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## Supplemental material

**Prophylactic cranial irradiation effect on survival in patients with small cell lung cancer:  
a comprehensive systematic review and meta-analysis**

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Supplementary Table 1. Search strategy used for PubMed search.	
1	(Brain[Title/Abstract] OR "Brain"[MeSH Terms] OR Cerebr*[Title/Abstract] OR "Cerebrum"[MeSH Terms] OR Cerebell*[Title/Abstract] OR Intracranial[Title/Abstract]. OR cranial[Title/Abstract])
2	("Small cell Lung cancer"[Title/Abstract] OR "Small-cell Lung cancer"[Title/Abstract] OR "Small-cell lung carcinoma"[Title/Abstract] OR "Small cell lung carcinoma"[Title/Abstract] OR "Small Cell Lung Carcinoma"[MeSH Terms])
3	(Radiotherap*[Title/Abstract] OR Radiosurg*[Title/Abstract] OR LINAC[Title/Abstract] OR linear accelerator[Title/Abstract] OR Gamma Knife[Title/Abstract] OR Cyberknife[Title/Abstract] OR "x knife"[Title/Abstract] OR stereotactic*[Title/Abstract] OR fraction*[Title/Abstract] OR irradiat*[Title/Abstract] OR radiat*[Title/Abstract] OR WBRT[Title/Abstract] OR SRS[Title/Abstract] OR SFRT[Title/Abstract] OR Radiotherapy[MeSH Terms] OR Dose fractionation[MeSH Terms] OR Cranial Irradiation[MeSH Terms] OR Radiosurgery[MeSH Terms])
4	(Prophyl*[Title/Abstract] OR Prevent*[Title/Abstract])
	1 & 2 & (3 & 4)

Supplementary Table 2. Characteristics of the included studies.								
Author	Country	Study Type	Stage	PCI	NPCI	Dose	Main Previous Treatment	Data Source
Rosen, 1983 <sup>1</sup>	USA	Retrospective	L & E	76	176	NA	Chemoradiotherapy	NHR
Fleck, 1990 <sup>2</sup>	USA	Retrospective	L	38	20	>25 Gy	Chemoradiotherapy	NHR
Russell, 1991 <sup>3</sup>	USA	Prospective	O	93	94	>25 Gy	Chemoradiotherapy	NHR
Rosenstein, 1992 <sup>4</sup>	USA	Retrospective	L	36	26	>25 Gy	Chemoradiotherapy	NHR
Ohonoshi, 1993 <sup>5</sup>	Japan	Prospective	L & E	23	23	>25 Gy	Chemoradiotherapy	NHR
Slotman, 1993 <sup>6</sup>	Netherland	Retrospective	L	54	21	NA	Chemoradiotherapy	NHR
Shaw, 1994 <sup>7</sup>	USA	Retrospective	L & E	571	51	>25 Gy	Chemoradiotherapy	NHR
Arriagada, 1995 <sup>8</sup>	France	Prospective	L & E	145	149	≤25 Gy	Chemoradiotherapy, Surgery	NHR
Liengswangwong, 1995 <sup>9</sup>	USA	Retrospective	L	24	19	>25 Gy	Chemoradiotherapy	NHR
Rubenstein, 1995 <sup>10</sup>	USA	Retrospective	L	82	107	≤25 Gy	Chemoradiotherapy, Surgery	NHR
Work, 1996 <sup>11</sup>	Denmark	Prospective	L	157	42	>25 Gy	Chemoradiotherapy	NHR
Alexopoulos, 1997 <sup>12</sup>	Greece	Retrospective	L & E	51	28	>25 Gy	Chemoradiotherapy	NHR
Gregor, 1997 <sup>13</sup>	UK	Prospective	L	194	120	>25 Gy	Chemoradiotherapy	HR
Laplanche, 1998 <sup>14</sup>	France	Prospective	L & E	100	111	≤25 Gy	Chemoradiotherapy	NHR
Wolfson, 2001 <sup>15</sup>	USA	Retrospective	L	15	12	>25 Gy	Chemoradiotherapy	NHR
Arriagada, 2003 <sup>16</sup>	Spain	Prospective	L & E	245	260	≤25 Gy	Chemoradiotherapy	NHR
Cao, 2005 <sup>17</sup>	China	Prospective	L	26	25	>25 Gy	Chemoradiotherapy	NHR
Slotman, 2007 <sup>18</sup>	Netherland	Prospective	E	143	143	≤25 Gy	Chemoradiotherapy	HR

