Table 1: Study characteristics of included studies comparing between primary endocrine therapy (PET) and primary surgical therapy (PST)

Name of trial	Author, year	Type of study	Study period	Definition of older	n		Treatment			ER status	Longest follow-up (median time)
					PET	PST	PET	PST	Adjuvant ET		
Nottingham 2 (EPSII)	Johnston, 2012	RCT	1989-1996	≥70	100	53	TAM 20mg OD	Simple Mastectomy	All patients	All positive (H score ≥100)	20 years (78 months)
Nottingham 1 (EPSI)	Chakrabarti, 2011	RCT	1982-1987	>70	65	66	TAM 20mg BD	Wedge mastectomy	No	NR	20 years
GRETA	Mustacchi, 2003	RCT	Mar 1987-Jun 1992	≥70	235	239	TAM 160 mg day 1, then 20 mg/day	NR	All patients	PET: NR PST: 72% (n=82/114)	13 years (80 months)
St Georges	Gazet, 2011	RCT	1982-1989	>70	100	100	TAM 20mg OD	WLE/mastectomy	No	All positive	28 years
Cancer Research Campaign	Fennessy, 2004	RCT	1984-1991	≥70	230	225	TAM 40mg OD	WLE/simple mastectomy/quandrantectomy/modified mastectomy	All patients	NR	(12.7 years)
	Bates, 1991*	RCT	Not specified	≥70	183	171	TAM	Simple excision or mastectomy	All patients	NR	(34 months)*
NA	Nicholson, 1988	PCS	NR	≥60	61	33	TAM 20mg OD or low dose aminoglutethimide 125mg BD (4.9%) + hydrocortisone 20mg BD	NR	No	PET: 60% (n=9/15) PST: 67% (n=22/33)	5 years (14 months)
	Traa, 2011	RCS	1985-2005	≥75	113	233	TAM	NR	Yes for 52.4% (n=122/23)	PET: 91.2% (n=52/57) PST: 69.6% (n=128/184)	10 years (mean 4.1 years for PET, 6.5 years for PST)
	Wink, 2012	RCS	2001-2008	≥75	184	1504	TAM (55%) or AI (45%)	NR	NR	PET: 94.2% (N=145/154) PST: NR	8.48 years (mean 2.6 years)
	Rao, 2007	RCS	1992-2002	≥80	62	48	TAM (87.1%) or AI (12.9%)	WLE (37.5%) / Mastecto	Yes for 93.8% (n=45/48)	PET: 94.7% (n=18/19)	154 months (41 months)

								my (62.5%)		PST: 71.4% (n=15/21)	
	Syed, 2011	RCS	1973-2009	≥70	449	616	TAM or AI	WLE / mastectomy	Yes for 50% (n=97) in WLE, 61.6% (n=157) in mastectomy	All positive	PET: 16.8 years, PST: 19.2 years (49 months)
	Nayyar, 2020	RCS	1 Jan 2008-31 Dec 2013	≥70	778	8006	TAM or AI	NR	Yes for 53% (n=4215)	Either ER or PR positive	NR
	Suen, 2020	RCS, PSM[#]	2008-2017	≥70	83	209	TAM (55%) or AI (45%)	Lumpectomy/mastectomy /radical mastectomy	All patients	All positive	Mean 67.2 months
Bridging the Age Gap in Breast Cancer	Morgan, 2021	PCS, PSM[#]	Feb 2013-June 2018	≥70	238	422	TAM (4.4%) or AI (90.4%) unknown (5.2%)	WLE or Mastectomy + AC +/- CT +/- RT +/- ET	≥70	All positive	(52 months)
	Wyld, 2021	PCS, PSM[#]	Jan 2013-Jun 2018								

[*]This study was not included in quantitative analysis as newer study was performed by Fennessy et al. in 2004. This study was described in this table as this study included clinical response to PET which was not included in the newer study. Follow-up was ongoing at the time of study publication.
[#]Only data from the PSM cohort is included

