Application Checklist (for your use only)

To be sent by email attachment to the SEER-Medicare contact:

X☐ Application:

X☐ Your description of the project **must** include:

- statement of main hypothesis / specific research question
- description of study subjects and cancer sites/phases to be included in the analysis
- brief explanation of how key components of the study will be obtained/identified within the PEDSF and/or claims data– specifically:
  - cohort selection criteria
  - covariates
  - outcomes
- a list of requested files and how each will be used, (for example: MEDPAR will be used …. NCH will be used….).
- how the 5% population (non-cancer and/or cancer) will be used, if requested
- description of the planned analyses (e.g. logistic regression will be used to assess….)
- description of the personnel involved
- timeline for completion
- references can be included, if relevant.

X☐ You **must** include an explanation of data storage and protection. Please **be specific** as to the location of all files and media and all protections that will be in place.

X☐ Completed and signed Data Use Agreement (DUA)

X☐ Documentation of IRB approval

X☐ Completed and signed Request form for restricted variables (if applicable)

☐ Letter from funder (if applicable)

Please send any questions to the SEER-Medicare contact at yaniskoe@imsweb.com

APPLICATION FOR SEER-MEDICARE DATA
(Please complete all information in this form)

I. Contact information

Project Title: Incorporating real-world economic and epidemiologic inputs into prospective economic evaluations of cancer-related health technologies

Principal Investigator: (*students or fellows may NOT be listed as the PI)*

Name:	ANIRBAN BASU
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Alternate contact: Student / fellow contact / assistant / Co-PI: (indicate type)

Name:	
Institution:	
Address:	
City, State Zip	
Email:	
Phone:	

II. Project Description:

A. Title **Incorporating real-world economic and epidemiologic inputs into prospective economic evaluations of cancer-related health technologies**

B. Brief overview of your project (one or two sentences) This project aims to use SEER-Medicare linked data to inform the costs, effectiveness, adherence and diffusion parameters for cost-effectiveness models intended to evaluate cancer technologies.

C. Cancer sites being requested (e.g.Lung): Breast, prostate, lung, colorectal, leukemia, Melanoma, Non-Hodgkin Lymphoma, CML, Endometrial, bladder, kidney and liver

D. Description of the Project (between 1-5 pages).

The CHOICE Institute at the University of Washington collaborates with the Institute of Clinical and Economic Review (ICER) to generate cost-effectiveness and budget impact models for healthcare technologies that ICER identifies as high-value targets based on a diverse stakeholder inputs. Results from these models are beginning to influence health care policy in the United States, in terms of drug pricing and value-based purchasing and also facilitating discussions around value for multiple stakeholders. Most of these evaluations that we have done in the past correspond to cancer treatments. We envision that we will continue to do a lot more in this space. One of the challenges that we face is obtaining precise inputs for the parameter for these model and, especially, the lack of real-world data to inform these inputs. This project aims to use SEER-Medicare linked data to inform the costs, effectiveness, adherence and diffusion parameters for these models intended to evaluate cancer technologies. Over the next five years, our goal is to estimate these parameters across multiple sites of cancer by exploiting variations in the use of innovations and access across multiple sites and use them in future modeling projects. Because the specific cancer site for which we will be asked to develop a model in the future is currently unknown, we plan to use SEER-Medicare data on a large range of cancer sites that include breast, prostate, lung, colorectal, leukemia, Melanoma, Non-Hodgkin Lymphoma, CML, Endometrial, bladder, kidney and liver. All analyses relating to the use of these data and for our project will present group-level results.

Aim1: To estimate total and sector-specific (e.g. hospital) health care costs by cancer sites and age (in comparison to general non-cancer population), cancer treatment phases, drug combinations used and over the remaining lifetime of the elderly patients.
Aim2: To estimate the incidence of adverse events related to specific drugs and other interventions such as surgery and radiation therapies.
Aim3: To estimate different adherence measures to cancer drugs and biologics.
Aim4: To estimate diffusion of cancer technologies over time since their introduction.
Aim5: To estimate changes in mortality among cancer patients over time and associate them with changes to the standard of care.

For Aim 1, we will run econometric methods that deal with censoring and account for the idiosyncratic distributions of costs to estimate attributable costs.

