

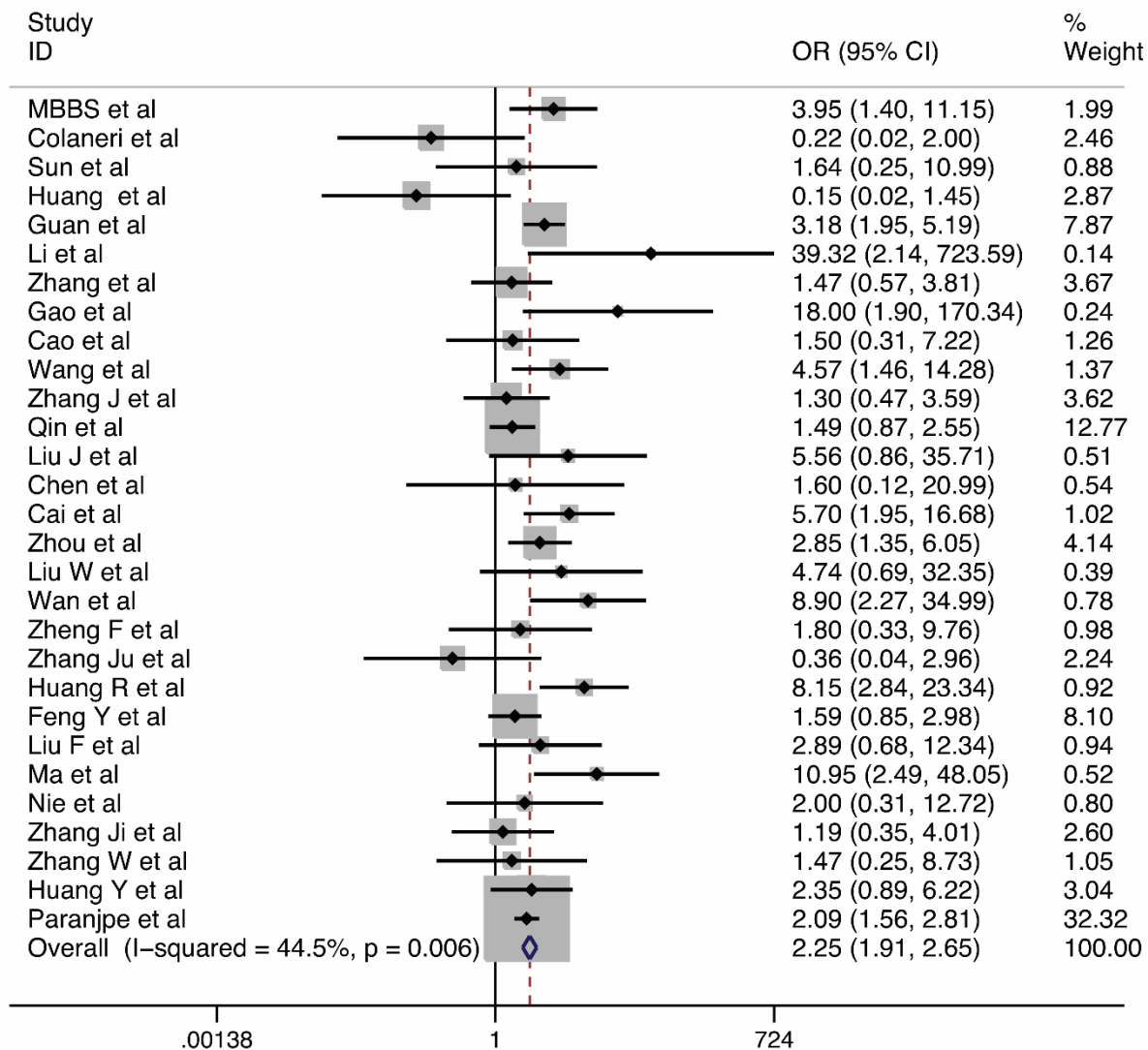
## **Multi-organ Dysfunction in Patients with COVID-19: A Systematic Review and Meta-analysis**

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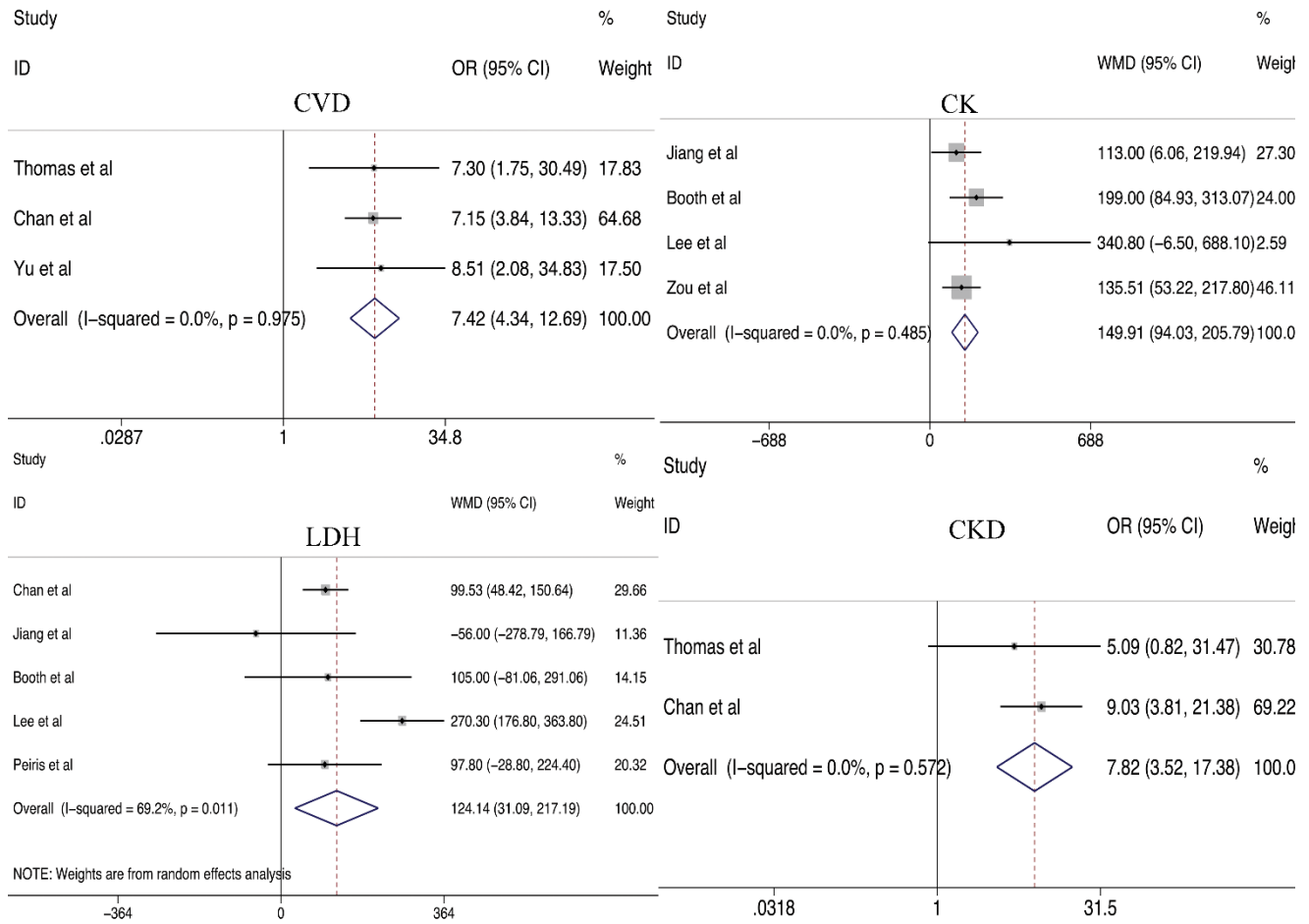
# SUPPLEMENTARY DATA

