

Appendix: Harmonization of Prostate Cancer Stage and Grade Outcome Data in the “Pooling Project of Diet and Cancer”

I. Classifying prostate cancer cases by stage

The following tumor classification methods were used:

- Tumor Nodes Metastases Staging System (TNM) (American Joint Committee on Cancer 1997);
- AJCC Stage Grouping (American Joint Committee on Cancer 1997);
- SEER Summary Stage (see: <http://seer.cancer.gov/tools/codingmanuals/>);
- SEER Extent of Disease (for definitions of codes, please see: <http://seer.cancer.gov/tools/codingmanuals/historical.html>).

Our definitions for advanced prostate cancer were created considering the different methods used to code stage information in each cohort and to be able to allow all cohorts to be included in the analyses. Some studies have collected stage data using multiple methods. In our definitions of advanced stage, if stage was coded using more than one method, we classified the case according to the most advanced stage variable for that case.

Three definitions for “advanced” prostate cancer were used in this study:

1. **“Periprostatic advanced”** (equivalent to T3, T4, N1, M1 or fatal - **not an outcome in our analysis**, only used to define localized cases). Periprostatic advanced prostate cancer (extension to periprostatic tissue or higher – cases meet at least one of the following criteria:
 - a) Death due to prostate cancer as an underlying cause of death (ICD-9 185, ICD-10 C61 or study-specific variable indicating death from prostate cancer as underlying cause);
 - b) AJCC stage III or IV;
 - c) TNM staging (equivalent to T3N0M0 or higher) defined as one of the following combinations:
 - i. T3, N0 or NX, M0 or MX
 - ii. T4, N0 or NX, M0 or MX
 - iii. Any T*, N1 or N2 or N3 (N2, N3 are codes from older manuals), M0 or MX
 - iv. Any T, any N*, M1 or (M1a or M1b or M1c);
 - d) SEER extent of disease defined as one of the following:
 - i. Clinical/pathological extension: equivalent to “periprostatic extension” or higher (codes ≥ 41 but < 90)
 - ii. Lymphnode extension equivalent to N1 or higher (codes ≥ 1 but < 9);
 - e) SEER summary stage defined by one of the following:
 - i. regional by direct extension only
 - ii. regional by lymphnodes only
 - iii. regional by both direct extension and regional lymphnode(s)
 - iv. regional NOS
 - v. distant disease/distant site(s)/lymphnode(s) involved.
2. **“Advanced”** (equivalent to T4, N1, M1 or fatal – an outcome in our analyses). Advanced prostate cancer cases meet at least one of the following criteria:
 - a) Death due to prostate cancer as underlying cause of death (ICD-9 185, ICD-10 C61 or study specific variable indicating death from prostate cancer as underlying cause);
 - b) AJCC stage IV;
 - c) TNM staging (equivalent to T4N0M0 (i.e. “tumor is fixed or invades adjacent structures other than seminal vesicles: bladder neck, external sphincter, rectum, levator muscles

and/or pelvic wall” (American Joint Committee on Cancer 1997)) or higher defined as one of the following combinations:

- i. T4, N0 or NX, M0 or MX
- ii. Any T, N1 or N2 or N3 (N2, N3 are codes from older manuals), M0 or MX
- iii. Any T, any N, M1 or M1a or M1b or M1c;
- d) SEER extent of disease defined as one of the following:
 - i. Clinical/pathological extension: equivalent to “extension to fixation to adjacent structures other than seminal vesicles” or higher (codes ≥ 50 but < 90)
 - ii. Lymphnode extension: equivalent to N1 or higher (codes ≥ 1 but < 9);
- e) SEER summary stage defined by one of the following:
 - i. regional by lymphnodes only
 - ii. regional by both direct extension and regional lymphnode(s)
 - iii. distant disease/distant site(s)/lymphnode(s) involved.

Please note: For this definition of more advanced cases we excluded cases coded as “regional by direct extension only” and “regional NOS” because in the SEER summary stage manual, the category “regional by direct extension only” does not distinguish between T3N0M0 and T4N0M0.

3. “Advanced restricted” (equivalent to T4, N1, M1 or fatal, but excludes all localized cases as well as cases with missing stage at diagnosis who died during follow-up – an outcome in our analysis). Advanced restricted prostate cancer (advanced_restricted) is defined in the same way as advanced prostate cancer, except that it excludes fatal cases initially diagnosed as “localized” and fatal cases with missing stage at diagnosis.

II. Non-advanced (localized prostate cancers)

Localized (non-advanced) prostate cancer were defined as all cases that have information on stage and are **not defined as advanced using the 1st advanced outcome definition (regional/periprostic extension or higher).**

III. Classifying prostate cancer cases by grade

The following methods were used to code grade:

1. Gleason summary score;
2. Histological grade (for examples, please see <http://seer.cancer.gov/manuals/codeman.pdf>, p. 102; http://seer.cancer.gov/manuals/2004Revision%201/SPM_2004_maindoc.r1.pdf, p. 95-96).

Some cohorts collected information on both histological grade and Gleason score. If grade was coded using more than one method cases were classified according to the highest grade variable for that case.

1. High grade cases were defined as:
 - a) Gleason summary score ≥ 8 OR;
 - b) “Poorly differentiated or undifferentiated.”
2. Low grade cases were defined as:
 - a) Gleason summary score < 8 OR;
 - b) “Well or moderately differentiated.”

Reference

(American Joint Committee on Cancer (1997). AJCC Cancer Staging Manual. Philadelphia, PA, Lippincott-Raven Publishers)