For Aim 2, we will use logistic regression and count data model, with generalized estimating equations to account for clustering, to estimate the incidence of any and number of adverse events related to specific technology use. We will also explore advanced econometric methods that will exploit geographic and physician level variations in technology-use to generate causal effects

For Aim 3, we will describe rates of alternative adherence measures under various treatments.

For Aim 4, we will estimate parameters of the Bass model of diffusion of technology as a function of target population and technology characteristics.

For Aim 5, we will use advanced survival techniques to estimate mortality effects of various interventions and also over time for various target populations.

The study cohort will include all patients ages 66 and above diagnosed with breast, prostate, lung, colorectal, leukemia, Melanoma, Non-Hodgkin Lymphoma, CML, Endometrial, bladder, kidney or liver cancer. We request all data relating to these sites so that we can focus on specific population within these sites as needed by a future prospective economic evaluation studies identified by ICER.

Measures:

PATIENT BASELINE CHARACTERISTICS	**SOURCE**
Incident xxxx cancer	PEDSF
Socio-demographics: age, race/ethnicity	PEDSF
Health status and comorbid conditions	MEDPAR, Outpatient and NCH files for year prior to incident cancer
Medicare entitlement and HMO indicators	PEDSF
PATIENT SOCIOECONOMIC STATUS	
Individual level poverty indicator based on dual enrollee status; enrollment in state buy-in low income subsidy programs	PEDSF
Per capita income and Proportion educational attainment in neighborhood;	SEER-provided variables at Census tract level (PEDSF) supplemented by Census tract data
EXTENT OF DISEASE	
Tumor size and grade; lymph node status, HR status, distant disease status, site of primary tumor, AJCC stage	PEDSF
INITIAL TREATMENT	
Cytotoxic chemotherapy	Outpatient, NCH
Radiation therapy	MEDPAR, Outpatient, NCH, PEDSF
Surgery	MEDPAR, Outpatient, NCH
ADVERSE EVENTS	
Hospitalization for surgical complications (bleeding, wound infections, pneumonia, MI)	MEDPAR
Hospitalization for chemotherapy complications (neutropenia, infection, anemia)	MEDPAR PEDSF PEDSF
Second primary cancer	
Death from cancer	

Utilizations and Costs	MEDPAR, NCH, Outpatient claims, HHA, Hospice, DME, and Part D

Personnel

Study personnel will include faculty at The CHOICE Institute at the University of Washington, Seattle, who are involved in the ICER project. They include Anirban Basu, Josh Carlson, Dave Veenstra, Aasthaa Bansal, Beth Devine, Ryan Hansen, Douglas Barthold, Davene Wright, Zach Marcum, and Shelley Gray. Responsibilities for these personnel are details below:

Anirban Basu is the Principal Investigator on this project. He will supervise all analysis pertaining to SEER-Medicare data.

Josh Carlson, Dave Veenstra, Aasthaa Bansal, Beth Devine, Ryan Hansen, Douglas Barthold, Davene Wright, Zach Marcum, and Shelley Gray are faculty at the CHOICE Institute who take turns to lead ICER economic evaluation projects. Each will work with Prof. Basu to discuss the needs for their project, whether those questions can be answered using the SEER-Medicare data and then carry out the necessary analysis with the data to inform their models. Prof. Basu will be involved in every step on the analysis.

Timeline

- Oct 2018 – Sep 2023: Multiple cycles of data-cleaning and preparation, analysis and using these results as inputs to ICER economic evaluation models and publications.

E. Data Storage and Protection:

The CD-ROMS containing the SEER-Medicare data files will be stored in locked cabinets in Dr. Basu's office. The data files will be loaded and stored in an encrypted and password protected Windows Server in the CHOICE Institute at the University of Washington. Users can only access these datasets on the server. Sharing of data files will be restricted to members of this research group. The departmental network is isolated on its own router and authorized logins are restricted to a single "gateway" machine that holds no sensitive data. Remote access via secured VPN capabilities provide protected access to data servers. Network-intensive services such as mail and Web service are on separate nodes that hold no project data. Data tapes and servers are located in a locked room accessible by a secured keypad only to computing personnel.

