eligibility criteria of the randomized trial whenever possible. For each trial we used three Cox regression models to determine hazard ratios (HRs) for overall survival: univariable, multivariable, and propensity score adjusted models. Multivariable analyses controlled for potential confounders including demographic, comorbidity, clinical, treatment and tumor-related variables. Each NCDB survival analysis was defined as discordant if the HR for the NCDB analysis fell outside the 95% confidence interval of the corresponding randomized trial. Separately, we also assessed for disagreement with statistical significance, with $p<0.05$ for NCDB and $p>0.05$ for the clinical trial (or vice versa) defined as discordant.

Results: Thirty-two randomized trials met inclusion criteria. NCDB analyses produced hazard ratios for survival discordant with randomized trials in 16 (50%) univariable analyses, 10 (31%) multivariable analyses, and 12 (37%) propensity score analyses. NCDB analyses produced p-values discordant with randomized trials with 26 (81%) univariable analyses, 22 (69%) multivariable analyses, and 20 (62%) propensity score analyses. We did not identify any clinical trial characteristics specifically associated with discordance between NCDB analyses and randomized trials including disease site, severity of cancer, or era of trial.

Conclusion: Comparative effectiveness research involving radiation therapy using NCDB frequently produces results discordant to randomized data. Multivariable or propensity score analysis modestly improves concordance between NCDB and clinical trials. Caution should be used when interpreting comparative effective research with cancer registry data.

Author Disclosure: **A. Kumar**: Independent Contractor; Sympto Health. Consultant; Sympto Health. **Z.D. Guss**: None. **V. Nalawade**: None. **R.R. Sarkar**: None. **B.S. Rose**: None. **P. Sheridan**: None. **R. Xu**: None. **J.D. Murphy**: None.

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Nomogram to Predict Survival Benefit of Postoperative Radiotherapy for Major Salivary Gland Cancers

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Purpose/Objective(s): There are no randomized data to support the use of postoperative radiotherapy (PORT) for major salivary gland malignancies. Our objective was to develop and validate a nomogram to estimate overall survival (OS) with and without PORT.

Materials/Methods: Adults in the National Cancer Database diagnosed with invasive non-metastatic major salivary gland cancer between 2004-2015 were identified. Exclusion criteria included prior malignancy, pT1N0, no/unknown surgery, neoadjuvant therapy, PORT dose <50 Gy or >75 Gy, PORT to a non-head/neck site, PORT started >9 weeks from surgery, and PORT duration >9 weeks. Ratio of nodal positivity (N+ ratio) was defined as number of nodes positive among nodes resected. Cox proportional hazards models determined the effect of covariates on OS. A multivariate regression model was used to generate a nomogram to predict 2-, 5-, and 10-year OS. Cross-validation using 500 random 50-50 hold-out samples was performed. All p-values are two-sided.

Results: There were 18,400 subjects who met inclusion criteria, of which 9,721 (53%) received PORT. Subjects who received PORT had significantly worse adverse pathologic features compared to those treated with surgery alone: pT3-4 (54% vs 39%, $p<0.01$), high grade (60% vs 35%, $p<0.01$), lymphovascular invasion (34% vs 17%, $p<0.01$), >0.1 N+ ratio (36% vs 23%, $p<0.01$), extranodal extension (23% vs 15%, $p<0.01$), major nerve involvement (12% vs 6%, $p<0.01$), and positive margin (45% vs 25%, $p<0.01$). Median age at diagnosis for both cohorts was 65 ($p=0.07$). Distribution of gland involvement was 86% parotid, 13% submandibular, and 1% sublingual. Median follow-up for living subjects was 4.9 years. PORT was significantly associated with improved OS for the following subgroups by log-rank test: pT3 ($p<0.01$), pT4 ($p<0.01$), high grade ($p<0.01$), node positive ($p<0.01$), and positive margin ($p<0.01$). The variables listed in the table below were incorporated into a nomogram using data from 6,138 subjects. The resulting nomogram demonstrated good accuracy in predicting OS, with a concordance index of 0.719.

Conclusion: Our cross-validated nomogram predicts the 2-, 5-, and 10-year differences in OS based on receipt of PORT for major salivary gland cancers using readily available clinicopathologic features. The nomogram will be made publicly available online.