## Diabetes



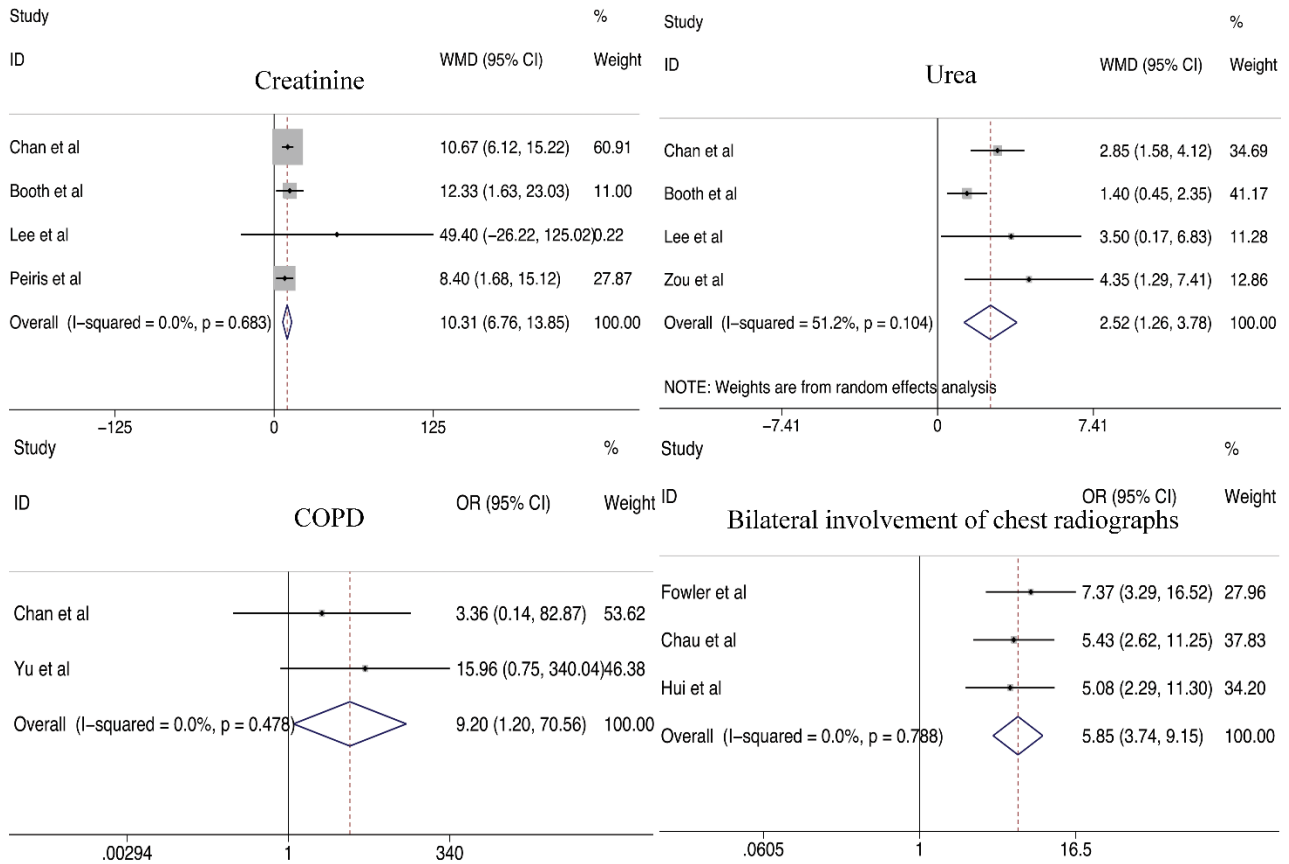
Supplementary Figure 1. Relationship between diabetes and COVID-19 severity.