No attempt will be made to identify individual patients or providers. We will abide by the no reported cell size less than 11 rule.

F. Funding Source: The current project is being funded by resources from within the School of Pharmacy at the University of Washington.

G. Restricted Variables:

We are requesting permission for access to patient's census tract and ZIP code, physician ZIP code, and hospital ZIP code in order to carry out some of the advanced econometric methods proposed.

Specifically, the primary purpose of using zip codes and NPIs will be to construct instrumental variables in order to address unobserved confounding or confounding by indication when comparing different modalities of treatment in the real-world setting. For example, physician-specific preferences based on past levels of use of a certain treatment or drug can often be used to induce pseudo-randomized allocation of treatments to current patients. Similarly, in some cases geographic variations and distances measures are used as instrumental variables, both of which require zipcode data. In other cases, geographic identifiers are used as controls in the analyses. Several application of these methods using SEER-Medicare data have been published, including some by this group. No attempt will be made to identify individual patients or providers.

Here is a list of publications that have applied these methods to SEER-Medicare data:

1. Macleod LC, Odisho AY, Tykodi SS, Holt SK, Harper JD, Gore JL. Comparative Effectiveness of Initial Surgery vs Initial Systemic Therapy for Metastatic Kidney Cancer in the Targeted Therapy Era: Analysis of a Population-based Cohort. *Urology* 2018 Mar;113:146-152.

2. Mehta HB, Vargas GM, Adhikari D, Dimou F, Riall TS. Comparative effectiveness of chemotherapy vs resection of the primary tumour as the initial treatment in older patients with Stage IV colorectal cancer. *Colorectal Dis* 2017 Jun;19(6):O210-O218.

3. Pollom EL, Wang G, Harris JP, Koong AC, Bendavid E, Bhattacharya J, Chang DT. The Impact of Intensity Modulated Radiation Therapy on Hospitalization Outcomes in the SEER-Medicare Population With Anal Squamous Cell Carcinoma. *Int J Radiat Oncol Biol Phys* 2017 May 01;98(1):177-185.

4. Lu-Yao GL, Kim S, Moore DF, Shih W, Lin Y, DiPaola RS, Shen S, Zietman A, Yao SL. Primary radiotherapy vs conservative management for localized prostate cancer--a population-based study. *Prostate Cancer Prostatic Dis* 2015 Dec;18(4):317-24.

5. Mack CD, Brookhart MA, Glynn RJ, Meyer AM, Carpenter WR, Sandler RS, Stürmer T. Comparative Effectiveness of Oxaliplatin Versus 5-flourouricil in Older Adults: An Instrumental Variable Analysis. *Epidemiology* 2015 Sep;26(5):690-9.

6. Winn AN, Shah GL, Cohen JT, Lin PJ, Parsons SK. The real world effectiveness of hematopoietic transplant among elderly individuals with multiple myeloma. *J Natl Cancer Inst* 2015 Aug;107(8).

7. Wan F, Small D, Bekelman JE, Mitra N. Bias in estimating the causal hazard ratio when using two-stage instrumental variable methods. *Stat Med* 2015 Jun 30;34(14):2235-65.

8. Deepak JA, Ng X, Feliciano J, Mao L, Davidoff AJ. Pulmonologist involvement, stage-specific treatment, and survival in adults with non-small cell lung cancer and chronic obstructive pulmonary disease. *Ann Am Thorac Soc* 2015 May;12(5):742-51.

9. Bekelman JE, Mitra N, Handorf EA, Uzzo RG, Hahn SA, Polsky D, Armstrong K. Effectiveness of androgen-deprivation therapy and radiotherapy for older men with locally advanced prostate cancer. *J Clin Oncol* 2015 Mar 01;33(7):716-22.

10. Li J, Fine J, Brookhart A. Instrumental variable additive hazards models. *Biometrics* 2015 Mar;71(1):122-130.

11. Basu A, Gore JL. Are Elderly Patients With Clinically Localized Prostate Cancer Overtreated? Exploring Heterogeneity in Survival Effects. *Med Care* 2015 Jan;53(1):79-86.