Patel, 2009 <sup>19</sup>	USA	Retrospective	L	670	7325	≤25 Gy	Chemoradiotherapy	HR
Giuliani, 2010 <sup>20</sup>	Canada	Retrospective	L	127	80	NA	Chemoradiotherapy	HR
Sas-Korczyńska, 2010 <sup>21</sup>	Poland	Retrospective	L	86	43	>25 Gy	Chemoradiotherapy	NHR
Stanic, 2010 <sup>22</sup>	Slovenia	Retrospective	L	24	143	>25 Gy	Chemoradiotherapy	NHR
Schild, 2012 <sup>23</sup>	USA	Retrospective	L & E	459	280	>25 Gy	Chemoradiotherapy	HR
Eaton, 2013 <sup>24</sup>	USA	Retrospective	L	138	1788	NA	Surgery	HR
Tai, 2013 <sup>25</sup>	Canada	Retrospective	L	177	112	NA	Chemoradiotherapy	NHR
Bettington, 2013 <sup>26</sup>	Australia	Retrospective	L	37	30	>25 Gy	Chemoradiotherapy	HR
Zhu, 2014 <sup>27</sup>	China	Retrospective	L	67	126	≤25 Gy	Surgery	HR, NHR
Ozawa, 2015 <sup>28</sup>	Japan	Retrospective	L	29	95	NA	Chemoradiotherapy, Surgery	NHR
Yokouchi, 2015 <sup>29</sup>	Japan	Retrospective	L & E	13	140	≤25 Gy	Surgery	HR
Chen, 2016 <sup>30</sup>	China	Retrospective	E	45	159	≤25 Gy	Chemoradiotherapy	HR
Salama, 2016 <sup>31</sup>	USA	Prospective	E	41	44	≤25 Gy	Chemoradiotherapy	HR
Yang, 2016 <sup>32</sup>	USA	Retrospective	L	5	388	NA	Surgery	HR
Eze, 2017 <sup>33</sup>	Germany	Retrospective	L	71	113	>25 Gy	Chemoradiotherapy	HR, NHR
Farooqi, 2017 <sup>34</sup>	USA	Retrospective	L	364	294	≤25 Gy	Chemoradiotherapy	HR, NHR
Lok, 2017 <sup>35</sup>	USA	Retrospective	L	115	93	≤25 Gy	Chemoradiotherapy, Surgery	HR
Takahashi, 2017 <sup>36</sup>	Japan	Prospective	E	113	111	≤25 Gy	Chemoradiotherapy	HR, NHR
Verma, 2017 <sup>37</sup>	USA	Retrospective	L	17	54	≤25 Gy	Chemoradiotherapy	NHR
Xu, 2017 <sup>38</sup>	China	Retrospective	L	115	234	NA	Surgery	HR, NHR
Wu, 2017 <sup>39</sup>	USA	Retrospective	L	116	167	NA	Chemoradiotherapy, Surgery	HR
Zhang, 2017 <sup>40</sup>	China	Retrospective	L	94	76	NA	Chemoradiotherapy	HR
Sas-Korczyńska, 2018 <sup>41</sup>	Poland	Retrospective	L	167	104	>25 Gy	Chemoradiotherapy	HR
Bang, 2018 <sup>42</sup>	Canada	Retrospective	E	68	87	≤25 Gy	Chemoradiotherapy	HR
Chen, 2018 <sup>43</sup>	China	Retrospective	L	19	33	≤25 Gy	Surgery	HR, NHR
Mamesaya, 2018 <sup>44</sup>	Japan	Retrospective	L	60	20	≤25 Gy	Chemoradiotherapy	HR
Matutino, 2018 <sup>45</sup>	Brazil	Retrospective	E	16	30	≤25 Gy	Chemoradiotherapy	HR
Nakamura, 2018 <sup>46</sup>	Japan	Retrospective	L	93	69	≤25 Gy	Chemoradiotherapy	HR
Sharma, 2018 <sup>47</sup>	USA	Retrospective	E	473	3784	NA	Chemoradiotherapy	HR

