brighton and sussex medical school

Decision making in frail patients with breast cancer

Professor Malcolm Reed and Professor Juliet Wright

Reduction in breast cancer mortality 1989-2006

- Women < 50 years = 37%
- Women > 69 years = 2%

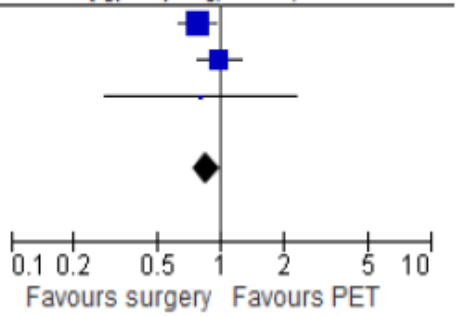
Autier BMJ 2010 341 3620

Cochrane review of surgery plus adjuvant Tamoxifen versus Tamoxifen only

2.1 Survival - overall

Study or Subgroup	Surgery Events	Surgery Total	PET Events	PET Total	O-E	Variance	Weight	Peto Odds Ratio Exp[(O-E) / V], Fixed, 95% CI
CRC	159	225	187	230	-21.71	85.27	55.4%	0.78 [0.63, 0.96]
GRETA	130	239	144	235	-1.29	65.19	42.4%	0.98 [0.77, 1.25]
Nottingham 2	8	53	14	94	-0.75	3.4	2.2%	0.80 [0.28, 2.32]
Total (95% CI)		**517**		**559**			**100.0%**	**0.86 [0.73, 1.00]**
Total events	297		345					

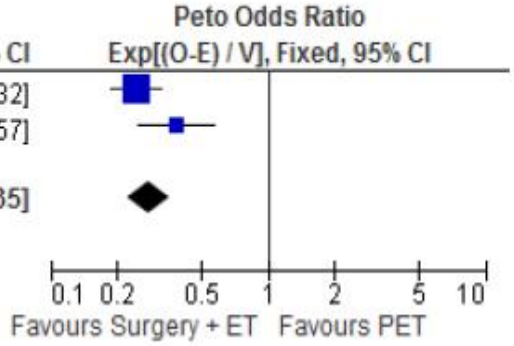
Heterogeneity: Chi² = 2.05, df = 2 (P = 0.36); I² = 3%
Test for overall effect: Z = 1.91 (P = 0.06)



