Respond Aim 1 Aggressive PCa Outcome definitions

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| **Outcome** | **Registries** | **Years of diagnosis** | **Variables** | **Comments** |
| **Advanced stage (not confined to the prostate)** | CA, GA, LA, MI, NJ, TX | 2000 | seerSummaryStage1977 | Only outcome can assess for all registries and all years |
| 2001-2003 | seerSummaryStage2000 |
| 2004-2013 | derivedSs2000 |
|  | | | | |
| **High grade (Gleason 8-10)** | CA, GA, LA, MI, NJ, TX | 2000-2002 | Grade | Use path > bx hierarchy. Need to check SSF 10 and 8 even in earlier years because may be populated instead of SSF 6 depending on when case abstracted |
| CA, GA, LA, MI, NJ | 2004-2013 | Cssitespecificfactor6  csSiteSpecificfactor10  csSitespecificFactor8 |
| TX | 2011-2013 | csSiteSpecificfactor10  csSitespecificFactor8 |
|  | | | | |
| **Combined risk grouping (M1,N1,T3/T4, Gleason 8-10, or PSA >20 ng/ml)** | CA, GA, LA, MI, NJ | 2004-2009 | Derivedajcc6T  derivedAjcc6N  derivedAjcc6M  Cssitespecificfactor6  csSiteSpecificfactor10  csSitespecificFactor8  csSitespecificFactor1 | Using path>bx hierarchy for all variables because of registry data collection limitations. Therefore can use derived AJCC items  PSA completeness for TX < other registries |
| 2010-2013 | Derivedajcc7T  derivedAjcc7N  derivedAjcc7M  csSiteSpecificfactor10  csSitespecificFactor8  csSitespecificFactor1 |
| TX | 2011-2013 | Derivedajcc7T  derivedAjcc7N  derivedAjcc7M  csSiteSpecificfactor10  csSitespecificFactor8  csSitespecificFactor1 |
|  | | | | |
| **Combined risk grouping, not considering PSA**  **(M1,N1,T3/T4, or Gleason 8-10)** | CA, GA, LA, MI, NJ | 2004-2009 | Derivedajcc6T  derivedAjcc6N  derivedAjcc6M  Cssitespecificfactor6  csSiteSpecificfactor10  csSitespecificFactor8 | Using path>bx hierarchy for all variables because of registry data collection limitations. Therefore can use derived AJCC items |
| 2010-2013 | Derivedajcc7T  derivedAjcc7N  derivedAjcc7M  csSiteSpecificfactor10  csSitespecificFactor8 |
| TX | 2011-2013 | Derivedajcc7T  derivedAjcc7N  derivedAjcc7M  csSiteSpecificfactor10  csSitespecificFactor8 |

**Notes:**

Advanced stage

* TX did not collect EOD extension and lymph node involvement 2000-2003
* When comparing the SEER summary stage- based definition to a definition based on tumor extension (path>clinical), lymph node involvement, and metastasis, overall agreement for advanced stage high 98%. 99% of advanced stage identified by extension was also identified by summary stage. 89% of advanced stage identified by summary stage was also identified by extension.
  + Disagreement is disproportionately coming from years 2000-2003.
* When compared to using lymph node involvement, metastases, and clinical extension, agreement is lower at 92%. While 98% of advanced stage identified by clinical extension was also identified by summary stage only 50% of advanced summary stage was identified using clinical extension.

High grade

* Requires use of grade and site-specific factors
* Grade definition not consistent throughout entire time span
* Completeness of grade variable is higher than completeness of site specific factors necessary for Gleason score determination. Larger proportion of population would be included in years 2000-2002 compared to 2004-2013
* Excluding 2003 altogether because of misclassification.
  + In 2003 intermediate and high grade are collapsed. Proportion of intermediate disease which will by definition be included in the “high grade” outcome if using grade variable 2003+ is much larger than proportion of high grade disease. For years where both Gleason 8-10 and Grade 3/4 can be compared, % of grade 3/4 much higher than %Gleason 8-10
    - Using grade 3/4 ~45-59% would be classified as “high”
    - Using Gleason score 8-10 ~14-18% are classified as “high”
* Excluding Texas from 2003- 2010 for same reason
  + Texas did not collect site-specific factors from 2004-2010 and would require using grade variable with high misclassification
* Discrepancy in source of grade between grade variable and combined SSF variables. Highest in any specimen (grade) vs largest specimen (SSF hierarchy)

Combined outcomes

* Limit to 2004-2013 because of availability of PSA and Gleason score
* TX did not collect SSF 2004-2010 and is therefore excluded from those years. TX only contributes 3 years of data to this outcome
* Using path > clinical hierarchy. For years 2004-2009 cannot distinguish path and bx Gleason.
* For simplicity using derived AJCC rather than the CS path extension, CS clinical extension, lymph node, and mets at dx fields. Results should be the same with the path>clinical hierarchy as long as histology is in AJCC inclusion list
* Note that NCCN groups use clinical T stage.
* Because TX had much higher % of unknown PSA, doing version of outcome that does not consider PSA value

Other considerations

* Using the path takes precedence over clinical hierarchy because majority of data we have was collected that way
* Creates bias because path data available only for men who had prostatectomy
  + Sensitivity analyses using clinical stage