

Supplementary File 9: Additional Tables for Chapter 2, Results: Decision impact studies

Table 1: Study characteristics: Oncotype DX

Study	Country (area)	N patients	Population	Nodal status	Prosp / retro	N centres	Pre-test	Pre-test by (based on)	Post-test	Post-test by (based on)	Risk group (%)		
											Low	Inter	High
UK studies													
Hassan 2015 ¹ ; Hassan 2015 ²	UK (Bolton)	26	ER+ HER2- (assumed)	LN0 (assumed)	Prosp	1	Recomm	MDT (NR)	Decision	MDT & patient (NR)	81%		19%
Holt 2013 ³ Albanell 2016 ⁴ (subgroup)	UK (Wales)	All: 142 Sub: 94	All: ER+ HER2+/- Sub: ER+ HER2-	All: LN0/N1mi Sub: LN0	Prosp	1	Decision	Physician & patient (CP factors+AOL)	Decision	Physician & patient (NR)	All: 56% Sub: NR	All: 28% Sub: NR	All: 17% Sub: NR
Kiernan 2016 ⁵	UK	50	ER+ HER2- (assumed)	LN0 (assumed)	Retro	2	Recomm	Physician (NR)	Recommendation	Physician	NR	NR	NR
Kuchel 2016 ⁶	UK	135	ER+ HER2-	LN0-3	Prosp	Multi	Recomm and Decision	NR	Recomm and Decision	NR	52%	42%	6%
Loncaster 2017 ⁷	UK (Manchester)	All: 201 LN0: 136 LN+: 65	ER+ HER2-	LN0 68% LN+ 32%	Pilot + retro.	NR	Recomm	MDT (CP factors + PREDICT)	Decision	NR (test for low/high RS; test + patient discussion for inter RS)	All: 43% LN0: 34% LN+: 62%	All: 44% LN0: 51% LN+: 29%	All: 13% LN0: 15% LN+: 9%
Some data was submitted by the company in confidence and cannot be reported here.													
European studies													
Albanell 2012 ⁸ (trans-GEICAM)	Spain	107	ER+ HER2-	LN0	Prosp	6	Recomm	Physician (CP factors)	Recomm	Physician	58%	33%	9%
Bodmer 2015 ⁹	Switzerland	60	ER+ HER2- Pre/postmeno Inter clin risk	LN0 or LN+	Prosp	1 area	Recomm	Physician (CP factors)	Recomm	MDT	52%	40%	8%
De San Vicente 2015 ¹⁰	Spain	37	HR+ HER2- Inter O-DX	LN0, 73% LN+, 27%	Retro	1	Recomm	Physician (CP factors)	Decision	Physician & patient	0%	100%	0%
Dieci 2016 ¹¹	Italy	123	ER+ HER2- T1-3 Inter clin risk	LN0	Prosp	9	Recomm	Physician (NR)	Recomm & Decision	Physician & patient	61%	33%	6%
Dreyfus 2015 ¹²	France	39	HR+ HER2- Indicated for CT	LN0, 39% LN1-3, 51%	Prosp	2	Recomm	MDT	Recomm	MDT	49%	46%	5%