2.2 Local disease control

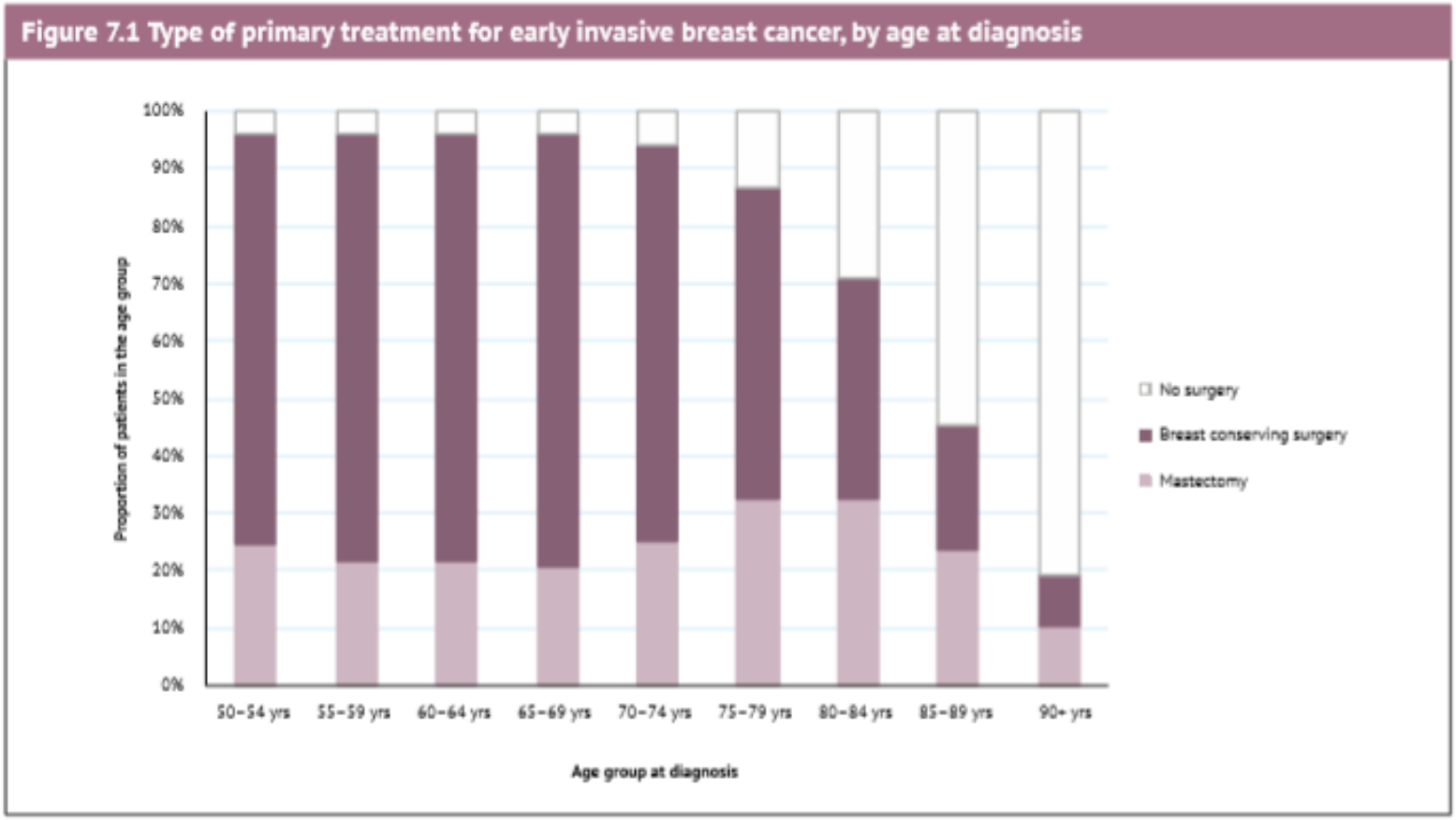
Study or Subgroup	Surgery Events	Surgery Total	PET Events	PET Total	O-E	Variance	Weight	Peto Odds Ratio Exp[(O-E) / V], Fixed, 95% CI
CRC	36	225	115	230	-73.63	52.83	69.6%	0.25 [0.19, 0.32]
GRETA	27	239	95	235	-22.37	23.09	30.4%	0.38 [0.25, 0.57]
Total (95% CI)		**464**		**465**			**100.0%**	**0.28 [0.23, 0.35]**
Total events	63		210					

Heterogeneity: Chi² = 2.90, df = 1 (P = 0.09); I² = 66%
Test for overall effect: Z = 11.02 (P < 0.00001)



Hind, Wyld and Reed 2007

Surgical omission related to Age



NABCOP Annual Report 2018

NICE Guidance 2009

"Treat patients with early invasive breast cancer, irrespective of age, with surgery and appropriate systemic therapy, rather than endocrine therapy alone, unless significant comorbidity precludes surgery."

