Appendix Data for Wheeler, Heidenreich, Froelicher, Hlatky, and Ashley "Cost effectiveness of pre-participation screening for prevention of sudden cardiac death in young athletes"

Appendix Table 1. Assumptions

Baseline Medical Cost per Year	Base Case	Low Estimate	Low CI for Simulation	High CI for Simulation	High estimate
Age 6-17	1285(35)	1000	1100	1400	1600
Age 18-44	2631(35)	2200	2500	2800	3000
Age 45-64	5224(35)	4400	5100	5300	6000
Age 65+	8906(35)	7800	8500	9500	10000
Utilities					
Athlete	0.94(49)	0.87	0.93	0.95	1
Secondary Screen – Year 1	0.939*	0.87	0.929	0.949	1
Non-Athlete	0.94*	0.87	0.93	0.95	1
Heart disease – Newly diagnosed	0.89(49)	0.76	0.85	0.93	1
Heart disease – after diagnosis year 4 on	0.94*	0.76	0.93	0.95	1
False Negative, Disease not Discovered	0.94*	0.90	0.93	0.95	1

Appendix Table 1, Cont'd.

Test Characteristics					
ECG alone Sensitivity	40	10 (27)	25	45	65
ECG alone Specificity	98	61.5 (27)**	95.2	98.8	99
ECG alone Cost	34	5	25	65	304
Miscellaneous					
Max. Life span	100*				
Age at screening	16*	12	14	18	22
Years of Extra Risk	8*	3	5	10	15
Annual Discount Rate	0.03(60)	0.00	0.025	0.04	0.07
Probability Heart Disease Discovery in Primary False Negative per year	0.01*§	0.001	0.008	0.012	0.075
Number of athletes screened#	3700000†	1000000	2000000	5000000	20000000

Appendix Table 1, Cont'd.

Prevalence (%)			
Hypertrophic Cardiomyopathy	0.2(61)	0.003(62)	0.3(63)
Anomalous Coronary Anatomy	0.2(64)	0.05(65)	1.3(66)
Left Ventricular Hypertrophy	1.7(67)	1	8(43)
Myocarditis	0.05(68)	0.0015(68)	0.1
Aortic Aneurysm	0.01*	0.005	0.13(30)
Arrhythmogenic Right Ventricular Cardiomyopathy	0.02(69)	0.01	0.05
Premature Coronary Artery Disease	0.1(70)	0.005	5(70)
Dliated Cardiomyopathy	0.05(71)	0.003(62)	0.2(72)
Mitral Stenosis	0.06(73)	0.03	0.1
Long QT	0.02(74)	0.01	0.06
Mitral Valve Prolapse	1.3(30)	0.34(73)	5(29)
Brugada	0.06(75, 76)	0.02(77)	0.6(78)
Wolfe-Parkinson-White	0.2(79, 80)	0.05	0.4
Pulmonary Arterial Hypertension	0.0003(81)	0.0001(82)	0.003
Marfan	0.02(83)	0.005(84)	0.03(83)
Coarctation	0.025(85)	0.017(86)	0.04
Bicuspid Aortic Valve	0.25(73)	0.1	0.5

* Author consensus estimates †Based on number of sports participants in high-risk sports divided by average number of sports per athlete for high school and college athletes (5, 87,88). ** ECG alone using mildly abnormal ECG findings as positive initial screening

(44). § Disease discovery in Primary Testing False Negative in base case is 10fold more frequent than in the Secondary Testing False Negative group, as the Secondary Testing False Negative will be less likely to have readily discoverable disease if disease is not demonstrated on secondary testing, while there is a substantial proportion of individuals with underlying disease in the Primary Testing False Negative group who have disease easily discovered by echocardiography or other imaging technologies. # Not included in probabilistic sensitivity analyses. Probability distributions for probabilistic sensitivity analyses were defined with the base case as the median input and the low and high estimates of the median set as the 95% confidence interval limits of two one-sided normal distributions, with all values limited to positive numbers (or values between 0 and 1 for utilities and test characteristics). CI: confidence interval.

Appendix Table 2 – Cost Effectiveness Ratios Using Relative Risk as Multipliers of the Baseline Risk of Death*

In the base case we used conservative estimates for the propagation of risk associated with discovered underlying heart disease through screening, by reducing the risk of death to the background population risk after the age of thirty-five. In this sensitivity analysis, we used the ratio of the risk of death due to the presence of underlying heart disease to that for those without underlying heart disease as a multiplier in comparison to the baseline, actuarial yearly risk of death. In this analysis, as subjects with underlying heart disease age in the model, their risk of sudden cardiac death becomes substantially larger than those of unaffected contemporaries or those in the base-case model.

Screening Method	Recommended to undergo secondary testing, number of athletes	Identified at increased risk of sudden death, number of athletes	Athletic sudden deaths, cases*	Life Years saved (discounted years)	Life Years Saved per 1000 athletes, discounted years	Total incremental cost versus no screening, discounted $ millions	Discounted cost per Athlete	Incremental Cost-Effectiveness Ratio compared to no screening ($/Life Year Saved)	Incremental Cost-Effectiveness Ratio, Compared with next cheaper Non-dominated strategy	Incremental Cost-Effectiveness Ratio Quality adjusted (Discounted $/Quality Adjusted Life Year Saved)
No screening			1070						Cheapest	
ECG alone	73,100	17,700	818	10200	2.8	$328	$89	$32,200	$32,200	$40,300
H&P	110,000	6700	980	3730	1	$422	$114	$113,000	Dominated	Dominated
ECG plus H&P	180,000	30,200	650	17250	1.90	$794	$215	$46,000	$65,500	$83,600

* Multiplicative model assumes having underlying heart disease increases the relative risk of death above baseline throughout the individual's lifetime. Hazard ratios of 0.997 for individuals without heart disease, 1.61 for individuals with undiscovered heart disease, and 1.30 for individuals with discovered heart disease were multiplied by the

baseline actuarial rate of death at each age until the age of 99. These ratios are derived from the ratio of the risk of SCD in non-athletes with occult cardiovascular abnormalities or diagnosed cardiovascular disease (9) to the incidence of any cause of death at age 24 (89) (at completion of competitive athletic activity for most individuals). The average life expectancy for athletes with heart disease in this model is 56.8 years from the time of screening versus 61.93 years for those without underlying heart disease.