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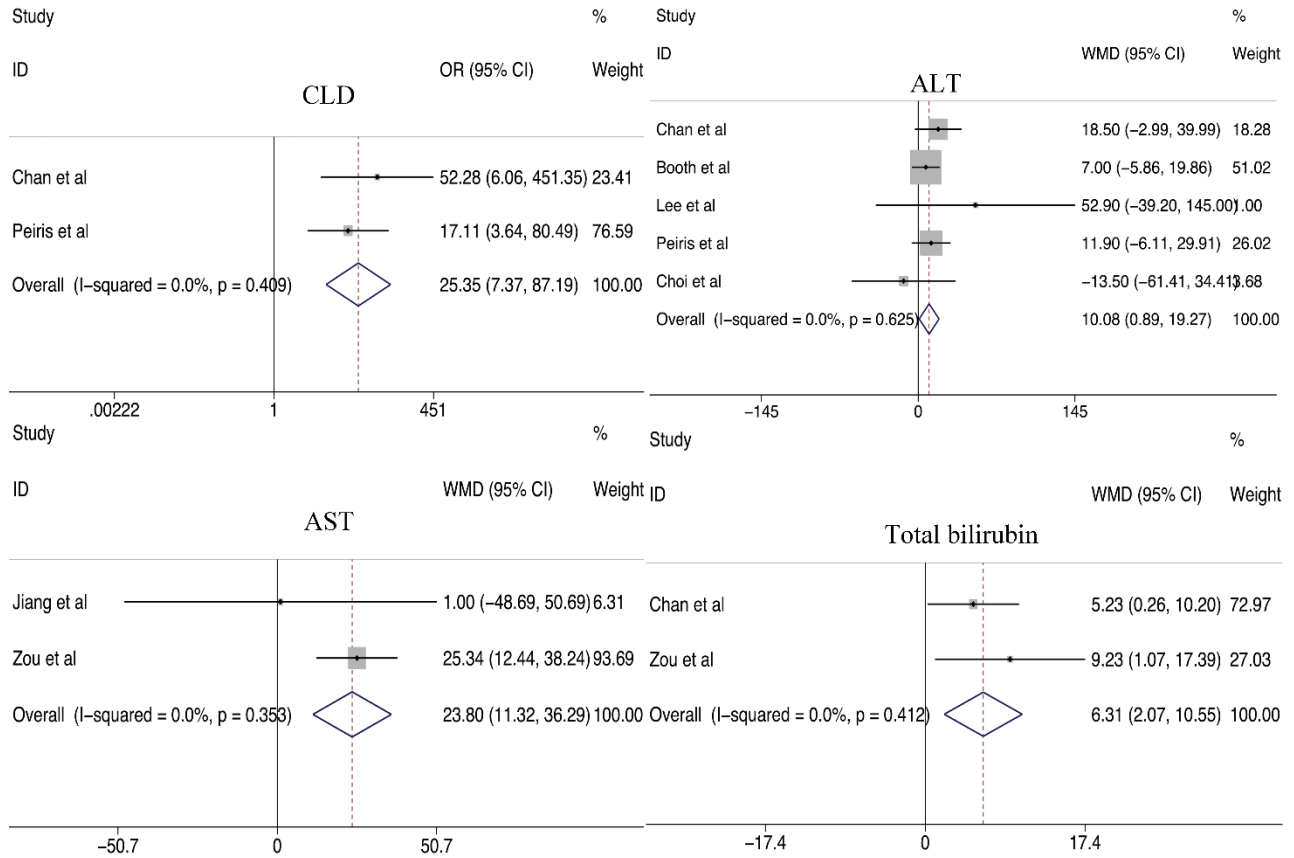
**Supplementary Figure 2.** Relationship between organ dysfunction (CVD, CK, LDH and CK) and SARS severity.

# SUPPLEMENTARY DATA



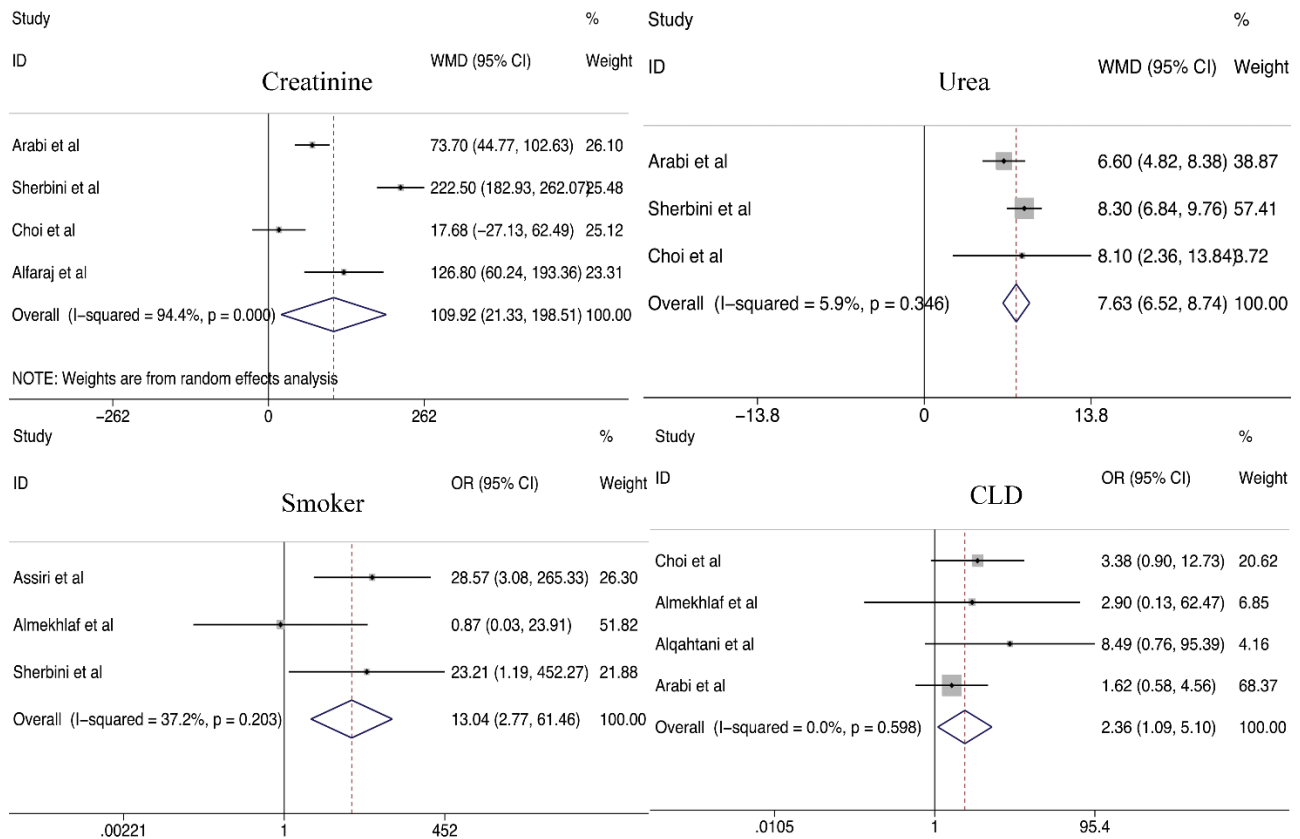
**Supplementary Figure 3.** Relationship between organ dysfunction (Creatinine, Urea, COPD and Bilateral involvement of chest radiographs) and SARS severity.