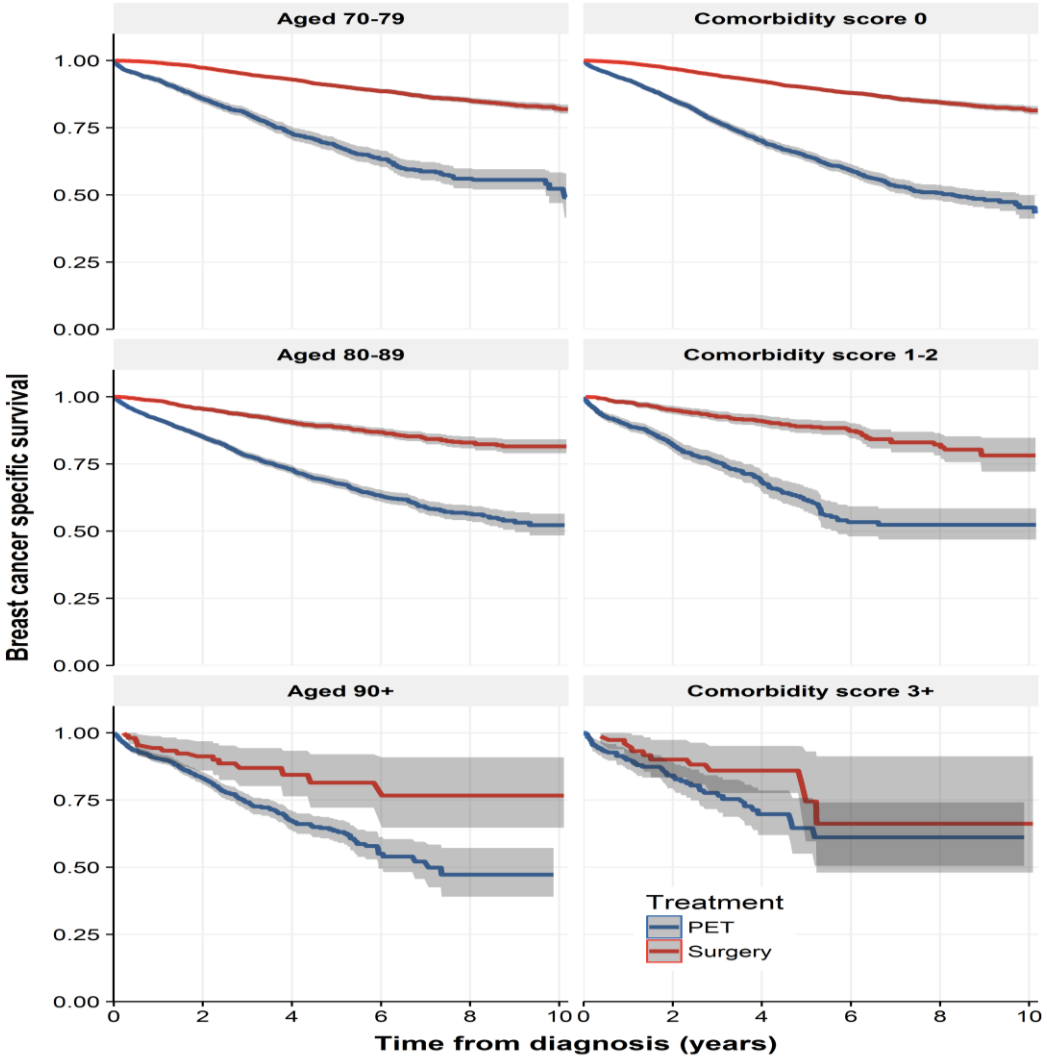
US practice is surgery for all

- Recent US study of ~6000 nursing home residents in the USA with breast cancer undergoing surgery (Tang et al, JAMA Surgery, 2018)
- The 30-day mortality rates were 8% after lumpectomy, 4% after mastectomy, and 2% after ALND….compared to 0.1% in the UK for all ages (and 0% out of 2500 women over 70 in Age Gap)
- The 1-year mortality rates were 41% after lumpectomy, 30% after mastectomy, and 29% after ALND.
- Among 1-year survivors, the functional decline rate was 56% to 60%. The mean MDS-ADL score increased (signifying greater dependency) by 3 points for lumpectomy, 4 points for mastectomy, and 5 points for ALND.

‘Age Gap’ multicentre cohort study

- Collect data on disease characteristics, treatment type, age, quality of life, co-morbidity and functional status at baseline
- Short term follow up via direct site returns up to 2 years
- Long term follow up via cancer registries
- Survival and quality of life key outcomes
- Propensity score matched analysis to adjust for baseline variables
- Use of data to validate an on line tool.

