

**Patient ranking of late
symptoms after breast and
prostate cancer and their
influence on self initiated
nutritional therapies**

The Bedford Real World Study

Australia

MASCC/ISOO

ANNUAL MEETING ON
SUPPORTIVE CARE IN CANCER

Adelaide, Australia | 23-25 June, 2016



Background and aims

To explore whether asking patients from a real world population to rank their troublesome late toxicities would give a difference profile than expected from RCT data who to be:

- Older
- Ethnically more diverse
- More co-morbidities
- Be in other trials
- Have had previous malignancies

Precise knowledge of toxicities are important to:

- Counsel patients on the risks and benefits of adjuvant therapies
- Advise appropriate exercise / lifestyle strategies
- Educate physicians on what to expect in the follow up period
- Help priorities clinical trials to patient needs



Personal disclosures

Funding: The Primrose Oncology Research Fund. No commercial input

| <i>Company Name</i> | <i>Honoraria/ Expenses</i> | <i>Consulting/ Advisory Board</i> | <i>Funded Research</i> | <i>Royalties/ Patent</i> | <i>Stock Options</i> | <i>Ownership / Equity Position</i> | <i>Employee</i> | <i>Other (please specify)</i> |
|----------------------------------|--------------------------------|---|----------------------------|------------------------------|--------------------------|--|-----------------|-----------------------------------|
| Astrazeneca | X | X | | | X | | | |
| Jansen-cilag | X | X | | | | | | |
| Prostate Cancer | | | X | | | | | |
| Helsinn | X | X | | | | | | |
| Nature-medical Ltd | X | | | | X | | | |
| Health Education Publications | | | | | | X | | |

Studies have reported 50-65% cancer patients take OTCS^{1,2}

This study aimed to established whether:

- Treatment pathways and the level of side effects influence OTC supplement intake.
- Which supplements are taken and for what reason

1. Bauer et al *Integrative Cancer Therapies* 2012;11(2): 83-89.

2. Uzzo et al. *British Journal of Urology International* 2004;93(7): 955-960.

Every patients with Ca prostate & breast, >6months post sx, rxt or chemo - Primrose unit
Data recorded during their routine consultation by one of 5 oncologist or 2 specialist nurses.

Bedford Hospital NHS Trust

Long Term Toxicity Ranking of Symptoms

Hospital label: _____

Tumour site:
☐ Breast ☐ Prostate

Past treatment:
☐ Chemotherapy (>6 months previous) ☐ No chemotherapy ☐ Radiotherapy

Last treatment details:

Current treatment:
☐ Hormones ☐ No hormones

Details:

What are the symptoms, in order of rank, which trouble you the most, and have you undertaken any complementary measures to alleviate them?

Rank:

1. Symptom description: _____ Complementary therapy: _____


Do they help? ☐ Yes ☐ No Did you discuss with the doctor? ☐ Yes ☐ No If "yes", was the discussion helpful? ☐ Yes ☐ No ☐ Did not discuss

2. Symptom description: _____ Complementary therapy: _____

Do they help? ☐ Yes ☐ No Did you discuss with the doctor? ☐ Yes ☐ No If "yes", was the discussion helpful? ☐ Yes ☐ No ☐ Did not discuss

3. Symptom description: _____ Complementary therapy: _____

Do they help? ☐ Yes ☐ No Did you discuss with the doctor? ☐ Yes ☐ No If "yes", was the discussion helpful? ☐ Yes ☐ No ☐ Did not discuss



4. Symptom description: _____ Complementary therapy: _____

Do they help? ☐ Yes ☐ No Did you discuss with the doctor? ☐ Yes ☐ No If "yes", was the discussion helpful? ☐ Yes ☐ No ☐ Did not discuss

5. Symptom description: _____ Complementary therapy: _____


Do they help? ☐ Yes ☐ No Did you discuss with the doctor? ☐ Yes ☐ No If "yes", was the discussion helpful? ☐ Yes ☐ No ☐ Did not discuss

Do you take any other supplements? ☐ Yes ☐ No If "yes", please describe: _____

Do they help? ☐ Yes ☐ No Did you discuss with the doctor? ☐ Yes ☐ No If "yes", was the discussion helpful? ☐ Yes ☐ No ☐ Did not discuss

Clinician: _____ Date: ____/____/____

Thank you very much for taking the time to complete this questionnaire



Sept 15
to
Feb 16.