Study	Country (area)	N patients	Population	Nodal status	Prosp / retro	N centres	Pre-test	Pre-test by (based on)	Post-test	Post-test by (based on)	Risk group (%)		
											Low	Inter	High
Eiermann 2013 ¹³	Germany	244 LN0 122 LN+	ER+ HER2-	LN0, 67% LN1-3, 33%	Prosp	15	Recomm	MDT (CP factors & local protocol)	Recomm	MDT	54%	38%	8%
Gligorov 2015 ¹⁴ (SWITCH)	France	95	ER+ HER2-	LN0-mic	Prosp	7	Recomm	MDT (CP factors + French guidelines)	Recomm	MDT	55%	40%	5%
Hejduk 2016 ¹⁵ Petrakova 2016a, b ^{16, 17}	Czech Republic	196	ER+ HER2-grade 2 + other risk factor	LN0	Prosp	13	Recomm	NR	Recomm	NR	56%	38%	6%
Mouysset 2016 ¹⁸	France	603	ER+ HER2-	LN0, 61% LN+, 39%	Prosp	Multi	Recomm	MDT (CP factors)	Recomm	MDT	60%	34%	6%
Novas 2016 ¹⁹	Spain	35	NR	N1mic	Retro	NR	Recomm	Physician (NR)	Recomm	Physician	54%	43%	3%
Pestalozzi 2015 ²⁰	Switzerland	221	ER+ HER2-	pN0 or pN1a	Prosp	Multi	Recomm	MDT (NR)	Recomm	MDT	NR	NR	NR
Wassermann 2015 ²¹	France	72	HR+ HER2- Pre/postmeno	LN0, 86% LNmic, 6% LN1-3, 9%	Prosp	4	Recomm	MDT (NR)	Recomm	MDT	NR	NR	NR

N, number of patient; AOL, Adjuvant! Online; HR+, hormone receptor positive; HER2, human epidermal growth factor receptor; ER+, oestrogen receptor positive; LN, lymph node; RS, Oncotype DX recurrence score; Inter, intermediate; sub, subgroup; NR, not reported; Prosp, prospective; Retro, retrospective; Multi, multinational; CP, clinicopathological; Recomm, recommendation; MDT, multidisciplinary team; pre/postmeno, pre and post menopausal women

Table 2: Study characteristics: EndoPredict (EPClin)

Study	Country (area)	N patients	Population	Nodal status	Prosp / retro	N centres	Pre-test	Pre-test by (based on)	Post-test	Post-test by (based on)	Risk group (%)		
											Low		
UK studies													
Bloomfield 2017 ²² (abstract)	UK	149	ER+ HER2-	NR	Prosp	8	Decision	Physician & patient (CP factors)	Decision	Physician & patient	50%	-	50%
European studies													
Ettl 2015 ²³	Germany	217	ER+ HER2-	LN0, 73% LN+, 27%	Prosp	1	Recomm	MDT (CP factors + uPA/PAI-1)	Recomm	MDT	61%	-	39%
Muller 2013 ²⁴	Germany	130	ER+ HER2-	LN0, 62% LN1-3, 35.5% LN4+, 2.5%	Retro	1	Recomm	Physician (CP factors)	Recomm	Physician	48%	-	52%
Penault-Llorca 2016 ²⁵ (ADENDOM)	France	200	ER+ HER2- Clinically inter. risk	LN0-mic	Prosp		Recomm	MDT (CP factors)	Recomm & Decision	MDT	67%	-	33%
N, number of patient; HR+, hormone receptor positive; HER2, human epidermal growth factor receptor; ER+, oestrogen receptor positive; LN, lymph node; Inter, intermediate; -, not reported; Prosp, prospective; Retro, retrospective; CP, clinicopathological; Recomm, recommendation; MDT, multidisciplinary team;													

Table 3: Study characteristics: IHC4+C

Study	Country (area)	N patients	Population	Nodal status	Prosp / retro	N centres	Pre-test	Pre-test by (based on)	Post-test	Post-test by (based on)	Risk group (%)		
											Low		
UK studies													
Yeo 2015 ²⁶	UK (London)	124	ER+ HER2-	LN0 74% LN1-3 26%	Prosp	1 (Royal Marsden)	Recomm	MDT (NR)	Recomm	MDT	NR	NR	NR
European studies													
None													
N, number of patient; HR+, hormone receptor positive; HER2, human epidermal growth factor receptor; ER+, oestrogen receptor positive; LN, lymph node; Inter, intermediate; -, not reported; Prosp, prospective; Recomm, recommendation; MDT, multidisciplinary team													

