

**Inhaled anti-asthma therapies following hormone therapy in women: A nationwide cohort study**

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**Online data supplement**

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## **Abbreviations**

HT – Hormone therapy

ICS – Inhaled corticosteroids

LABA – Long-acting beta<sub>2</sub>-agonists

STROBE - Strengthening the Reporting of Observational studies in Epidemiology

SABA – Short-acting beta<sub>2</sub>-agonists

ATC – Anatomical Therapeutic Chemical system

ICD – International Classification of Diseases Online tables

**Table S1: Budesonide equivalents**

<b>Substance</b>	<b>Multiplying factor</b>
Budesonide	1.0
Beclometasone	2.0
Ciclesonide	2.5
Fluticasone propionate	2.0
Mometasone	1.4
Fluticasone furoate	4

**Table S1:** Multiplying factors to calculate budesonide equivalents. Example: 200 micrograms of ciclesonide =  $200 \times 2.5 = 500$  micrograms of budesonide.

**Table S2: ATC-codes of inhaled anti-asthma medication**

<b>Substance</b>	<b>ATC</b>
<b>Inhaled corticosteroids</b>	
Budesonide	R03BA02, R03AK07, R03AK12
Beclometasone	R03BA01, R03AK08
Ciclesonide	R03BA08
Fluticasone propionate	R03BA05, R03AK06, R03AK11
Mometasone	R03BA07, R03AK09, R03AK14
Fluticasone furoate	R03BA09, R03AK10
<b>Long-acting beta<sub>2</sub>-agonists</b>	
Salmeterol	R03AC12, R03AK06, R03AK12
Vilanterol	R03AK10
Indacaterol	R03AC18, R03AK14
Formoterol	R03AC13, R03AK07, R03AK08, R03AK09, R03AK11
<b>Short-acting beta<sub>2</sub>-agonists</b>	
Salbutamol	R03AC02
Terbutaline	R03AC03

**Table S2:** Overview of ATC-codes for inhaled anti-asthma medications. If a given drug was a combined drug (e.g. R03AK12 – Budesonide/Salmeterol) the components were separated into long-acting beta<sub>2</sub>-agonists and inhaled corticosteroids. ATC, Anatomical Therapeutic Classification system.

**Table S3: Adjusted odds ratios of increased use of ICS in hormone therapy users**

<b>Time points (months)</b>	<b>Any increase (&gt;0 µg) OR (95%CI)</b>	<b>P value</b>	<b>Increase (&gt;100 µg) OR (95%CI)</b>	<b>P value</b>
<b>Hormone therapy</b>				
<b>3</b>	0.99 (0.95-1.03)	0.6	1.05 (1.00-1.09)	0.031
<b>6</b>	1.04 (1.00-1.08)	0.060	1.08 (1.04-1.13)	<0.001
<b>9</b>	1.00 (0.96-1.04)	1.00	1.07 (1.03-1.11)	0.001
<b>12</b>	0.98 (0.94-1.01)	0.20	1.02 (0.98-1.06)	0.39
<b>Hormone therapy by type</b>				
<b><i>Systemic estrogen</i></b>				
<b>3</b>	0.91 (0.83-0.99)	0.023	1.08 (1.02-1.19)	0.092
<b>6</b>	1.00 (0.92-1.08)	0.9	1.12 (1.02-1.23)	0.014
<b>9</b>	0.92 (0.84-1.00)	0.055	1.08 (0.98-1.19)	0.099
<b>12</b>	0.85 (0.78-0.93)	<0.001	1.01 (0.92-1.11)	0.8
<b><i>Combination</i></b>				
<b>3</b>	0.94 (0.90-0.99)	0.027	1.06 (1.00-1.12)	0.053
<b>6</b>	0.95 (0.90-1.00)	0.058	1.06 (1.00-1.13)	0.036
<b>9</b>	0.99 (0.94-1.04)	0.6	1.09 (1.03-1.16)	0.003
<b>12</b>	0.92 (0.87-0.97)	0.002	1.02 (0.96-1.08)	0.6
<b><i>Progestogens</i></b>				
<b>3</b>	0.82 (0.77-0.87)	<0.001	0.97 (0.91-1.04)	0.42

<b>6</b>	0.87 (0.82-0.93)	<0.001	1.00 (0.94-1.08)	0.9
<b>9</b>	0.86 (0.81-0.91)	<0.001	0.96 (0.90-1.03)	0.32
<b>12</b>	0.83 (0.78-0.88)	<0.001	0.91 (0.85-0.98)	0.014
<b><i>Local estrogen</i></b>				
<b>3</b>	0.94 (0.91-0.97)	<0.001	1.03 (0.99-1.07)	0.092
<b>6</b>	0.94 (0.91-0.97)	<0.001	1.00 (0.97-1.04)	0.8
<b>9</b>	0.94 (0.91-0.97)	<0.001	0.99 (0.96-1.03)	0.7
<b>12</b>	0.90 (0.87-0.94)	<0.001	0.96 (0.93-1.00)	0.050

**Table S3:** Odds ratios of being increased in ICS at the four timepoints. Reference for all odds ratios is “No hormone therapy”. ICS, inhaled corticosteroids; CI, confidence interval