830 (97%) filled questionnaire

480 men (Prostate) and 350 women (Breast Cancer)

Average age 63 years (Range 36-87 years)

437 (53%) on hormone therapies:

- LHRH agonists
- Tamoxifen
- Anastrozole
- Exemestane
- Letrozole



Level of self reported troublesome toxicities

(≥ 1):

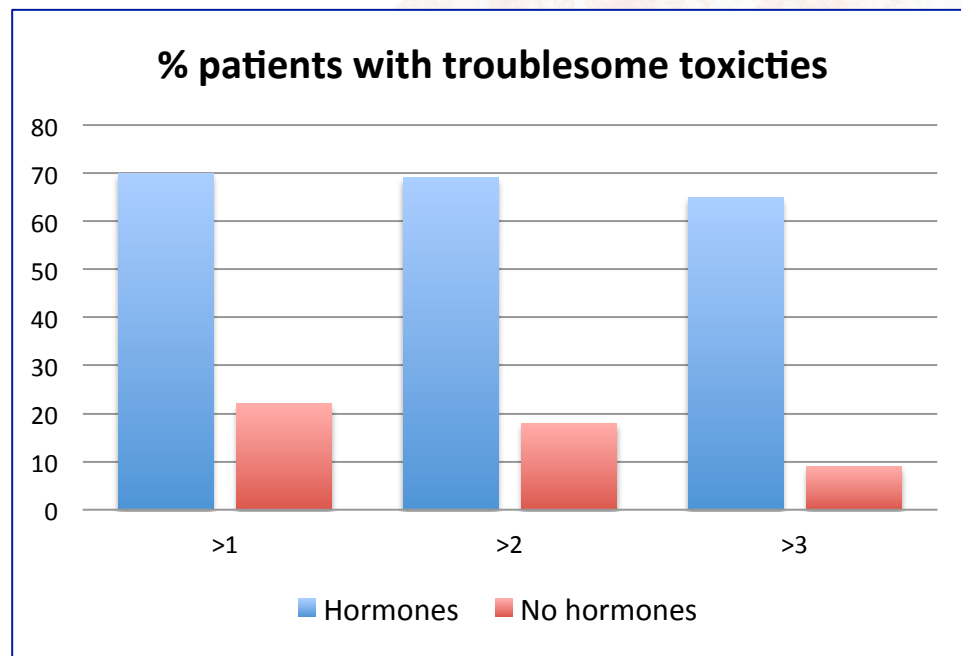
- Overall 393 of 830 (47%)
 - Hormones 305 of 437 (70%)
 - No hormones 88 of 393 (22%)
- Diff 48% (Chi^2 P= 0.002)

(≥ 2):

- Overall 370 of 830 (45%)
 - Hormones 300 of 437 (69%)
 - No hormones 70 of 393 (18%)
- Diff 51% (Chi^2 P= 0.001)

(≥ 3):

- Overall 319 of 830 (38%)
 - Hormones 284 of 437 (65%)
 - No hormones 35 of 393 (9%)
- Diff 56% (Chi^2 P= 0.001)



Ranking of distress

Women:

| | |
|----------------|-----|
| 1. Hot flushes | 62% |
| 2. Arthralgia | 55% |
| 3. Fatigue | 42% |
| 4. Mood | 29% |
| 5. Weight gain | 28% |
| 6. Vag dryness | 10% |

Men:

| | |
|-----------------|-----|
| 1. Hot flushes | 61% |
| 2. Fatigue | 42% |
| 3. Arthralgia | 39% |
| 4. ED / Libido* | 25% |
| 5. Mood | 15% |
| 6. Weight gain | 15% |

* Afro-Caribbean men ranked erectile dysfunction over hot flushes.



Established Arthritis incidence

Women

Anastrozole Tamoxifen

| Musculoskeletal | | |
|------------------------|----------|----------|
| Arthritis | 512 (17) | 445 (14) |
| Arthralgia | 467 (15) | 344 (11) |
| Osteoporosis | 325 (11) | 226 (7) |
| Fracture | 315 (10) | 209 (7) |
| Bone pain | 201 (7) | 185 (6) |
| Arthrosis | 207 (7) | 156 (5) |
| Joint Disorder | 184 (6) | 160 (5) |
| Myalgia | 179 (6) | 160 (5) |

Men

LHRH analogues (%)

| | |
|---------------------------------------|----|
| Hot Flashes | 62 |
| Sexual Dysfunction | 21 |
| Decreased Erections | 18 |
| Lower Urinary Tract Symptoms | 13 |
| Lethargy | 8 |
| Pain (worsened in the first 30 days) | 8 |
| Edema | 7 |
| Upper Respiratory Infection | 7 |
| Rash | 6 |
| Sweating | 6 |
| Anorexia | 5 |
| Chronic Obstructive Pulmonary Disease | 5 |
| Congestive Heart Failure | 5 |
| Dizziness | 5 |
| Insomnia | 5 |
| Nausea | 5 |

Arthralgia & cancer treatments

- Osteoarthritis
- Chemotherapy (Taxotere)
- Tamoxifen
- Aromatase inhibitors
- Herceptin
- Tyrosine kinase inhibitors



Patient information materials

**WE ARE
MACMILLAN.
CANCER SUPPORT**



Arimidex (anastrozole)

Contents and links: Breast cancer | Tamoxifen | Arimidex | Aromasin | Bone health | Exercise | Diet | Joint pains | Lifestyle advice | Lifestyle guide



Your doctor has recommended a medication called Arimidex. This leaflet summarises possible side effects and methods to manage them.