Abstract 1147; Table 1

Variable	HR	95% CI	P
Age at diagnosis	1.04	1.03 – 1.04	<0.01
Male sex (ref: female)	1.28	1.17 – 1.39	<0.01
Charlson-Deyo comorbidity score (ref: 0)			
1	1.19	1.08 – 1.31	<0.01
2	1.58	1.32 – 1.90	<0.01
≥3	1.80	1.33 – 2.44	<0.01
Primary site (ref: parotid)			
Submandibular	1.31	1.16 – 1.48	<0.01
Sublingual	0.68	0.38 – 1.23	0.21
Pathologic T-stage (ref: 1)			
2	1.14	0.96 – 1.35	0.13
3	1.59	1.35 – 1.88	<0.01
4	1.89	1.60 – 2.23	<0.01
N+ ratio (ref: 0)			
>0 and ≤0.10	1.45	1.29 – 1.63	<0.01
>0.1 and <0.5	1.74	1.58 – 1.93	<0.01
≥0.5	2.13	1.91 – 2.37	<0.01
Tumor grade (ref: low)			
Intermediate	1.70	1.43 – 2.02	<0.01
High	2.09	1.77 – 2.47	<0.01
Positive margin (ref: negative)	1.28	1.18 – 1.38	<0.01
Yes PORT (ref: no PORT)	0.63	0.58 – 0.68	<0.01

Author Disclosure: **C.D. Jacobs**: None. **R. Kahmke**: None. **D.J. Rocke**: None. **I. Barak**: None. **S. Jung**: None. **G. Suneja**: Employee; University of North Carolina. Research Grant; National Institutes of Health. Honoraria; National Comprehensive Cancer Network. Travel Expenses; National Comprehensive Cancer Network, Radiation Oncology Institute, American Board of Radiology. **Y.M. Mowery**: Employee; Duke Health.

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Revisiting the role of SBRT in Localized Hepatocellular Carcinoma (HCC): Accounting for Selection Biases in National Cancer Database (NCDB) Analyses

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Purpose/Objective(s): Observational data are used increasingly to compare efficacy between cancer treatment modalities when level 1 evidences are lacking. Compared with randomized clinical trials (RCTs), these studies are prone to confounding by indication and selection biases that may threaten the validity despite efforts to account for them. A recent NCDB study that utilized propensity score (PS) methods suggested radiofrequency ablation (RFA) may yield better survival than SBRT for patients (pts) with non-surgically managed localized HCC. Significant

concerns about selection biases of pts referred for SBRT and their impact on the study findings remain. Our objective is to investigate the impacts of selection biases that cannot be readily accounted for by conventional PS methods.

Materials/Methods: We consider an unbiased comparison between SBRT and RFA can be obtained from a "super-population" (e.g., P1), consisting of candidate pts had a RCT of SBRT vs. RFA were conducted hypothetically. Conventional PS analyses use a subset of this "super-population" (e.g., P2) who were eventually referred for SBRT and RFA to obtain an unconfounded treatment comparison. When P2 is biasedly selected from P1, naïve PS analyses based on P2 alone cannot fully recover the underlying treatment difference due to selection biases. We used so-called Inverse Probability of Selection Weighting (IPSW) method to account for selection biases that cannot be addressed by PS. IPSW-based Kaplan-Meier method and Cox model were used to report and compare Overall survival (OS), defined as the interval btw treatment and death or last follow-up (f/u).

Results: The super-population (P1) consists of 6,041 cases diagnosed with primary HCC in 2004 to 2014, including 499 (8.3%) and 5,542 (91.7%) who received SBRT and RFA, respectively. The selected sample (P2) for naïve PS analysis consists of 3,513 cases (7.6% SBRT vs. 92.4% RFA) w/ median f/u 3.8 yrs. Potential selection biases were observed. Without accounting for selection biases, hazard ratio (HR) for OS (SBRT vs. RFA) using naïve PS analysis is 1.46 (95% CI: 1.08-1.97, p=0.01). Using the proposed IPSW method, the HR was reduced to 1.10 (95% CI: 0.79-1.52, p=0.57). The estimated OS rates at 1, 3, and 5 year (yr) w/o and w/ accounting for selection biases are summarized in the Table.

Conclusion: Our study suggests selection biases may exist and substantially impact findings when naïve PS analysis are performed. Additional residual confounding may still remain due to incomplete key prognostic factors. Analyses based on observational database for comparative effectiveness research requires extra cautions to minimize the impacts of confounders and selection biases.

