A Practice Tool for Combined Hormonal Contraceptives

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ABBREVIATIONS

BTB	breakthrough bleeding	**IHD**	ischemic heart disease
CHC	combined hormonal contraceptive	**IUC**	intrauterine contraception
COC	combined oral contraceptive	**LARC**	long acting reversible contraceptive
Cu-IUD	copper intrauterine device	**LNG-IUS**	levonorgestrel intrauterine system
CVD	cardiovascular disease	**MI**	myocardial infarction
EE	ethinyl estradiol	**VTE**	venous thromboembolism
HFI	hormone free interval		

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Initiating and Managing Combined Hormonal Contraceptives (CHC)

Step 1: Assess if CHC is Appropriate

- ☐ Gather patient history
- ☐ Screen for contraindications
- ☐ Screen for drug interactions
- ☐ Perform blood pressure measurement
- ☐ Refer if required

Step 2: Initiate a CHC Product

- ☐ Select a product
- ☐ Choose a regimen

Step 3: Patient Education for CHC

- ☐ Choose a start date
- ☐ Provide general patient education on:
  - how to use CHC
  - adherence and missed CHC
  - side effects and management
  - back-up contraception
- ☐ Create a follow-up plan

Step 4: Follow-up Monitoring of CHC

- ☐ Assess patient satisfaction
- ☐ Check adherence
- ☐ Ask about side effects
- ☐ Check if changes with health status
- ☐ Perform blood pressure measurement

STEP 1: Assess If CHC is Appropriate

☐ Gather patient history

Patient Demographics

☐ Age ☐ Weight ☐ Height

Medical History

☐ Screen for risk of VTE, CVD, breast cancer, migraines with aura, liver disease - see contraindications.

Social History

Do you currently smoke?
How many cigarettes do you smoke per day?

Menstrual History

When was your last menstrual period?
How often do you get your periods? Are they regular or irregular? Are your periods heavy?
Do you get spotting or bleeding in between periods? Has it been assessed?

Past & Current Contraceptive Use

What type of contraception are you currently using? Have you been on hormonal contraception in the past?
Which ones and for how long? Did you have any side effects?
Were you satisfied with past contraceptives? Why or why not?

Possibility of Pregnancy

Have you had unprotected intercourse since your last menstrual period?
Is there a possibility of pregnancy? Recommend pregnancy test.*

* If possibility of pregnancy → **Refer**.

Assess if a LARC is appropriate

Do you want to become pregnant in the next year?
How important is it for you not to be pregnant right now?
Would you be interested in using a LARC?*

* If interested in LARC → **Refer**.

If the woman is seeking contraception, consider LARC, such as an IUC or implant as very effective, reversible, and longer-term form of contraception. IUCs include LNG-IUS and Cu-IUD.

NOTE: Pelvic exam and pap smear are NOT required prior to providing CHC, though should be part of a woman's normal reproductive care.

☐ Screen for contraindications:*

Cardiovascular Disease Risk	• Smokes ≥ 15 cigarettes/day and over the age of 35 years • Cardiovascular disease (MI, IHD etc) • Hypertension (systolic ≥ 140 mmHg or diastolic ≥ 90 mmHg)	• History of stroke • Migraines with aura • Diabetes with microvascular complications
VTE Risk	• VTE – current or past history	• Thrombophilia
Breast cancer	• Breast Cancer – current or past history	
Liver Disease	• Active or past liver disease	
Other	• Given birth in the last 3 weeks • Breastfeeding <6 weeks postpartum • Rheumatic diseases such as lupus	• Other active cancers/chemotherapy • Undiagnosed abnormal uterine bleeding

* If contraindications are present → **Refer**.

☐ Screen for drug interactions:*

Screen for inducers of EE/progestins:	• Anticonvulsants (phenytoin, carbamazepine, primidone, topiramate, phenobarbital, oxcarbazepine) • Rifampin • Antiretrovirals (efavirenz, nevirapine ritonavir) • St John's Wort
Other interactions:	• Lamotrigine (EE can induce metabolism) • Concurrent use of potassium sparing drugs (i.e. ACE inhibitors, spironolactone) with drospirenone containing CHC

* If drug interactions are present → **Refer**.

☐ Perform Blood Pressure Measurement*

* If BP ≥140/90 → **Refer**.

☐ Refer if any of the following:

- ☐ BP is ≥ 140/90 mmHg
- ☐ Smoker and over 35 years
- ☐ Abnormal uterine bleeding
- ☐ One or more contraindications listed above
- ☐ Potential for drug interaction(s)
- ☐ Possibility of pregnancy

The questions provided above are suggestions to guide patient assessment, rather than an all inclusive list. In addition, clinicians may expand assessment to include sexual history, etc.

STEP 2: Initiate a CHC Product

☐ Select a Product:

CHC products contain an estrogen and a progestin.

- Progestin is responsible for the main contraception effect.
- Estrogen helps stabilize endometrium and helps with menstrual cycle control.

There are no advantages of the multiphasic products over monophasic. All CHC options are equally effective in preventing pregnancy.

CHC route options include: oral tablets, transdermal patch, and vaginal ring.