# SUPPLEMENTARY DATA



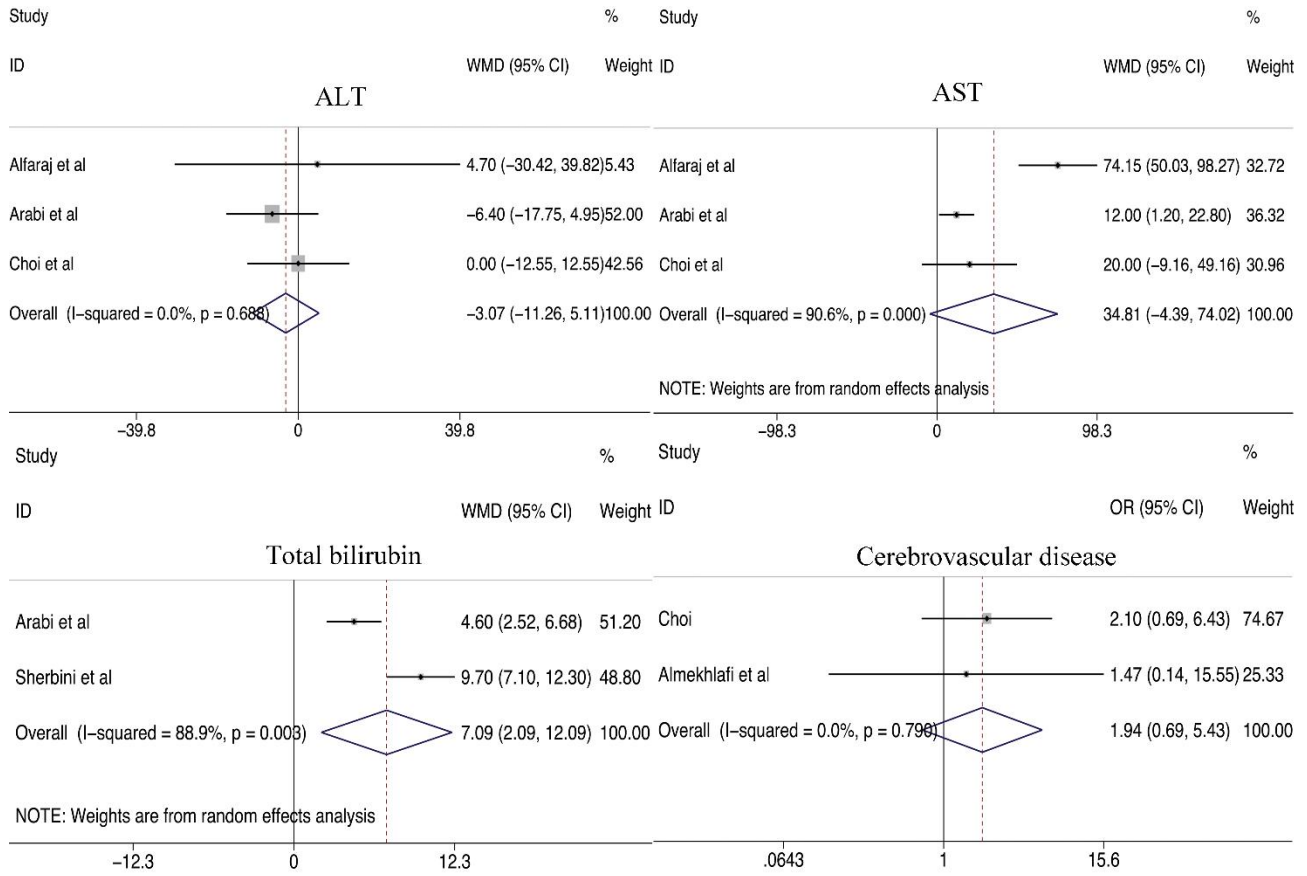
**Supplementary Figure 4.** Relationship between organ dysfunction (CLD, ALT, AST and Total bilirubin) and SARS severity.