Breast cancer specific survival



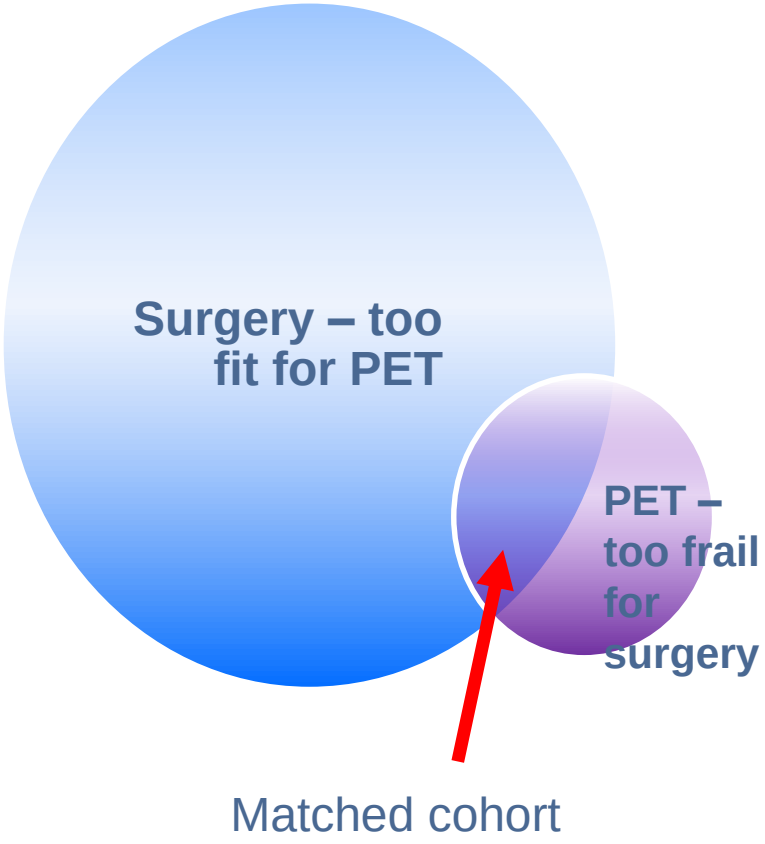
Breast cancer specific survival (BCSS) by age group (left) and by comorbidity score (right) for surgery and PET treatment arms