Abstract 1148; Table 1 OS rates (95% CI) w/o and w/ accounting for selection biases

	w/o adjustment		w/ adjustment		
	RFA	SBRT	RFA	SBRT	SBRT-RFA
1yr	81%(80,82)	63% (55,73)	80%(79,82)	68%(61,75)	-12%(-19,-5)
3yr	52%(50,54)	36%(27,47)	49%(47,52)	42%(33,50)	-8%(-16,1)
5yr	36%(34,38)	29%(20,42)	34%(31,36)	36%(27,45)	3%(-7,12)

Author Disclosure: **C. Hu**: Employee; Food and Drug Administration. Research Grant; National Cancer Institute. Consultant; Merck & Co. **Y. Cheng**: None. **H. Tsai**: None. **H. Jing**: None. **J.J. Meyer**: Research Grant; Peregrine Pharmaceuticals, Inc. clinical trials support; D-fine Inc. Honoraria; UpToDate, Inc.

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Radiotherapy and Receptor Tyrosine Kinase Inhibition for Solid Cancers: An International Meta-Analysis of 11 Studies with 5,284 Patients

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Purpose/Objective(s): Receptor tyrosine kinase inhibitors (RTKIs), defined as either monoclonal antibodies (e.g. cetuximab, bevacizumab) or small molecule TKIs (e.g. erlotinib, lapatinib, gefitinib), are hypothesized to improve outcomes of radiation therapy (RT)-based standard of care therapies for multiple cancers. Our objective is to evaluate the efficacy and toxicity of the addition of RTKIs to RT-based therapy for solid cancers. We hypothesized that the addition of RTKIs to RT-based therapy do not increase overall survival.

Materials/Methods: PICOS/PRISMA/MOOSE methods were used to identify prospective randomized studies on PubMed, 2008 to 2018, including patients with solid tumor cancers treated RT +/- RTKIs. Extracted variables included use of RT vs chemo-RT (CRT), RTKI type (antibody vs small molecule), overall survival hazard ratios (HRs) with 95% confidence intervals (CIs) of survival, and grade 3+ toxicity. The primary endpoint was overall survival. The secondary endpoint was grade 3+ toxicity. Random-effects meta-analyses were performed using DerSimonian and Laird methods.

Results: A total of 405 studies met initial search criteria, and 11 (N) prospective randomized trials of RT+/-TKI met inclusion criteria, encompassing 5,284 patients (n). The trials included cancers of the head and neck (N=4, n=2808), esophagus (N=3, n=762), lung (N=3, n=793), or brain (N=1, n=921). Four studies examined a small molecule RTKIs and RT treatment with 1,192 patients, and 7 studies evaluated receptor tyrosine kinase antibodies and RT treatment with 4,092 patients. The addition of RTKIs to RT-based therapy did not improve overall survival, HR 0.97 (95%CI 0.85, 1.09); among all patients, it did not worsen toxicity rates 1.09 (95%CI 0.95-1.25). On subgroup analysis (not mutually exclusive, Table 1), addition of RTKI to RT alone increased grade 3+ toxicity, RR 1.31 (1.05, 1.63).

Conclusion: Use of receptor tyrosine kinase inhibition in addition to RT did not confer a significant survival advantage. For patients receiving RT alone, adding a TKI worsens toxicity. The risks of TKI-related toxicity should be weighed against any benefits that TKIs afford in progression-free survival.

Author Disclosure: **E. Batchelder**: None. **E.J. Lehrer**: None. **L. Tchelebi**: None. **J. Drabick**: None. **D.M. Trifiletti**: None. **N.G. Zaorsky**: None.

Abstract 1149; Table 1 Outcomes and toxicities of RTKIs added to RT-based therapy for the treatment of solid cancers

		Overall survival					Toxicity				
Subgroup stratification	Treatment (not mutually exclusive)	studies	patients	HR	% weight	I^2 %	studies	patients	RR	% weight	I^2 %
RT or CRT	CRT + any type of RTKI	8	4775	0.98 (0.84, 1.11)	74.6	52.3	5	2970	1.01 (0.88, 1.15)	74.05	81.4
	RT + any type of RTKI	3	974	0.98 (0.65, 1.31)	25.4	69.3	2	550	1.31 (1.05, 1.63)	25.95	36.7
Drug type	RT or CRT + small molecule TKI	4	1192	1.07 (0.74, 1.40)	27.95	68.1	2	773	1.28 (0.95, 1.73)	26.0	56.2
	RT or CRT + antibody RTKI	7	3231	0.96 (0.83, 1.08)	72.05	49.8	7	2747	1.03 (0.95, 1.22)	74.0	86.3
Overall		**11**	**5284**	**0.97 (0.85, 1.09)**	**100**	**53.0**	**7**	**3520**	**1.09 (0.95-1.25)**	**100**	**85.2**