

How much of differences in cancer survival can be explained by variation in stage at diagnosis: An example from breast cancer and melanoma in the East of England

Mark J. Rutherford¹, Gary A. Abel², Sally R. Wilkes³,
Lucy Ironmonger⁴, Nick Ormiston-Smith⁴, David C. Greenberg^{2,5},
Paul C. Lambert^{1,6}, and Georgios Lyratzopoulos^{2,7}

¹Department of Health Sciences,
University of Leicester, UK.

²Cambridge Centre for Health Services Research,
University of Cambridge, UK.

³Centre of Evidence Based Dermatology,
University of Nottingham, UK.

⁴Statistical Information Team,
Cancer Research UK.

⁵National Cancer Registration Service,
Public Health England, Eastern Office, Cambridge

⁶Department of Medical Epidemiology and Biostatistics,
Karolinska Institutet, Sweden.

⁷Health Behaviour Research Centre,
University College London, UK.

mark.rutherford@le.ac.uk

NAEDI Conference. 27th March, 2015.

Motivation

Impact of
variation in
stage on
survival

Background

Methods

Melanoma

Breast -
Deprivation

Breast - Age

Conclusions

References

- It has been well established that stage at diagnosis varies across population groups (e.g. deprivation groups, age-groups, gender) for some cancer sites.
- It is also well known that survival heavily depends on stage at diagnosis.

Question:

What would happen to survival at a population level if we could remove these inequalities in stage at diagnosis?

This is a different question to how many lives would be saved if differences in relative survival across population groups could be completely removed.

Three studies

Impact of
variation in
stage on
survival

Background

Methods

Melanoma

Breast -
Deprivation

Breast - Age

Conclusions

References

- ① Melanoma - investigate the impact on survival of variation in stage at diagnosis for:
 - (a) Sex: Males vs Females.
 - (b) Deprivation quintiles: 5 groups based on postcodes (1 - least deprived, 5 - most deprived).
 - (c) Combined effect of sex and deprivation.
- ② Breast Cancer - investigate the impact of stage variation by deprivation groups across age (30-99).
- ③ Breast Cancer - investigate the impact of stage variation by age-groups for those aged 70+. Four age-groups (70-74, 75-79, 80-84, and 85+).

- Use data from the East of England with good stage completeness (during 2006-2010) for both melanoma and breast.
- Diagnoses over a 5-year calendar period; with follow-up on mortality until early 2012.
- We use region- and deprivation-specific lifetables provided by the Cancer Research UK Cancer Survival Group at LSHTM.
- We use a reweighting approach to approximate the relevant estimates for England as a whole - taking into account differences in age, sex and deprivation distributions between the East of England and the rest of England.

General Approach

Impact of
variation in
stage on
survival

Background

Methods

Melanoma

Breast -
Deprivation

Breast - Age

Conclusions

References

- 1 Calculate the stage distribution observed in each of the relevant groups.
- 2 Define an “improved” stage distribution by selecting the “best” group’s stage distribution.
- 3 Calculate the standardised survival under the two different stage distributions.
- 4 Report the difference as the number of deaths avoided within a given timeframe.

Note:

We model relative survival using a flexible parametric excess mortality model.

Necessary to convert to all-cause survival to report the number of avoidable deaths.

Methods Example - Sex Melanoma: Stage Distributions - Age 60-69, Least Deprived

Impact of
variation in
stage on
survival

Males

Stage at Diagnosis	Number (%)
Stage I	135 (64.6%)
Stage II	46 (22.0%)
Stage III/IV	28 (13.4%)
Total	209 (100%)

Females

Stage at Diagnosis	Number (%)
Stage I	104 (76.5%)
Stage II	18 (13.2%)
Stage III/IV	14 (10.3%)
Total	136 (100%)

- The stage distributions vary between males and females, with females having a higher proportion diagnosed at an earlier stage.