Wang, 2018 <sup>48</sup>	China	Retrospective	L & E	11	80	≤25 Gy	Surgery	HR, NHR
Yin, 2018 <sup>49</sup>	China	Retrospective	L	160	109	>25 Gy	Chemoradiotherapy, Surgery	HR
Kim, 2019 <sup>50</sup>	South Korea	Retrospective	L	139	95	≤25 Gy	Chemoradiotherapy	HR
Kou, 2019 <sup>51</sup>	China	Retrospective	L	394	2178	NA	Chemoradiotherapy	HR
Resio, 2019 <sup>52</sup>	USA	Retrospective	L	202	657	NA	Surgery	HR
Chen, 2019 <sup>53</sup>	China	Retrospective	L	69	69	≤25 Gy	Chemoradiotherapy, Surgery	HR
Jeong, 2019 <sup>54</sup>	South Korea	Retrospective	L	56	45	≤25 Gy	Chemoradiotherapy	HR
Chung, 2020 <sup>55</sup>	South Korea	Retrospective	E	48	48	≤25 Gy	Chemoradiotherapy	HR
Elegbede, 2020 <sup>56</sup>	Canada	Retrospective	L & E	107	253	NA	Chemoradiotherapy, Surgery	HR
Iqbal, 2020 <sup>57</sup>	UK	Retrospective	L	46	4	≤25 Gy	Chemoradiotherapy	NHR
Lou, 2020 <sup>58</sup>	China	Retrospective	L & E	46	100	NA	Surgery	HR
Pezzi, 2020 <sup>59</sup>	USA	Retrospective	L	84	84	>25 Gy	Chemoradiotherapy	HR
Yu, 2020 <sup>60</sup>	China	Retrospective	E	21	97	≤25 Gy	Chemoradiotherapy	HR, NHR
Ghanta, 2021 <sup>61</sup>	USA	Retrospective	L	83	83	>25 Gy	Chemoradiotherapy, Surgery	HR
Inoue, 2021 <sup>62</sup>	Japan	Retrospective	L	32	32	≤25 Gy	Chemoradiotherapy	NHR
Keller, 2021 <sup>63</sup>	USA	Retrospective	E	57	57	≤25 Gy	Chemoradiotherapy	HR
Li, 2021 <sup>64</sup>	China	Retrospective	L	69	69	≤25 Gy	Chemoradiotherapy	HR
Yan, 2021 <sup>65</sup>	Canada	Retrospective	L	81	196	≤25 Gy	Chemoradiotherapy	HR
Yang, 2021 <sup>66</sup>	China	Retrospective	L	124	540	NA	Surgery	HR
Zhou, 2021 <sup>67</sup>	USA	Retrospective	L	43	143	≤25 Gy	Surgery	HR
Chen, 2022 <sup>68</sup>	China	Retrospective	L	324	324	>25 Gy	Chemoradiotherapy, Surgery	HR
Held, 2022 <sup>69</sup>	Denmark	Retrospective	L & E	39	39	≤25 Gy	Chemoradiotherapy	HR, NHR
Hou, 2022 <sup>70</sup>	China	Retrospective	L	58	58	NA	Chemoradiotherapy	HR
Lim, 2022 <sup>71</sup>	South Korea	Retrospective	L & E	43	186	≤25 Gy	Chemoradiotherapy, Surgery	HR
Pan, 2022 <sup>72</sup>	China	Retrospective	L	83	33	≤25 Gy	Chemoradiotherapy	HR
Qi, 2022 <sup>73</sup>	China	Retrospective	L	75	75	≤25 Gy	Chemoradiotherapy	HR, NHR
Ueki, 2022 <sup>74</sup>	Japan	Retrospective	L	24	38	≤25 Gy	Chemoradiotherapy	HR, NHR

