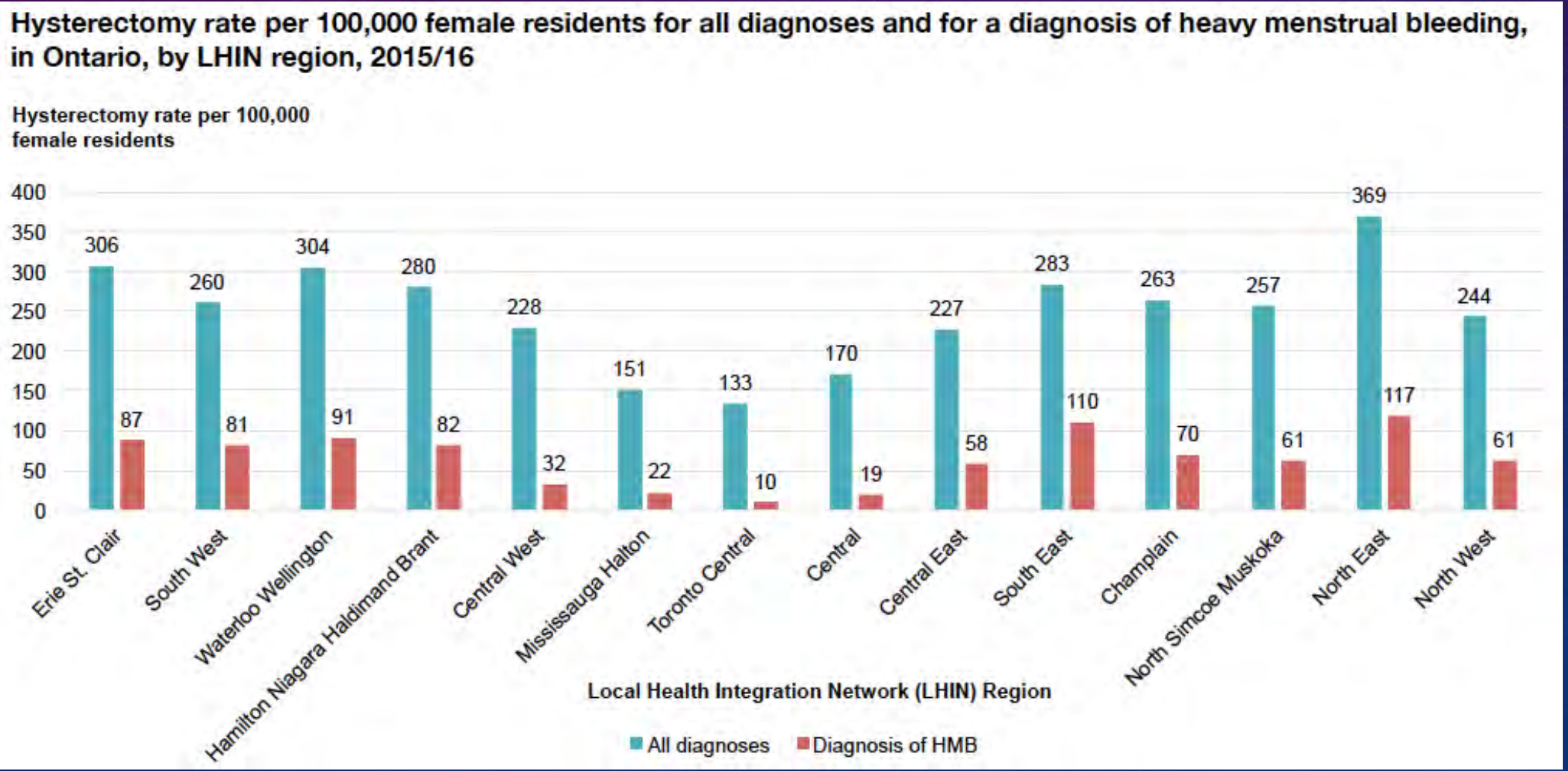


DISCUSS THE ROLE OF IRON REPLACEMENT IN WOMEN WITH HMB

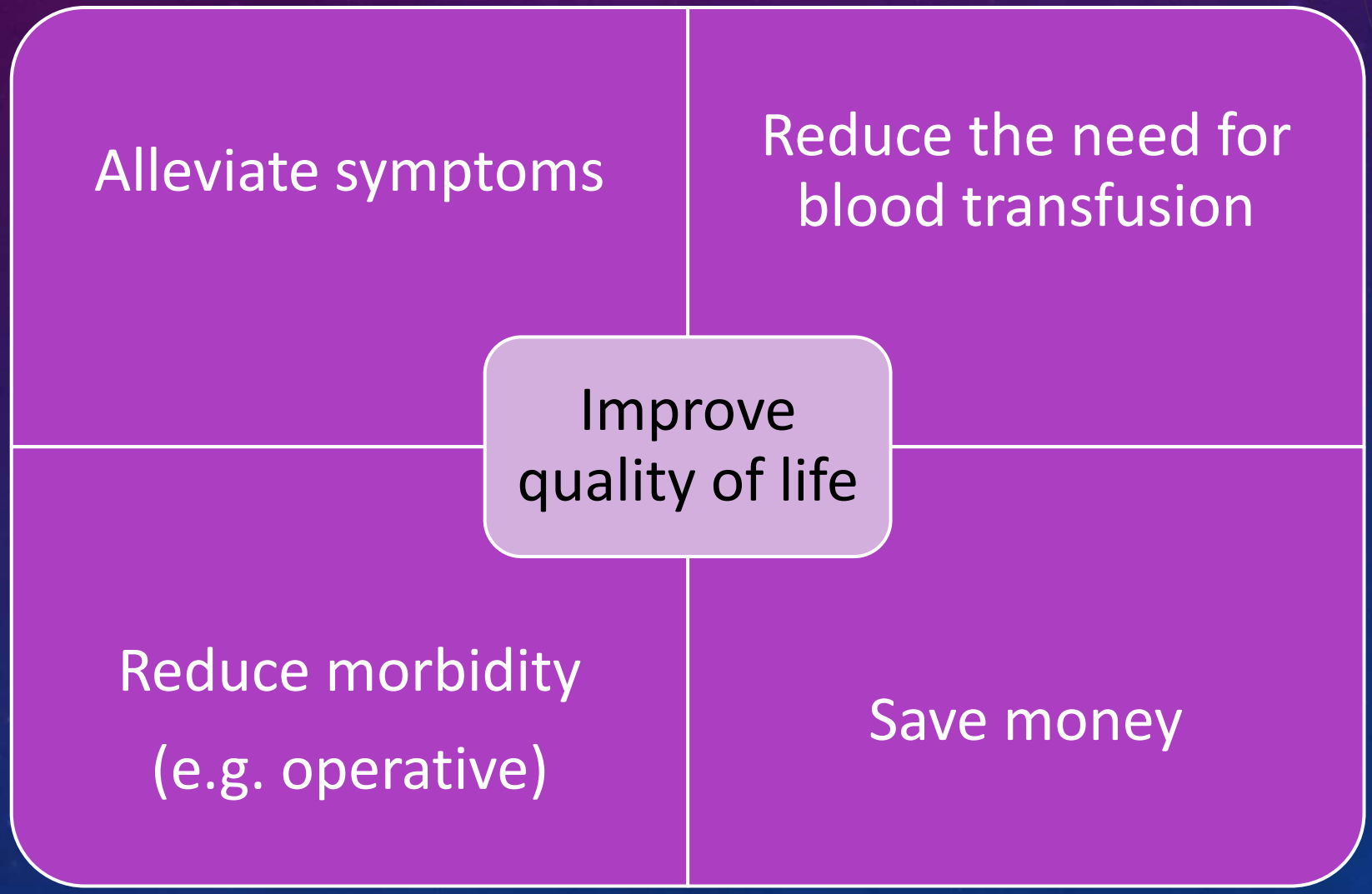
EVIDENCE-BASED OPTIONS

SOME PRACTICAL REALITIES

FULL SCOPE OF QUALITY CARE OF HMB AND IDA

HQO 2016.

WHY REPLACE IRON?



Hamilton Health Sciences
PATIENT EDUCATION

HHS ONTraC Patient Blood Management

Choosing an Iron Pill

ONTraC
ontario transfusion coordinators

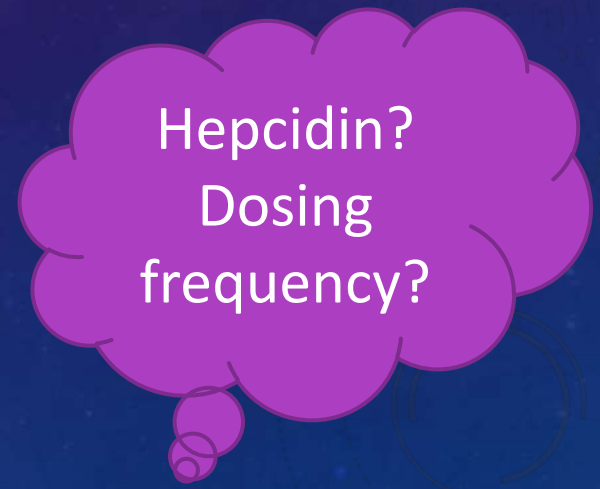
Always start with taking 1 pill a day. If you do not have side effects, and tolerate it well, increase the amount after 3 to 4 days to the recommended amount. The most common side effects are constipation or diarrhea, stomach discomfort and dark or black stool. This is more common with the last 3 pills listed below. If having side effects with high dose ferrous fumarate or ferrous sulfate, it may be easier to tolerate every other day or as per doctor's advice. Do not take iron at same time as antibiotics, Parkinson or thyroid medications.