Methods Example - Sex Melanoma: Stage Specific Survival - Age 60-69, Least Deprived

Impact of
variation in
stage on
survival

Background

Methods

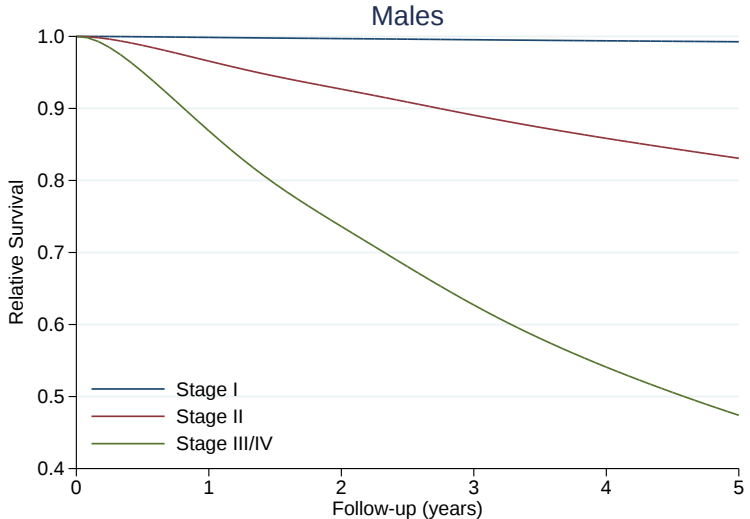
Melanoma

Breast -
Deprivation

Breast - Age

Conclusions

References



Methods Example - Sex Melanoma: Stage Specific Survival - Age 60-69, Least Deprived

Impact of
variation in
stage on
survival

Background

Methods

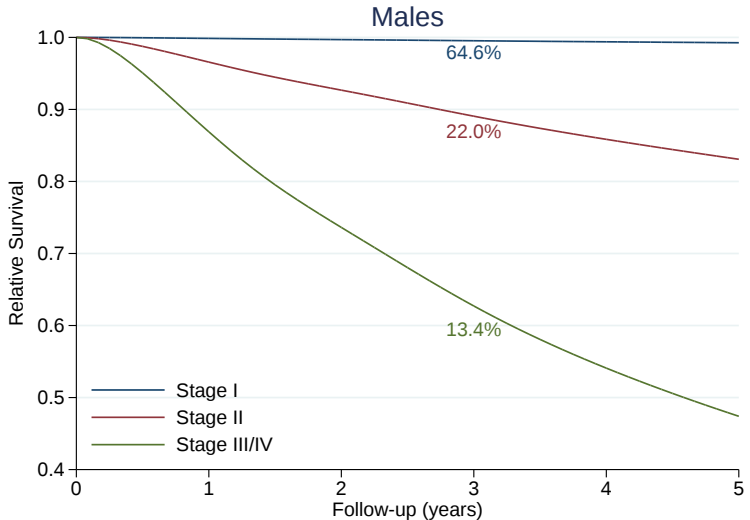
Melanoma

Breast -
Deprivation

Breast - Age

Conclusions

References



Methods Example - Sex Melanoma: Stage Specific Survival - Age 60-69, Least Deprived

Impact of
variation in
stage on
survival

Background

Methods

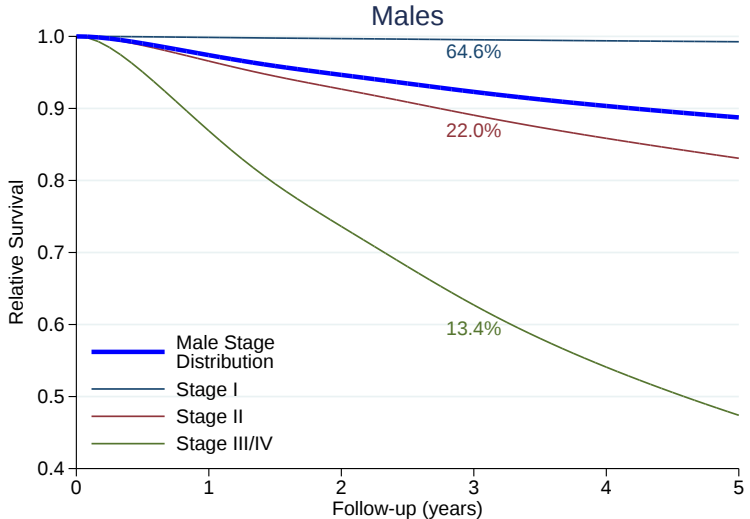
Melanoma

Breast -
Deprivation

Breast - Age

Conclusions

References



Methods Example - Sex Melanoma: Stage Specific Survival - Age 60-69, Least Deprived