HR: Hazard Ratio, NHR: Non-Hazard Ratio, L: Limited, E: Extensive

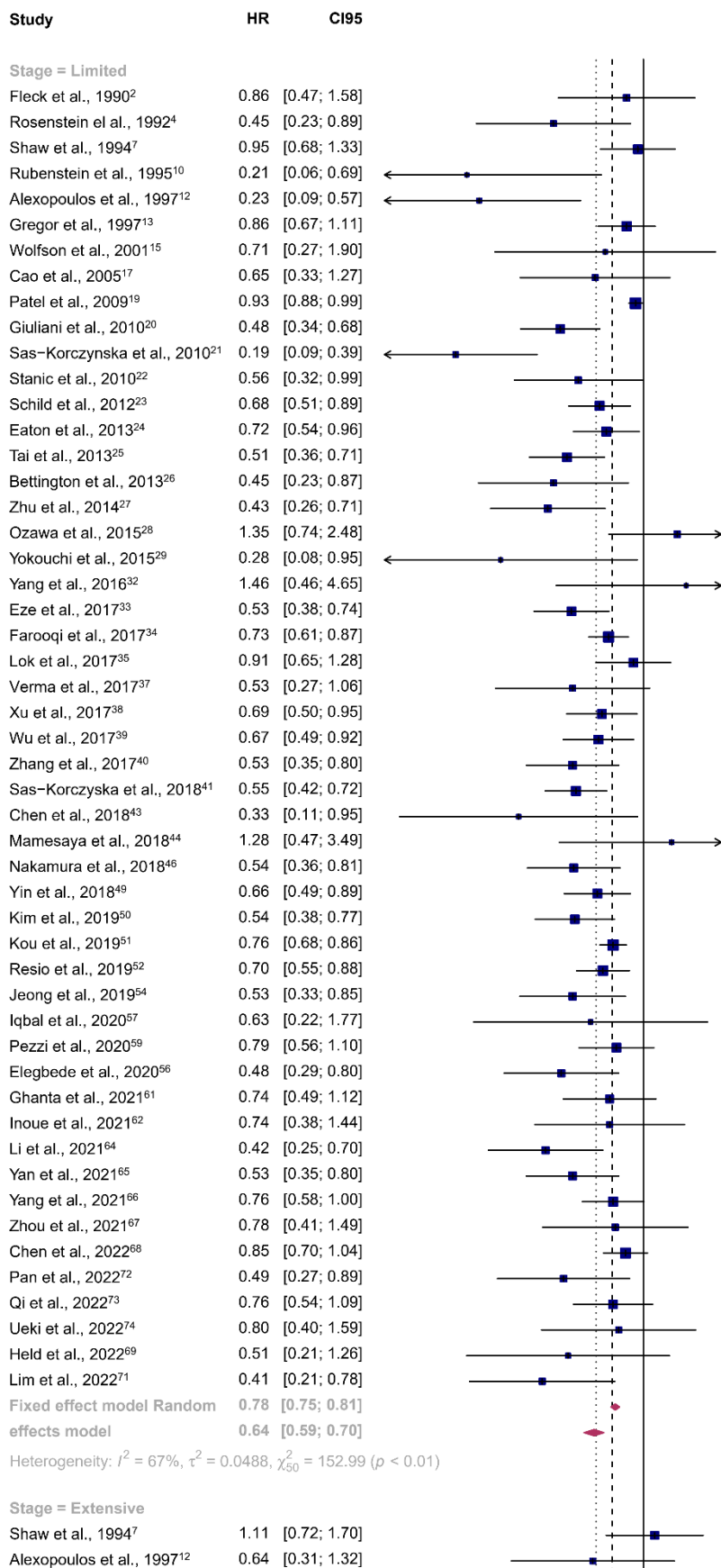
Supplementary Figure 1. Result of risk of bias assessment using ROBINS-I.