# SUPPLEMENTARY DATA



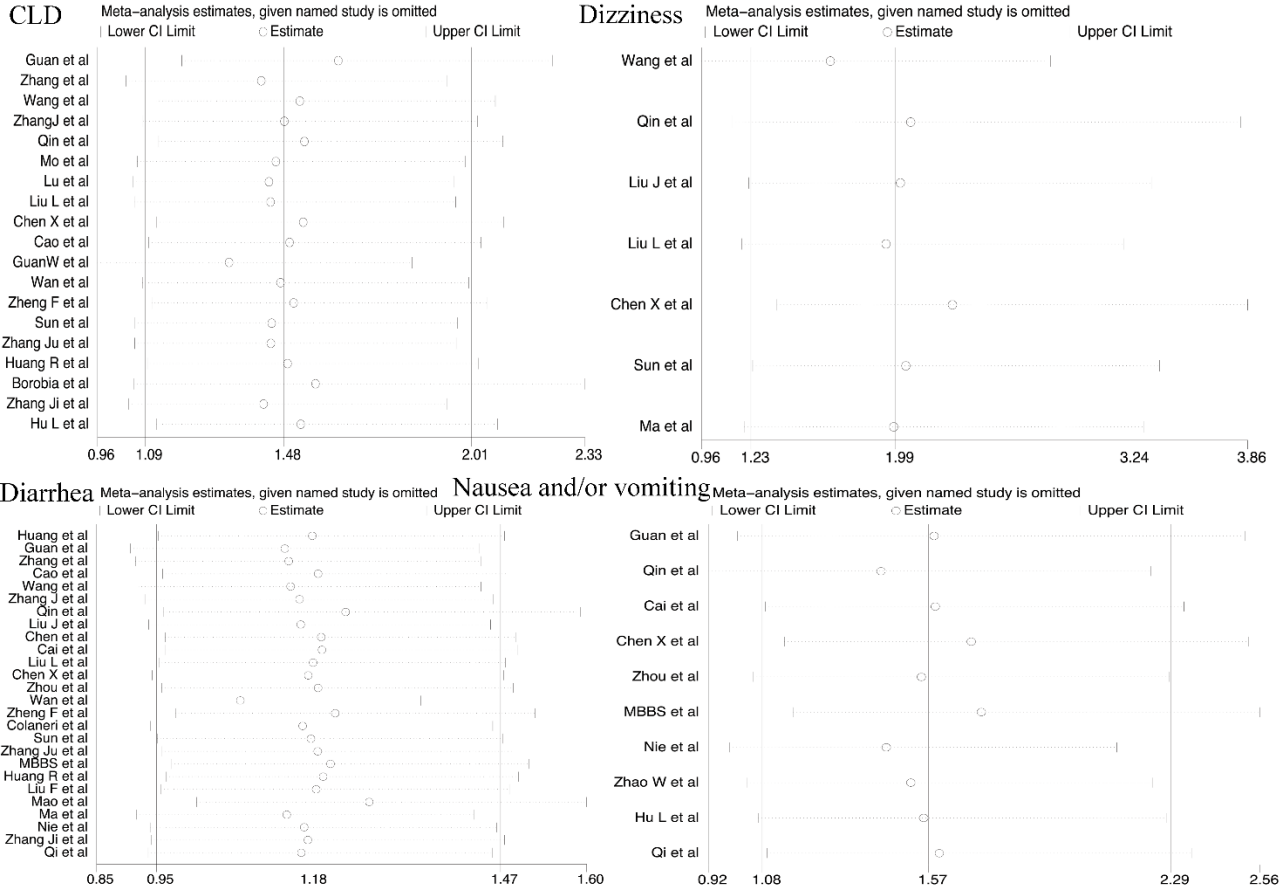
**Supplementary Figure 5.** Relationship between organ dysfunction (Creatinine, Urea, Smoker and CLD) and MERS severity.

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**Supplementary Figure 6.** Relationship between organ dysfunction (ALT, AST, Total bilirubin and Cerebrovascular disease) and MERS severity.

# SUPPLEMENTARY DATA



Supplementary Figure 7. Sensitivity analysis of outcomes: CLD, Dizziness, Nausea and/or vomiting and Diarrhea.



# SUPPLEMENTARY DATA

**Supplementary Table 1.** Characteristics of included studies.

First author	Date	Country	Patients (N)	Average Age	Sex Male (%)	Research Type	Clinical symptoms	Quality
<i>Huang et al</i> <sup>8</sup>	Dec 16 <sup>th</sup> 2019-Jan 2 <sup>nd</sup> 2020	China	41	49.0	73.0	Retrospective study	Fever 98% / Cough 76% Dyspnoea 55% Myalgia/fatigue 44%	High
<i>Zhao et al</i> <sup>15</sup>		China	101	44.44	55.4	Retrospective study	Fever 78.2% / Cough 62.4% Myalgia or fatigue 16.8% Sore throat 11.9% / Dyspnea 1.0%	Moderate
<i>Xu et al</i> <sup>16</sup>	Jan-Feb 2020	China	50	43.9	58	Retrospective study	Fever 86% / Cough 40% Fatigue 16% / Muscle ache 16% Expectoration 14%	High
<i>Guan et al</i> <sup>17</sup>	Dec 11 <sup>th</sup> 2019- Jan 29 <sup>th</sup> 2020	China	1099	47	58.1	Retrospective study	Fever 88.7% / Cough 67.8% Fatigue 38.1% Sputum production 33.7% Shortness of breath 18.7%	High
<i>Liu et al</i> <sup>11</sup>	Jan 21 <sup>st</sup> - Feb 3 <sup>rd</sup> 2020	China	73	41.6	56.2	Retrospective study	Fever 93 % / Cough 82% Fatigue 75 % / Anorexia 27 % Sputum production 53%	High
<i>Li et al</i> <sup>18</sup>	Jan-Feb 2020	China	83	45.5	53.0	Retrospective study	Fever 86.7% / Cough 78.3% Expectoration 18.1% Myalgia 18.1% / Headache 10.8%	High
<i>Wu et al</i> <sup>40</sup>	Jan 22 <sup>th</sup> - Feb 14 <sup>th</sup> 2020	China	80	46.1	48.75	Retrospective study	Fever 78.75% / Cough 63.75% Shortness of breath 37.50% Muscle ache 22.50% Headache/mental disorder 16.25%	High
<i>Qu et al</i> <sup>14</sup>	Jan-Feb 2020	China	30	50.5	53.3	Retrospective study		Moderate
<i>Zheng et al</i> <sup>20</sup>		China	103	44.39	53.4	Retrospective study		Moderate
<i>Qian et al</i> <sup>19</sup>	Jan-Feb 2020	China	91	50	40.66	Retrospective study	Fever 71.43% / Cough 60.44% Fatigue 43.96% /Anorexia 25.27% Expectoration 32.97%	Moderate
<i>Zhang et al</i> <sup>20</sup>	Jan 2 <sup>nd</sup> -Feb 10 <sup>th</sup> 2020	China	221	55	48.9	Retrospective study	Fever 90.5% / Fatigue 70.6% Cough 61.5% / Anorexia 36.2% Dyspnea 29.0%	High
<i>Qin et al</i> <sup>25</sup>	Jan 10 <sup>th</sup> - Feb 12 <sup>th</sup> 2020	China	452	58	52.0	Retrospective study	Fever 92.6% Shortness of breath 50.8% Expectoration 41.4% Fatigue 46.4%/Dry cough 33.3%	Moderate
<i>Tabata et al</i> <sup>22</sup>	Feb 11 <sup>th</sup> - Feb 25 <sup>th</sup> 2020	Japan	104	68	45.2	Retrospective study	Fever 34.6% / Cough 41.3% Malaise 21.2% Tachypnea 23.1% Runny nose 24.0%	Moderate
<i>Cao et al</i> <sup>23</sup>	Jan 20 <sup>th</sup> - Feb 15 <sup>th</sup> 2020	China	198	50.1	51.0	Retrospective study	Fever 86.9% / Cough 50.0% Sputum production 27.8% Myalgia or fatigue 29.8%	High