Appendix Table 3 – Probabilistic Sensitivity Analysis

Baseline	Comparator	Simulation 95% CI, Comparator False Positives	Simulation 95% CI, Comparator True Positives	Total Incremental Cost (mean of 10000 simulations, millions)	Simulation Mean (Median), ICER, $/LY	Simulation 95% CI, ICER, $/LY	Simulation Median‡, ICER, $/QALY	Simulation 95% CI, ICER, $/QALY
No screen	ECG	44,300-172,000	10,800-21,500	$319	$65,100 ($62,100)	$43,900-$102,100	$94,600	$24,400-dominated*
No screen	H&P	74,400-290,100	3,500-11,300	$433	$241,000 ($223,000)	$153,000-$412,000	$381,000	$85,300-QALY dominated*
No screen	ECG+ H&P	112,000-255,000	21,400-35,700	$733	$87,600 ($84,700)	$62,400-130,000	$130,000	$58,800-QALY dominated*
H&P	ECG	44,300-172,000	10,800-21,500	Cost Saving (-$115)	Cost and life saving	Cost and life saving-$1,520	Cost and QALY saving	Cost and QALY saving - dominated*
H&P	ECG+ H&P	112,000-255,000	21,400-35,700	$302	$45,700 ($45,200)	$21,200-$71,300	$66,200	$15,300-dominated*
ECG	ECG+ H&P	112,000-255,000	21,400-35,700	$414	$122,000 ($117,000)	$79,600-$233,200	$190,000	$44,200-dominated*

Simulations were run as pairwise comparisons, ignoring dominance and weak dominance. ‡Simulation median given as mean not meaningful due to proportion of QALY costing simulations. *Due to significant effect of changes in utilities varied over the estimated range, incremental cost effectiveness ratios for each methodology were dominated versus all strategies with a decrease in QALY in a substantial fraction of simulations. Comparator was found to be QALY costing in 24% of simulations (ECG alone vs no screening), 28% of simulations (H&P vs no screening), 21% of simulations (ECG alone vs H&P), 25% of simulations (ECG plus H&P vs ECG alone), 25% of simulations (ECG plus H&P vs. no screening), 23% of simulations (ECG plus H&P vs H&P). Abbreviations: ICER, incremental cost effectiveness ratio; LY, life years saved; CI, confidence interval; QALY, quality adjusted life years; H&P, cardiovascular focused history and physical; ECG + H&P, 12-lead electrocardiogram plus cardiovascular focused history and physical; ECG, 12-lead electrocardiogram.

Appendix Table 4A. Comparison of cost effectiveness of different screening methods for reducing sudden death in young athletes.

Screening Method	Screening Method Sensitivity	Screening Method Specificity	Reference	Criteria	False Positive, #	Number Identified as High Risk, Year One*	Life Years Saved per 1000 Athletes	Discounted Life Years Saved per 1000 Athletes	Total Cost (millions)	Cost (per athlete)	Discounted Cost (per athlete)	Discounted $/Life Year Saved	Discounted $/QALY	Incremental cost per athlete*	Incremental Life Years Saved/1000 athletes	Incremental Cost-Effectiveness Ratio, Versus next cheaper Non-dominated strategy
No screen	0%	100%							$0							Cheapest
Family History	5%	97.1%	27	unexplained death in young family member	106000	2200	0.40	0.16	$166	$65	$45	$274,900	$559,000			Weakly dominated
ECG alone	25%	98.8%	27	ECG abnormal	43900	11100	2.43	0.97	$230	$74	$62	$64,000	$92,300			Weakly dominated
ECG alone	40%	98.0%	51	ECG abnormal	73100	17760	3.89	1.55	$295	$100	$80	$51,400	$74,200	$80	1.55	$51,400
ECG alone	45%	95.2%	44	markedly abnormal elite athletes	175500	19980	4.29	1.72	$402	$148	$109	$63,400	$94,000			Weakly dominated
CV H&P	15%	97.0%		base case	109700	6660	1.39	0.56	$410	$133	$111	$199,200	$310,000			Dominated
ECG+ history	25%	97.5%	27	ECG abnormal, serious symptoms or family history	91400	11100	2.39	0.96	$544	$168	$147	$153,900	$228,000			Dominated
ECG alone	55%	89.7%	44	distinctly abnormal, elite athletes	376500	24400	5.10	2.05	$614	$243	$166	$81,100	$125,000			Weakly dominated
ECG+ H&P	68%	95.0%		base case	182800	30200	6.56	2.62	$737	$244	$199	$76,100	$111,000			Weakly dominated
ECG+ H&P	73%	93.1%	52	ECG or H&P positive	252200	32400	7.00	2.79	$815	$278	$220	$78,800	$116,000			Weakly dominated
ECG+ H&P	34%	84.7%	26	ECG or history positive	559300	15100	2.86	1.16	$1,001	$377	$270	$232,500	$425,000			Dominated
CG+ H&P	90%	84.9%	13	ECG plus H&P	552000	39960	8.41	3.37	$1,018	$390	$275	$81,600	$125,000	$195	1.82	$107,000
Family History	5%	70.1%	27	any heart disease in family member	1093000	2200	-0.49	-0.14	$1,080	$489	$292	Net life costing	Dominated			Dominated
ECG alone	75%	61.5%	44	mildly abnormal, elite athletes	1407000	33300	6.16	2.51	$1,621	$704	$438	$174,400	$335,000			Dominated
ECG alone	85%	35.0%	27	LVH by isolated Sokolow-Lyon	2376000	37700	6.28	2.60	$2,545	$1,129	$688	$264,200	$655,000			Dominated

Appendix Table 4 Footnotes. Note that the validity of comparison among strategies may be limited as the test characteristics derived or estimated from the cited publications may not be fully applicable to the population utilized for the model nor reproducible in wide clinical practice. *Cost versus next cheaper, non-dominated strategy. Dominated strategies are those that are more expensive and less effective than cheaper strategies. Weakly dominated strategies are those that are incrementally less cost-effective per life year saved than more costly strategies, such that a combination of the more expensive and less expensive non-dominated strategies would be preferable to use of the weakly dominated strategy.

Appendix Table 4B. Comparison of cost effectiveness of different screening methods for reducing sudden cardiac death in young athletes using cardiovascular history and physical as baseline comparator.

Screening Method	Screening Method Sensitivity	Screening Method Specificity	Reference	Criteria	False Positive, #	Number Identified as High Risk, Year One*	Life Years Saved per 1000 Athletes	Discounted Life Years Saved per 1000 Athletes	Total Cost (millions)	Discounted Cost (per athlete)	Discounted $/Life Year Saved	Discounted $/QALY	Incremental cost per athlete*	Incremental Effectiveness (Life Years Saved per 1000 athletes)	Incremental Cost-Effectiveness Ratio, Compared with next cheaper Non-dominated strategy
CV H&P	15%	97.0%		Base Case											
ECG plus history	25%	97.5%	27	ECG abnormal, serious symptoms or family history	-18278	4440	1.01	0.40	$134	$36	$90,800	$125,000			Weakly dominated
ECG plus H&P	68%	95%		Base case	73112	23532	5.18	2.06	$328	$89	$42,900	$61,600	$89	2.06	$42,900
ECG plus H&P	73%	93.1%	52	ECG or H&P positive	142568	25752	5.61	2.24	$405	$109	$48,900	$71,100			Weakly dominated
ECG plus H&P	34%	84.7%	26	ECG or history positive	449639	8436	1.48	0.61	$591	$160	$263,000	$571,000			Dominated
ECG plus H&P	90%	84.9%	13	ECG plus H&P	442327	33300	7.02	2.81	$607	$164	$58,356	$310,000	$75	0.75	$101,000

Note that the validity of comparison among strategies may be limited as the test characteristics derived or estimated from the cited publications may not be fully applicable to the model nor reproducible in wide clinical practice. *Cost versus next cheaper, non-dominated strategy. Dominated strategies are those that are more expensive and less effective than cheaper strategies. Weakly dominated strategies are those that are incrementally less cost-effective per life year saved than more costly strategies, such that a combination of the more expensive and less expensive non-dominated strategies would be preferable to use of the weakly dominated strategy.