Iron pills	Amount	Cost per day	Information
Heme-Iron Polypeptide example — **Proferrin**	One tablet 1 to 3 times a day or per doctor's advice	**$1.01 to $3.03 a day** $30.29 for 30 tablets = $1.01 a tablet	Very easily absorbed. Taken with or without food. Does not need acid in the stomach to get absorbed. Good choice if you take medicines that reduce stomach acid.*** Note to vegetarians and vegans: product is made from animal proteins (bovine source). Do not take if you have an allergy to cow products.
Polysaccharide-Iron Complex example — **FeraMAX 150** or generic	One capsule once daily or as per doctor's advice (Also available in powder form)	**67¢ a day** $19.99 for 30 capsules = 67¢ a capsule	Taken with or without food. Does not need acid in the stomach to get absorbed. Good choice if you take medications that reduce stomach acid.*** Note to vegetarians and vegans: capsule coating is made from an animal source. Capsule can be opened and contents mixed into water or sprinkled over soft food. Virtually tasteless.
Ferrous fumarate 300 mg tablets examples — **Eurofer, Palafer**	One to two tablets once daily or as per doctor's advice	**19¢ to 38¢ a day** $5.69 for 30 tablets = 19¢ a tablet	Needs acid in the stomach to get absorbed. Take on an empty stomach — at least 1 hour before or 2 hours after eating, with orange juice or vitamin C. Absorption may be decreased if you take antacids or medications that reduce stomach acid.***
Ferrous sulphate 300 mg tablets examples — **Feosol, Fer-In-Sol**	One to two tablets once daily or as per doctor's advice	**10¢ to 20¢ a day** $10.19 for 100 tablets = 10¢ a tablet	Needs acid in the stomach to aid in absorption. Take on an empty stomach — at least 1 hour before or 2 hours after eating, with orange juice or vitamin C. Absorption may be decreased if you take antacids or medications that reduce stomach acid.***
Ferrous gluconate 300 mg tablets	One to three tablets once daily or as per doctor's advice	**4¢ to 12¢ a day** $3.89 for 100 tablets = 4¢ a tablet	Needs acid in the stomach to aid in absorption. Take on an empty stomach — at least 1 hour before or 2 hours after eating, with orange juice or vitamin C. Absorption may be decreased if you take antacids or medications that reduce stomach acid.***

Prices are approximate and subject to change.

***Examples of some common brand name medicines that reduce stomach acid are:
Prevacid, Nexium, Tecta, Pantoloc, Losec, Prilosec, Zantac

Hamilton Health Sciences, 2016
June 23, 2016



http://www.hamiltonhealthsciences.ca/documents/Patient%20Education/IronPillChoosing-th.pdf

Prepared by Michelle Zeller, MD FRCPC and Linda Pickrell, RN, OnTRAC

WHEN DO WE MOVE TO PARENTERAL IRON?

- Refractory IDA
  - Failure to respond to/tolerate treatment at a dose of at least 100 mg of elemental iron per day after 4 to 6 weeks of therapy (can take ≥ 6 months)
  - Failure to respond to/tolerate 2 different categories of oral iron for minimum 3 months
- Prevent need for urgent transfusion or serious sequelae
  - Pregnancy, preoperative, severely symptomatic

- **Should parenteral iron be a first line therapy?**

Lopez Lancet 2015, Koch Anemia 2015, Hershko, Camaschella Blood 2014

PARENTERAL IRON IN HMB

- RCT comparing ferrous sulphate (65mg elemental iron TID x 6wks) to ferric carboxymaltose (1000mg x1 dose over 15 min) in 477 women)
- Results:
  - Hb increase of ≥20 g/L (82% FC vs. 62% FS)
  - Correction of anemia (73% FC vs. 50% FS)
  - Patients receiving FC reported increased QOL
  - No serious adverse drug events

Van Wyck Transfusion 2009

PRACTICAL REALITIES OF IRON REPLACEMENT

- Parenteral iron is increasingly hard to access in Ontario
  - Generally given in a hospital setting
  - Generally not funded by the hospital

- What can we do to help our patients?
  - Focus on treating the CAUSE of iron deficiency
  - Proactively discuss cost of parenteral iron, insurance options, EAP funding
  - Develop streamlined care pathways
  - **Advocate! Iron deficiency in women is a PUBLIC HEALTH PROBLEM!**

POP QUIZ!

3 questions to test your knowledge and attitudes about iron deficiency anemia and HMB

WHAT SHOULD YOUR FIRST STEP BE IN ASSESSING A PATIENT WITH SUSPECTED HMB?

a) Order a serum ferritin

b) Take a thorough history

c) Administer a pictorial blood loss assessment chart

d) Order a pelvic ultrasound

e) Refer to hematology

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WHICH HORMONAL THERAPY FOR HMB OFFERS THE GREATEST AVERAGE REDUCTION IN MENSTRUAL BLOOD LOSS?

a) Progestin IUD

b) Progestin IUD + combined OCP

c) Combined OCP

d) Cyclic oral progestogen

e) They are all similarly effective

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c) Ulipristal (Fibristal®)

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e) Tranexamic acid

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