How do they work? Some tumours such as breast cancer can cause the cancer cells to stop growing and in some cases produce hormones by stopping the production of oestrogen.

How are they taken? Arimidex is prescribed as a tablet. Some women prefer to take it with food as it may cause nausea. Stick to it as it is easier to remember to take the tablets in the long term.

If you forget to take your tablet don't panic – levels of the drug in your body will stay in the blood for a couple of weeks before you run out of the tablets and make sure you have a supply.

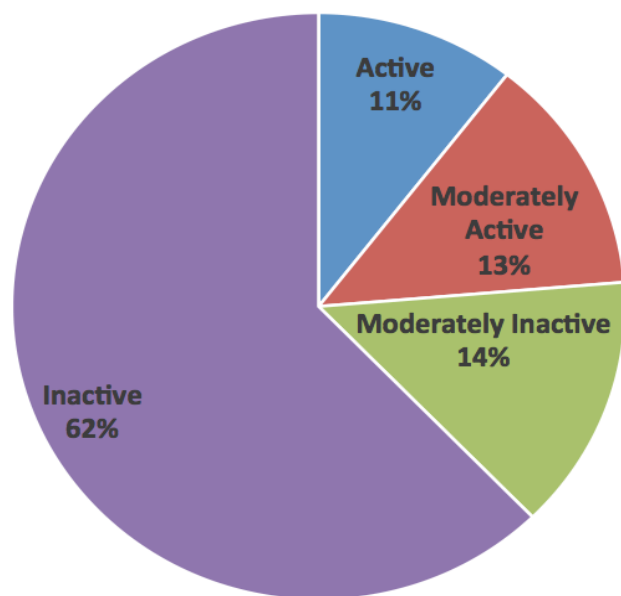
What are they taken for? There are 6 main reasons why postmenopausal women are given Arimidex:

- To control or shrink an established breast cancer (palliation). e.g. if the cancer has spread to the bones.
- To shrink a tumour in the breast before surgery (neo-adjuvant therapy).
- Given in a frail or elderly women to control a tumour in the breast.
- In the adjuvant setting (given after the main therapies such as surgery).
- There is also evidence that some women may be better off taking Arimidex than tamoxifen.
- Finally they have been shown to be slightly more effective in some cases where the cancer was initially aggressive (grade 3) or had spread to the nodes, were



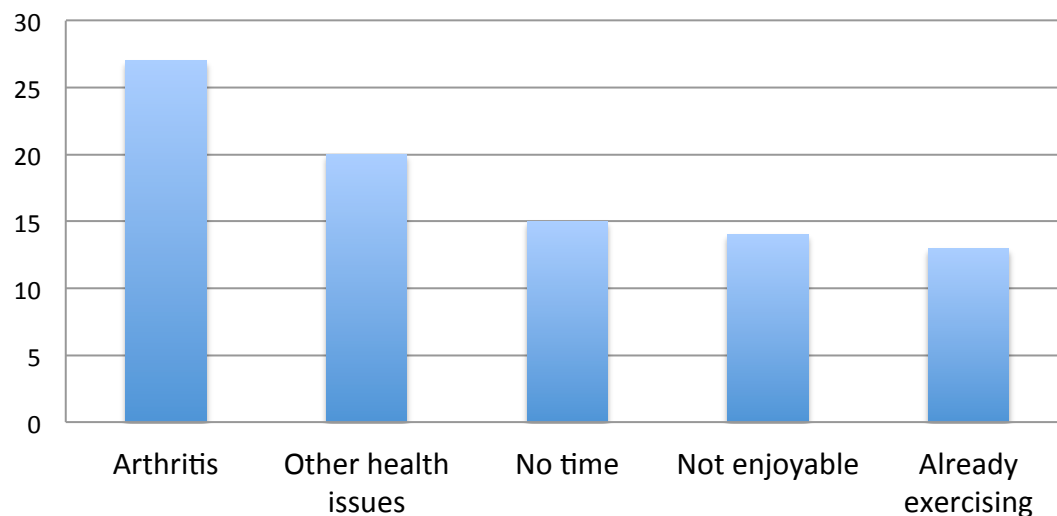
Exercise after Cancer

Current exercise levels GPPAQ



Thomas et al *Clinical Oncology* (2013) 25 (4) 246-51

Barriers to exercise



Benefits of physical activity after cancer

BMJ

Meta-analysis of 33 RCT

Significant benefits for Fatigue, Mood, QoL.

