Comparative effectiveness of angiotensin converting enzyme inhibitors (ACEI) and thiazide or thiazide-like diuretics (THZ)

Version: 1.1.0

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1.1.1   Cohort Entry Events

People with continuous observation of 365 days before event may enter the cohort when observing any of the following:

1. drug exposure of '[LEGEND HTN] ACE inhibitors' for the first time in the person's history.

Limit cohort entry events to the earliest event per person.

Restrict entry events to with all of the following criteria:

1. having no drug exposures of '[LEGEND HTN] Hypertension drugs', starting anytime prior to cohort entry start date.

2. having at least 1 condition occurrence of 'Hypertensive disorder', starting between 365 days before and 0 days after cohort entry start date.
3. having exactly 1 distinct standard concepts from drug era of '[LEGEND HTN] Hypertension drugs', starting between 0 days before and 7 days after cohort entry start date.

1.1.2   Cohort Exit

The cohort end date will be based on a continuous exposure to '[LEGEND HTN] ACE inhibitors': allowing 30 days between exposures, adding 0 days after exposure ends, and using days supply and exposure end date for exposure duration.

1.1.3   Cohort Eras

Entry events will be combined into cohort eras if they are within 0 days of each other.

1.1.4   Concept: Hypertensive disorder

Concept ID	Concept Name	Code	Vocabulary	Excluded	Descendants	Mapped
316866	Hypertensive disorder	38341003	SNOMED	NO	YES	NO

1.1.5   Concept: [LEGEND HTN] First-line hypertension drugs

Concept ID	Concept Name	Code	Vocabulary	Excluded	Descendants	Mapped
1332418	Amlodipine	17767	RxNorm	NO	YES	NO
40235485	azilsartan	1091643	RxNorm	NO	YES	NO
1335471	benazepril	18867	RxNorm	NO	YES	NO
1351557	candesartan	214354	RxNorm	NO	YES	NO
1340128	Captopril	1998	RxNorm	NO	YES	NO
1395058	Chlorthalidone	2409	RxNorm	NO	YES	NO
1328165	Diltiazem	3443	RxNorm	NO	YES	NO
1341927	Enalapril	3827	RxNorm	NO	YES	NO
1346686	eprosartan	83515	RxNorm	NO	YES	NO
1353776	Felodipine	4316	RxNorm	NO	YES	NO
1363749	Fosinopril	50166	RxNorm	NO	YES	NO
974166	Hydrochlorothiazide	5487	RxNorm	NO	YES	NO
978555	Indapamide	5764	RxNorm	NO	YES	NO
1347384	irbesartan	83818	RxNorm	NO	YES	NO
1326012	Isradipine	33910	RxNorm	NO	YES	NO
1308216	Lisinopril	29046	RxNorm	NO	YES	NO
1367500	Losartan	52175	RxNorm	NO	YES	NO
907013	Metolazone	6916	RxNorm	NO	YES	NO
1310756	moexipril	30131	RxNorm	NO	YES	NO
1318137	Nicardipine	7396	RxNorm	NO	YES	NO

1318853	Nifedipine	7417	RxNorm	NO	YES	NO
1319880	Nisoldipine	7435	RxNorm	NO	YES	NO
40226742	olmesartan	321064	RxNorm	NO	YES	NO
1373225	Perindopril	54552	RxNorm	NO	YES	NO
1331235	quinapril	35208	RxNorm	NO	YES	NO
1334456	Ramipril	35296	RxNorm	NO	YES	NO
1317640	telmisartan	73494	RxNorm	NO	YES	NO
1342439	trandolapril	38454	RxNorm	NO	YES	NO
1308842	valsartan	69749	RxNorm	NO	YES	NO
1307863	Verapamil	11170	RxNorm	NO	YES	NO