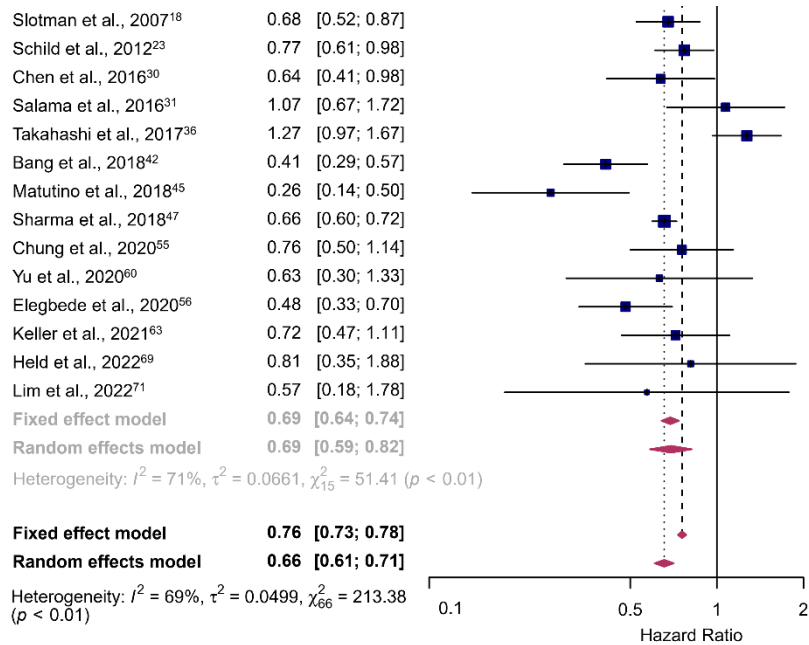
Study	Risk of bias domains							Overall
	D1	D2	D3	D4	D5	D6	D7	
Rosen, 1983 <sup>1</sup>	⊗	⊗	?	?	?	+	+	⊗
Fleck, 1990 <sup>2</sup>	⊗	-	+	?	?	+	+	⊗
Russell, 1991 <sup>3</sup>	+	+	+	+	?	+	+	+
Rosenstein, 1992 <sup>4</sup>	⊗	-	-	?	?	?	+	⊗
Ohonoshi, 1993 <sup>5</sup>	+	+	+	?	?	+	+	+
Slotman, 1993 <sup>6</sup>	-	⊗	?	?	?	?	+	⊗
Shaw, 1994 <sup>7</sup>	-	+	+	?	?	+	+	-
Arriagada, 1995 <sup>8</sup>	+	⊗	+	?	?	+	+	⊗
Liengswangwong, 1995 <sup>9</sup>	⊗	⊗	-	?	?	+	+	⊗
Rubenstein, 1995 <sup>10</sup>	-	+	+	?	?	+	+	-
Work, 1996 <sup>11</sup>	-	⊗	+	⊗	?	?	+	⊗
Alexopoulos 1997 <sup>12</sup>	⊗	⊗	-	?	?	?	+	⊗
Gregor, 1997 <sup>13</sup>	+	+	+	+	?	+	+	+
Laplanche, 1998 <sup>14</sup>	+	+	+	+	?	+	+	+
Wolfson, 2001 <sup>15</sup>	+	+	+	+	?	+	+	+
Arriagada, 2003 <sup>16</sup>	+	+	+	+	?	+	+	+
Cao, 2005 <sup>17</sup>	-	?	+	?	?	+	+	-
Slotman, 2007 <sup>18</sup>	+	+	+	+	?	+	+	+
Patel, 2009 <sup>19</sup>	-	⊗	+	?	?	+	+	⊗
Giuliani, 2010 <sup>20</sup>	-	-	?	-	?	+	+	-
Sas-Korczynska, 2010 <sup>21</sup>	-	⊗	-	?	?	+	+	⊗
Stanic, 2010 <sup>22</sup>	⊗	?	+	?	?	?	+	⊗
Schild, 2012 <sup>23</sup>	-	+	+	?	?	+	+	-
Eaton, 2013 <sup>24</sup>	-	⊗	?	?	?	+	+	⊗
Tai, 2013 <sup>25</sup>	-	⊗	?	?	?	?	+	⊗
Bettington, 2013 <sup>26</sup>	⊗	⊗	+	?	?	-	+	⊗
Zhu, 2014 <sup>27</sup>	-	⊗	+	-	?	+	+	⊗
Ozawa, 2015 <sup>28</sup>	-	+	?	?	?	+	+	-
Yo kouchi, 2015 <sup>29</sup>	-	+	+	?	?	+	+	-
Chen, 2016 <sup>30</sup>	-	⊗	+	?	?	+	+	⊗
Salama, 2016 <sup>31</sup>	+	+	+	+	?	+	+	+
Yang, 2016 <sup>32</sup>	-	⊗	?	?	?	?	+	⊗
Eze, 2017 <sup>33</sup>	-	-	+	?	?	+	+	-
Farooqi, 2017 <sup>34</sup>	-	⊗	+	-	?	+	+	⊗
Lok, 2017 <sup>35</sup>	-	?	?	+	?	+	+	-
Takahashi, 2017 <sup>36</sup>	+	+	+	+	?	+	+	+
Verma, 2017 <sup>37</sup>	⊗	⊗	+	?	?	?	+	⊗
Xu, 2017 <sup>38</sup>	-	⊗	-	?	?	+	+	⊗
Wu, 2017 <sup>39</sup>	⊗	-	?	?	?	?	+	⊗
Zhang, 2017 <sup>40</sup>	-	⊗	+	?	?	+	+	⊗
Sas-Korczynska, 2018 <sup>41</sup>	-	⊗	+	?	?	+	+	⊗
Bang, 2018 <sup>42</sup>	-	-	+	?	?	+	+	-
Chen, 2018 <sup>43</sup>	⊗	+	+	?	?	+	+	⊗
Mamesaya, 2018 <sup>44</sup>	-	+	+	?	?	+	+	-
Matutino 2018 <sup>45</sup>	⊗	-	+	?	?	?	+	⊗
Nakamura, 2018 <sup>46</sup>	-	⊗	+	-	?	+	+	⊗
Sharma, 2018 <sup>47</sup>	+	-	+	?	?	+	+	-
Wang, 2018 <sup>48</sup>	-	+	+	?	?	+	+	-
Yin, 2018 <sup>49</sup>	⊗	⊗	+	-	?	+	+	⊗
Kim, 2019 <sup>50</sup>	-	⊗	+	-	?	+	+	⊗
Kou, 2019 <sup>51</sup>	-	⊗	?	?	?	+	+	⊗
Resio, 2019 <sup>52</sup>	-	⊗	?	?	?	+	+	⊗
Chen, 2019 <sup>53</sup>	-	⊗	+	?	?	?	+	⊗
Jeong, 2019 <sup>54</sup>	-	+	+	?	?	+	+	-
Chung, 2020 <sup>55</sup>	+	-	+	?	?	+	+	-
Elegbede, 2020 <sup>56</sup>	-	⊗	?	?	?	?	+	⊗
Iqbal, 2020 <sup>57</sup>	⊗	-	+	?	?	?	+	⊗
Lou, 2020 <sup>58</sup>	-	⊗	?	?	?	+	+	⊗
Pezzi, 2020 <sup>59</sup>	-	+	+	?	?	+	+	-
Yu, 2020 <sup>60</sup>	⊗	?	+	?	?	+	+	⊗
Ghanta, 2021 <sup>61</sup>	-	+	+	?	?	+	+	-
Inoue, 2021 <sup>62</sup>	-	+	+	?	?	+	+	-
Keller, 2021 <sup>63</sup>	-	⊗	?	?	?	+	+	⊗
Li, 2021 <sup>64</sup>	-	+	+	?	?	+	+	-
Yan, 2021 <sup>65</sup>	-	⊗	+	?	?	+	+	⊗
Yang, 2021 <sup>66</sup>	⊗	?	?	?	?	+	+	⊗
Zhou, 2021 <sup>67</sup>	-	⊗	+	?	?	+	+	⊗
Chen, 2022 <sup>68</sup>	-	-	+	?	?	+	+	-
Held, 2022 <sup>69</sup>	⊗	⊗	+	?	?	+	+	⊗
Hou, 2022 <sup>70</sup>	-	?	?	?	?	+	+	-
Lim, 2022 <sup>71</sup>	-	-	?	?	?	+	+	-
Pan, 2022 <sup>72</sup>	-	-	+	?	?	+	+	-
Qi, 2022 <sup>73</sup>	-	-	+	?	?	?	+	-
Ueki, 2022 <sup>74</sup>	-	+	+	?	?	?	+	-