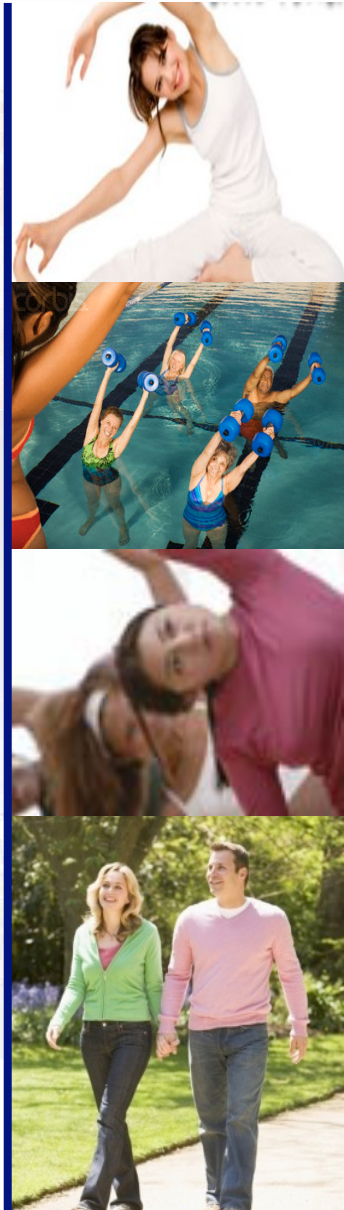
Fong, Bourke et al *BMJ* 2012; 344:

Evidence review of international studies

Hot flushes, peripheral neuropathy, weight gain

2-4 hrs PA a week linked to 30-40% reduction in relapse

Thomas et al *BJMP* 2015; 7 (1) 2-9.



Exercise for arthritis

HOPE study New York 2014

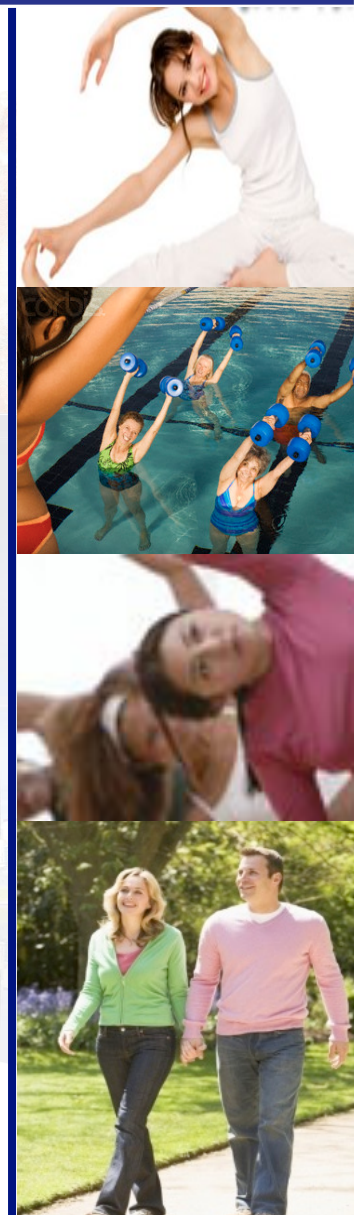
121 patients

Usual post
treatment care

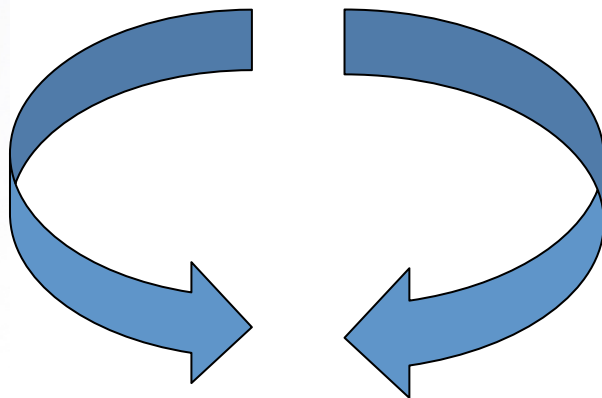
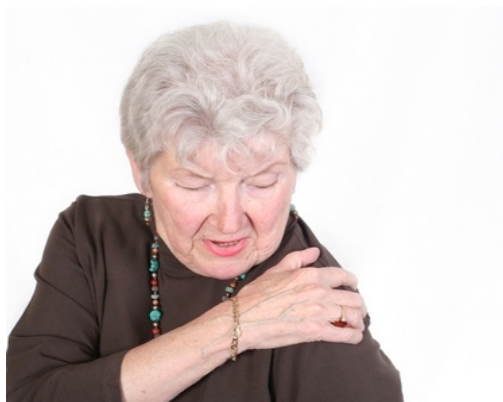
30 mins 4 times/wk
aerobic exercise

30% better pain, stiffness and
qol at 12 weeks

Irwin et al JCO 2015,(33),10.