Impact of
variation in
stage on
survival

Background

Methods

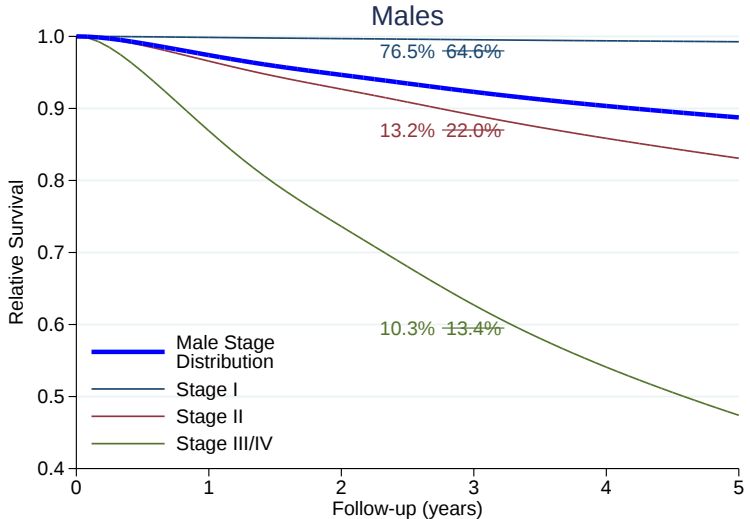
Melanoma

Breast -
Deprivation

Breast - Age

Conclusions

References



Methods Example - Sex Melanoma: Stage Specific Survival - Age 60-69, Least Deprived

Impact of
variation in
stage on
survival

Background

Methods

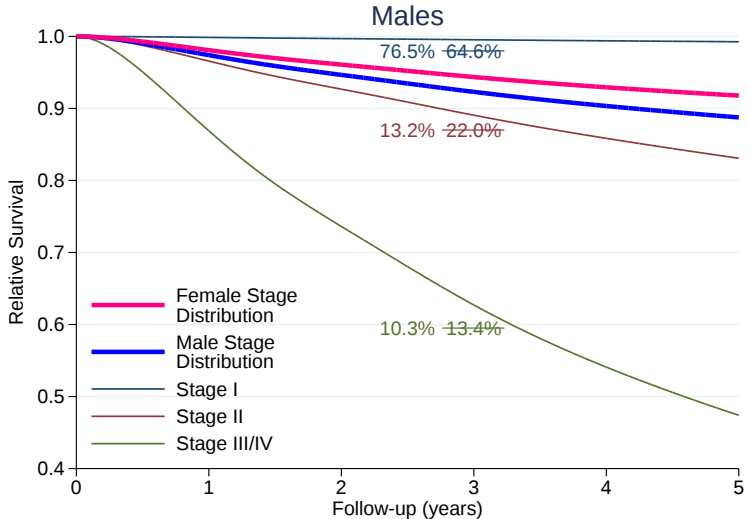
Melanoma

Breast -
Deprivation

Breast - Age

Conclusions

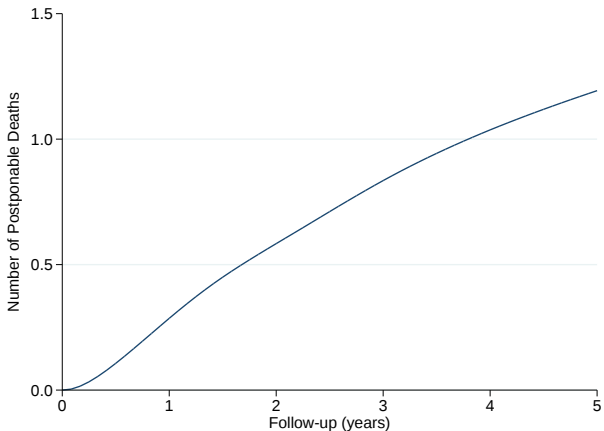
References



Avoidable Deaths - Age 60-69, Least Deprived. Males having female stage distribution

