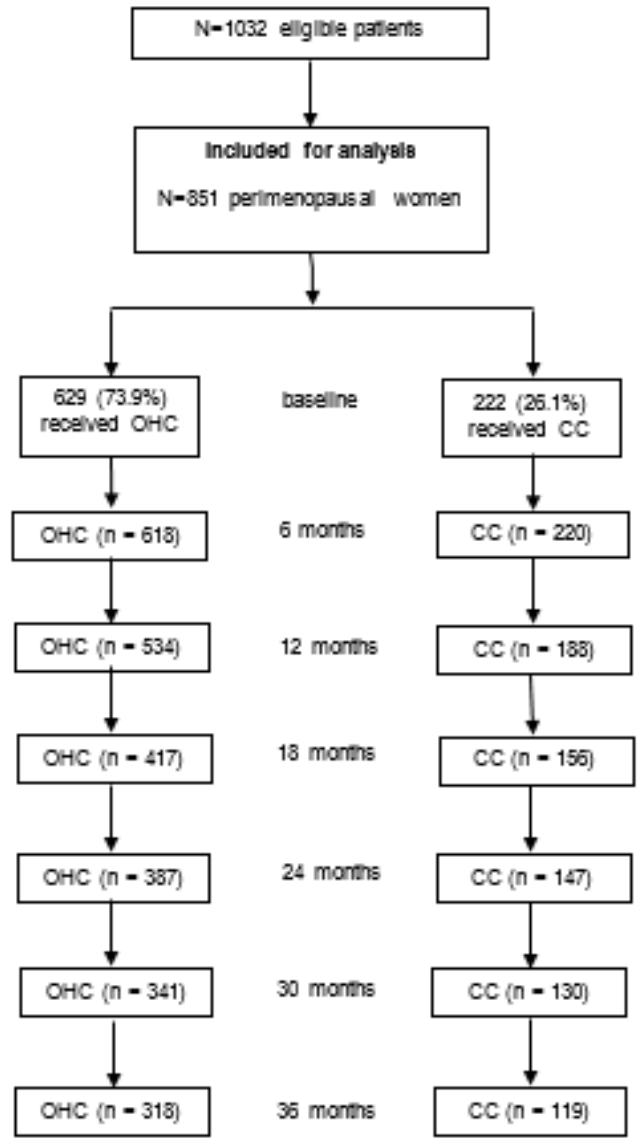
1. Participant Flow



OHC, ossein-hydroxyapatite complex; CC, calcium carbonate

2. Baseline Characteristics

Variable	OHC (n=629)	CC (n=222)	*p*
Age (years), mean (SD) only	47.3 (3.0)	47.1 (2.8)	0.485
Number of children (range 0-12), mean (SD)	1.9 (1.0)	1.9 (1.2)	0.627
Concomitant treatment (not calcium supplements), n (%)	131 (20.8)	41 (18.5)	0.452
Age at menarche (years), mean (SD)	12.2 (1.4)	12.3 (1.4)	0.268
Past contraceptive treatment, n (%) Duration (years), mean (SD)	213 (42.6) 7.0 (4.4)	86 (45.7) 6.6 (4.5)	0.458 0.572
Menstrual cycle: Regular (last 12 months), n (%) Periodicity changes (last 3 months), n (%) Amenorrhea (last 3-11 months), n (%)	 191 (30.9) 228 (36.9) 199 (32.2)	 70 (32.3) 71 (32.7) 76 (35)	 0.531 0.452 0.458
Risk factors (habits)			
Smoking status Current smoking, n (%) Cigarettes per day, mean (SD) Smoking habit (years), mean (SD) Former smoker, n (%) Years after smoking cessation, mean (SD)	 172 (27.9) 13.5 (8.4) 19.8 (7.9) 60 (23.4) 8.6 (6.5)	 73 (33.2) 14.1 (7.5) 18.1 (8.7) 16 (19.3) 11.6 (6.4)	 0.137 0.583 0.157 0.429 0.108
Frequent alcohol use Drinks a day (units), mean (SD)	47 (7.9) 1.50 (0.76)	19 (8.6) 1.42 (0.51)	0.732 0.681
Caffeine use, n (%)	249 (44.6)	100 (50.3)	0.171
Reported calcium intake (mg/day), mean (SD)	992 (503)	996 (475)	0.973
Regular exercise, n (%)	226 (44.1)	92 (47.9)	0.358

BMI: body mass index; BMD: bone mineral density; OHC: ossein-hydroxyapatite complex; CC: calcium carbonate.

3. Outcome Measures

Adverse drug reactions:

Adverse drug reaction	OHC (n=629) n (%)	CC (n=222) n (%)	P value
Total	17 (2.7)	17 (7.7)	0.001
Gastrointestinal complaints†	13 (2.1)	13 (5.9)	0.005
Headache	3 (0.5)	1 (0.5)	1.000*
Dizziness	0	1 (0.5)	0.261*
Dysgeusia	0	1 (0.5)	0.261*
Back pain	0	1 (0.5)	0.261*
Eczema	1 (0.2)	0	1.000*
Weight gain	1 (0.2)	0	1.000*

OHC: ossein-hydroxyapatite complex; CC: calcium carbonate.

† Including: Dyspepsia, abdominal pain, flatulence, vomiting, esophagitis.

* Not statistically significant

Bone mineral density at the lumbar spine (T-score and g/cm2):

	Ossein-hydroxyapatite complex			Calcium carbonate			Between group P value[b]
Visit	n	Mean (SD)	P value[a]	n	Mean (SD)	P value[a]	
T-score							
Baseline	601	-0.61 (1.11)	-	206	-0.75 (0.98)	-	0.250
V7-Baseline	299	0.01 (0.82)	0.19	107	-0.23 (0.76)	0.001	<0.001
BMD (g/cm²)							
Baseline	578	1.03 (0.15)	-	204	1.01 (0.13)	-	0.057
V7-Baseline	280	0.00 (0.11)	0.34	102	-0.03 (0.11)	<0.001	<0.001

[a]Wilcoxon test for change from baseline within groups

[b]Mann-Whitney U test for difference between treatment groups

BMD: bone mineral density

V7: visit at 36 months of follow-up

4. Adverse Events

Adverse drug reaction	OHC (n=629) n (%)	CC (n=222) n (%)	P value
Total	17 (2.7)	17 (7.7)	0.001
Gastrointestinal complaints†	13 (2.1)	13 (5.9)	0.005
Headache	3 (0.5)	1 (0.5)	1.000*
Dizziness	0	1 (0.5)	0.261*
Dysgeusia	0	1 (0.5)	0.261*
Back pain	0	1 (0.5)	0.261*
Eczema	1 (0.2)	0	1.000*
Weight gain	1 (0.2)	0	1.000*

OHC: ossein-hydroxyapatite complex; CC: calcium carbonate.

† Including: Dyspepsia, abdominal pain, flatulence, vomiting, esophagitis.

* Not statistically significant