Appendix Table 5A. Comparison of screening modalities assuming 36th Bethesda Conference parameters or Base Case Parameters. Effects of multiple testing, repeat follow up testing, and screened population size.

Screening Method	Sensitivity	Specificity	Total Incremental Cost (discounted Millions)	Per athltete incremental Cost (non-discounted)	Per athlete incremental Discounted Cost	Life Years Saved per 1000 Athletes	Discounted Life Years Saved per 1000 Athletes	Incremental Cost-effectiveness Raito (Discounted $/Life Year Saved)	False Positive Tests, #	Number Identified as High Risk, Year One†
Statement Assumptions, 10 million Screened, Single Screen per Athlete										
CV H&P Base case	15%	97%	$970	$108	$97	0.29	0.13	$757,000*	299700	1500
ECG plus H&P base	68%	95%	$1,510	$174	$151	2.02	0.83	$183,000	499500	6800
ECG plus H&P (13)	90%	85%	$1,960	$252	$196	1.97	0.85	$230,000*	1498500	9000
Base Case Assumptions 3.7 million Screened Yearly Screen per Athlete, Recurring Follow-up Testing Costs										
CV H&P Yearly	15%	97%	$2,780	$862	$751	1.39	0.56	$1,350,000*	880000	6600
ECG plus H&P, Yearly	68%	95%	$4,380	$1,366	$1,184	6.56	2.62	$452,100	1464000	30200
Statement Assumptions, 10 million Screened, Yearly Screen per Athlete, Recurring Follow-up Testing Costs										
CV H&P Yearly	15%	97%	$7,320	$831	$732	0.29	0.13	$5,717,000*	2397600	1500
ECG plus H&P, Yearly	90%	85%	$13,300	$1,549	$1,334	1.97	0.85	$1,563,000	11988000	9000
Base Case Assumptions, 3.7 million Screened, Yearly Screen per Athlete, No Recurring Follow-up Testing Costs										
CV H&P, Yearly	15%	97%	$2,300	$717	$623	1.39	0.56	$1,121,000*	880000	6600
ECG plus H&P, Yearly	68%	95%	$3,500	$1,100	$950	6.56	2.62	$363,000	1464000	30200
Statement Assumptions, 10 million Screened, Yearly Screen per Athlete, No Recurring Follow-up Testing Costs										
CV H&P, Yearly	15%	97%	$6,090	$692	$609	0.29	0.13	$4,760,000*	2397600	1500
ECG plus H&P, Yearly	90%	85%	$7,230	$853	$723	1.97	0.85	$850,000	11988000	9000

Comparator is no screening. *Dominated strategy. † Number of athletes screened to be at high risk. In yearly screen analyses, only athletes identified at year one are included. Abbreviations: CV H&P, cardiovascular focused history and physical; ECG plus H&P, 12-lead electrocardiogram plus cardiovascular focused history and physical.

Appendix Table 5B. Comparison of screening modalities assuming 36th Bethesda Conference document parameters or Base Case Parameters, as compared to baseline of history and physical. Effects of multiple testing, repeat follow up testing, and screened population size.

Screening Method	Comparator	Sensitivity	Specificity	Total Incremental Cost (millions, discounted)	Incremental Life Years Saved per 1000 Athletes	Incremental Discounted Life Years Saved per 1000 Athletes	Incremental Cost per athlete, non-discounted	Incremental Discounted Cost per athlete	Difference in Discounted $/Life Year Saved, Screening Method vs. Comparator	Difference in False Positive Test Results, #	Difference in Number Identified as High Risk, Year One†
Statement Assumptions, 10 million Screened, Single Screen per Athlete											
ECG plus H&P (13)	CV H&P Base case	90%	85%	$990	1.69	0.73	$144	$99	$136,400	1198800	7500
Base Case Assumptions 3.7 million Screened Yearly Screen per Athlete, Recurring Follow-up Testing Costs											
ECG plus H&P Yearly	CV H&P, Yearly	68%	95%	$1,600	2.18	2.06	$504	$433	$210,000	584000	23600
Statement Assumptions, 10 million Screened, Yearly Screen per Athlete, Recurring Follow-up Testing Costs											
ECG plus H&P Yearly	CV H&P, Yearly	68%	95%	$3,760	1.73	0.69	$434	$376	$539,300	1598400	5300
ECG plus H&P, Yearly	CV H&P, Yearly	90%	85%	$6,030	1.69	0.73	$718	$603	$830,700	9590400	7500
Base Case Assumptions, 3.7 million Screened, Yearly Screen per Athlete, No Recurring Follow-up Testing Costs											
ECG plus H&P, Yearly	CV H&P, Yearly	68%	95%	$1,210	2.18	2.06	$383	$327	$158,600	584000	23600
Statement Assumptions, 10 million Screened, Yearly Screen per Athlete, No Recurring Follow-up Testing Costs											
ECG plus H&P, Yearly	CV H&P, Yearly	90%	85%	$1,140	1.69	0.73	$161	$114	$157,400	1598400	7500
ECG plus H&P Yearly	CV H&P, Yearly	68%	95%	$2,930	1.73	0.69	$339	$293	$420,000*	9590400	5300

*Dominated strategy. † Number of athletes screened to be at high risk. In yearly screen analyses, only athletes identified at year one are included. Abbreviations: CV H&P, cardiovascular focused history and physical; ECG plus H&P, 12-lead electrocardiogram plus cardiovascular focused history and physical.

Appendix Figure Legends

Appendix Figure 1. Characteristics of the unscreened student athlete population. Student athletes harboring cardiac abnormalities placing them at potential increased risk for SCD. Numbers of athletes in at-risk athletic activities expected to have underlying cardiac abnormalities are listed next to chart labels. Total number of student athletes in at-risk activities estimated to be 3.7 million. Note that mitral valve prolapse and left ventricular hypertrophy do not carry similar risk of early death as compared to other findings in the population.

Appendix Figure 2. Expected prevalence and risk of sudden death per year in the young athlete population. (A) Expected frequencies of student-athletes harboring underlying cardiac abnormalities were calculated from figures for total student-athlete participants and prevalence of cardiac abnormalities in adolescent and young adult sampled populations (Appendix Table 1 for references). The number of athletes at risk was then divided by the number of athletes found to have SCD in registry data (13) to generate an estimated yearly risk for SCD by underlying diagnosis (B). Note that many athletes harboring potential causes of sudden cardiac death have comparatively low risk versus others. Sudden deaths in the left ventricular hypertrophy group are assumed to be due to subclinical forms of hypertrophic cardiomyopathy; those with mitral valve prolapse may be due to mechanical or arrhythmic causes. CAD, coronary artery disease; ARVC, arrhythmogenic right ventricular cardiomyopathy.