Barrier to exercise is arthralgia ^{ISOO}



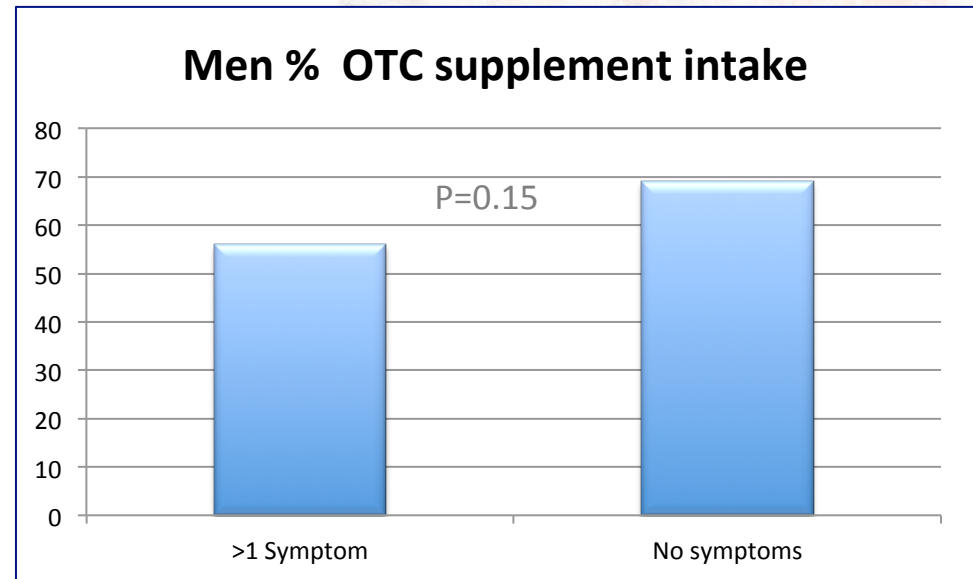
OTC supplementation - men



Total group 498 of 830 (60%) took OTCS

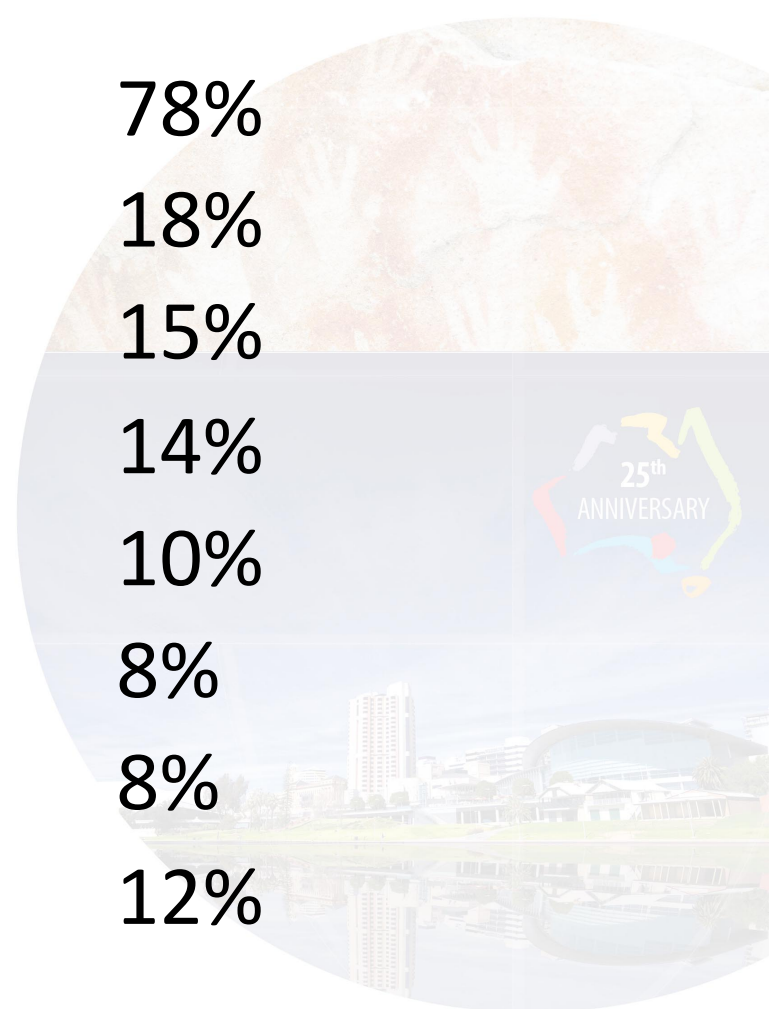
Men (prostate cancer) -

- Overall 309 of 480 (64%) took OTCS
- ≥ 1 symptoms 107 of 191 (56%)
- No symptoms 202 of 289 (69%)*
Diff 13% (χ^2 $p=0.15$).



*78% of men managed on active surveillance took Pomi-T or other polyphenol rich OTCS.