Impact of
variation in
stage on
survival

- Approximate annual incidence: $\frac{209}{5}$. (Number of males in this category and 5 years of incidence data.)
- **Accounting for expected survival.**



Background

Methods

Melanoma

Breast -
Deprivation

Breast - Age

Conclusions

References

Melanoma Study

Impact of
variation in
stage on
survival

Background

Methods

Melanoma

Breast -
Deprivation

Breast - Age

Conclusions

References

- ① Melanoma - investigate the impact on survival of variation in stage at diagnosis for:
 - (a) Sex: Males vs Females.
 - (b) Deprivation quintiles: 5 groups based on postcodes (1 - least deprived, 5 - most deprived).
 - (c) Combined effect of sex and deprivation.
- 5,122 individuals with Melanoma diagnosed in the East of England with complete stage information (2006-2010).
- Combined Stage III/IV into a single group because of small numbers and because both are metastatic (regional/distant).
- Large differences in stage distribution across both gender and deprivation.

Stage Distribution Example - Age 60-69

Impact of
variation in
stage on
survival

Background

Methods

Melanoma

Breast -
Deprivation

Breast - Age

Conclusions

References

Females - least deprived

Stage at Diagnosis	Number (%)
Stage I	104 (76.5%)
Stage II	18 (13.2%)
Stage III/IV	14 (10.3%)
Total	136 (100%)

Females - most deprived

Stage at Diagnosis	Number (%)
Stage I	15 (55.6%)
Stage II	8 (29.6%)
Stage III/IV	4 (14.8%)
Total	27 (100%)

Males - least deprived

Stage at Diagnosis	Number (%)
Stage I	135 (64.6%)
Stage II	46 (22.0%)
Stage III/IV	28 (13.4%)
Total	209 (100%)

Males - most deprived

Stage at Diagnosis	Number (%)
Stage I	13 (50.0%)
Stage II	8 (30.8%)
Stage III/IV	5 (19.2%)
Total	26 (100%)

Stage Distribution Example - Age 60-69

Stage Standardisation by Sex

Impact of
variation in
stage on
survival

Background

Methods

Melanoma

Breast -
Deprivation

Breast - Age

Conclusions

References

Females - least deprived

Stage at Diagnosis	Number (%)
Stage I	104 (76.5%)
Stage II	18 (13.2%)
Stage III/IV	14 (10.3%)
Total	136 (100%)

Females - most deprived

Stage at Diagnosis	Number (%)
Stage I	15 (55.6%)
Stage II	8 (29.6%)
Stage III/IV	4 (14.8%)
Total	27 (100%)

Males - least deprived

Stage at Diagnosis	Number (%)
Stage I	135 (64.6%)
Stage II	46 (22.0%)
Stage III/IV	28 (13.4%)
Total	209 (100%)

Males - most deprived

Stage at Diagnosis	Number (%)
Stage I	13 (50.0%)
Stage II	8 (30.8%)
Stage III/IV	5 (19.2%)
Total	26 (100%)

Stage Distribution Example - Age 60-69

Stage Standardisation by Deprivation

Impact of
variation in
stage on
survival

Background

Methods

Melanoma

Breast -
Deprivation

Breast - Age

Conclusions

References

Females - least deprived

Stage at Diagnosis	Number (%)
Stage I	104 (76.5%)
Stage II	18 (13.2%)
Stage III/IV	14 (10.3%)
Total	136 (100%)

Males - least deprived

Stage at Diagnosis	Number (%)
Stage I	135 (64.6%)
Stage II	46 (22.0%)
Stage III/IV	28 (13.4%)
Total	209 (100%)

Females - most deprived

Stage at Diagnosis	Number (%)
Stage I	15 (55.6%)
Stage II	8 (29.6%)
Stage III/IV	4 (14.8%)
Total	27 (100%)

Males - most deprived

Stage at Diagnosis	Number (%)
Stage I	13 (50.0%)
Stage II	8 (30.8%)
Stage III/IV	5 (19.2%)
Total	26 (100%)