Appendix Figure 3. Cost effectiveness of screening athletes to prevent sudden cardiac death. Evaluation of different screening modalities and test characteristics derived from the athlete screening literature. Test modalities and reported test results were used as inputs in the model and compared to a strategy of no screening. The discounted incremental life years gained per 1000 athletes screened is plotted against the cost per athlete screened for each modality. The incremental cost effectiveness ratio, screening method, and threshold for a positive test results are shown together with the reference from which test characteristic estimates were derived. Note due to significant heterogeneity between the populations studied and methods used in the papers compared, the test characteristics derived from each study may not be entirely applicable to the screened population described for the base case. Additionally, the methods of family history, history, and physical are not uniform across the studies referenced. Number in parentheses is reference from which input estimates have been derived. Details of incremental cost-effectiveness ratio versus no screening for each study (references in parentheses) can be found in Appendix Table 4A; comparison to a baseline of history and physical for those including history can be found in Appendix Table 4B. Estimated test sensitivity and specificity for each graphed incremental cost effectiveness ratio is shown, derived from reference in parentheses. Incremental cost effectiveness ratios versus no screening are as follows: $51,400 (40%,98%), $63,400 (45%,95.2%), $64,000 (25%,98.8%), $76,100 (68%, 95%), $78,800 (73%,93.1%), $81,000 (55%,89.7%), $81,600 (90%,84.9%), $153,900 (25%,97.5%), $174,000 (75%,61.5%), $199,200 (15%,97%), $232,500 (34%,84.7%), $264,000 (85%,35%), $275,000 (5%,97.1%); life costing (5%,70.1%). LVH, left ventricular hypertrophy; ECG + history, 12-lead ECG and concerning or severe historical features; FH, family history.

Appendix Figure 4. Univariate sensitivity analyses for ECG strategies. The incremental cost-effectiveness ratios of (A) ECG alone versus no screening, (B) ECG plus cardiovascular focused history and physical versus ECG alone were compared by varying critical parameters through possible ranges. The comparison of ECG alone versus cardiovascular focused history and physical alone is not shown as the ECG alone strategy is dominant (costs less and is more effective) in all cases except when ECG specificity is low, ECG cost is more than $65 and history and physical cost is less than $42. For each graph, the base case estimates are shown (vertical lines). Horizontal solid boxes represent the incremental cost effectiveness ratio resulting from inputting the described variable over the expected range of the mean value (also used in probabilistic sensitivity analysis); horizontal lines represent incremental cost effectiveness ratio found using expected minimum and maximum inputs, which may be applicable to specific subgroups or to particular payors. The accompanying table lists, from left to right: the low value input, the low input used for probabilistic sensitivity analysis, the high value input used for probabilistic sensitivity analysis, and the high value input for each variable or combination of variables. Risk ratio, Athlete vs. DQ represents the ratio of risk reduction associated with disqualification and treatment of athletes with underlying occult heart disease. SN, sensitivity; SP, specificity. † ECG plus H&P cost and life saving versus comparator. * Base case assumption.

Appendix Figure 5. Probabilistic sensitivity analysis results evaluating screening athletes using ECG alone versus other screening modalities. A) Scatter plot of life saving versus incremental increase in cost for each of 10,000 Monte Carlo simulations randomly varying each variable over estimated ranges (Table 1, Appendix Table 1 for inputs). ECG alone sensitivity of 40% and specificity of 98% based on data of Nora et al. (51) together with estimate of prevalence of screened athletes potentially at risk (Appendix Table 1). Lines representing willingness to pay threshold incremental cost effectiveness ratios of $50,000 per life year and $100,000 per life year are shown for comparison. Simulations with negative incremental cost are cost-saving versus the comparator. Average values and confidence intervals for incremental cost effectiveness ratios based on probabilistic simulations are shown in Appendix Table 3. B) Cost effectiveness acceptability curve, showing proportion of simulations below incremental cost effectiveness ratio at given values in discounted dollars per discounted life years saved. The probability of preferring ECG alone compared to no screening is 12.6% at a willingness to pay threshold of $50,000 per life year and 97% at $100,000 per life year. ECG alone is cost- and life-saving in more than 93.6% of simulations vs. H&P alone, and below $50,000 per life year saved in more than 99.9% of simulations.

Appendix Figure 6. Effect of multiple testing on screening cost-effectiveness. As the primary analysis assumes a single episode of screening, yet current recommendation statements advise yearly or biannual screening, the effects of repeated screening for each methodology in terms of change in cost-effectiveness were modeled. Yearly screening cost (screening test plus secondary testing costs) are assumed to recur with each additional year of screening, as an upper bound of cost of screening (see also Appendix Table 5). More conservative estimates regarding the cost of repeated screening in terms of reduction of repeated secondary testing costs may lead to costs intermediate between those shown and the base case estimate. Efficacy was assumed to be independent of number of tests, though the veracity of this assumption is not well known.

Appendix Figure 7. Sensitivity analysis of cost effectiveness of screening as a function of total student and student athlete number potentially at risk for sudden cardiac death, assuming constant number of athletic sudden cardiac deaths. A. Sensitivity analysis examining total number of athletes at risk versus cost-effectiveness ratio for ECG plus history and physical or cardiovascular focused history and physical, compared to no screening. Total number of athletic sudden cardiac deaths was assumed to be independent of the number screened for this analysis, however non-athletic death and background non-sudden cardiac death remained constant on a per individual basis for each risk group. 26 million students is the total middle school and high school age population in the United States (90). Ten million students is the estimated total school age population participating in any sports. 3.7 million students (base case) is the estimated total high school and college age population participating in high intensity, interscholastic and intercollegiate sport. B. Sensitivity analysis examining total number of athletes at risk versus incremental cost effectiveness ratio assuming underlying at risk heart disease prevalence of 0.1%; with proportionally higher yearly incidence of death in the high risk subgroups, modeled after the risk estimates in (13).