What OTCS are men taking?



| | |
|----------------------|-----|
| • Pomi-T | 78% |
| • Saw palmetto | 18% |
| • Lycopene | 15% |
| • Selenium or/+ Zinc | 14% |
| • Multivitamins | 10% |
| • Apricot kernels | 8% |
| • Turmeric | 8% |
| • Other | 12% |

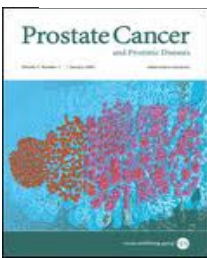
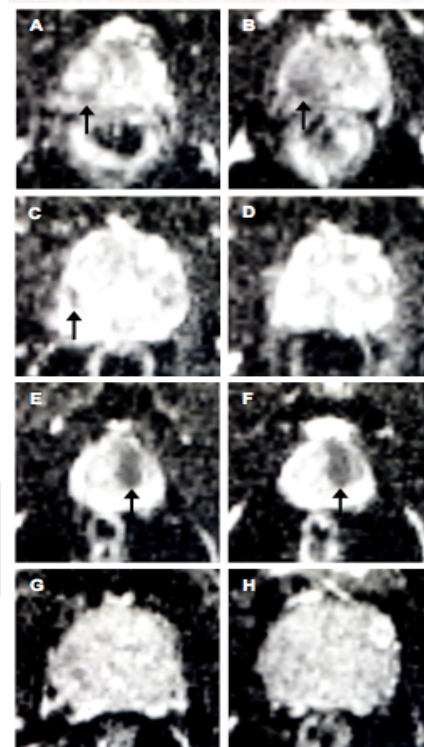
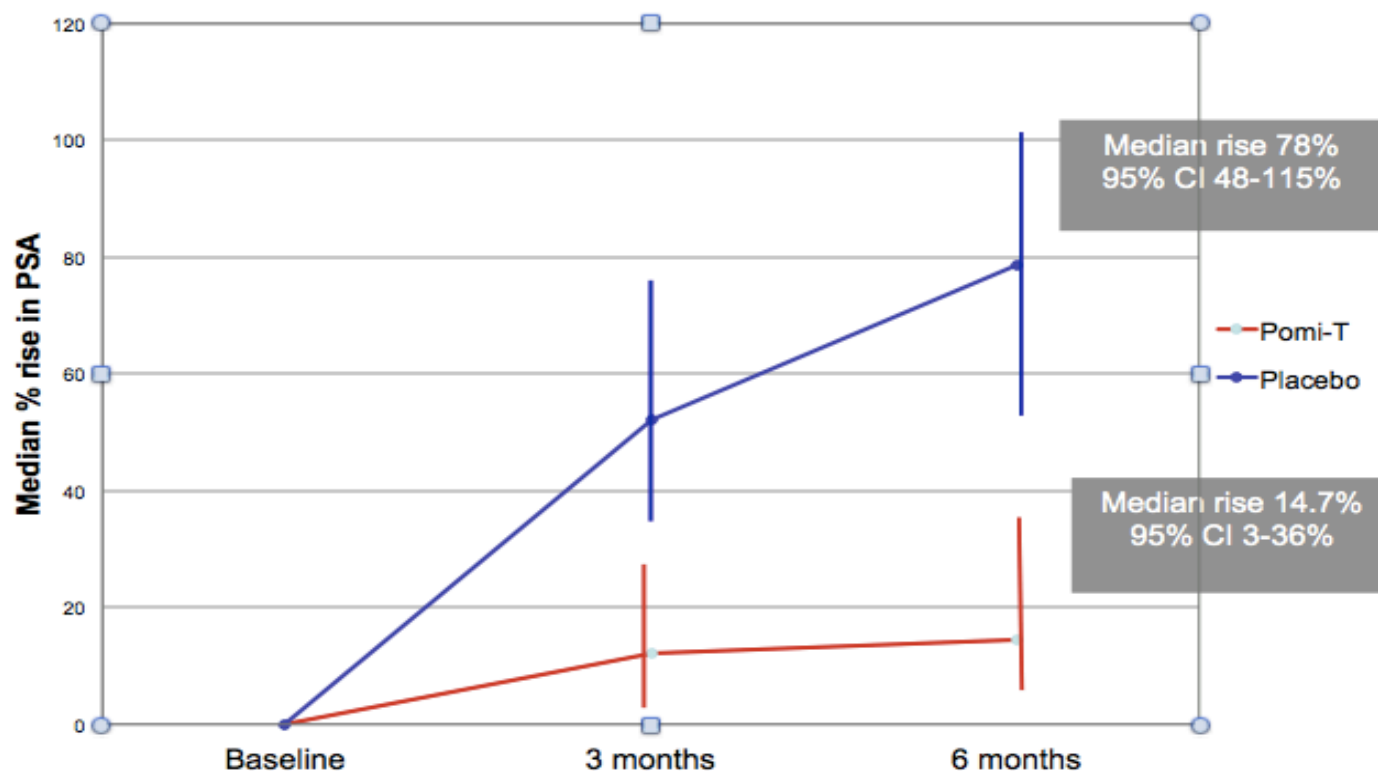


Pomi-T



Median percentage rise in PSA between the two randomised groups

Difference 63.8% ANCOVA $p=0.0008$



Thomas et al The Pomi-T study Prostate cancer & Prostate diseases 2014, (17)

Thomas et al. J Lifestyle Med. 2015 (1) 01



HPF: Men taking Zn 100mg/day - prostate ca worse [Leitzmann]

SELECT : Vit E & selenium- prostate ca worse [Klein].