AC: Axillary clearance; AI: Aromatase inhibitors; BD: Twice a day dosing; CT: Chemotherapy; ER: Estrogen receptor; ET: Endocrine therapy; NA: Not applicable; NR: Not reported; OD: Once a day dosing; PCS: Prospective cohort study; PET: Primary endocrine therapy; PR: Progesterone receptor; PSM: Propensity score matched; PST: Primary surgical therapy; RCS: Retrospective cohort study; RCT: Randomised controlled trial; RT: Radiotherapy; TAM: Tamoxifen; WLE: Wide local excision

Table 2: Summary of overall survival (OS) and breast-cancer specific survival (BCSS) in included studies

Name of trial	Author, year	Overall survival			Breast-cancer specific survival		
		PET	PST	HR / RR / p-value	PET	PST	HR / RR / p-value
		Median (months) / five-year (%) / 10-year (%) months	Median (months) / five-year (%) / 10-year (%) months		Median (months) / five-year (%) / 10-year (%) months	Median (months) / five-year (%) / 10-year (%) months	
Nottingham 2 (EPSII)	Johnston, 2012	- / 74.0 / 64.0	- / 83.0 / 66.0	p-value: 5-year: 0.206 10-year: 0.802	- / 92 / 89	- / 92.5 / 86.8	p-value: 5-year: 0.921 10-year: 0.687
Nottingham 1 (EPSI)	Chakrabarti, 2011	73.0 / - / -	74.0 / - / -	p-value: 0.446	- / - / -	- / - / -	-
GRETA	Mustacchi, 2003	71.2 / - / -	70.9 / - / -	Unadjusted RR: 1.02, 95% CI: 0.8-1.3, p=0.89	- / - / -	- / - / -	Unadjusted RR: 1.38, 95% CI: 0.94-2.04, p=0.09
St Georges	Gazet, 2011	- / - / -	- / - / -	**Unadjusted HR: 1.3, 95% CI: 1.05-1.60**	- / - / -	- / - / -	**Unadjusted HR: 1.68, 95% CI: 1.15-2.47**
Cancer Research Campaign	Fennessy, 2004	- / 59.5 / 28.8	- / 67.4 / 37.7	**adjusted HR: 1.3, 95% CI: 1.05-1.60**	- / - / -	- / - / -	**Unadjusted HR: 1.68, 95% CI: 1.15-2.47**
NA	Nicholson, 1988	- / - / -	- / - / -	Cumulative OS: NS	- / - / -	- / - / -	-
	Traa, 2011	- / 41.0 / 5.1	- / 61.8 / 27.8	p-value: 5-year: 0.4 10-year: 0.3	- / 85 / 79.5	- / 87.3 / 78.3	p-value: 5-year: 0.421 10-year: 0.324 Adjusted HR: 0.68, 95% CI: 0.33-1.42
	Wink, 2012	- / 27.0 / -	- / 62.3 / -	Cumulative OS: **<0.001**	- / - / -	- / - / -	-
	Rao, 2007	42.0 / 6.3 / 1.6	71.0 / 52.1 / 12.9	Cumulative OS for stage I, II: **0.0002** Cumulative OS for stage III, IV: **0.03**	- / - / -	- / - / -	-
	Syed, 2011	- / - / -	- / - / -	-	not reached / 84 / -	not reached / 95 / -	p-value **5-year: <0.001**
	Nayyar, 2020	- / 78.0 / -	- / 89.6 / -	**adjusted HR: 1.69, 95% CI: 1.35-2.13**	- / 95.3 / -	- / 98.2 / -	**adjusted HR: 1.92, 95% CI: 1.11-3.33**
	Suen, 2020	- / 70.0 / 24.7	- / 70.6 / 61.5	5-year: 0.63 10-year: **0.0029**	- / - / -	- / - / -	-
Bridging the Age Gap in Breast Cancer	Morgan, 2021 Wyld, 2021	- / - / -	- / - / -	**adjusted HR: 1.39, 95% CI: 1.02-1.89, p=0.037**	- / - / -	- / - / -	adjusted HR: 1.35, 95% CI: 0.73-2.50, p=0.34

Bold indicates statistically significant results.

BCSS: Breast cancer-specific survival; CI: Confidence interval; HR: Hazards ratio; NA: Not applicable; NS: Not significant; PET: Primary endocrine therapy; OS: Overall survival; PST: primary surgical therapy; RR: Risk ratio