Domains:  
D1: Bias due to confounding.  
D2: Bias due to selection of participants.  
D3: Bias in classification of interventions.  
D4: Bias due to deviations from intended interventions.  
D5: Bias due to missing data.  
D6: Bias in measurement of outcomes.  
D7: Bias in selection of the reported results.

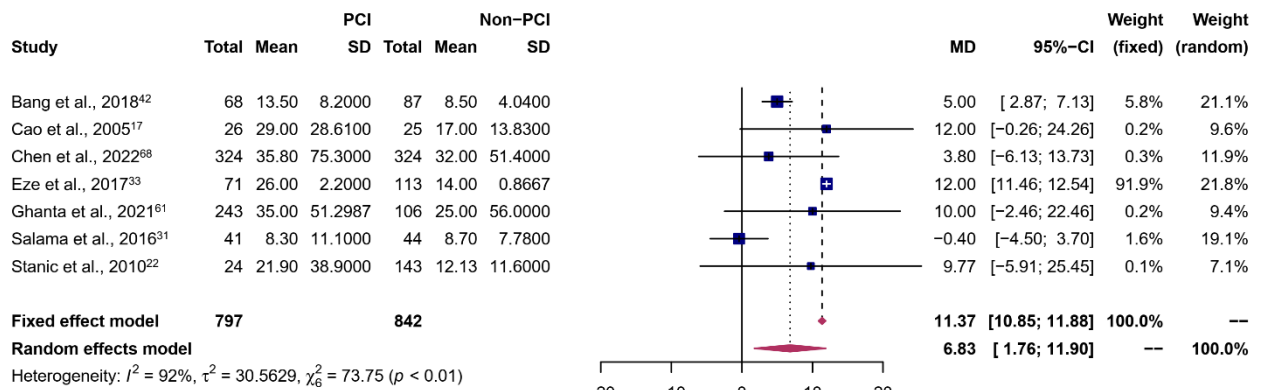
Judgement  
⊗ Serious  
- Moderate  
+ Low  
? No information