CV247: RCT - no benefit of Cu, Mg, Vit C over lifestyle [Thomas]

VITAL cohort: Lycopene, Saw Palmetto, Genistein – no effect [Brasky]

VITAL cohort: prostate cancer lower with grape seed extract [Brasky]

RCT of saw palmetto: – No effect on BPH or cancer [Brent]

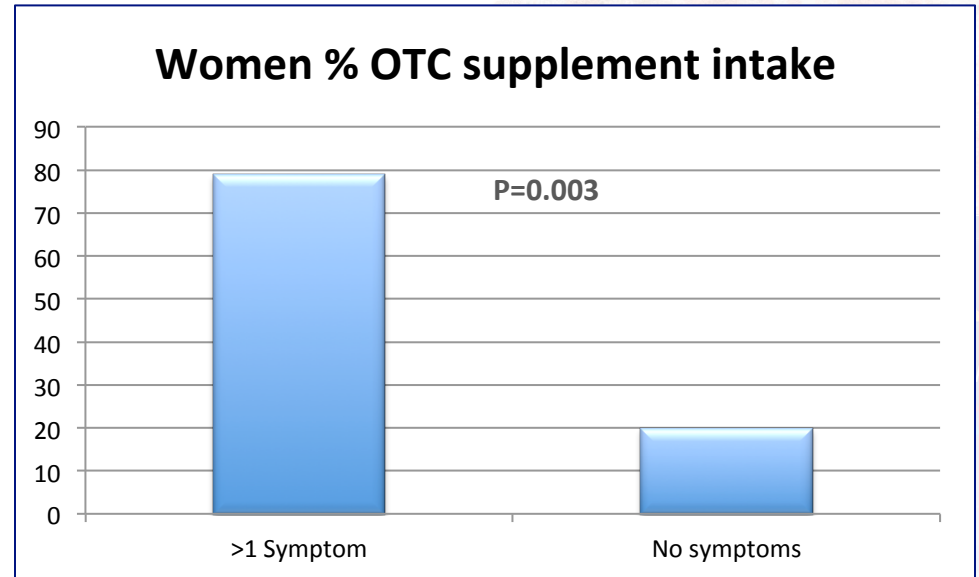
Phase II: genistein no psa effect, increased IFGF [Spentzos]

RCT (x2): lycopene – no effect on psa [Barber, Clark]

OTC supplementation - women

Women (breast cancer)

- Overall 189 of 350 (54%) took PTCS
- ≥ 1 symptoms 159 of 202 (79%)
- No symptoms 30 of 148 (20%)
Diff 59% (χ^2 $p=0.003$).



OTCS among women with symptoms

Evening primrose / Starflower oil
Glucosamine or/+ Chondroitin
Fish oils
Multivitamins
Pomi-T
St Johns wart
Grape seed
Other
Total

| % taking* | helpful |
|-----------|---------|
| 45% | 45% |
| 41% | 30% |
| 21% | 48% |
| 12% | 50% |
| 8% | 85% |
| 5% | 74% |
| 10% | 70% |
| 12% | 50% |
| 54% | 63% |

*at time of survey

Supplements for arthritis

Glucosamine – 13 RCT - Two Meta-analysis - Doubtful benefit

Chondroitin - 22 RCT - Two meta-analysis - Doubtful benefit

Fish oils - 17 RCT Rheumatoid arthritis benefits but not OA

Wandel et al meta-analysis. BMJ 2010; 341.