Stage Distribution Example - Age 60-69

Stage Standardisation by Sex & Deprivation

Impact of
variation in
stage on
survival

Background

Methods

Melanoma

Breast -
Deprivation

Breast - Age

Conclusions

References

Females - least deprived

Stage at Diagnosis	Number (%)
Stage I	104 (76.5%)
Stage II	18 (13.2%)
Stage III/IV	14 (10.3%)
Total	136 (100%)

Males - least deprived

Stage at Diagnosis	Number (%)
Stage I	135 (64.6%)
Stage II	46 (22.0%)
Stage III/IV	28 (13.4%)
Total	209 (100%)

Females - most deprived

Stage at Diagnosis	Number (%)
Stage I	15 (55.6%)
Stage II	8 (29.6%)
Stage III/IV	4 (14.8%)
Total	27 (100%)

Males - most deprived

Stage at Diagnosis	Number (%)
Stage I	13 (50.0%)
Stage II	8 (30.8%)
Stage III/IV	5 (19.2%)
Total	26 (100%)

Results Melanoma - East of England (stacked)

Impact of
variation in
stage on
survival

Background

Methods

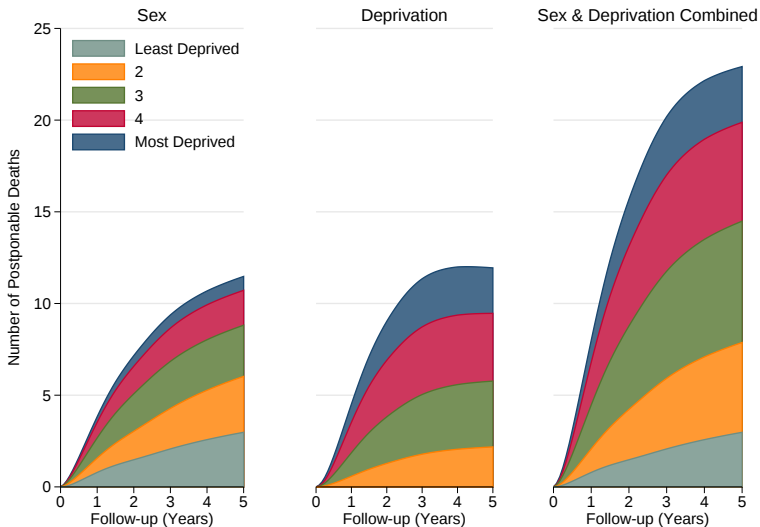
Melanoma

Breast -
Deprivation

Breast - Age

Conclusions

References



Results Melanoma - England (stacked)

Impact of
variation in
stage on
survival

Background

Methods

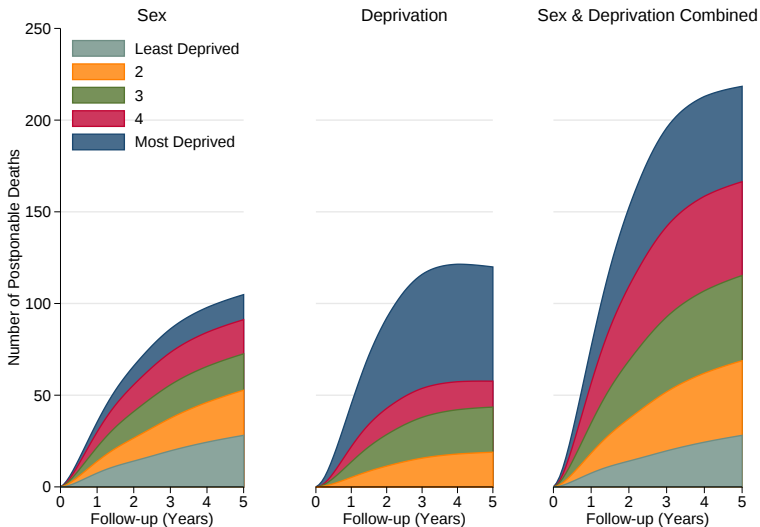
Melanoma

Breast -
Deprivation

Breast - Age

Conclusions

References



Breast Deprivation Study

Impact of
variation in
stage on
survival

Background

Methods

Melanoma

Breast -
Deprivation

Breast - Age

Conclusions

References

- ② Breast Cancer - investigate the impact of stage variation by deprivation groups across age (30-99).
 - 20,738 women with breast cancer diagnosed in the East of England with complete stage information (2006-2010).
 - Notable differences in the stage distributions across the 5 deprivation groups.
 - Women from more deprived areas more likely to be diagnosed with advanced stage disease.
 - Relative survival also varies hugely across stage at diagnosis; those diagnosed at Stage I have very little excess mortality.