**Supplementary Figure 2.** Forest plot of the pooled HR on the effect of PCI on OS in patients with E-and L-SCLC.

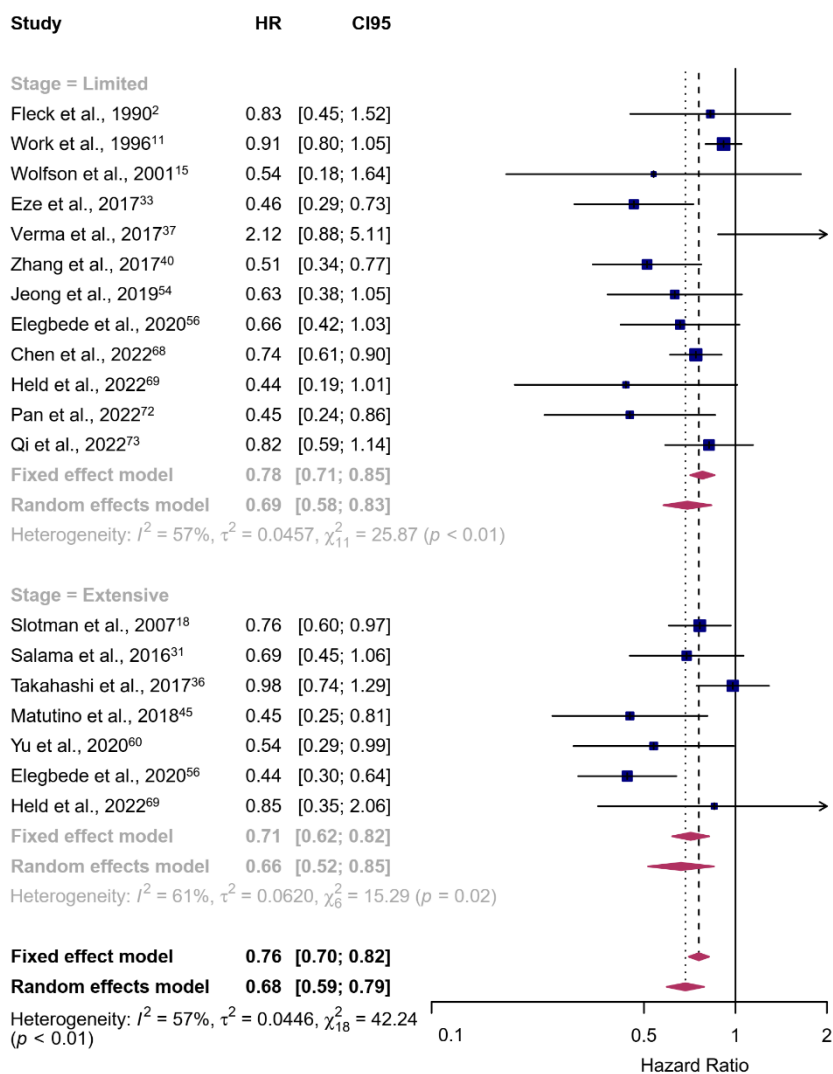




**Supplementary Figure 3.** Forest plot showing mean difference of overall survival time.

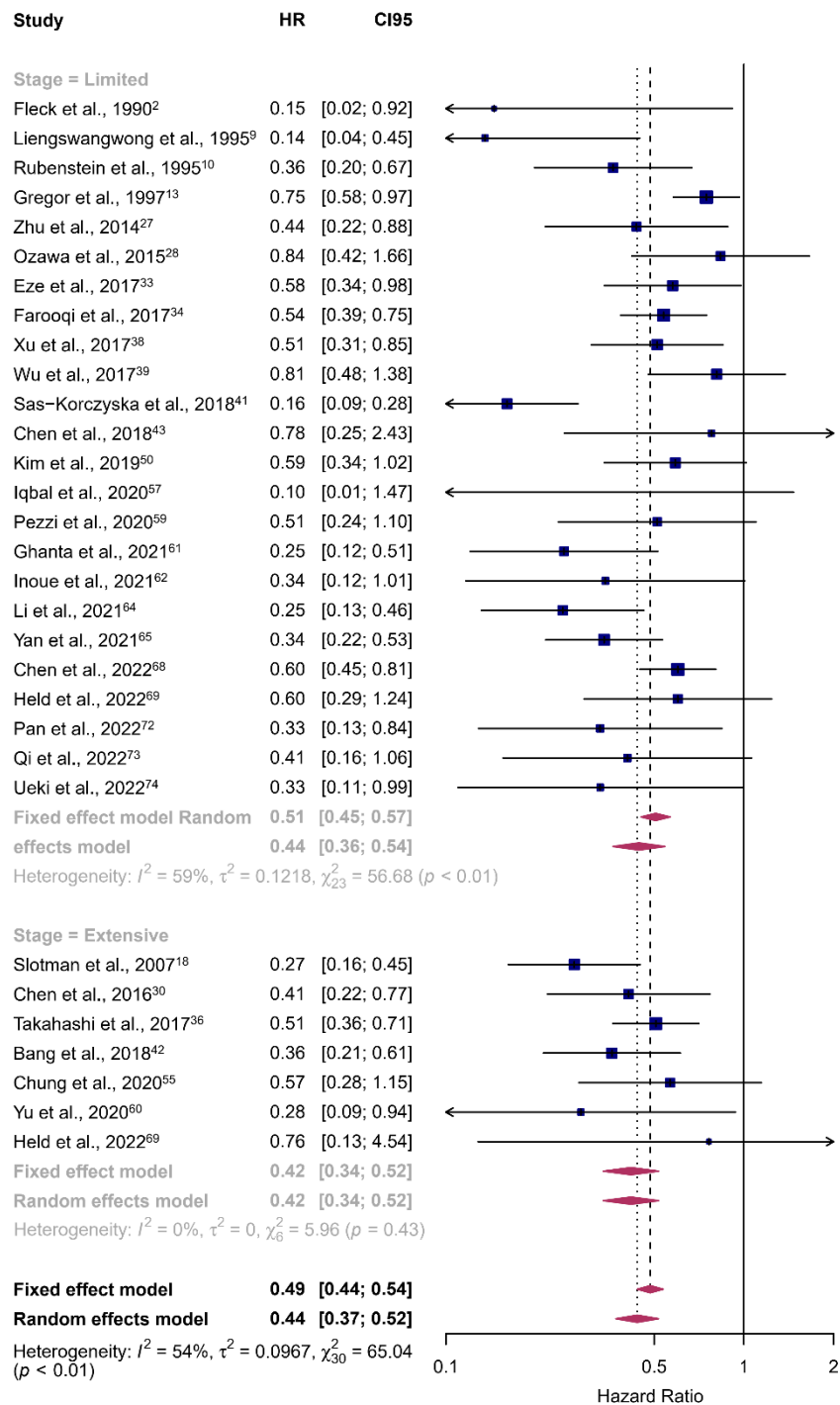


**Supplementary Figure 4.