Observational data from registry sources

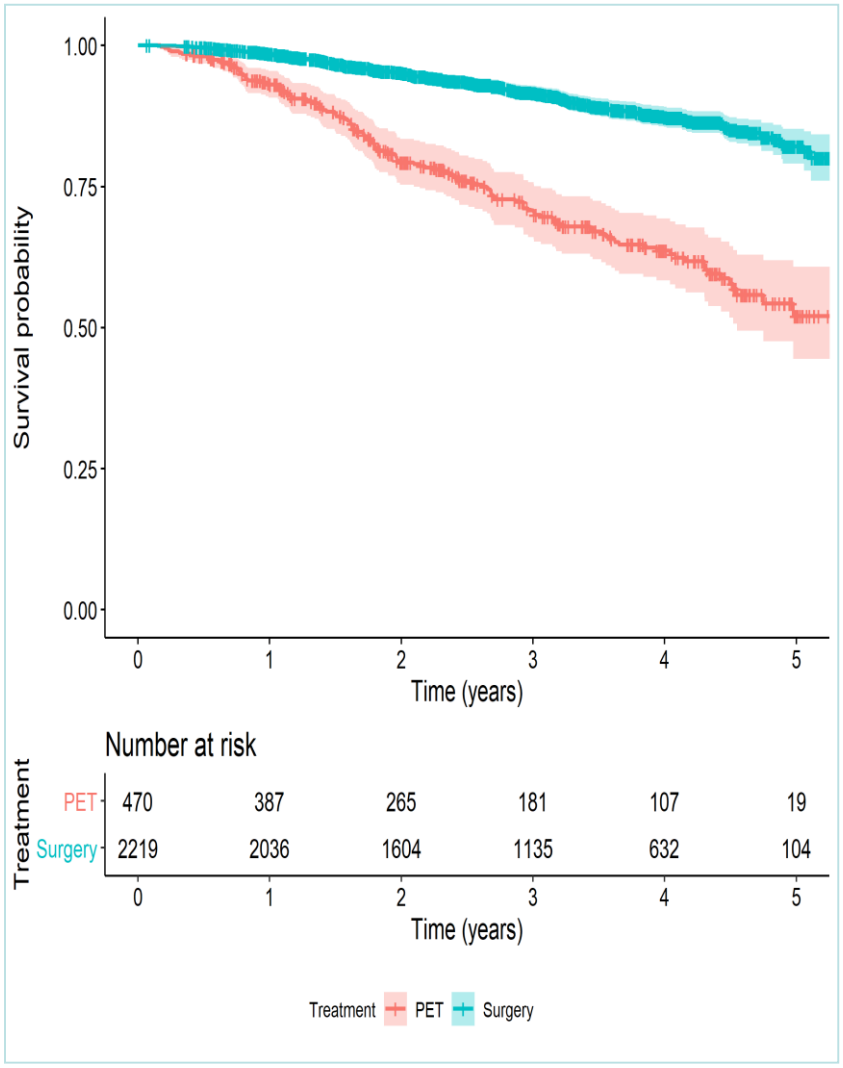
Propensity matching

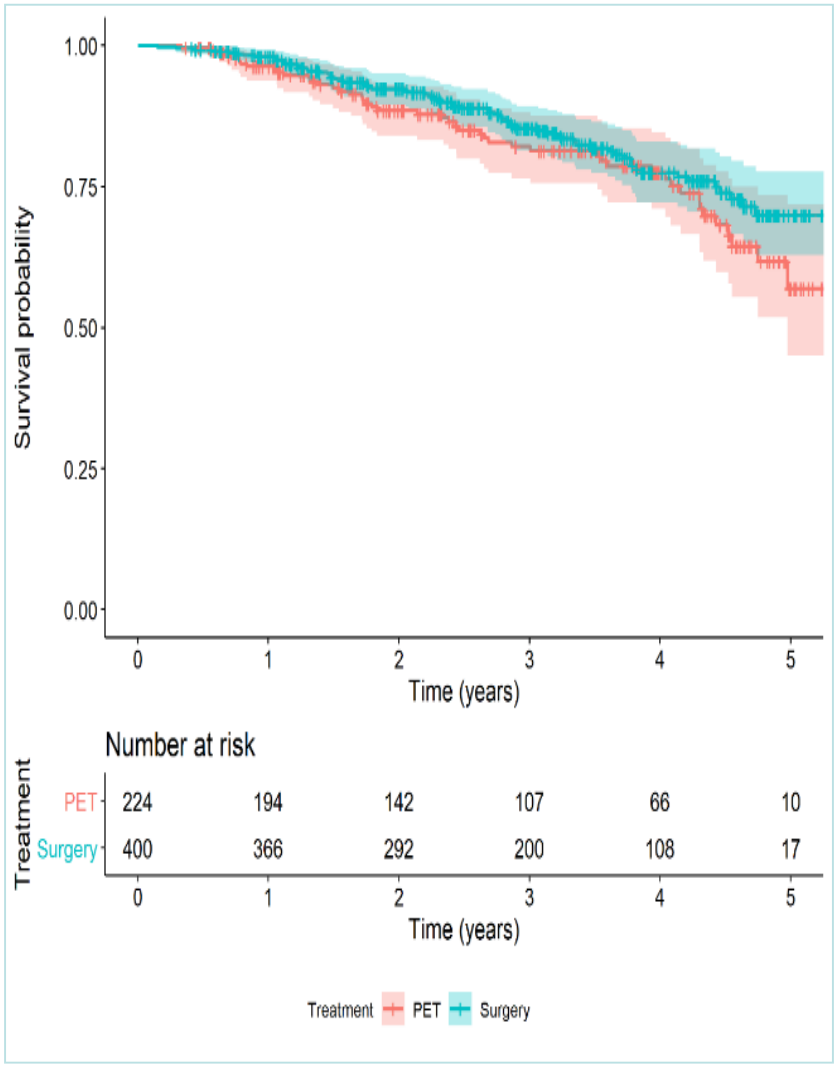
- Surgical and PET patients assigned propensity score

- 1:1 matching
  - Age
  - Co-morbidities (Modified Charlson Score Index (MCCI))
  - Frailty (Activities of Daily Living Score (ADL))
  - Pre-operative tumour size, grade and nodal status
  - Oestrogen receptor +ve



Cause specific survival unmatched (a) versus propensity score matched(b)





‘Age Gap’ cohort study - survival

- Unmatched patients Surgery > PET – similar to cohort studies.
- Difference almost disappears with matched patients – similar to RCT’s
- Survival Curves similar to 3-4 years then surgery > PET
- What about impact of surgery on Quality of Life?