Table 4: Study characteristics: Prosigna

Study	Country (area)	N patients	Population	Nodal status	Prosp / retro	N centres	Pre-test	Pre-test by (based on)	Post-test	Post-test by (based on)	Risk group (%)		
											Low		
UK studies													
None													
European studies													
Martin 2015 ²⁷ (GEICAM)	Spain	200	ER+, HER2- Stage 1-2 T<5cm postmeno	LN0	Prosp	15	Recomm	Physician (CP variables or AOL & immunohistochemistry)	Recomm	Physician	51%	33%	17%
Van Asten 2016 ²⁸	Belgium	51	ER+, HER2- Unclear if CT needed	NR	Prosp	1	Recomm	MDT (CP factors)	Recomm	MDT	NR	NR	NR
Wuerstlein 2016 ²⁹	Germany	198	ER+, HER2- postmeno	LN0	Prosp	11	Recomm	Physician (CP factors)	Recomm	Physician	43%	35%	22%
N, number of patient; HR+, hormone receptor positive; HER2, human epidermal growth factor receptor; ER+, oestrogen receptor positive; LN, lymph node; Inter, intermediate; NR, not reported; Prosp, prospective; CP, clinicopathological; Recomm, recommendation; MDT, multidisciplinary team; postmeno, postmenopausal; AOL, Adjuvant! Online;													

Table 5: Study characteristics: MammaPrint

Study	Country (area)	N patients	Population	Nodal status	Prosp / retro	N centres	Pre-test	Pre-test by (based on)	Post-test	Post-test by (based on)	Risk group (%)		
											Low		
UK studies													
None													
European studies													
Bueno-de-Mesquita 2007 ³⁰ (RASTER)	Netherlands	427	80% ER+ 84% HER2- T1-4, M0 <61 yrs	LN0-micro	Prosp	16	Recomm	Physician (Dutch CBO guidelines)	Recomm & Decision	Physician; physician & patient	51%	-	49%
Cusumano 2014 ³¹	Netherlands, Belgium, Italy, Spain	151	ER+ HER2- T1-3, M0	LN0 LN1-3	Prosp	4	Recomm	MDT (NR)	Recomm	MDT	NR	-	NR
Drukker 2014 ³² (subset of RASTER)	Netherlands, Germany, France, Italy, Portugal	37	ER+/- HER2+/- T1-3, M0	LN0	Selected cases	12 oncologists	Recomm	Physician (tools & CP factors)	Recomm	Physician	NR	-	NR
Exner 2014 ³³	Austria	75	ER+ HER2- Grade 1-2 T 1-3cm	LN0	Prosp	1 hospital	Recomm	MDT (closely followed St Gallen 2009)	Recomm	MDT	76%	-	24%
Hartmann 2012 ³⁴	Germany	60	HR+ HER2- ≥60 years Grade 2-3 T >1cm	LN0 LN1-3	Prosp	2 hospitals	Decision	MDT (national guidelines) + patient preference	Recomm	MDT	63%	-	37%
Kuijjer 2016 ³⁵	Netherlands	377	ER+ (HER2 NR)	NR	Prosp	33 hospitals	Recomm	Physician (CP factors)	Recomm	Physician	57%	-	43%
Rullan 2016 ³⁶	Spain	129	HR+ HER2- 35-70 yr T 1-3cm, grade 2	94% LN0-mic	NR	3 hospitals	Recomm	Physician (CP factors & local protocol)	Decision	Physician + patient	NR	-	NR
Wuerstlein 2016 ³⁷ (WSG PRIME)	Germany	430	HR+ HER2-	LN0 (72%) LN1-3 (28%)	Prosp	27 hospitals	Recomm	Physician (CP factors and/or IHC for ER/PR/Ki67)	Recomm (unclear)	Physician	NR	-	NR

N, number of patient; HR+, hormone receptor positive; HER2, human epidermal growth factor receptor; ER+, oestrogen receptor positive; LN, lymph node; Inter, intermediate; NR or -, not reported; Prosp, prospective; Retro, retrospective; CP, clinicopathological; Recomm, recommendation; MDT, multidisciplinary team

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