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							Headache or Dizziness 12.1%	
<i>Wang et al</i> <sup>12</sup>	Jan 1 <sup>st</sup> -Jan 28 <sup>th</sup> 2020	China	138	56	54.3	Retrospective study	Fever 98.6% / Fatigue 69.6% Dry cough 59.4%/Myalgia 34.8% Anorexia 39.9%	High
<i>Zhang J et al</i> <sup>24</sup>	Jan 16 <sup>th</sup> -Feb 3 <sup>rd</sup> 2020	China	140	57	50.7	Retrospective study	Fever 91.7% / Cough 75.0% Fatigue 75.0% Gastrointestinal symptoms 39.6%	High
<i>Chen X et al</i> <sup>33</sup>	Jan 23 <sup>rd</sup> - Feb 14 <sup>th</sup> 2020	China	291	46	49.8	Retrospective study	Fever 68.7% / Cough 60.5% Fatigue 31.6% / Myalgia 9.3% Headache 6.9%	High
<i>Mo et al</i> <sup>26</sup>	Jan 1 <sup>st</sup> - Feb 5 <sup>th</sup> 2020	China	155	54	55.5	Retrospective study	Fever 81.3%/ Cough 62.6% Chest distress 39.4% Fatigue 73.2% Myalgia or arthralgia 61.0%	High
<i>Liu J et al</i> <sup>27</sup>	Jan 5 <sup>th</sup> - Jan 24 <sup>th</sup> 2020	China	40	48.7	37.5	Retrospective study	Fever 90.0% / Cough 82.5% Sputum production 52.5% Chill 25% / Fatigue 55% Fever 100% / Cough 80%	Moderate
<i>Chen et al</i> <sup>28</sup>	Dec 19 <sup>th</sup> 2019-Jan 27 <sup>th</sup> 2020	China	21	56.3	81.0	Retrospective study	Fatigue 85% / Myalgia 40% Sputum production 25% Fever 64.4% / Cough 18.1%	High
<i>Cai et al</i> <sup>29</sup>	Jan 11 <sup>th</sup> - Feb 6 <sup>th</sup> 2020	China	298	47	50	Retrospective study	Fatigue 2.0% / Headache 1.3% Diarrhea 2.0% Fever 90.9% / Fatigue 25.3%	High
<i>Lu et al</i> <sup>31</sup>	Before Feb 7 <sup>th</sup> 2020	China	265			Retrospective study	Cough 49.4%/ Inappetence 11.7% Expectoration 23.0% Fever 84.3% / Cough 74.5%	Moderate
<i>Lie L et al</i> <sup>32</sup>	Jan 20 <sup>th</sup> - Feb 3 <sup>rd</sup> 2020	China	51	45	62.7	Retrospective study	Fatigue 43.1% / Dyspnea 21.6% Muscular soreness 11.8%	High
<i>Gao et al</i> <sup>21</sup>	Jan 23 <sup>rd</sup> -Feb 2 <sup>nd</sup> 2020	China	43	43.74	60.47	Retrospective study		Moderate
<i>Liu W et al</i> <sup>41</sup>	Dec 30 <sup>th</sup> 2019- Jan 15 <sup>th</sup> 2020	China	78	38	50	Retrospective study	Cough 43.6%	Moderate
<i>Zhang Y et al</i> <sup>44</sup>	Up to Feb 11 <sup>th</sup> 2020	China	44672		51.4	Retrospective study		Moderate
<i>Guan W et al</i> <sup>42</sup>	Dec 30 <sup>th</sup> 2019- Jan 31 <sup>st</sup> 2020	China	1590	48.9	57.3	Retrospective study	Fever 88% Coughing 70.2% Fatigue 42.8% productive cough 36% Fever 76.5% / Cough 58.4%	High
<i>Yang et al</i> <sup>34</sup>	Jan 17 <sup>th</sup> - Feb 10 <sup>th</sup> 2020	China	149	45.11	54.4	Retrospective study	Expectoration 32.2% Sore throat 14.09% / Chill 14.09%	High
<i>Chen N et al</i> <sup>35</sup>	Jan 1 <sup>st</sup> - Jan 20 <sup>th</sup> 2020	China	99	55.5	67.7	Retrospective study	Fever 83% / Cough 82% Shortness of breath 31% Muscle ache 11% / Confusion 9%	High
<i>Xu X et al</i> <sup>36</sup>	Jan 10 <sup>th</sup> - Jan 26 <sup>th</sup> - 2020	China	62	41	56	Retrospective study	Fever 77%/ Myalgia/fatigue 52% Cough 81% / Expectoration 56%	Moderate