Breast Stage Distributions Example: Age 60-64

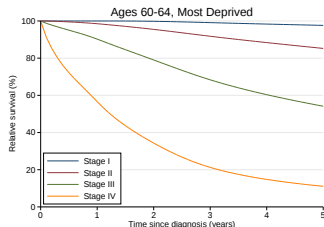
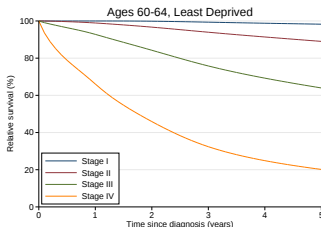
Impact of
variation in
stage on
survival

Least deprived

Stage at Diagnosis	Number (%)
Stage I	443 (54.6%)
Stage II	294 (36.3%)
Stage III	52 (6.4%)
Stage IV	22 (2.7%)
Total	811 (100%)

Most deprived

Stage at Diagnosis	Number (%)
Stage I	65 (45.5%)
Stage II	58 (40.6%)
Stage III	13 (9.1%)
Stage IV	7 (4.9%)
Total	143 (100%)



Breast Stage Distributions Example: Age 60-64

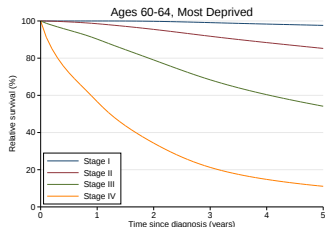
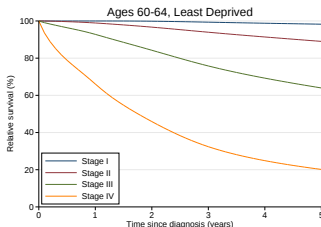
Impact of
variation in
stage on
survival

Least deprived

Stage at Diagnosis	Number (%)
Stage I	443 (54.6%)
Stage II	294 (36.3%)
Stage III	52 (6.4%)
Stage IV	22 (2.7%)
Total	811 (100%)

Most deprived

Stage at Diagnosis	Number (%)
Stage I	65 (45.5%)
Stage II	58 (40.6%)
Stage III	13 (9.1%)
Stage IV	7 (4.9%)
Total	143 (100%)



Results Deprivation Inequalities Breast - England (stacked)

Impact of
variation in
stage on
survival

Background

Methods

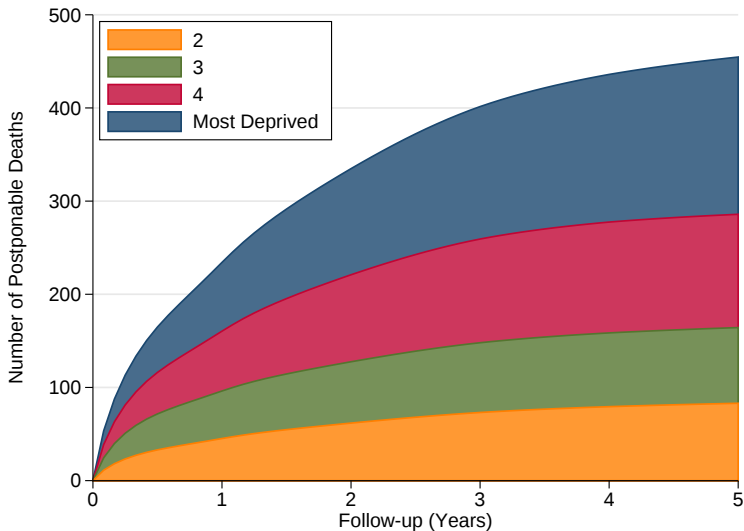
Melanoma

Breast -
Deprivation

Breast - Age

Conclusions

References



Breast Older Age Study

Impact of
variation in
stage on
survival

Background

Methods

Melanoma

Breast -
Deprivation

Breast - Age

Conclusions

References

- ③ Breast Cancer - investigate the impact of stage variation by age-groups for those aged 70+. Four age-groups (70-74, 75-79, 80-84, and 85+).
- 6,478 women aged 70+ with breast cancer diagnosed in the East of England with complete stage information (2006-2010).
- Use 4 age-groups to investigate stage variation in older women.
- We used 70-74 as the group with the stage distribution to match to - younger groups would have influence of screening on stage distribution.