1.1.6 Concept: [LEGEND HTN] Hypertension drugs

Concept ID	Concept Name	Code	Vocabulary	Excluded	Descendants	Mapped
1319998	Acebutolol	149	RxNorm	NO	YES	NO
1317967	aliskiren	325646	RxNorm	NO	YES	NO
991382	Amiloride	644	RxNorm	NO	YES	NO
1332418	Amlodipine	17767	RxNorm	NO	YES	NO
1314002	Atenolol	1202	RxNorm	NO	YES	NO
40235485	azilsartan	1091643	RxNorm	NO	YES	NO
1335471	benazepril	18867	RxNorm	NO	YES	NO
1322081	Betaxolol	1520	RxNorm	NO	YES	NO
1338005	Bisoprolol	19484	RxNorm	NO	YES	NO
932745	Bumetanide	1808	RxNorm	NO	YES	NO
1351557	candesartan	214354	RxNorm	NO	YES	NO
1340128	Captopril	1998	RxNorm	NO	YES	NO
1346823	carvedilol	20352	RxNorm	NO	YES	NO
1395058	Chlorthalidone	2409	RxNorm	NO	YES	NO
1398937	Clonidine	2599	RxNorm	NO	YES	NO
1328165	Diltiazem	3443	RxNorm	NO	YES	NO
1363053	Doxazosin	49276	RxNorm	NO	YES	NO
1341927	Enalapril	3827	RxNorm	NO	YES	NO
1309799	eplerenone	298869	RxNorm	NO	YES	NO
1346686	eprosartan	83515	RxNorm	NO	YES	NO
1353776	Felodipine	4316	RxNorm	NO	YES	NO
1363749	Fosinopril	50166	RxNorm	NO	YES	NO
956874	Furosemide	4603	RxNorm	NO	YES	NO
1344965	Guanfacine	40114	RxNorm	NO	YES	NO
1373928	Hydralazine	5470	RxNorm	NO	YES	NO
974166	Hydrochlorothiazide	5487	RxNorm	NO	YES	NO
978555	Indapamide	5764	RxNorm	NO	YES	NO
1347384	irbesartan	83818	RxNorm	NO	YES	NO
1326012	Isradipine	33910	RxNorm	NO	YES	NO
1386957	Labetalol	6185	RxNorm	NO	YES	NO
1308216	Lisinopril	29046	RxNorm	NO	YES	NO
1367500	Losartan	52175	RxNorm	NO	YES	NO
1305447	Methyldopa	6876	RxNorm	NO	YES	NO
907013	Metolazone	6916	RxNorm	NO	YES	NO
1307046	Metoprolol	6918	RxNorm	NO	YES	NO
1309068	Minoxidil	6984	RxNorm	NO	YES	NO
1310756	moexipril	30131	RxNorm	NO	YES	NO
1313200	Nadolol	7226	RxNorm	NO	YES	NO
1314577	nebivolol	31555	RxNorm	NO	YES	NO
1318137	Nicardipine	7396	RxNorm	NO	YES	NO
1318853	Nifedipine	7417	RxNorm	NO	YES	NO
1319880	Nisoldipine	7435	RxNorm	NO	YES	NO
40226742	olmesartan	321064	RxNorm	NO	YES	NO
1327978	Penbutolol	7973	RxNorm	NO	YES	NO

1373225	Perindopril	54552	RxNorm	NO	YES	NO
1345858	Pindolol	8332	RxNorm	NO	YES	NO
1350489	Prazosin	8629	RxNorm	NO	YES	NO
1353766	Propranolol	8787	RxNorm	NO	YES	NO
1331235	quinapril	35208	RxNorm	NO	YES	NO
1334456	Ramipril	35296	RxNorm	NO	YES	NO
970250	Spironolactone	9997	RxNorm	NO	YES	NO
1317640	telmisartan	73494	RxNorm	NO	YES	NO
1341238	Terazosin	37798	RxNorm	NO	YES	NO
942350	torsemide	38413	RxNorm	NO	YES	NO
1342439	trandolapril	38454	RxNorm	NO	YES	NO
904542	Triamterene	10763	RxNorm	NO	YES	NO
1308842	valsartan	69749	RxNorm	NO	YES	NO
1307863	Verapamil	11170	RxNorm	NO	YES	NO

