INTERVAL ESTIMATION FOR OPERATING CHARACTERISTIC OF CONTINUOUS BIOMARKERS WITH CONTROLLED SENSITIVITY OR SPECIFICITY

Yijian Huang[1], Isaac Parakati[2],

Dattatraya H. Patil[1], and Martin G. Sanda[1]

[1]*Emory University*

and [2]*Ann & Robert H. Lurie Children's Hospital of Chicago*

Supplementary Material

Additional simulations, with unequal case and control sizes, were conducted; other features of the setups were the same as those in the main paper. For the single-biomarker evaluation, Figures S.1 and S.2 show the results when $n_\bullet = n_\circ/2$, whereas Figures S.3 and S.4 pertain to the situations with $n_\bullet = n_\circ \times 2$. Both sets are counterparts of Figures 1 and 2 in the main paper. For the two-biomarker comparison, Table S.1 reports situations with both $n_\bullet = n_\circ/2$ and $n_\bullet = n_\circ \times 2$, in parallel to Table 1 in the main paper.

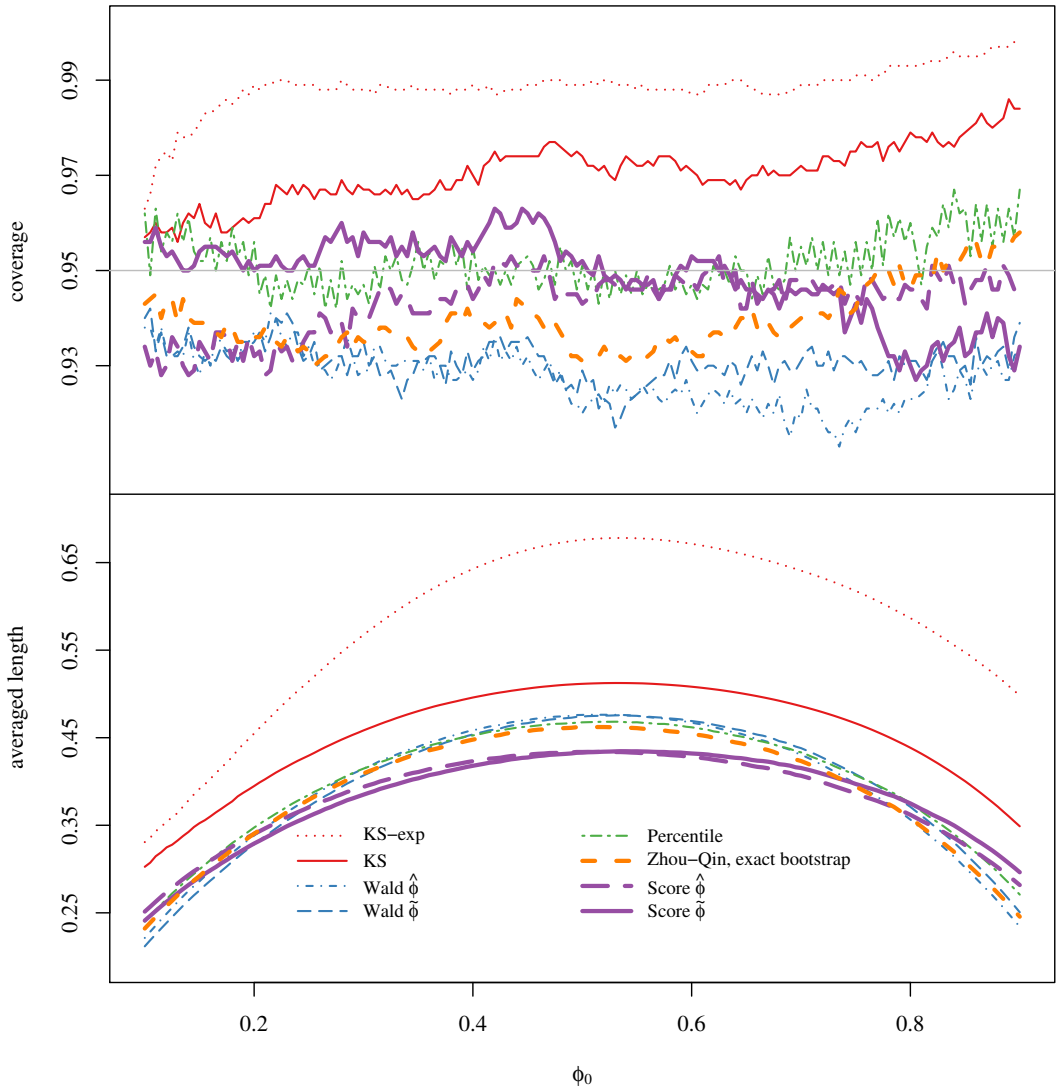

Figure S.1: Simulation summaries of 95% confidence intervals for specificity at controlled 95% sensitivity in the single-biomarker evaluation, under fixed sizes, $n_\bullet = 50$ and $n_\circ = 100$, and variable ϕ_0. KS is the kernel smoothing-based Wald confidence intervals, as in Pepe (2003), whereas KS-exp corresponds to the KS applied to exponentially transformed biomarker data.