** Forest plot of the pooled HR on the effect of PCI on PFS in patients with E-and L-SCLC.

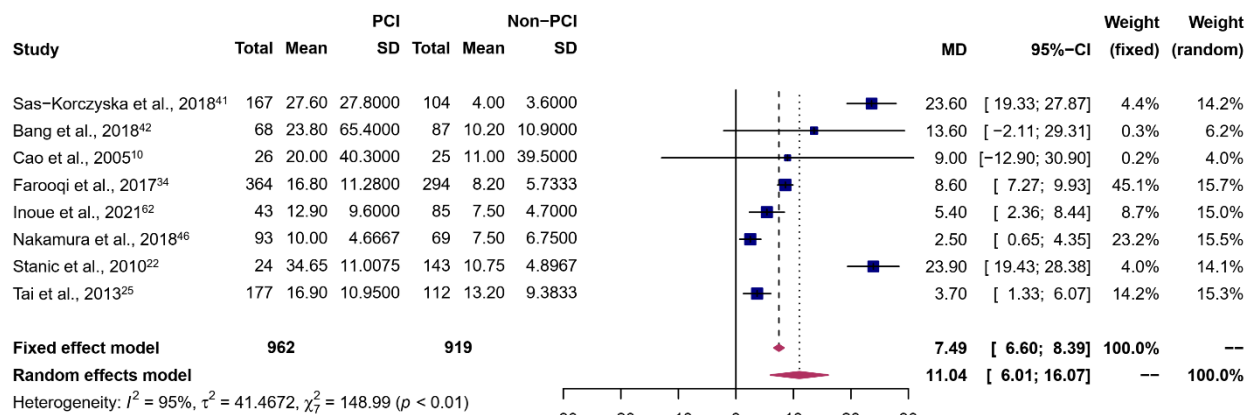




**Supplementary Figure 5.** Forest plot of the pooled HR on the effect of PCI on BMFS in patients with E-and L-SCLC.



**Supplementary Figure 6.** Forest plot showing mean difference of time to brain metastases.



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