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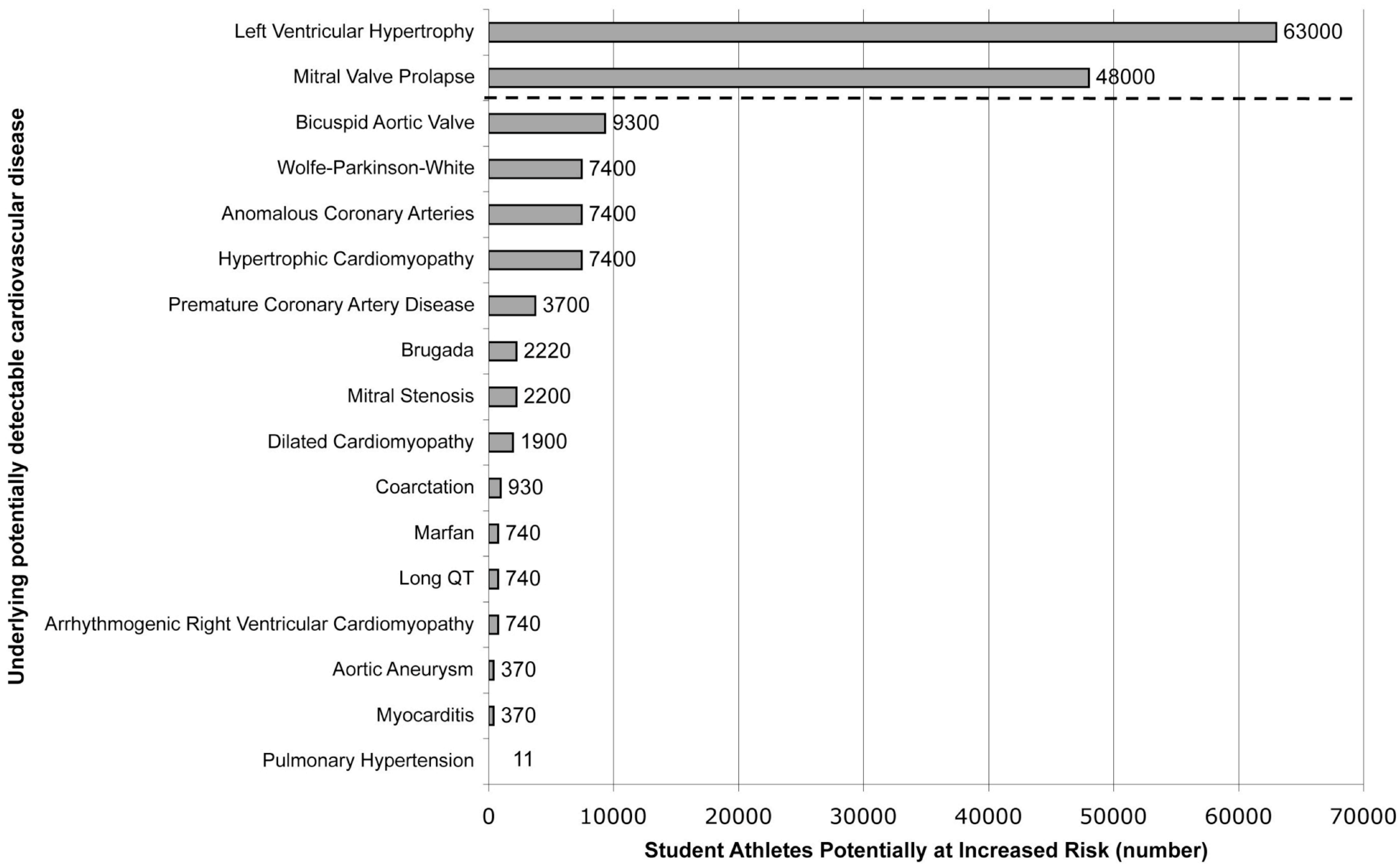
Appendix Figure 1.



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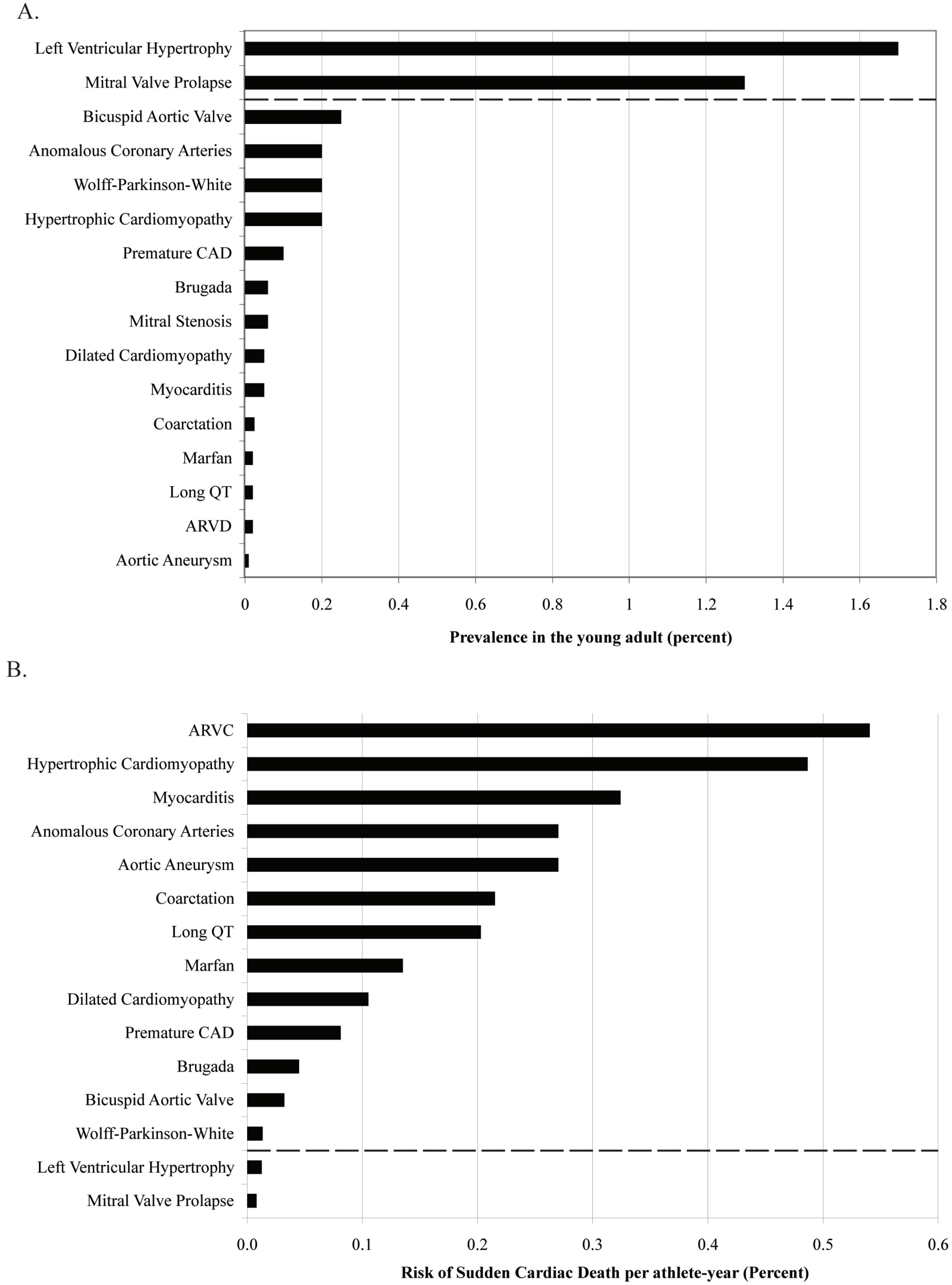