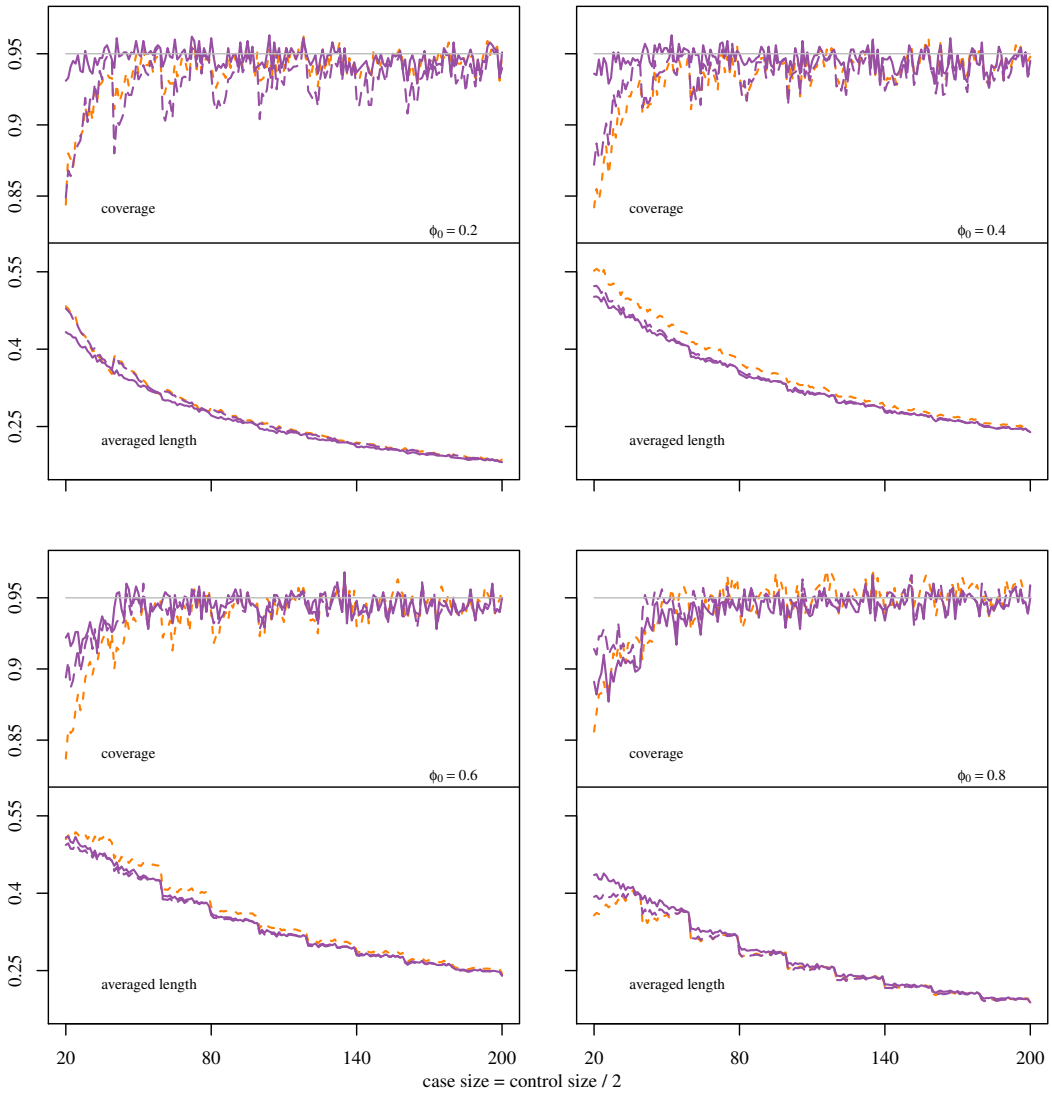

Figure S.2: Simulation summaries of 95% confidence intervals for specificity at controlled 95% sensitivity in the single-biomarker evaluation, under fixed ϕ_0 and variable sizes $n_\bullet = n_\circ/2$. Score intervals, based on $\widehat{\phi}$ and $\widetilde{\phi}$, and the exact bootstrap-based Zhou–Qin are included, with the same labeling as in Figure S.1.