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<i>Shi et al</i> <sup>37</sup>	Dec 20 <sup>th</sup> 2019-Jan 23 <sup>rd</sup> 2020	China	81	49.5	52	Retrospective study	Headache 34% Fever 73% / Dyspnoea 42% Cough 59% / Rhinorrhea 26% Chest tightness 22%	Moderate
<i>Zhou et al</i> <sup>38</sup>	Dec 29 <sup>th</sup> 2019- Jan 31 <sup>st</sup> 2020	China	191	56	62	Retrospective study	Fever 94% / Cough 79% Sputum 23% / Myalgia 15% Fatigue 23%	High
<i>Liu K et al</i> <sup>39</sup>	Dec 30 <sup>th</sup> 2019- Jan 24 <sup>th</sup> 2020	China	137	57	44.5	Retrospective study	Fever 81.8% / Coughing 48.2% Muscle pain or fatigue 32.1% Dyspnea 19.0% / Headache 9.5%	Moderate
<i>Wan et al</i> <sup>45</sup>	Jan 23 <sup>th</sup> -Feb 8 <sup>th</sup> 2020	China	135	46	53.3	Retrospective study	Fever 88.9% Cough 76.5% myalgia or fatigue 32.5% Headache 17.7%	High
<i>Zhao W et al</i> <sup>48</sup>	Jan 21 <sup>st</sup> -Feb 8 <sup>th</sup> 2020	China	77	52	44.2	Retrospective study	Fever 85.7% /Cough 63.7% Fatigue 27.3% Shortness of breath 20.8% Headache or dizziness 13.0%	Moderate
<i>YangYet et al</i> <sup>43</sup>	Up to Jan 26 <sup>th</sup> 2020	China	4021	49	55	Retrospective study		Moderate
<i>Ma et al</i> <sup>49</sup>	Jan 21 <sup>st</sup> - Mar2 <sup>nd</sup> 2020	China	84	48	57.1	Retrospective study	Fever 64.3% /Cough 51.2% Expectoration 33.3% Fatigue 19.0%/Anorexia 16.7%	Moderate
<i>Nie et al</i> <sup>50</sup>	9 <sup>th</sup> – 28 <sup>th</sup> Feb 2020	China	97	39	35.1	Retrospective study	Fever 58.8% /Cough 55.7% Fatigue 33% / Diarrhea 12.45% Sputum production 15.5%	High
<i>Xu Xi et al</i> <sup>46</sup>	Jan 23 <sup>th</sup> -Feb 4 <sup>th</sup> 2020	China	90	50	44.5	Retrospective study	Fever 78% / Coughing 63% Fatigue 21%/Myalgia 28% Sore throat 26%	Moderate
<i>Qi et al</i> <sup>47</sup>	Jan 19 <sup>th</sup> - Feb 16 <sup>th</sup> 2020	China	267	48	55.8	Retrospective study	Fever 84.3%/ Cough 70.8% Fatigue 77.8%/ Dyspnea 16.2% Nasal congestion 19.9%	High
<i>Hu L et al</i> <sup>51</sup>	Jan 8 <sup>th</sup> - Feb 20 <sup>th</sup> 2020	China	323	61	51.4	Retrospective study	Fever 83.9% Cough50.8% Dyspnea 4.3% /Chest distress 0.9% Headache 0.9%	High
<i>Levinson et al</i> <sup>53</sup>	Mar 10 <sup>th</sup> - 23 <sup>rd</sup> 2020	Israel	42	34	44.2	Retrospective study	Cough 69% /Fatigue 69% Myalgia or arthralgia 57% Headache 48% /Dyspnea 43%	Moderate
<i>Petrilli et al</i> <sup>52</sup>	Mar 1 <sup>st</sup> -Apr 2 <sup>nd</sup> 2020	United States	4103			Retrospective study		High
<i>Huang Y et al</i> <sup>54</sup>	Jan 1 <sup>st</sup> -Mar 8 <sup>th</sup> 2020	China	223	62.0	56.5	Retrospective study	Fever 78.9% /Cough 69.1% Fatigue 56.5%/Diarrhea 6.7% Rhinitis 38.3% Cough 35.4%	Moderate
<i>Fontanet et al</i> <sup>55</sup>	Mar 30 <sup>th</sup> - 4 <sup>th</sup> Apr 2020	France	661	37	38.0	Retrospective study	Headache 30.9% /Asthenia 29.6% Sore throat 26.8%	Moderate
<i>Paranjpe et al</i> <sup>56</sup>	Feb 27 <sup>th</sup> - Apr 2 <sup>nd</sup> 2020	United States	2199	65	58.8	Retrospective study		Moderate