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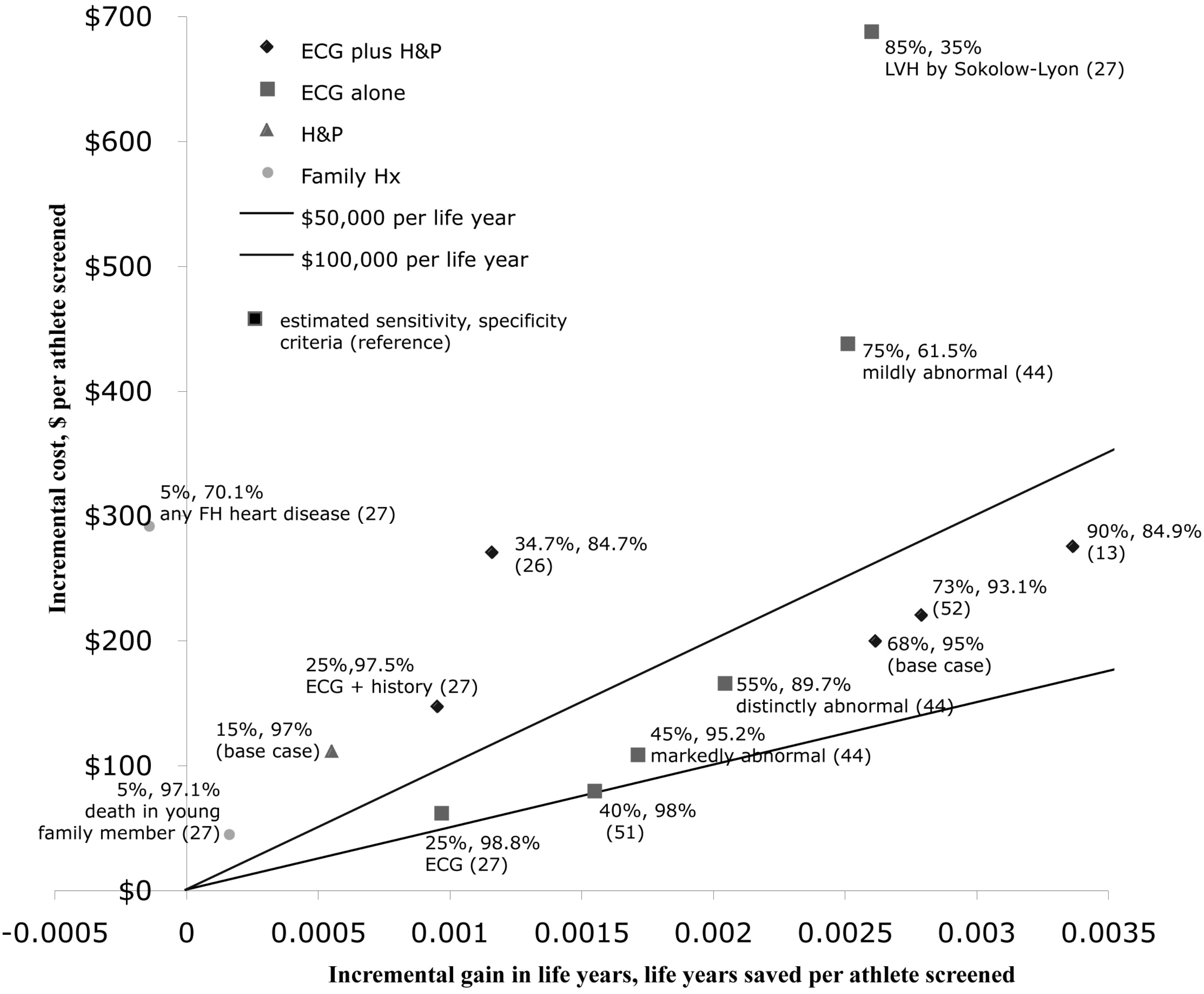

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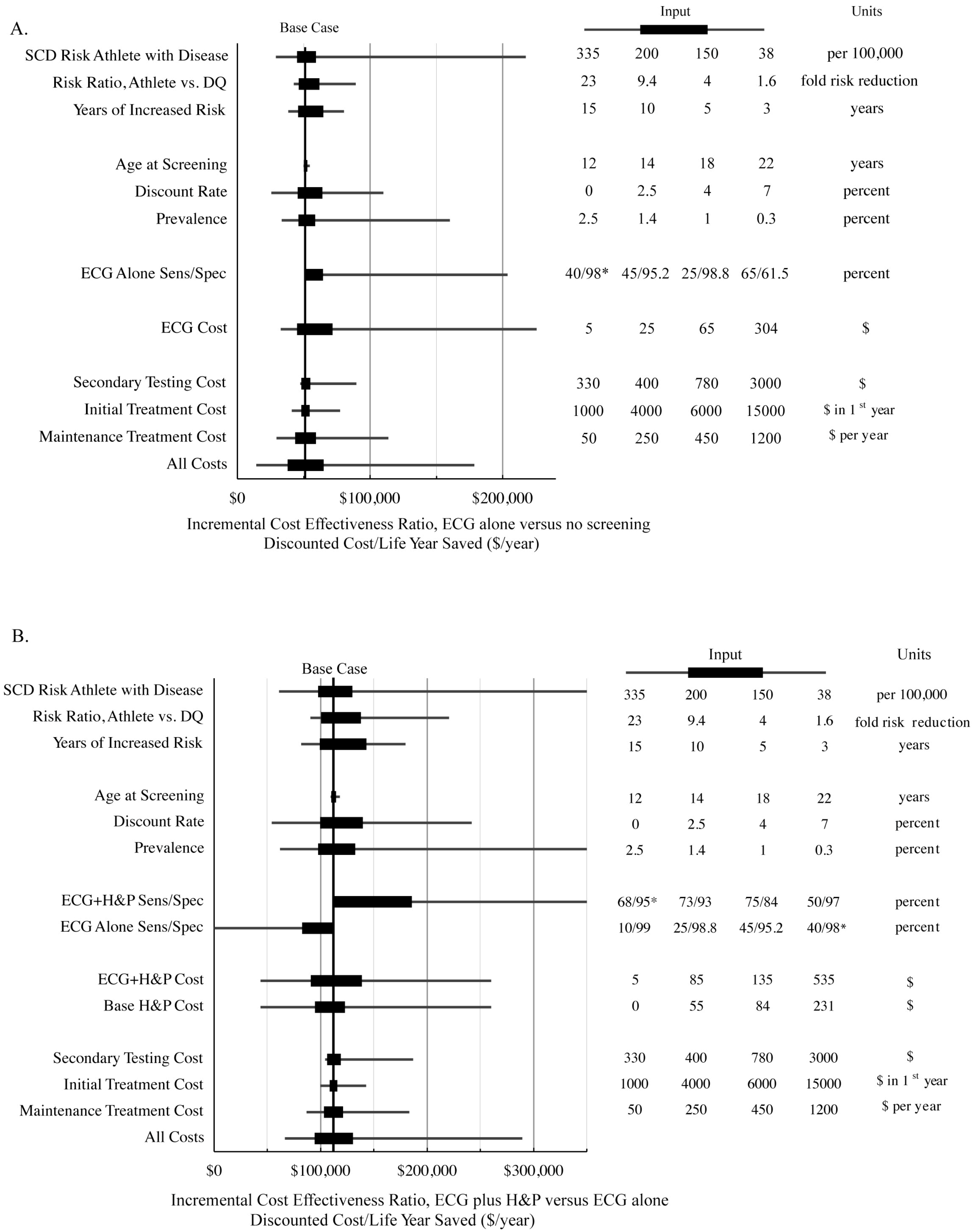
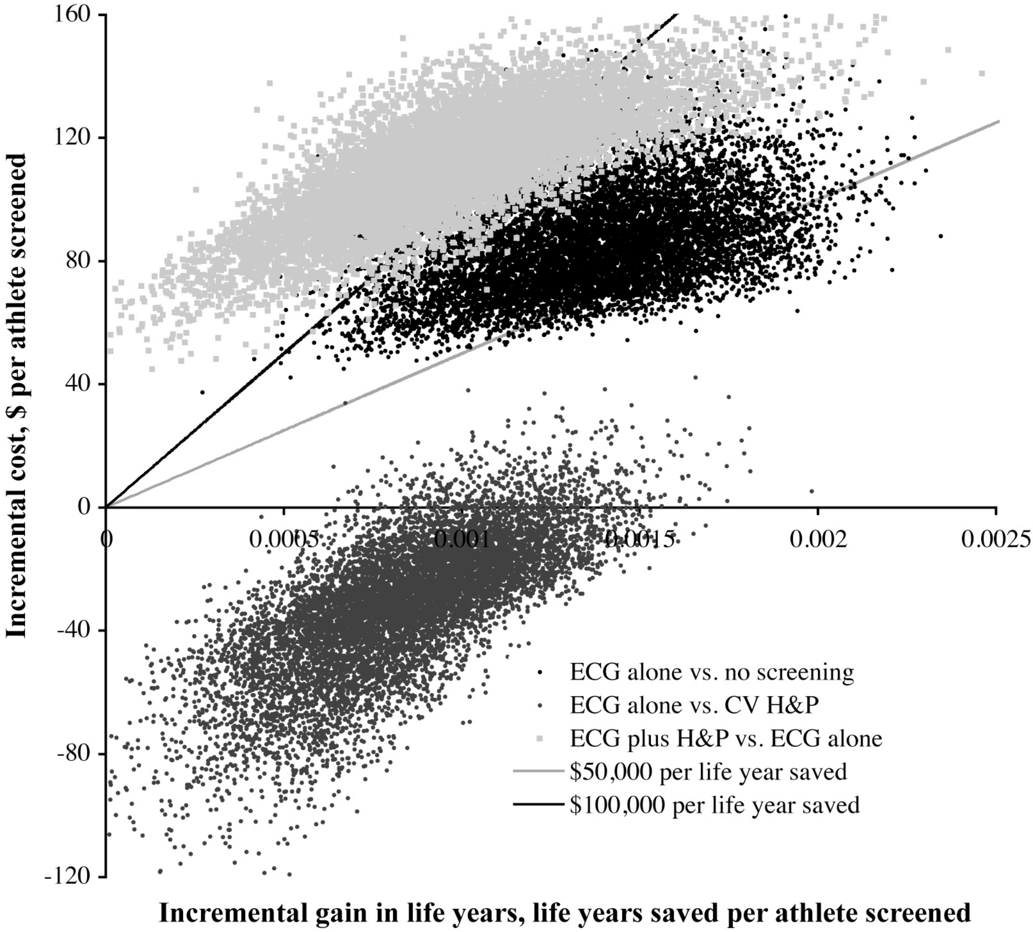