1.1.7 Concept: [LEGEND HTN] ACE inhibitors

Concept ID	Concept Name	Code	Vocabulary	Excluded	Descendants	Mapped
1335471	benazepril	18867	RxNorm	NO	YES	NO
1340128	Captopril	1998	RxNorm	NO	YES	NO
1341927	Enalapril	3827	RxNorm	NO	YES	NO
1363749	Fosinopril	50166	RxNorm	NO	YES	NO
1308216	Lisinopril	29046	RxNorm	NO	YES	NO
1310756	moexipril	30131	RxNorm	NO	YES	NO
1373225	Perindopril	54552	RxNorm	NO	YES	NO
1331235	quinapril	35208	RxNorm	NO	YES	NO
1334456	Ramipril	35296	RxNorm	NO	YES	NO
1342439	trandolapril	38454	RxNorm	NO	YES	NO

1.2 THZ New-Users

1.2.1 Cohort Entry Events

People with continuous observation of 365 days before event may enter the cohort when observing any of the following:

1. drug exposure of '[LEGEND HTN] Thiazide or thiazide-like diuretic' for the first time in the person's history.

Limit cohort entry events to the earliest event per person.

Restrict entry events to with all of the following criteria:

1. having no drug exposures of '[LEGEND HTN] Hypertension drugs', starting anytime prior to cohort entry start date.

2. having at least 1 condition occurrence of 'Hypertensive disorder', starting between 365 days before and 0 days after cohort entry start date.
3. having exactly 1 distinct standard concepts from drug era of '[LEGEND HTN] Hypertension drugs', starting between 0 days before and 7 days after cohort entry start date.

1.2.2 Cohort Exit

The cohort end date will be based on a continuous exposure to '[LEGEND HTN] Thiazide or thiazide-like diuretic': allowing 30 days between exposures, adding 0 days after exposure ends, and using days supply and exposure end date for exposure duration.

1.2.3 Cohort Eras

Entry events will be combined into cohort eras if they are within 0 days of each other.

1.2.4 Concept: Hypertensive disorder

Concept ID	Concept Name	Code	Vocabulary	Excluded	Descendants	Mapped
316866	Hypertensive disorder	38341003	SNOMED	NO	YES	NO

1.2.5 Concept: [LEGEND HTN] First-line hypertension drugs

Concept ID	Concept Name	Code	Vocabulary	Excluded	Descendants	Mapped
1332418	Amlodipine	17767	RxNorm	NO	YES	NO
40235485	azilsartan	1091643	RxNorm	NO	YES	NO
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974166	Hydrochlorothiazide	5487	RxNorm	NO	YES	NO
978555	Indapamide	5764	RxNorm	NO	YES	NO
1347384	irbesartan	83818	RxNorm	NO	YES	NO
1326012	Isradipine	33910	RxNorm	NO	YES	NO
1308216	Lisinopril	29046	RxNorm	NO	YES	NO
1367500	Losartan	52175	RxNorm	NO	YES	NO
907013	Metolazone	6916	RxNorm	NO	YES	NO
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1318853	Nifedipine	7417	RxNorm	NO	YES	NO
1319880	Nisoldipine	7435	RxNorm	NO	YES	NO
40226742	olmesartan	321064	RxNorm	NO	YES	NO
1373225	Perindopril	54552	RxNorm	NO	YES	NO
1331235	quinapril	35208	RxNorm	NO	YES	NO
1334456	Ramipril	35296	RxNorm	NO	YES	NO
1317640	telmisartan	73494	RxNorm	NO	YES	NO
1342439	trandolapril	38454	RxNorm	NO	YES	NO
1308842	valsartan	69749	RxNorm	NO	YES	NO
1307863	Verapamil	11170	RxNorm	NO	YES	NO

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978555	Indapamide	5764	RxNorm	NO	YES	NO
1347384	irbesartan	83818	RxNorm	NO	YES	NO
1326012	Isradipine	33910	RxNorm	NO	YES	NO
1386957	Labetalol	6185	RxNorm	NO	YES	NO
1308216	Lisinopril	29046	RxNorm	NO	YES	NO
1367500	Losartan	52175	RxNorm	NO	YES	NO
1305447	Methyldopa	6876	RxNorm	NO	YES	NO
907013	Metolazone	6916	RxNorm	NO	YES	NO
1307046	Metoprolol	6918	RxNorm	NO	YES	NO
1309068	Minoxidil	6984	RxNorm	NO	YES	NO
1310756	moexipril	30131	RxNorm	NO	YES	NO
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1319880	Nisoldipine	7435	RxNorm	NO	YES	NO
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1327978	Penbutolol	7973	RxNorm	NO	YES	NO