Bridging the Gap – Quality of Life Outcomes

Surgery has significant adverse effects for at least 2 years on:

- Global QoL
- Physical function
- Pain
- Fatigue
- Breast symptoms (short term)
- Arm symptoms

PET – no significant change at two years

Overall Summary - Age GapTrial

- This study has shown that recruiting women over the age of 70 to clinical trials is achievable -the oldest recruit was 102 and women with cognitive impairment and severe frailty were recruited.
- In common with other cohort studies, overall survival is significantly reduced in un-matched women on PET compared to surgery.
- When matched patients are studied as in RCT's or using propensity score matching as in Age Gap there is no survival benefit for surgery for up to 4 years.
- Surgery results in significantly worse QoL for at least two years.
- PET can be safely recommended for those with ER + positive cancer with an estimated life expectancy of less than 4 years
- This currently equates to to a fit woman of 90 or a les fit woman in her mid 80s. Age Gap has developed Decision Aids and online outcome predictors to facilitate selection.

Moving beyond age in decision making

- Age gives us useful information about groups not individuals
- Strong evidence of conscious and unconscious bias
- Multiple screening tools for frailty
- Prognostic indicators (eg Predict) do not include patient comorbidities and other characteristics
- Age Gap Decision Aid **does** include comorbidities and frailty assessment (Charlson Index – Activities of Daily Living) to give an estimated prediction of life expectancy
- Current screening tools and clinician judgement (often overly dependent on age) result in continued inappropriate allocation to PET and/or surgery

How can we identify and manage patients with breast cancer and potential frailty?

Performance Status (WHO / ECOG)

Performance Status (WHO / ECOG)

0 – Asymptomatic (Fully active, able to carry on all predisease activities without restriction)

1 – Symptomatic but completely ambulatory (Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature. For example, light housework, office work)

2 – Symptomatic, <50% in bed or chair during the day (Ambulatory and capable of all self care but unable to carry out any work activities. Up and about more than 50% of waking hours)

3 – Symptomatic, >50% in bed or chair, but not bedbound (Capable of only limited self-care, confined to bed or chair 50% or more of waking hours)

4 – Bedbound (Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair)

What is frailty?

- Age-related decline in multiple physiological systems
- Threshold of homeostatic reserve reached, resulting in:
  - An ‘at risk’ state
  - Vulnerability to minor stressor events
- **Disproportionate changes** in health status:
  - From mobile to immobile
  - From lucid to confused
  - From independent (‘managing’) to requiring help
- An increased risk of adverse events

Underpins the ‘non-specific nature’ of some medical presentations in older adults

Clegg A et al. Lancet. 2013:381(9868):752–76.

Common presentations of frailty

- Fatigue, unintentional weight loss, frequent infections[1]
- Falls (a non-faller may fall due to a minor stress event)[1]
- Over time failure of postural and gait systems (vision, balance, muscle strength)[2]
- Unable to guarantee safe navigation of undemanding environments – spontaneous, recurrent falls may occur[2]
- Delirium: Present in 15–30% elderly patients on admission to hospital[3]
- Fluctuating disability ('good' and 'bad' days)[1]

1. Chen X, Mao G and Leng SX. Clin Interv Aging 2014;9:433–41;
2. 2. Eeles E and Low Choy N. Frailty and Mobility, in Theou O, Rockwood K (eds). Frailty in Aging. Biological, Clinical and Social Implications. Interdiscipl Top Gerontol Geriatr. Basel, Karger, 2015, vol 41, pp 107–20;
3. 3. Inouye SK. Clin Geriatr Med 1998;14(4):745–64.

Frailty index

An alternative frailty model, which utilises a multi-dimensional approach where deficits accumulate across a range of functional, physical and cognitive domains (Rockwood and Mitnitski, 2011) as part of the Canadian Study of Health and Aging. Basedon Comprehensive Geriatric Assessment (CGA)

- Deficit accumulation
  - Deficits = symptoms, signs, disease states, specific functional deficits
  - Markers of the decline in physiological reserve
  - The more you have the more likely you are to be frail
  - So if 10/40 deficits present, their FI = 0.25
  - Adverse outcomes proportional to deficits - more you have, worse you do
  - Cut off between fitness and frailty around 0.25
  - Upper FI threshold around 0.67, where any more leads to death

FI, frailty index

Rockwood K and Mitnitski A, Clin Geriatr Med 2011;27(1):17–26.

Is frailty permanent?

