

**Supplementary Figure S1.** Risk of bias assessment of included studies

		Risk of bias domains					
		D1	D2	D3	D4	D5	Overall
Study	ABCSDG-12						
	E-3193, INT-0142						
	SOFT						
	TEXT						

Domains:  
D1: Bias arising from the randomization process.  
D2: Bias due to deviations from intended intervention.  
D3: Bias due to missing outcome data.  
D4: Bias in measurement of the outcome.  
D5: Bias in selection of the reported result.

Judgement  
 Some concerns  
 Low

**Supplementary Table SI.** Common Terminology Criteria for Adverse Events (CTCAE) v3.0 definition of adverse events of interest

Adverse event	Grade 1	Grade 2	Grade 3	Grade 4
Hypertension	Asymptomatic, transient (20 mm Hg (diastolic) or to > 150/100 if previously within normal limits; intervention not indicated	Recurrent or persistent ( $\geq 24$ h) or symptomatic increase by > 20 mm Hg (diastolic) or to > 150/100 if previously within normal limits; monotherapy may be indicated	Requiring more than 1 drug or more intensive therapy than previously	Life-threatening consequences (e.g. hypertensive crisis)
Weight gain	5 – < 10% of baseline	10 – < 20% of baseline	$\geq 20\%$ of baseline	–
Cardiac ischaemia	Asymptomatic arterial narrowing without ischaemia	Asymptomatic and testing suggesting ischaemia; stable angina	Symptomatic and testing consistent with ischaemia; unstable angina; intervention indicated	Acute myocardial infarction
Thrombosis	–	Deep vein thrombosis or cardiac thrombosis; intervention (e.g., anticoagulation, lysis, filter, invasive procedure) not indicated	Deep vein thrombosis or cardiac thrombosis; intervention (e.g., anticoagulation, lysis, filter, invasive procedure) indicated	Embolic event including pulmonary embolism or life-threatening thrombus
Glucose intolerance	Asymptomatic, intervention not indicated	Symptomatic; dietary modification or oral agent indicated.	Symptoms interfering with activities of daily living; insulin indicated.	Life-threatening consequences (e.g., ketoacidosis, hyperosmolar non-ketotic coma)
Hyperglycaemia*	> ULN – 160 mg/dl > ULN – 8.9 mmol/l	> 160–250 mg/dl >8.9–13.9 mmol/l	> 250–500 mg/dl > 13.9–27.8 mmol/l	> 500 mg/dl > 27.8 mmol/l or acidosis

ADL – activities of daily living. \*Fasting unless otherwise specified in protocol.

**Supplementary Table SII.** Baseline characteristics of participants in included studies

Study	Treatment (n)	Age, median (IQR)	Receptor status, n (%)				Tumour grade, n (%)		Tumour size, n (%)	
			LN negative	ER positive	PgR positive	HER2 positive	Grade 1 or 2	Grade 3	≤ 2 cm	> 2 cm
ABCSG-12	Tamoxifen + OFS (451)	45.5 (27.6–6.5)	301 (66.7)	421 (93.3)	397 (88.0)	NR	344 (76.3)	93 (20.6)	NR	NR
	Tamoxifen + OFS + zoledronic acid (449)	45.3 (27.5–6.3)	295 (65.7)	414 (92.2)	401 (89.3)	NR	344 (76.6)	89 (19.8)	NR	NR
	Anastrozole + OFS (453)	45.0 (25.9–56.3)	303 (66.9)	427 (94.3)	407 (89.9)	NR	344 (75.9)	97 (21.4)	NR	NR
	Anastrozole + OFS + zoledronic acid (450)	44.5 (28.8–6.4)	302 (67.1)	421 (93.6)	402 (89.3)	NR	339 (75.3)	98 (21.8)	NR	NR
E-3193, INT-0142 <sup>a</sup>	Tamoxifen alone (167)	46 (26–55)	167 (100)	161 (96.4)	153 (91.6)	NR	NR	NR	139 (83.3)	28 (16.8)
	Tamoxifen + OFS (170)	44 (30–54)	170 (100)	165 (97.1)	154 (90.6)	NR	NR	NR	141 (82.9)	29 (17.1)
SOFT <sup>b,c</sup>	Tamoxifen alone (1018)	43 (38–46)	662 (65.0)	NR	NR	857 (84.2)	767 (75.3)	227 (22.3)	676 (66.4)	315 (30.9)
	Tamoxifen + OFS (1015)	43 (38–47)	662 (65.2)	NR	NR	867 (85.4)	779 (76.8)	212 (20.9)	656 (64.6)	334 (32.9)
	Exemestane + OFS (1014)	43 (38–47)	671 (66.2)	NR	NR	857 (84.5)	791 (78)	201 (19.8)	678 (66.9)	315 (31.1)
TEXT <sup>b,c</sup>	Tamoxifen + OFS (1328)	44 (40–46)	690 (52)	NR	NR	1155 (87)	969 (73)	345 (26)	797 (60)	518 (39)
	Exemestane + OFS (1332)	43 (39–46)	692 (52)	NR	NR	1159 (87)	959 (72)	360 (27)	786 (59)	532 (40)

ABCSG-12 – Austrian Breast and Colorectal Cancer Study Group trial 12, E-3193 INT-0142 – Comparison of Tamoxifen versus Tamoxifen Plus Ovarian Function Suppression in Premenopausal Women with Node-

Negative, Hormone Receptor-Positive Breast Cancer, ER – oestrogen receptor, GnRH – gonadotropin-releasing hormone, HER2 – human epidermal growth receptor 2, LN – lymph node, NR – not reported, OFS – ovarian function suppression, PgR – progesterone receptor, SOFT – Suppression of Ovarian Function Trial, TEXT - Tamoxifen and Exemestane Trial. <sup>a</sup>8 patients excluded from final analysis due to ineligibility. <sup>b</sup>Baseline characteristics from SOFT and TEXT trials were retrieved from their original articles. <sup>c</sup>Inclusion criteria required immunohistochemistry confirming oestrogen and/or progesterone receptor positive but did not report breakdown of included participants.

**Supplementary Table SIII.** Summary of outcomes reported in included studies

Study	Hypertension	Weight gain	Cardiac ischaemia	Thrombosis	Glucose intolerance	Hyperglycaemia
ABCSG-12	X	✓	X	✓	X	X
E-3193, INT-0142	✓	✓	X	X	X	X
SOFT + TEXT	✓	X	✓	✓	✓	✓

**Supplementary Table SIV.** Common cardiovascular risk factors that can be assessed at the bedside

<b>Demographics</b>	Age Race Height Weight Body mass index (BMI)
<b>Medical history</b>	Hypertension Diabetes Dyslipidaemia Chronic kidney disease Heart failure Angina/ischaemic heart disease Atrial fibrillation Stroke/transient ischaemic attack (TIA) Peripheral vascular disease
<b>Family history</b>	Premature atherosclerotic cardiovascular disease Sudden cardiac death
<b>Social history</b>	Smoking
<b>Clinical parameters and biomarkers</b>	Resting heart rate and blood pressure Electrocardiogram (ECG) Blood glucose Lipid profile Renal function Cardiac biomarkers – troponin and NT-ProBNP