1373225	Perindopril	54552	RxNorm	NO	YES	NO
1345858	Pindolol	8332	RxNorm	NO	YES	NO
1350489	Prazosin	8629	RxNorm	NO	YES	NO
1353766	Propranolol	8787	RxNorm	NO	YES	NO
1331235	quinapril	35208	RxNorm	NO	YES	NO
1334456	Ramipril	35296	RxNorm	NO	YES	NO
970250	Spironolactone	9997	RxNorm	NO	YES	NO
1317640	telmisartan	73494	RxNorm	NO	YES	NO
1341238	Terazosin	37798	RxNorm	NO	YES	NO
942350	torsemide	38413	RxNorm	NO	YES	NO
1342439	trandolapril	38454	RxNorm	NO	YES	NO
904542	Triamterene	10763	RxNorm	NO	YES	NO
1308842	valsartan	69749	RxNorm	NO	YES	NO
1307863	Verapamil	11170	RxNorm	NO	YES	NO

1.2.7 Concept: [LEGEND HTN] Thiazide or thiazide-like diuretic

Concept ID	Concept Name	Code	Vocabulary	Excluded	Descendants	Mapped
1395058	Chlorthalidone	2409	RxNorm	NO	YES	NO
974166	Hydrochlorothiazide	5487	RxNorm	NO	YES	NO
978555	Indapamide	5764	RxNorm	NO	YES	NO
907013	Metolazone	6916	RxNorm	NO	YES	NO

2 Outcome Cohorts

2.1 Primary Outcome: Hospitalization with Heart Failure Events

2.1.1 Cohort Entry Events

People enter the cohort when observing any of the following:

1. visit occurrences of 'Inpatient or ER visit'; having at least 1 condition occurrence of '[LEGEND HTN] Heart Failure', starting between 0 days before and all days after 'Inpatient or ER visit' start date and starting anytime on or before 'Inpatient or ER visit' end date.

2.1.2 Cohort Exit

The cohort end date will be offset from index event's end date plus 0 days.

2.1.3 Cohort Eras

Entry events will be combined into cohort eras if they are within 7 days of each other.

2.1.4 Concept: Inpatient or ER visit

Concept ID	Concept Name	Code	Vocabulary	Excluded	Descendants	Mapped
262	Emergency Room and Inpatient Visit	ERIP	Visit	NO	YES	NO
9203	Emergency Room Visit	ER	Visit	NO	YES	NO
9201	Inpatient Visit	IP	Visit	NO	YES	NO

2.1.5 Concept: [LEGEND HTN] Heart Failure

Concept ID	Concept Name	Code	Vocabulary	Excluded	Descendants	Mapped
315295	Congestive rheumatic heart failure	82523003	SNOMED	YES	YES	NO
316139	Heart failure	84114007	SNOMED	NO	YES	NO

2.2 Competing Outcome: Acute Myocardial Infarction Events

2.2.1 Cohort Entry Events

People may enter the cohort when observing any of the following:

1. condition occurrences of '[LEGEND HTN] Acute myocardial Infarction'.

Restrict entry events to having at least 1 visit occurrence of 'Inpatient or ER visit', starting anytime on or before cohort entry start date and ending between 0 days before and all days after cohort entry start date.

2.2.2 Cohort Exit

The cohort end date will be offset from index event's start date plus 7 days.

2.2.3 Cohort Eras

Entry events will be combined into cohort eras if they are within 180 days of each other.

2.2.4 Concept: Inpatient or ER visit

Concept ID	Concept Name	Code	Vocabulary	Excluded	Descendants	Mapped
262	Emergency Room and Inpatient Visit	ERIP	Visit	NO	YES	NO
9203	Emergency Room Visit	ER	Visit	NO	YES	NO
9201	Inpatient Visit	IP	Visit	NO	YES	NO

2.2.5 Concept: [LEGEND HTN] Acute myocardial Infarction

Concept ID	Concept Name	Code	Vocabulary	Excluded	Descendants	Mapped
4329847	Myocardial infarction	22298006	SNOMED	NO	YES	NO
314666	Old myocardial infarction	1755008	SNOMED	YES	YES	NO