Appendix Figure 5 .

A.



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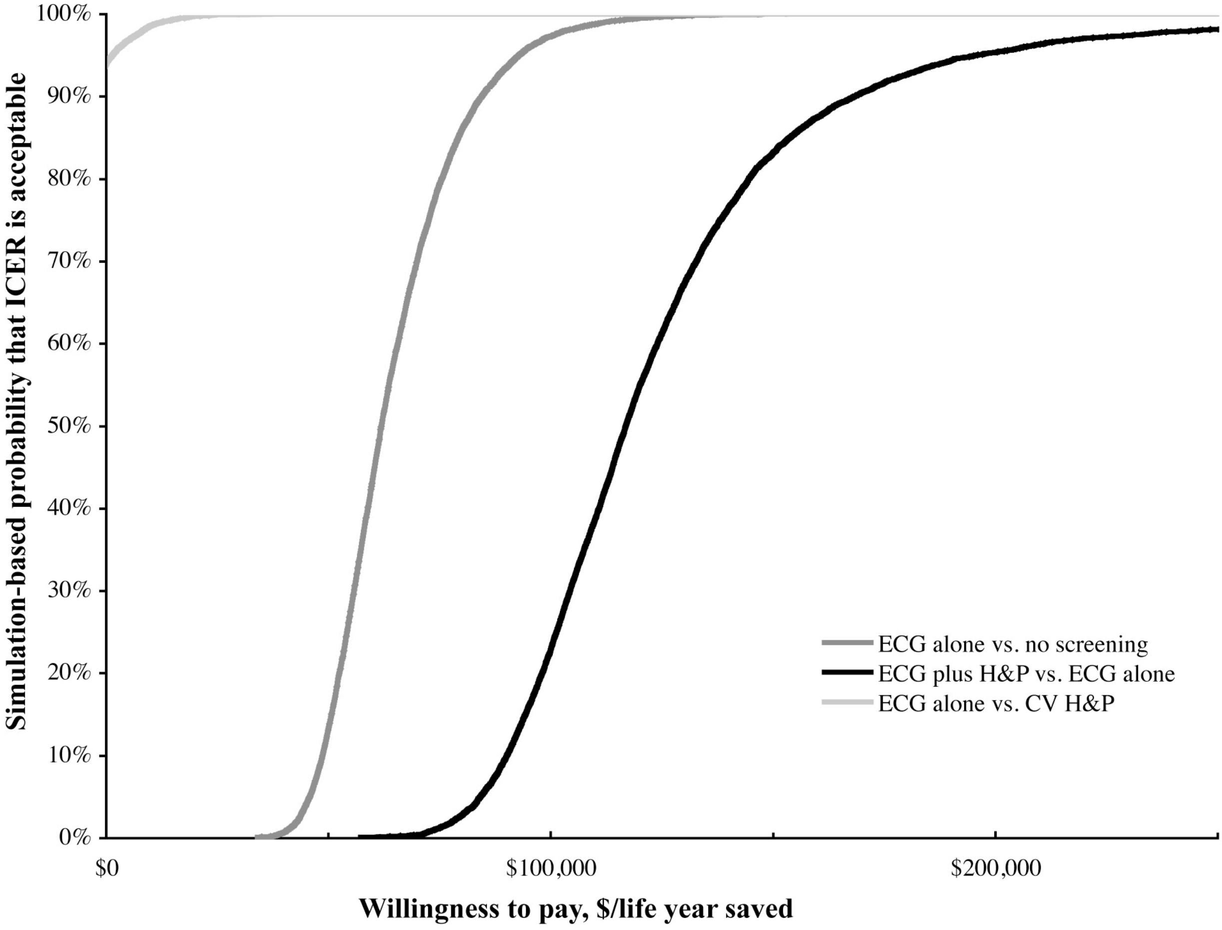