- Not necessarily!
- Frailty does appear to be a dynamic process[1]
- But… trajectory is mainly toward more frail states[1]
- Very rare to revert from frail to non-frail (0–0.9% chance)[1]
- In most people, frailty is progressive

1. Gill TM et al. Archives of Internal Medicine 2006;166(4):418–23;
2. Fried LP et al. J Gerontol A Biol Sci Med Sci 2001;56:M146–56.

Risk factors: Potential targets for intervention

- Alcohol misuse
- Cognitive impairment
- Falls
- Functional impairment
- Hearing problems
- Mood disorder
- Poor nutritional status
- Physical inactivity
- Obesity avoidance
- Polypharmacy
- Smoking
- Social isolation
- Loneliness
- Poor vision
- Incontinence

Stuck AE et al. Soc Sci Med 1999;48:445–69.

Brighton Breast Clinic

Referral criteria:

- No age threshold
- Newly diagnosed with breast cancer, considered unfit for or declining surgery
- Patients on primary endocrine treatment who develop disease progression
- Geriatrician and surgeon
- Parallel oncology clinic
- Specialist nurse input

Joint Assessment ‘Same Time’ Assessment

‘CGA’ geriatrician led

- Functional status
- Cognitive status
- Polypharmacy
- Management of comorbidities
- Optimisation of medical issues
- Referral to other specialties

Breast cancer assessment - surgeon led

- Joint formulation of management plan
- Breast cancer treatment options
- Pre-operation planning
- Monitoring response to PET

Brighton Breast Clinic

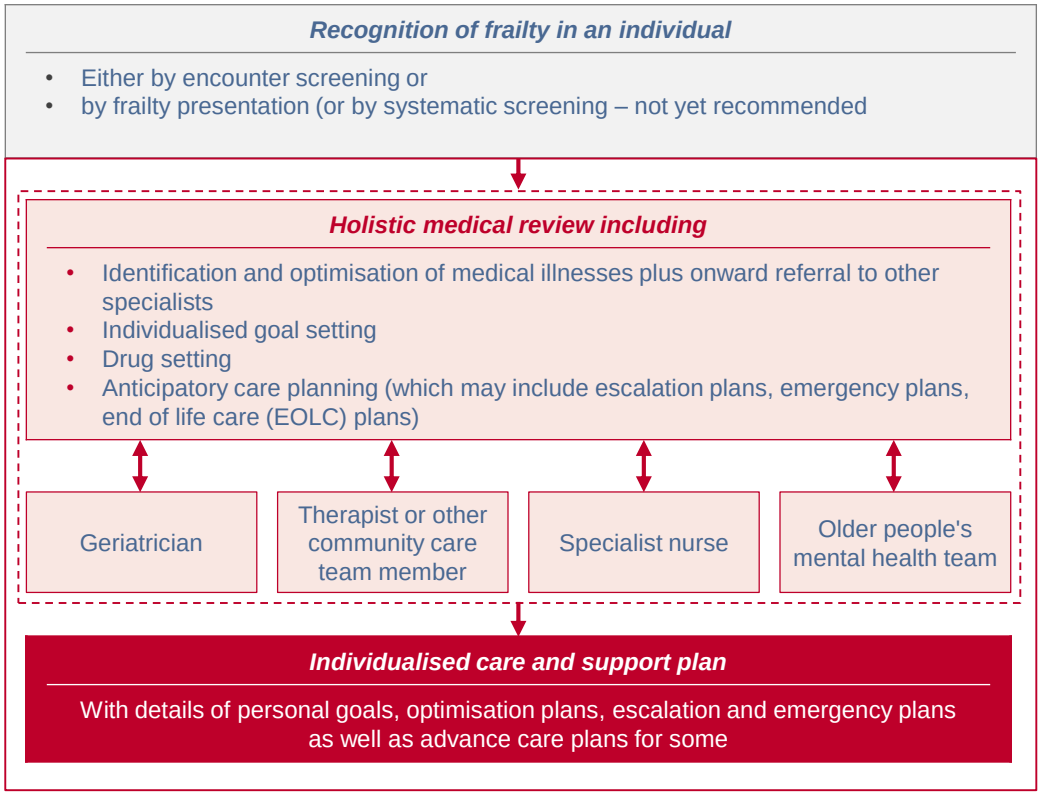
Comprehensive Geriatric Assessment (CGA)

Full CGA likely to take 1.5–2.5 hours

Common problems:

Falls
Cognition
Continence
Mood
Mobility
Weight loss/nutrition
Polypharmacy
Physical inactivity
Alcohol excess
Smoking
Visual loss
Social isolation and loneliness

Physical exam – eyes, ears, neuro – VITAL



Holistic review likely to take 45–60 minutes

Capacity should be assessed

Care and support plan:

Named individuals
Health and social care summary
Optimisation and maintenance plan
Escalation plan
Urgent care plan
Advanced care plan

British Geriatrics Society. Fit for Frailty. Available at: www.bgs.org.uk/campaigns/fff/fff_full.pdf

Brighton Breast Clinic

Age Gap Decision Tool

Compare surgery and primary endocrine therapy (PET)

DW

- 86 years
- Fungating tumour - left breast + inframammary fold (ER pos, PR neg, HER2 neg)
- Commenced PET (Letrozole) & referred to Joint clinic –
- PMH
  - Memory impairment – no formal diagnosis
  - Hypertension
  - Hypothyroidism
  - CKD Stage 3

DW

- Medication
  - Accrete D3 1 bd
  - Levothyroxine 150 mcg od
  - Ramipril 10 mg od
  - Not compliant with endocrine treatment
- Independently mobile – but memory impairment - wanders
  - MMSE 17/30
  - Lacked capacity to fully discuss medical treatment
  - Performance status zero

DW

- Largely symptom free and general examination normal
- Breast examination 15 cm mobile/fungating mass left breast

- CT head
- Staging CT thorax, abdomen, pelvis
- GABS - FBC, U&E, Glu, LFT, TFT, Corr Ca, B12, folate
- IM Fulvestrant
- Referral to memory assessment service
- Referral rapid response team - re home safety & same day discussion with GP

Age	Tumour grade	Tumour size	Disease nodes positive	Comorbidities	Frailty
86	2	100mm	No	Dementia, Moderate/Severe Renal Disease	ADL Stage 0

Chart (2yr) Chart (5yr) Survival (2yr) Survival (5yr) Table (2yr)

Table (5yr)

Statistics At Five Years

	Chance of survival	Chance of death due to breast cancer	Chance of death from other causes
Surgery	19.3%	8.8%	71.9%
PET	13.3%	24.2%	62.5%

DW

- Surgery planned for local control/symptoms - delayed because of surrounding infection
- Admitted to hospital – bleeding, infection and delirium
- Reviewed with oncologist – surgery preferable to palliative XRT - planned for mastectomy
- Subsequent deterioration - decline in compliance esp with personal care
- Elective admission 6 months after initial referral – with geriatric team aware of admission and complexities

DW

- Left palliative mastectomy (no SNB)
- Reasonable post op period/wound drain/antibiotics
- Good support from dementia nurse – patient reviewed from day 1 post op
- Transferred to geriatric ward
- Discharge planning complex – discharged day 37 to respite care

DW

- Seen in joint clinic
- Family delighted with surgical intervention
- Following respite care discharged home
- Independently mobile, symptom free
- No longer distressed by odour/pain bleeding/dressings
- Significant improvement in cognitive function
- Wound healed well
- Compliant with Letrozole

Joint Clinic

- April 2015-March 2020 182 patients were seen including three men
- 82 years (range 69-99 years).
- 57% of patients were followed up between 1-6 times.
- 13% of patients were referred for surgical treatment after initial PET.
- 10% of patients underwent a change in endocrine therapy.
- Medical management was changed in 35% of patients, typically for treatment optimisation, further investigations or referral to other specialists.

Future options

- ‘Brighton model’ very resource intensive
- Up-skill cancer services - challenging
- Training - curriculum reviews needed to match changing health delivery
  - undergraduate
  - postgraduate
  - ‘generalism’
- Role of screening tools in identification of patient needs or referral? (MacMillman ERG group)
- Development of geriatric liaison services though out the cancer pathway – joint working!

Discussion

- Assessment in the joint clinic resulted in more patients receiving surgical treatment.
- Cancer management was changed in over a third of the patients.
- About half of the patients required change of medical management to resolve issues identified by focused geriatric assessment.
- Liaison Geriatrician input crucial but model needs to be addressed to increase reach across oncology provision – liaison geriatrics is key for future improvements