Results Older Age Inequalities Breast - England (stacked)

Impact of
variation in
stage on
survival

Background

Methods

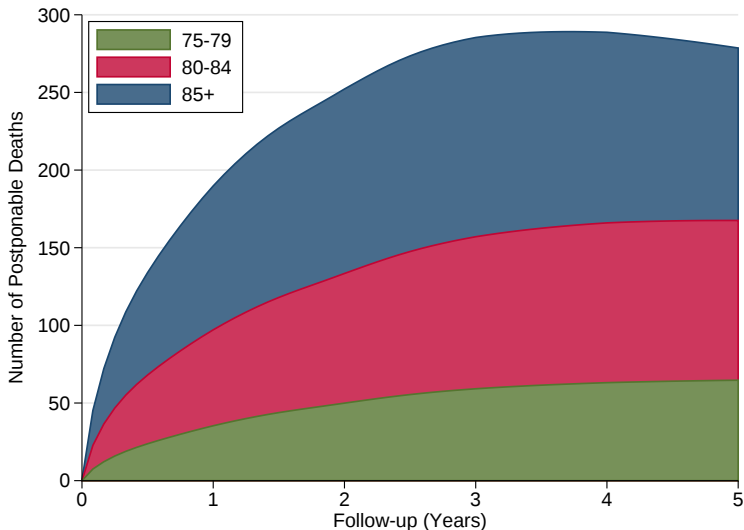
Melanoma

Breast -
Deprivation

Breast - Age

Conclusions

References



Concluding remarks

Impact of
variation in
stage on
survival

Background

Methods

Melanoma

Breast -
Deprivation

Breast - Age

Conclusions

References

- Inequalities in stage at diagnosis across sex and deprivation for melanoma, and deprivation and age for breast cancer, partially explain differences in cancer patient survival.
- Interventions designed to target early diagnosis for certain population groups are likely to reap substantial benefit in terms of extending patients' lives.
- Clearly, further improvements in survival could be achieved by diagnosing cancer earlier across the board - here we consider the impact of removing inequalities to match the "best" population group.
- Increasing national completeness for information on stage at diagnosis will mean that this analysis will soon be able to be conducted at a national level.

Selected References

Impact of
variation in
stage on
survival



G. Lyratzopoulos, G.A. Abel, C. Brown *et al.* Socio-demographic inequalities in stage of cancer diagnosis: evidence from patients with female breast, lung, colon, rectal, prostate, renal, bladder, melanoma, ovarian and endometrial cancer. *Ann Oncol*, 24:843-850, 2013.



P. Royston. and P.C. Lambert. Flexible Parametric Survival Analysis Using Stata: Beyond the Cox Model. *StataCorp LP*, 2011.



M.J. Rutherford, S.R. Hinchliffe, G.A. Abel *et al.* How much of the deprivation gap in cancer survival can be explained by variation in stage at diagnosis: An example from breast cancer in the East of England. *Int J Cancer*, 133 (9) :2192-2200, 2013.



M.J. Rutherford, L. Ironmonger, N. Ormiston-Smith *et al.* Estimating the potential survival gains by eliminating socioeconomic and sex inequalities in stage at diagnosis of melanoma. *BJC NAEDI Supplement*, 2015.



M.J. Rutherford, G.A. Abel, D.C. Greenberg *et al.* The impact of eliminating age inequalities in stage at diagnosis on breast cancer survival for older women. *BJC NAEDI Supplement*, 2015.

Background

Methods

Melanoma

Breast -
Deprivation

Breast - Age

Conclusions

References