12. Lu-Yao GL, Albertsen PC, Moore DF, Shih W, Lin Y, DiPaola RS, Yao SL. Fifteen-year survival outcomes following primary androgen-deprivation therapy for localized prostate cancer. *JAMA Intern Med* 2014 Sep;174(9):1460-7.

13. Basu A. Estimating person-centered treatment (PeT) effects using instrumental variables: an application to evaluating prostate cancer treatments. *J Appl Econ* 2014 Jun-Jul;29(4):671-691.

14. Gandaglia G, Sammon JD, Chang SL, Choueiri TK, Hu JC, Karakiewicz PI, Kibel AS, Kim SP, Konijeti R, Montorsi F, Nguyen PL, Sukumar S, Menon M, Sun M, Trinh QD. Comparative effectiveness of robot-assisted and open radical prostatectomy in the postdissemination era. *J Clin Oncol* 2014 May 10;32(14):1419-26.

15. Wright JD, Ananth CV, Tsui J, Glied SA, Burke WM, Lu YS, Neugut AI, Herzog TJ, Hershman DL. Comparative effectiveness of upfront treatment strategies in elderly women with ovarian cancer. *Cancer* 2014 Apr 15;120(8):1246-54.

16. Beadle BM, Liao KP, Elting LS, Buchholz TA, Ang KK, Garden AS, Guadagnolo BA. Improved survival using intensity-modulated radiation therapy in head and neck cancers: a SEER-Medicare analysis. *Cancer* 2014 Mar 01;120(5):702-10.

17. Sun M, Sammon JD, Becker A, Roghmann F, Tian Z, Kim SP, Larouche A, Abdollah F, Hu JC, Karakiewicz PI, Trinh QD. Radical prostatectomy vs radiotherapy vs observation among older patients with clinically localized prostate cancer: a comparative effectiveness evaluation. *BJU Int* 2014 Feb;113(2):200-8.

18. Sun M, Becker A, Tian Z, Roghmann F, Abdollah F, Larouche A, Karakiewicz PI, Trinh QD. Management of localized kidney cancer: calculating cancer-specific mortality and competing risks of death for surgery and nonsurgical management. *Eur Urol* 2014 Jan;65(1):235-41.

19. Parmar AD, Sheffield KM, Han Y, Vargas GM, Guturu P, Kuo YF, Goodwin JS, Riall TS. Evaluating comparative effectiveness with observational data: endoscopic ultrasound and survival in pancreatic cancer. *Cancer* 2013 Nov 01;119(21):3861-9.

20. Strope SA, Chang SH, Chen L, Sandhu G, Piccirillo JF, Schootman M. Survival impact of followup care after radical cystectomy for bladder cancer. *J Urol* 2013 Nov;190(5):1698-703.

21. Yao N, Mackley HB, Anderson RT, Recht A. Survival after partial breast brachytherapy in elderly patients with nonmetastatic breast cancer. *Brachytherapy* 2013 Jul-Aug;12(4):293-302.

22. Bekelman JE, Handorf EA, Guzzo T, Evan Pollack C, Christodouleas J, Resnick MJ, Swisher-McClure S, Vaughn D, Ten Have T, Polsky D, Mitra N. Radical cystectomy versus bladder-preserving therapy for muscle-invasive urothelial carcinoma: examining confounding and misclassification biasin cancer observational comparative effectiveness research. *Value Health* 2013 Jun;16(4):610-8.

23. Lu-Yao GL, Albertsen PC, Li H, Moore DF, Shih W, Lin Y, DiPaola RS, Yao SL. Does primary androgen-deprivation therapy delay the receipt of secondary cancer therapy for localized prostate cancer? *Eur Urol* 2012 Dec;62(6):966-72.

24. Wisnivesky JP, Halm EA, Bonomi M, Smith C, Mhango G, Bagiella E. Postoperative radiotherapy for elderly patients with stage III lung cancer. *Cancer* 2012 Sep 15;118(18):4478-85.

25. Kuo YF, Montie JE, Shahinian VB. Reducing bias in the assessment of treatment effectiveness: androgen deprivation therapy for prostate cancer. *Med Care* 2012 May;50(5):374-80.

26. Tan HJ, Norton EC, Ye Z, Hafez KS, Gore JL, Miller DC. Long-term survival following partial vs radical nephrectomy among older patients with early-stage kidney cancer. *JAMA* 2012 Apr 18;307(15):1629-35.