Towheed et al *Cochrane Database Sys Rev* 2005; 18(2):CD002946

Reichenbach et al *Anns of Int Med* 2007; 146(8):580

Cleland 2006, Fortin 1995

Polyphenol rich foods

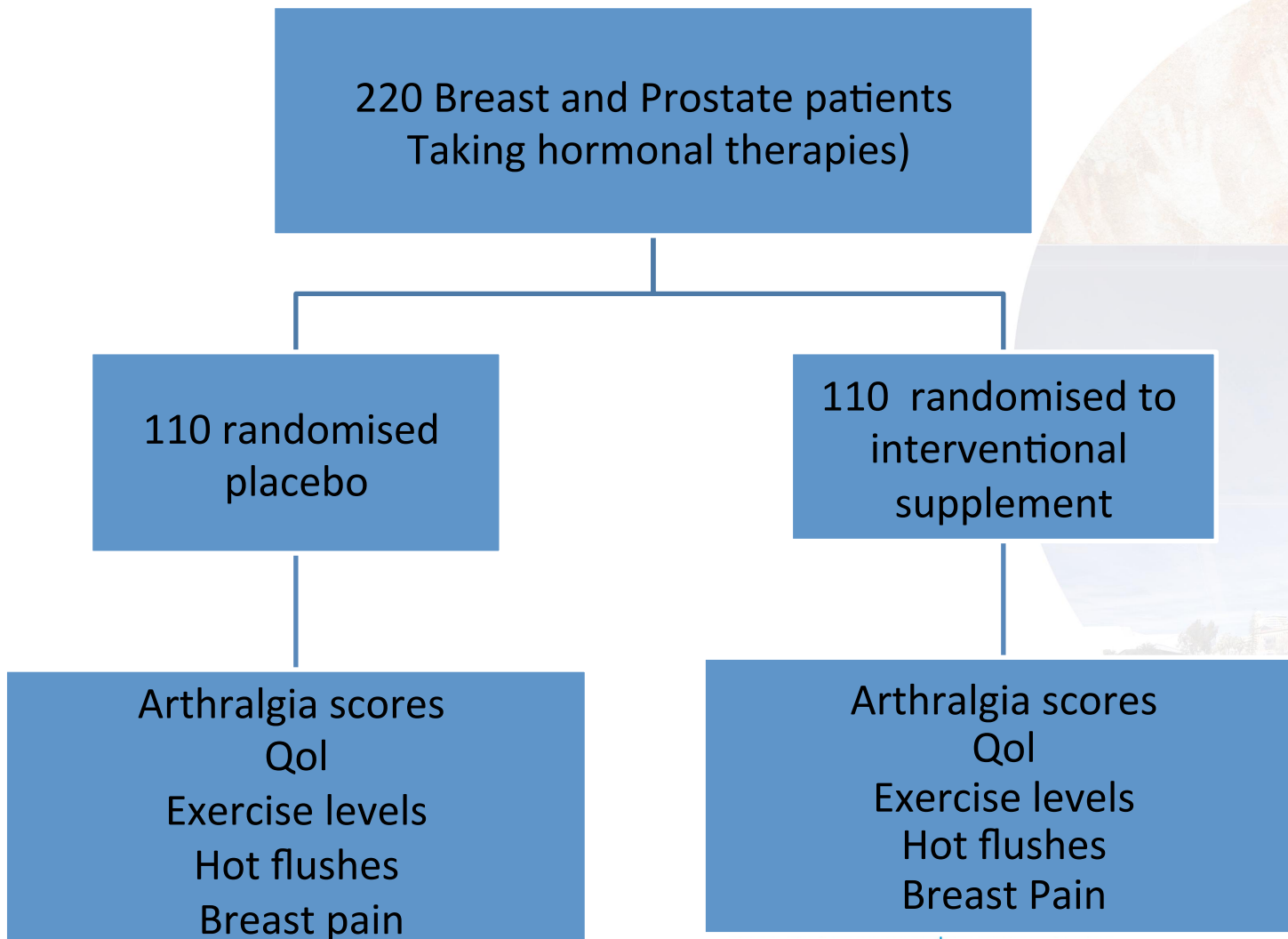
Populations who eat these foods have a lower incidence of arthritis and laboratory studies show they have cartilage protecting properties:

1. Anti-inflammatory properties, which reduce the discomfort and stiffness [Mitchel]
2. Anti-oxidant properties, which protect the joint from oxidative damage [Giovannucci, Stivala].
3. Anti-apoptotic effects on chondrocytes reducing cartilage degeneration [Shen].
4. Modulation metalloproteinases – remodels cartilage in arthritic joints [Dahlberg, Brinckerhoff].



A double blind RCT of phytochemical rich food for arthralgia post hormonal treatments

(EudraCT 2015-002018-66)



Conclusion

Asking a large real world group of patients to rank their most trouble symptoms reveals:

- Hormone therapies in men and women have a considerable burden of late effects
- Patients rank arthritis at considerable higher level than expected from previous RCT's
 - Counsel patients on the risks and benefits of adjuvant therapies
 - Improve accuracy and specificity of information tools
 - Educate physicians and patients – what to expect.
 - Preventative advice:
 - ✧ Weight control
 - ✧ Exercise and stretching
 - ✧ Polyphenol rich foods
- OTCS similar to previous studies but
 - In women >3 times more likely if troubled with symptoms - unmet needs?
 - In men common in AS – some of which appropriate
- Highlight the need for a National RCT evaluating whether polyphenol supplements and exercise will reduce arthritis incidence and improve wellbeing

Our ongoing research programme



CANCERNETUK