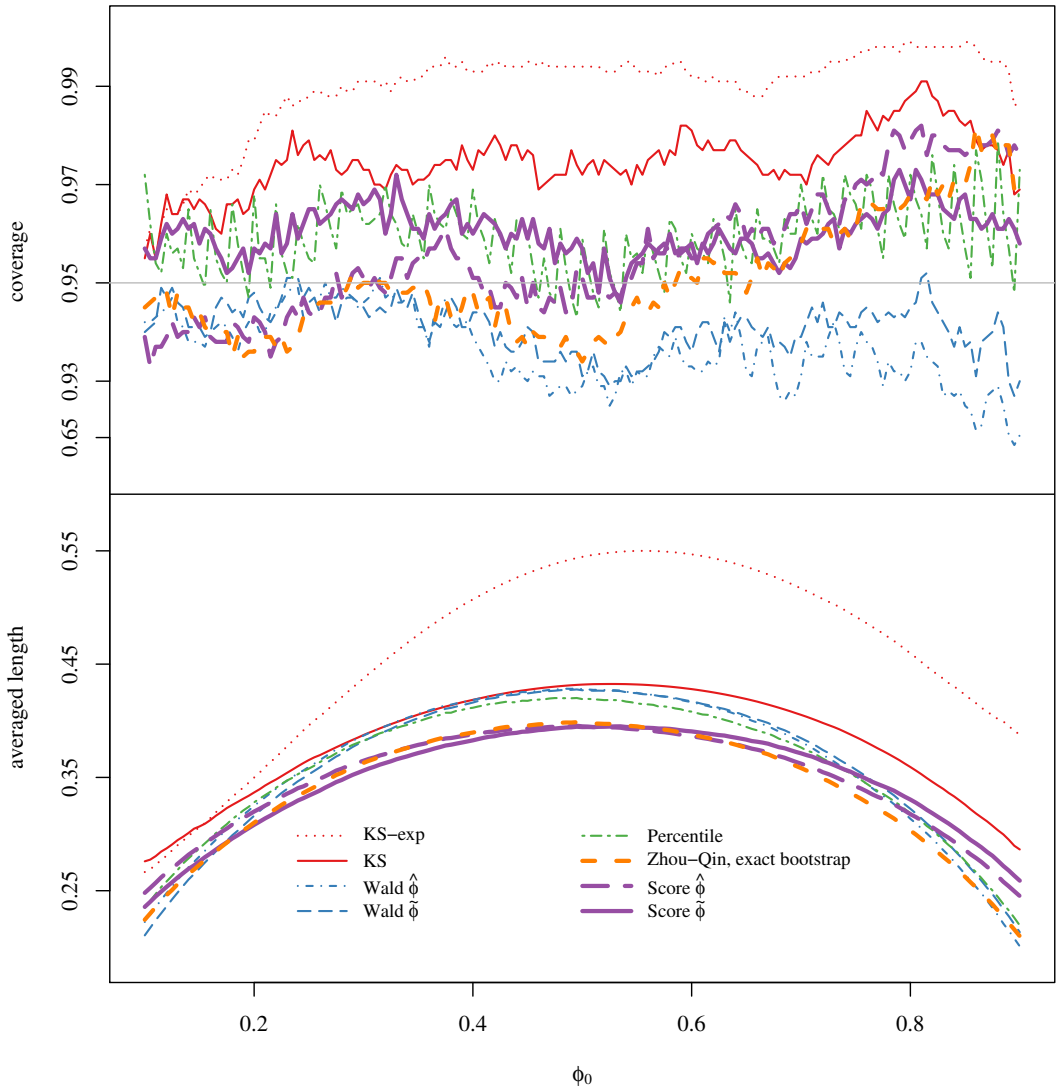

Figure S.3: Simulation summaries of 95% confidence intervals for specificity at controlled 95% sensitivity in the single-biomarker evaluation, under fixed sizes, $n_\bullet = 100$ and $n_\circ = 50$, and variable ϕ_0. KS is the kernel smoothing-based Wald confidence intervals, as in Pepe (2003), whereas KS-exp corresponds to the KS applied to exponentially transformed biomarker data.