27. Saito AM, Landrum MB, Neville BA, Ayanian JZ, Earle CC. The effect on survival of continuing chemotherapy to near death. *BMC Palliat Care* 2011 Sep 21;10:14.

28. Saito AM, Landrum MB, Neville BA, Ayanian JZ, Weeks JC, Earle CC. Hospice care and survival among elderly patients with lung cancer. *J Palliat Med* 2011 Aug;14(8):929-39.

29. Hadley J, Yabroff KR, Barrett MJ, Penson DF, Saigal CS, Potosky AL. Comparative effectiveness of prostate cancer treatments: evaluating statistical adjustments for confounding in observational data. *J Natl Cancer Inst* 2010 Dec 01;102(23):1780-93.

30. Gore JL, Litwin MS, Lai J, Yano EM, Madison R, Setodji C, Adams JL, Saigal CS, Urologic Diseases in America Project. Use of radical cystectomy for patients with invasive bladder cancer. *J Natl Cancer Inst* 2010 Jun 02;102(11):802-11.

31. Punglia RS, Saito AM, Neville BA, Earle CC, Weeks JC. Impact of interval from breast conserving surgery to radiotherapy on local recurrence in older women with breast cancer: retrospective cohort analysis. *BMJ* 2010 Mar 02;340:c845.

32. Wisnivesky JP, Halm E, Bonomi M, Powell C, Bagiella E. Effectiveness of radiation therapy for elderly patients with unresected stage I and II non-small cell lung cancer. *Am J Respir Crit Care Med* 2010 Feb 01;181(3):264-9.

33. Lu-Yao GL, Albertsen PC, Moore DF, Shih W, Lin Y, DiPaola RS, Yao SL. Survival following primary androgen deprivation therapy among men with localized prostate cancer. *JAMA* 2008 Jul 09;300(2):173-81.

34. Zeliadt SB, Potosky AL, Penson DF, Etzioni R. Survival benefit associated with adjuvant androgen deprivation therapy combined with radiotherapy for high- and low-risk patients with nonmetastatic prostate cancer. *Int J Radiat Oncol Biol Phys* 2006 Oct 01;66(2):395-402.

35. Earle CC, Tsai JS, Gelber RD, Weinstein MC, Neumann PJ, Weeks JC. Effectiveness of chemotherapy for advanced lung cancer in the elderly: instrumental variable and propensity analysis. *J Clin Oncol* 2001 Feb 15;19(4):1064-70.

III. Data Files Requested: Please list specific SEER-Medicare data files and years of data required. Project description **must** describe how each file will be used.

We are specifically requesting PEDSF files for the requested cancer sites. The sample sizes in these PEDSF files would be essential to carry out any meaning full analysis on health care utilizations and costs.

In addition, we are requesting the 5% non-cancer sample data in order to estimate attributable costs by cancer site and age in order to inform economic evaluation of screening intervention.

Name of file	Years available	Years requested
Patient Entitlement and Diagnosis Summary File (PEDSF) (SEER cases)	1973-2013	2008 - 2013
Summarized Denominator File (SUMDENOM) 5% non-cancer sample	1991-2013	2007 - 2013
MEDPAR	1991-2014	2007 - 2014
NCH - Carrier (physician/supplier)	1991-2014	2007 - 2014
Outpatient	1991-2014	2007 – 2014
Home Health (HHA)	1991-2014	2007 – 2014
Hospice	1991-2014	2007 – 2014
Durable Medical Equipment (DME)	1994-2014	2007 – 2014
Part D Event (PDE)	2007-2014	2007 - 2014
Chronic Conditions Flag	1999-2014	2007 - 2014
Hospital File	1996, 1998, 2000-2014	2007 - 2014

Note: Medicare claims prior to 1998 are available only for cases diagnosed with cancer before 2003. Cases diagnosed 2003-2005 have claims from 1998+; cases diagnosed 2006 -2007 have claims from 2000+; cases diagnosed 2008-2009 have claims from 2002+; cases diagnosed 2010-2011have claims 2004+; Cases diagnosed 2012-2013 have claims 2006+