CHC products in Canada contain:

Estrogen:
- EE 10 – 35 µg
- estetrol 15 mg

Progestins:
- 1st generation – norethindrone, ethynodiol
- 2nd generation – levonorgestrel
- 3rd generation – norgestimate, desogestrel
- 4th generation – drospirenone

☐ Choose a Regimen:

Regimen (COC, patch or ring)	
Cyclic (21/7):	Taken for 21 days followed by 7 day HFI
Shortened HFI (24/4):	Taken for 24 days followed by 4 days HFI (COC only)
Extended Cycle or Continuous Dosing:	• **Extended Cycle:** taken every day with 7 day HFI every 3 months • **Continuous:** taken every day with no HFI

Tips in choosing products:

- Most often clinicians start with EE 20 µg, and adjust dose based on side effect or BTB. Lower doses of EE are associated with fewer adverse effects but more breakthrough bleeding. For youth, consider starting with products of 30 µg or 35 µg EE. For women ≥ 35 years, consider products with less than or equal to 20 µg EE.
- All CHC's can improve acne. Antiandrogenic progestins (drospirenone, cyproterone) can also be considered with severe acne. Most of the variability with the CHC's is with the progestins.
- 1st and 2nd generation progestins may have a lower VTE risk compared to the other progestins. Study results have been inconsistent and this remains controversial. Canadian guidelines do not recommend preferential prescribing based upon progestin type.
- The transdermal contraceptive patch may be less effective in women with a weight ≥ 90kg.

Combined Hormonal Contraceptives in Canada

Composition	Product
Monophasic	
1st generation progestins	
EE 10 µg/norethindrone 1 mg x 24d, then EE 10 µg x 2d + HFI x 2d	LoLo
EE 35 µg/norethindrone 0.5 mg	Brevicon 0.5/35
EE 35 µg/norethindrone 1 mg	Brevicon 1/35 Select 1/35
2nd generation progestins	
EE 20 µg/levonorgestrol 0.1 mg	Alesse, generics
EE 30 µg/levonorgestrel 0.15 mg	Min-Ovral, generics
3rd generation progestins	
EE 30 µg/desogestrel 0.15 mg	Marvelon, generics
4th generation progestins/antiandrogenic progestins	
EE 20 µg/drospirenone 3 mg x 24d (HFI 4d)	Yaz, generics
EE 20 µg/drospirenone 3 mg + levomefolate 0.45 mg x 24d (HFI 4d with levomefolate tabs)	Yaz Plus
EE 30 µg/drospirenone 3 mg	Yasmin, generics
Estetrol 15 mg/drospirenone 3 mg x 24d (HFI 4d)	Nextstellis
Biphasic	
EE 35 µg/norethindrone 0.5 x 12d, 1mg x 9d	Synphasic
Triphasic	
EE 30 µg x 6d, EE 40 µg x 5 d, EE 30 µg x 10d/levonorgestrel 0.05 mg x 6d, 0.075 mg x 5d, 0.125 mg x 10d	Triquilar
EE 25 µg/desogestrel 0.1mg x 7d, 0.125 mg x 7 d, 0.15 mg x 7d	Linessa
EE 35 µg/ norgestimate 0.18mg x 7d, 0.215 mg x 7d, 0.25 mg x 7d	Tricira, Tri-Jordyna
EE 25 µg/ norgestimate 0.18mg x 7d, 0.215 mg x 7d, 0.25 mg x 7d	Tricira Lo
Extended Cycle Hormonal Contraceptive	
EE 30 µg/levonorgestrel 0.15 mg x 84d	Seasonale, generic
EE 30 µg/levonorgestrel 0.15 mg x 84d, then EE 10 µg x 7d	Seasonique
Combined Hormonal Contraceptive Patch	
EE 35 µg/norelgestromin 0.15 mg	Evra
Combined Hormonal Contraceptive Vaginal Ring	
EE 15 µg/etonogestrel 0.12 mg	Nuvaring, generics

Products listed in this table are based on current resources. Please check for any changes in availability.

STEP 3: Patient Education for CHC

☐ Choose a start date

Quick Start:	Sunday Start:	First Day Start:
Start any day of the week (start as soon as pick up prescription). **Back-up** contraception is required for **7 days**.*	Start on first Sunday after menstrual period begins. **Back-up** contraception is required for **7 days**.*	Start on the first day of the menstrual period. Back-up contraception is **not** required.

*Back-up contraception includes abstinence and barrier methods, such as condoms.

☐ Provide general patient information on:

- ☐ How to use CHC (see table below for route specific information)
- ☐ When to start CHC (Quick start is recommended method)
- ☐ When contraceptive efficacy starts
- ☐ How long to use back-up contraception when starting (for example 7 days after starting)
- ☐ Tips to help remember CHC
- ☐ What to do when CHC dose is missed or delayed
- ☐ Common side effects and management strategies, as well as risks of CHC
- ☐ Safe sex practices regarding STI prevention
- ☐ When to seek medical attention

☐ Create a follow-up plan:

- ☐ Follow-up at 1-3 months or next refill

Route specific patient education information:

COC	Take one pill daily at same time depending on regimen (see Regimens). Discuss daily routines and tips for adherence (e.g. take pill at the same time each day).
Patch	Apply new patch once a week depending on regimen (see Regimens). Apply at 1 of 4 sites: the buttock, abdomen, upper outer arm, upper torso (Do not apply to breasts).
Vaginal ring	Insert a new ring vaginally for three weeks depending on regimen (see Regimens). Rings should not interfere with intercourse. If ring is bothersome to either partner during intercourse, it may be removed and re-inserted after intercourse. Ring should not be left out of vagina for more than 3 hours.