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<i>Buscarini et al</i> <sup>57</sup>	Feb 21 <sup>st</sup> - Mar 13 <sup>th</sup> 2020	Italy	411		67.6	Retrospective study		Moderate
<i>Docherty et al</i> <sup>58</sup>	Feb 6 <sup>th</sup> - Apr 18 <sup>th</sup> 2020	United Kingdom	16749	72		Prospective study	Cough 70% /Fever 69% Shortness of breath 65% Fever 71.2% /Cough 61.7%	Moderate
<i>Borobia et al</i> <sup>59</sup>	Feb 25 <sup>th</sup> - Apr 19 <sup>th</sup> 2020	Spain	2226	61	48.2	Retrospective study	Dyspnea 49.8% /Myalgia 26.8% Diarrhea 21.7%	Moderate
<i>Cabaraux Lechien et al</i> <sup>60</sup>		France	86	41.7	34.9	Prospective study		High
<i>Zhang Ji et al</i>	Feb 1 <sup>st</sup> and Mar 15 <sup>th</sup> 2020	China	135	56	49.6	Retrospective study	Cough 100% /Fever 94.8% Fatigue 60.7% /Chest pain 34.1% Diarrhea 23.7%	Moderate
<i>Ji Wo et al</i> <sup>61</sup>	- Apr 8 <sup>th</sup> 2020	South Korea	65149	44	48.3	Retrospective study		Moderate
<i>Zheng F et al</i> <sup>63</sup>	Jan 17 <sup>th</sup> - Feb 7 <sup>th</sup> 2020	China	161	45	49.7	Retrospective study	Fever 75.8% /Cough 62.7% Fatigue 39.8% /Dyspnea 14.3% Muscle ache 11.2%	Moderate
<i>Wang Z et al</i> <sup>64</sup>	Jan 16 <sup>th</sup> - Jan 29 <sup>th</sup> 2020	China	69	42	46	Retrospective study	Fever 87% /Cough 55% Fatigue 42% /Myalgia 30% Sputum production 29%	Moderate
<i>Corbellini et al</i> <sup>67</sup>	23 <sup>rd</sup> - 25 <sup>th</sup> Mar 2020	Spain	111	61.4	60.4	Prospective study		Moderate
<i>Giacomelli et al</i> <sup>65</sup>	Mar 19 <sup>th</sup> 2020	Italy	59	60	67.8	Prospective study	Fever 72.8% /Cough 37.3% olfactory and/or taste disorders 33.9% Dyspnea 25.4%	Low
<i>Luers et al</i> <sup>66</sup>	22 <sup>th</sup> - 28 <sup>th</sup> Mar 2020	Germany	72	38	56.9	Retrospective study	Headache 77.8% / Sore Throat 62.5% Reduced olfaction 73.6% Muscle aches 70.8% /Cough 75%	Moderate
<i>Lu Lu et al</i> <sup>68</sup>	Jan 18 <sup>th</sup> - Feb 18 <sup>th</sup> 2020	China	304	44	59.9	Retrospective study		Moderate
<i>Colaneri et al</i> <sup>69</sup>	21 <sup>th</sup> - 28 <sup>th</sup> Feb 2020	Italy	44	/	63.6	Retrospective study		Moderate
<i>Vaira et al</i> <sup>70</sup>	Mar 31 <sup>st</sup> - Apr 6 <sup>th</sup> 2020	Italy	72	49.2	37.5	Prospective study	Fever 95.8% Cough 83.3% Asthenia 66.7%/Sore throat 51.4% Headache 41.6%	High
<i>Mao et al</i> <sup>71</sup>	Jan 16 <sup>th</sup> -Feb 19 <sup>th</sup> 2020	China	214	52.7	40.7	Retrospective study	Fever 61.7% Cough 60.0% Anorexia 31.8% /Diarrhea 19.2% Throat pain 14.5%	High
<i>Sun et al</i> <sup>72</sup>	Jan 20 <sup>th</sup> -Feb 15 <sup>th</sup> 2020	China	55	44	56.4	Retrospective study	Fever 81.8% Cough 47.3% Fatigue 25.5% /Expectoration 23.6% White sputum 16.4% Headache 70.3%/Loss of smell 70.2%	Moderate
<i>Lechien et al</i> <sup>73</sup>	Mar 22 <sup>nd</sup> - Apr 10 <sup>th</sup> 2020	France, Italy, Spain, Belgium, Switzerland	1566	39.17	32.3	Retrospective study	Nasal obstruction 67.8% Cough 63.2% Asthenia 63.3%	Moderate
<i>Zhang Ya et al</i> <sup>74</sup>	Jan 18 <sup>th</sup> - Feb 22 <sup>nd</sup> 2020	China	115	49.52	42.6	Retrospective study		Moderate
<i>Zheng Y et al</i> <sup>75</sup>	Jan 16 <sup>th</sup> - Feb 20 <sup>th</sup> 2020	China	99	49	52	Retrospective study		Moderate
<i>Wang R et al</i> <sup>76</sup>	Jan 20 <sup>th</sup> - Feb 9 <sup>th</sup> 2020	China	125	38.76	56.8	Retrospective study	Fever 92.8% /Cough 81.6% Shortness of breath 45.6% Sputum production 41.6%	High

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<i>Zhang Ju et al</i> <sup>77</sup>	Jan 13 <sup>th</sup> -Feb 16 <sup>th</sup> 2020	China	111	38	41.4	Retrospective study	Fever 71.2% Cough 37.8% Fatigue 18.0% /Dyspnea 16.2% Chest pain 10.8%	High
<i>Redd et al</i> <sup>78</sup>	on or before Apr 2 <sup>nd</sup> 2020	United States	318	63.4	54.7	Retrospective study	Fever 81.3% Fatigue 57.5% Myalgia 38.7% /Anorexia 34.8% Diarrhea 33.7%	Moderate
<i>Tomlins MBBS et al</i> <sup>79</sup>	10 <sup>th</sup> -30 <sup>th</sup> Mar 2020	United Kingdom	95	75	63	Retrospective study	Fever 72% /Cough 74% Shortness of breath 43% Confusion 21%/Myalgia 14%	Moderate
<i>Huang R et al</i> <sup>80</sup>	Jan 22 <sup>nd</sup> – Feb 10 <sup>th</sup> 2020	China	202	44	57.4	Retrospective study	Fever 77.2% Cough 59.4% Fatigue 21.8% /Sore throat 11.9% Muscle ache 10.4%	Moderate
<i>Feng Y et al</i> <sup>81</sup>	Jan 1 <sup>st</sup> - Feb 15 <sup>th</sup> 2020	China	476	53	56.9	Retrospective study	Fever 85.9% /Dry cough 59.4% Sputum production 35.5% Shortness of breath 24.4% Myalgia 12.6%	High
<i>Menni et al</i> <sup>82</sup>		United States United Kingdom	18401			Prospective study		Moderate
<i>Liu F et al</i> <sup>83</sup>	Jan 20 <sup>th</sup> -Feb 3 <sup>rd</sup> 2020.	China	134	51.5	47	Retrospective study	Fever 81.3% /Cough 39.6% Fatigue 19.4%/Poor appetite 9.7% Sputum production 17.9% Poor appetite 9.7%	High

**Supplementary Table 2.** Publication bias of indicators of multiorgan function and COVID-19 severity.

	Begg	Egger		Begg	Egger
Hypertension	0.195	1.479	CVD	0.116	0.117
Diabetes	0.896	0.551	CK	0.775	0.509
LDH	0.373	0.225	ALT	0.263	0.266
AST	0.902	0.911	Total bilirubin	0.300	0.899
Creatinine	0.661	0.719	Urea	0.474	0.430
ARDS	0.548	0.494	ACI	1.00	0.223
AKI	0.466	0.361	Smoker	0.152	0.268
COPD	0.65	0.009	CKD	0.075	0.006
Bilateral involvement of chest radiographs	0.101	0.120	CLD	0.234	0.561
Cerebrovascular disease	0.274	0.359	Headache	0.01	0.047
Anorexia	0.764	0.812	Dizziness	0.368	0.554
Abdominal pain	0.368	0.834	Diarrhea	0.537	0.629
Nausea and/or vomiting	0.371	0.909			