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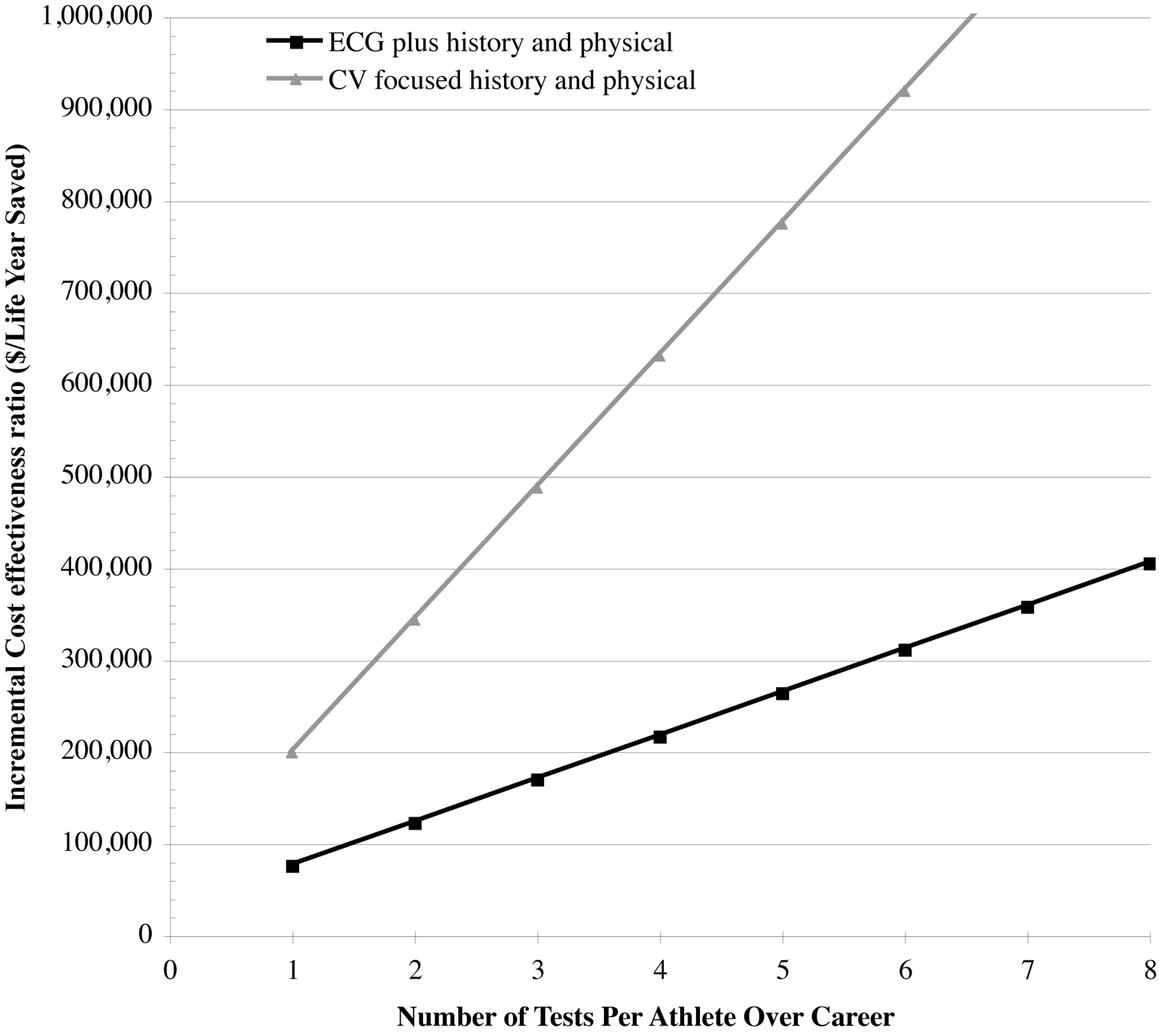
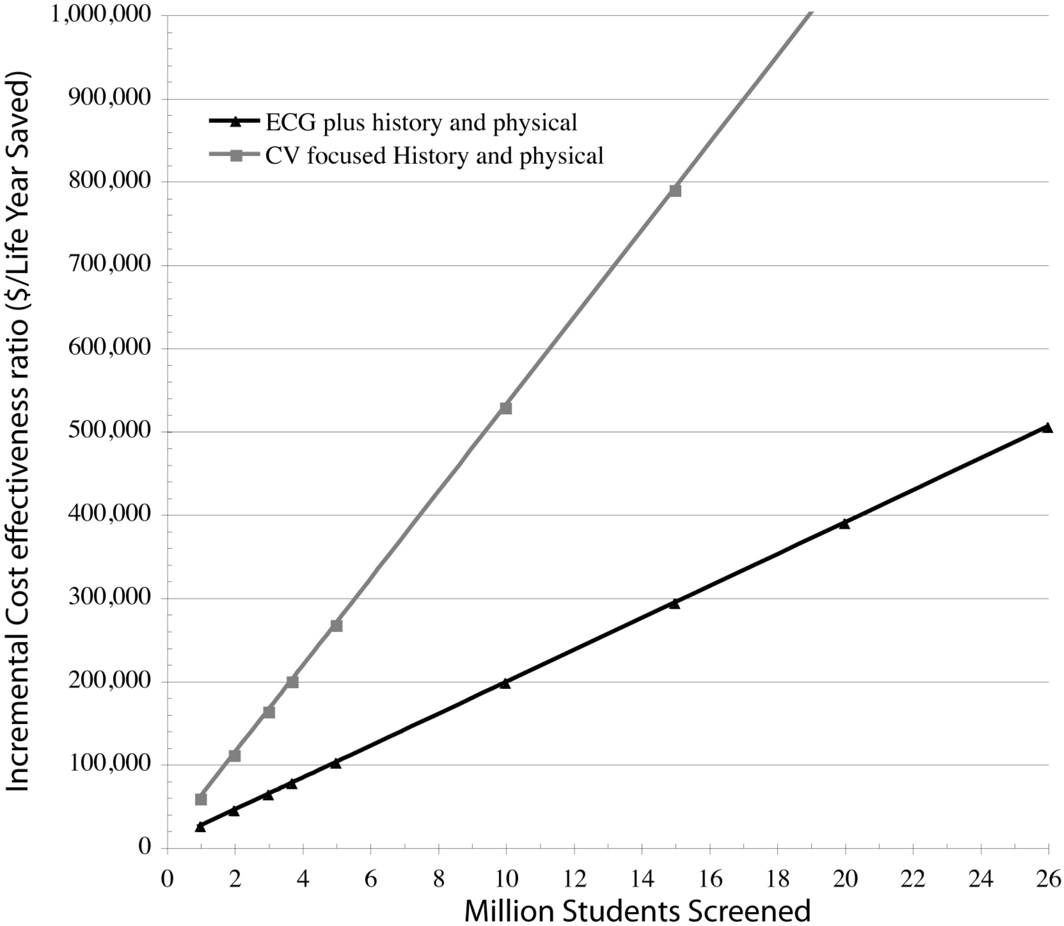


Appendix Figure 7.

A.



B.