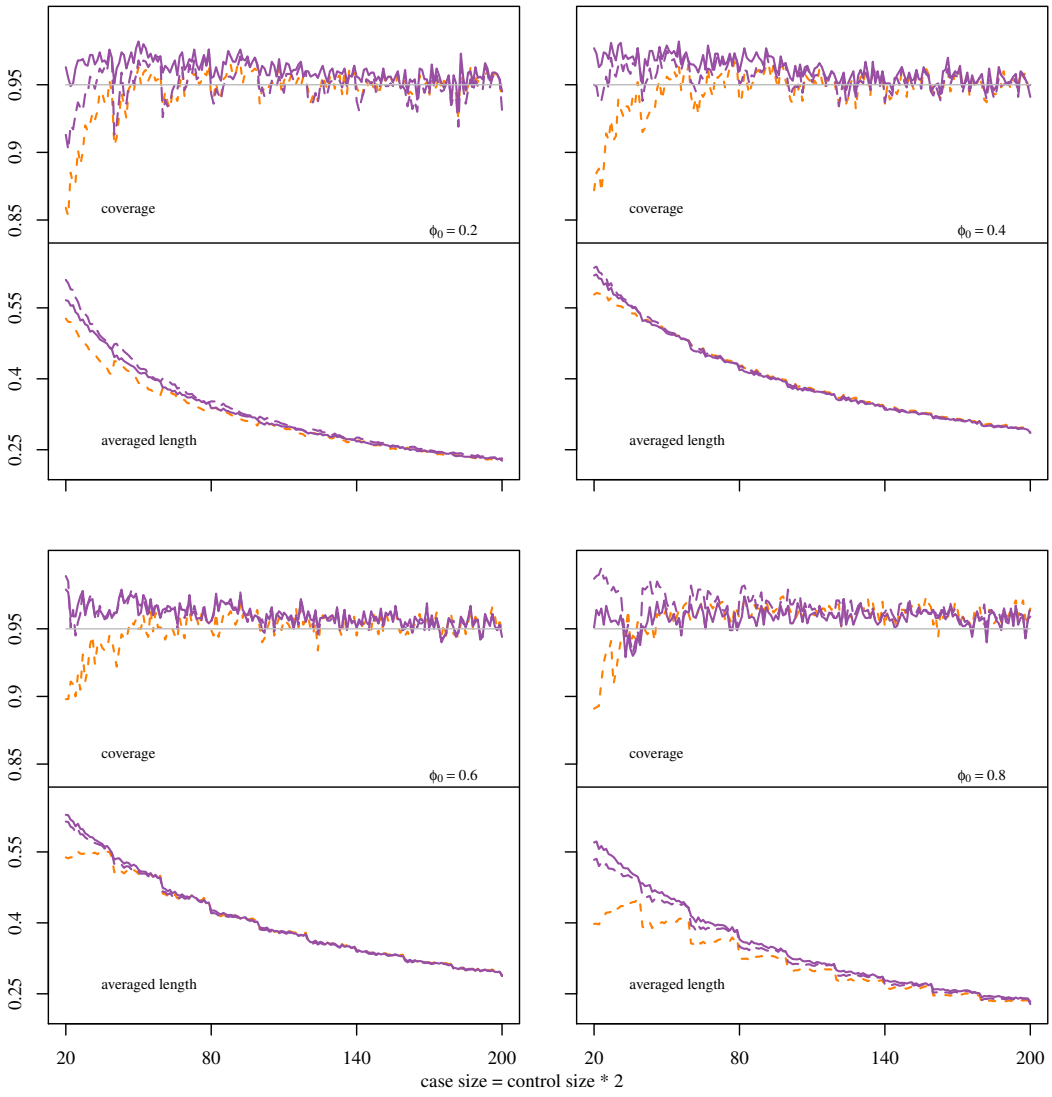

Figure S.4: Simulation summaries of 95% confidence intervals for specificity at controlled 95% sensitivity in the single-biomarker evaluation, under fixed ϕ_0 and variable sizes $n_\bullet = n_\circ \times 2$. Score intervals, based on $\widehat{\phi}$ and $\widetilde{\phi}$, and the exact bootstrap-based Zhou–Qin are included, with the same labeling as in Figure S.3.

Table S.1: Simulation summary statistics of exact bootstrap-based 95% confidence intervals for difference in specificity at controlled 95% sensitivity in the two-biomarker comparison.

				unpaired biomarkers					paired biomarkers				
				Wald		Pct	Score		Wald		Pct	Score	
ϕ_{0X}	δ_0	$n_\bullet/n_\circ$		$\widehat{\phi}$	$\widetilde{\phi}$		$\widehat{\phi}$	$\widetilde{\phi}$	$\widehat{\phi}$	$\widetilde{\phi}$		$\widehat{\phi}$	$\widetilde{\phi}$
0.2	0.0	75/150	C	960	967	977	962	968	964	971	985	967	975
			L	431	431	427	375	370	387	387	384	344	339
		150/75	C	960	967	981	962	964	959	959	984	963	962
			L	387	387	386	347	342	344	344	344	315	310
0.4	0.2	75/150	C	946	951	975	947	950	953	956	980	955	960
			L	510	510	502	443	439	460	460	453	409	405
		150/75	C	963	963	978	959	958	963	970	984	969	970
			L	449	449	447	403	400	401	401	399	367	364
	0.0	75/150	C	948	950	972	951	956	954	958	987	958	960
			L	576	576	568	495	492	519	519	511	457	455
		150/75	C	962	965	982	963	965	961	959	984	961	960
			L	502	502	500	447	445	444	444	443	405	403
0.6	0.4	75/150	C	950	953	975	944	944	955	958	979	943	951