**Table S4: Crude odds ratios of increased use of LABA among users of hormone therapy**

Timepoint	OR	Lower CI (95%)	Upper CI (95%)	P value	Type of LABA
Month 3	1.02	0.95	1.09	0.54	Formoterol
Month 3	1.04	0.95	1.12	0.42	Salmeterol
Month 3	1.04	0.45	2.42	0.91	Vilanterol
Month 3	0.51	0.24	1.02	0.06	Indacaterol
Month 6	1.09	1.01	1.17	0.022	Formoterol
Month 6	1.04	0.96	1.14	0.35	Salmeterol
Month 6	2.09	0.81	5.46	0.13	Vilanterol
Month 6	0.52	0.24	1.07	0.085	Indacaterol
Month 9	1.05	0.98	1.13	0.15	Formoterol
Month 9	1.05	0.96	1.15	0.25	Salmeterol
Month 9	0.73	0.25	2.00	0.54	Vilanterol
Month 9	0.68	0.31	1.43	0.31	Indacaterol
Month 12	1.06	0.98	1.14	0.12	Formoterol
Month 12	1.12	1.02	1.22	0.013	Salmeterol
Month 12	0.77	0.22	2.49	0.67	Vilanterol
Month 12	0.73	0.32	1.60	0.44	Indacaterol

**Table S4:** Crude odds ratios of having an increased use of LABA at the four different timepoints following the index date (HT initiation date). OR, Odds ratio; CI, confidence interval; LABA, long-acting beta<sub>2</sub>-agonist.

**Table S5: Adjusted odds ratios of increased use of LABA among users of hormone therapy**

Timepoint	OR	Lower CI (95%)	Upper CI (95%)	P value	Type of LABA
Month 3	1.02	0.95	1.10	0.56	Formoterol
Month 3	1.04	0.95	1.13	0.41	Salmeterol
Month 3	1.12	0.47	2.64	0.80	Vilanterol
Month 3	0.44	0.20	0.90	0.029	Indacaterol
Month 6	1.09	1.01	1.16	0.024	Formoterol
Month 6	1.04	0.96	1.14	0.35	Salmeterol
Month 6	1.99	0.75	5.33	0.17	Vilanterol
Month 6	0.45	0.20	0.96	0.044	Indacaterol
Month 9	1.05	0.98	1.13	0.17	Formoterol
Month 9	1.05	0.97	1.15	0.24	Salmeterol
Month 9	0.71	0.24	2.03	0.53	Vilanterol
Month 9	0.55	0.24	1.20	0.14	Indacaterol
Month 12	1.06	0.98	1.14	0.12	Formoterol
Month 12	1.12	1.03	1.22	0.012	Salmeterol
Month 12	0.67	0.18	2.28	0.53	Vilanterol
Month 12	0.74	0.31	1.68	0.47	Indacaterol

**Table S5:** Adjusted odds ratios of having an increased use of LABA at the four different timepoints following the index date (HT initiation date). Analyses were adjusted for household income, level of education and birth year. OR, Odds ratio; CI, confidence interval; LABA, long-acting beta<sub>2</sub>-agonist.



**Table S6: Crude odds ratios of increased use of SABA among users of hormone therapy**

<b>Timepoint</b>	<b>OR</b>	<b>Lower CI (95%)</b>	<b>Upper CI (95%)</b>	<b>P value</b>	<b>Type of SABA</b>
<b>Month 3</b>	1.01	0.96	1.07	0.64	Terbutaline
<b>Month 3</b>	1.00	0.93	1.08	0.99	Salbutamol
<b>Month 6</b>	0.98	0.93	1.03	0.42	Terbutaline
<b>Month 6</b>	1.00	0.93	1.08	0.97	Salbutamol
<b>Month 9</b>	0.95	0.90	1.00	0.035	Terbutaline
<b>Month 9</b>	0.98	0.91	1.06	0.66	Salbutamol
<b>Month 12</b>	0.94	0.89	0.99	0.020	Terbutaline
<b>Month 12</b>	0.95	0.88	1.03	0.21	Salbutamol

Table S6: Crude odds ratios of experiencing an increase in use of SABA in the 12 months following hormone therapy initiation. OR, Odds ratio; CI, confidence interval; SABA, short-acting beta<sub>2</sub>-agonists

**Table S7: Adjusted odds ratios of increased use of SABA among users of hormone therapy**

<b>Timepoint</b>	<b>OR</b>	<b>Lower CI (95%)</b>	<b>Upper CI (95%)</b>	<b>P value</b>	<b>Type of LABA</b>
<b>Month 3</b>	1.01	0.96	1.06	0.71	Terbutaline
<b>Month 3</b>	1.00	0.93	1.08	0.96	Salbutamol
<b>Month 6</b>	0.98	0.93	1.03	0.36	Terbutaline
<b>Month 6</b>	1.00	0.93	1.08	0.98	Salbutamol
<b>Month 9</b>	0.94	0.89	0.99	0.028	Terbutaline
<b>Month 9</b>	0.99	0.91	1.06	0.71	Salbutamol
<b>Month 12</b>	0.94	0.89	0.99	0.017	Terbutaline
<b>Month 12</b>	0.95	0.88	1.03	0.23	Salbutamol

Table S7: Adjusted odds ratios of experiencing an increase in use of SABA in the 12 months following hormone therapy initiation. Models are adjusted for baseline value, income level, household income and birth year. OR, Odds ratio; CI, confidence interval; SABA, short-acting beta<sub>2</sub>-agonists

**Figure S1: Analysis of changes in use of inhaled corticosteroids in women aged 54 years or older**

Figure S1: Plot displaying the differences in use of inhaled corticosteroids in the 12 months following initiation of hormone therapy among women  $\geq 54$  years of age. The results were similar to the main analyses.

**Figure S2: Analysis of changes in use of inhaled corticosteroids in women below 54 years of age**

Figure S2: Plot displaying the differences in use of inhaled corticosteroids in the 12 months following initiation of hormone therapy among women < 54 years of age. The results were similar to the main analyses.