Missed Combined Oral Contraceptive*

1 pill Delayed <24 hours	1 or more pills missed in 1st week	1-2 pills missed in weeks 2 or 3	3 or more pills missed in weeks 2 or 3
Take pill as soon as possible and continue taking pill once daily.	Take one pill as soon as possible and continue to end of pack. Use back-up contraception for 7 days or emergency contraception if unprotected intercourse in the past 5 days.	Take one pill as soon as possible and once daily until the end of the pack. Start the next cycle without a hormone free interval.	Take one pill as soon as possible and once daily until the end of the pack. Start the next cycle without a hormone free interval. Use back-up contraception for 7 days and consider emergency contraception if unprotected intercourse in the past 5 days.

*Refer to the appropriate product monograph for information regarding patch or vaginal ring.

Side Effects

Estrogen Related	Estrogen Deficiency	Progestin Related	Progestin Deficiency
• Nausea • Breast tenderness • Fluid retention • Headaches • Chloasma • Poor contact lens fit	• Early or micycle BTB/spotting • Hypomenorrhea • Menopausal symptoms (vasomotor, insomnia) • Mood (irritability, depression)	• Breast tenderness • Fluid retention • Bloating • Mood (irritability, depression) • Headache • Appetite changes	• Late BTB/spotting • Heavy menstrual flows • Delayed menses

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REFERENCES

Black A, Guilbert E, Costescu D, et al. Canadian Contraception Consensus (Part 3 of 4): Chapter 7--Intrauterine Contraception. *J Obstet Gynaecol* Can. 2016;38(2):182-222.

Black A, Guilbert E, Costescu D, et al. No. 329-Canadian Contraception Consensus Part 4 of 4 Chapter 9: Combined Hormonal Contraception. *J Obstet Gynaecol* Can. 2017;39(4):229-268 e225.

Hatcher RA, Nelson AL, Trussell J, Cwiak C, Cason P, Policar MS, Edelman A, Aiken ARA, Marrazzo J, Kowal D, eds. Contraceptive technology. 21st ed. New York, NY: Ayer Company Publishers, Inc., 2018.

STEP 4: Follow-up Monitoring of CHC

☐ **Assess patient satisfaction:**

How do you like your current method of contraception?

☐ **Check adherence:**

How many pills have you missed in the last week? How have you responded with regards to missed doses?

If using the patch or ring, have you missed any days applying a new patch or inserting a ring?

☐ **Ask about side effects:**

Have you experienced any side effects? When did they occur?

Have you had any breakthrough bleeding?

How have you been managing these side effects?

☐ **Check if changes with health status:**

Have you had any changes to your health, such as new medical conditions or new medications?

Has there been a change to your smoking status?

Has there been a change in weight?

☐ **Perform Blood Pressure Measurement***

*If BP ≥140/90 → Refer.

Managing Side Effects:

- Most minor side effects will disappear in the first few cycles.
- Always assess for other potential causes of a side effect. These should be ruled out prior to making changes to the CHC.

MANAGING SIDE EFFECTS*	
Breakthrough Bleeding:	BTB is common in the first 3 months after starting a new CHC. If BTB continues past the 3 months or if new onset: • Switch to CHC with higher EE dose OR change type of progestin **NOTE: if on continuous CHC regimen**, hold CHC for 3-4 days to see if BTB resolves (back-up contraception is not required during this timeframe if on continuous regimen). Refer if: ☐ Identified other possible causes for BTB ☐ BTB is heavy and occurs throughout the cycle ☐ BTB continues for longer than 3 months after adjustments in product/dose
Nausea	• Take at bedtime with food. • Change to CHC with lower estrogen dose if possible.
Water Retention	• Watch salt intake. • Change to CHC with lower estrogen doses. • Change to CHC with different progestin, consider antimineralocorticoid progestin (i.e. drospirenone) if fluid retention continuous.
Headache	• Assess when headache occurs, is it while on the CHC or during the HFI with cyclic? • If during the HFI, use continuously. • If while on CHC, switch to CHC with lower estrogen dose if possible. **If severe headache or migraine → Refer.**
Mood Changes	• Switch to CHC with different progestin. **If mood effects continue with switch → Refer.**
Acne	• Acne usually improves with time as most CHC will help improve acne. • If acne continues, switch to CHC with antiandrogenic properties. **If acne severe or continues → Refer.**
Weight Gain	• Assess for other causes of weight gain. • Assess if weight gain is from water/fluid retention. • In studies, weight gain has not been associated with CHC. **If weight gain continues → Refer.**

*Most of these recommendations apply more specifically to COC.