			L	521	521	509	459	458	473	474	461	426	425
		150/75	C	949	950	976	950	950	961	965	987	957	960
			L	448	448	445	408	407	404	404	402	375	374
	0.2	75/150	C	954	952	970	956	959	955	961	986	959	959
			L	586	586	576	505	505	530	530	518	468	468
		150/75	C	953	953	976	951	952	958	960	984	960	956
			L	501	501	500	448	448	446	446	444	407	407
	0.0	75/150	C	954	953	974	953	956	968	972	984	970	971
			L	597	597	584	511	513	539	539	526	473	476
		150/75	C	957	951	979	956	951	965	966	983	962	965
			L	503	503	501	448	450	445	445	443	405	408
0.8	0.6	75/150	C	956	955	969	931	933	960	962	978	937	935
			L	457	458	447	421	422	418	419	407	391	391
		150/75	C	942	949	977	955	946	960	965	982	938	942
			L	389	389	387	368	368	357	357	355	340	341
	0.4	75/150	C	966	967	969	943	945	965	968	980	942	947
			L	531	532	519	469	470	485	485	473	436	438
		150/75	C	961	957	974	960	964	955	949	986	940	949
			L	450	450	448	409	411	407	407	405	377	378
	0.2	75/150	C	961	959	964	952	953	966	970	979	959	962
			L	543	543	528	469	473	494	494	478	437	441
		150/75	C	957	959	972	954	951	967	962	992	956	962
			L	451	451	450	405	409	404	404	403	370	374
	0.0	75/150	C	969	966	976	963	964	968	970	981	964	966
			L	488	488	469	420	427	438	438	422	387	393
		150/75	C	966	962	986	966	964	976	974	992	978	972
			L	395	395	395	353	360	352	352	353	321	327

For unpaired comparison, $n_{\bullet X} = n_{\bullet Y}$ and $n_{\circ X} = n_{\circ Y}$ were set to $n_\bullet$ and $n_\circ$, respectively.
C: coverage probability (×1000); L: average interval length (×1000). Pct: percentile interval.