include determining a level of soluble ST2 in a biological sample from a subject, comparing the level of soluble ST2 in the biological sample to a reference level of soluble ST2, and selecting an anti-hypertensive treatment (also referred to herein as anti-hypertensive therapy) for a subject having an elevated level of soluble ST2 in the biological sample compared to the reference level of soluble ST2. Also provided are methods of treating a subject that include determining a level of soluble ST2 in a biological sample from a subject, comparing the level of soluble ST2 in the biological sample to a reference level of soluble ST2, and administering to a subject having an elevated level of soluble ST2 in the biological sample compared to the reference level of soluble ST2 an anti-hypertensive agent. Also provided are methods for selecting a subject for participation in a clinical study of a treatment for reducing the risk of developing hypertension, and methods of evaluating the risk of developing hypertension in a subject that include determining a level of soluble ST2 in a biological sample from a subject. Also provided are kits that contain an antibody that specifically binds to soluble ST2 for use in any of the methods described herein.

Also provided are methods for determining the efficacy of a treatment for reducing the risk of developing hypertension in a subject that include determining a first level of soluble ST2 in a biological sample obtained from a subject at a first time point, (2) determining a second level level of soluble ST2 in a biological sample obtained from the subject at a second time point, wherein between the first time point and the second time point, the subject is administered two or more (e.g., more than five, more than ten, or more than twenty) doses of a treatment (e.g., anti-hypertensive treatment, e.g., one or more anti-hypertensive agents), (3) comparing the second level and first level of soluble ST2, and (4) identifying the treatment administered to a subject having a decrease in the second level of soluble ST2 as compared to the first level of soluble ST2 as being effective for reducing the risk of developing hypertension in the subject, or alternatively, identifying the treatment administered to a subject having no substantial change or an elevation in the second level of soluble ST2 as compared to the first level of soluble ST2 as not being effective for reducing the risk of developing hypertension in a subject.

In one aspect, there is provided a method for selecting a treatment for a healthy subject who does not have hyptertension, the method comprising:

determining a level of soluble ST2 in a biological sample from a subject;

comparing the level of soluble ST2 in the biological sample to a reference level of soluble ST2, wherein the reference level of soluble ST2 is a level of soluble ST2 in a healthy subject who has a low risk of developing hypertension; and

selecting an anti-hypertensive therapy for a subject having an elevated level of soluble ST2 in the biological sample compared to the reference level of soluble ST2.

In one aspect, there is provided use of an anti-hypertensive agent in the manufacture of a medicament for ~~treating a healthy subject who does not have hypertension~~reducing the risk of developing hypertension in a subject, wherein the subject is

one whose biological sample has been determined to have an elevated level of soluble ST2 compared to a reference level of soluble ST2, wherein the reference level of soluble ST2 is a level of soluble ST2 in a healthy subject who has a low risk of developing hypertension.

In one aspect, there is provided a method for selecting a subject for participation in a clinical study of a treatment for reducing the risk of developing hypertension, the method comprising:

determining a level of soluble ST2 in a biological sample from a healthy subject who does not have hypertension;

comparing the level of soluble ST2 in the biological sample to a reference level of soluble ST2, wherein the reference level of soluble ST2 is a level of soluble ST2 in a healthy subject who has a low risk of developing hypertension; and

selecting a subject having an elevated level of soluble ST2 in the biological sample compared to the reference level of soluble ST2 for participation in a clinical trial of a treatment for reducing the risk of developing hypertension.

In one aspect, there is provided a method for evaluating the risk of developing hypertension in a healthy subject who does not have hypertension, the method comprising:

determining a level of soluble ST2 in a biological sample from a subject;

comparing the level of soluble ST2 in the biological sample to a reference level of soluble ST2, wherein the reference level of soluble ST2 is a level of soluble ST2 in a healthy subject who has a low risk of developing hypertension; and

identifying a subject having an elevated level of soluble ST2 in the biological sample compared to the reference level of soluble ST2 as having an increased risk of developing hypertension, or identifying a subject having decreased low level of soluble ST2 in the biological sample compared to the reference level of soluble ST2 as having a decreased risk of developing hypertension.

In one aspect, there is provided a kit comprising an antibody that specifically binds to soluble ST2 for use in a method as described herein, or use as described herein, and optionally instructions for performing any of the methods or use as described herein.

In any of the methods described herein, the subject is a healthy subject who does not have hypertension. In other embodiments of any of the methods described herein, the subject is a healthy subject who does not have hypertension and is not diagnosed with or presenting with two or more symptoms of any one of a cardiac disease, a cardiovascular disease, or a kidney disease.

WHAT IS CLAIMED IS:

1. A method of selecting a treatment for a healthy subject who does not have hypertension, the method comprising:

determining a level of soluble ST2 in a biological sample from a subject;

comparing the level of soluble ST2 in the biological sample to a reference level of soluble ST2, wherein the reference level of soluble ST2 is a level of soluble ST2 in a healthy subject who has a low risk of developing hypertension; and

selecting an anti-hypertensive therapy for a subject having an elevated level of soluble ST2 in the biological sample compared to the reference level of soluble ST2.

~~2. The method of claim 1, wherein the reference level of soluble ST2 is a level of soluble ST2 in a healthy subject who has a low risk of developing hypertension.~~

2.~~3.~~ The method of claim 1, wherein the biological sample comprises blood, serum, or plasma.

3.~~4.~~ The method of claim 1, further comprising:

determining the level of one or more additional biomarkers selected from the group consisting of: atrial natriuretic peptide (ANP), proANP, N-terminal (NT)-proANP, brain natriuretic peptide (BNP), proBNP, NT-proBNP, cardiac troponin ~~cardiac troponin I~~, C-reactive protein, creatinine, and Blood Urea Nitrogen (BUN) in the biological sample;

comparing the level of the one or more additional biomarkers in the biological sample to a reference level of the one or more additional biomarkers; and

selecting an anti-hypertensive therapy for a subject having an elevated level of the one or more additional biomarkers in the biological sample compared to the reference level of the one or more additional biomarkers.

4.~~5.~~ The method of claim 3, wherein the one or more additional biomarkers are selected from the group consisting of BNP, proBNP, and NT-proBNP.

5.~~6.~~ Use of an anti-hypertensive agent in the manufacture of a medicament for ~~treating~~ reducing the risk of developing hypertension in a subject ~~a healthy subject who does not have hypertension, wherein the subject is one~~ whose biological sample has been determined to have an elevated level of soluble ST2 as compared to a reference level of soluble ST2, wherein the reference level of soluble ST2 is a level of soluble ST2 in a healthy subject who has a low risk of developing hypertension.

~~7. The use of claim 6, wherein the reference level of soluble ST2 is a level of soluble ST2 in a healthy subject who has a low risk of developing hypertension.~~

6.~~8.~~The use of claim 5~~6~~, wherein the biological sample comprises blood, serum, or plasma.

7.~~9.~~ The use of claim 5~~6~~, wherein the biological sample has been further determined to have an elevated level of one or more additional biomarkers selected from the group consisting of: atrial natriuretic peptide (ANP), proANP, N-terminal (NT)-proANP, brain natriuretic peptide (BNP), proBNP, NT-proBNP, cardiac troponin ~~cardiac troponin I~~, C-reactive protein, creatinine, and Blood Urea Nitrogen (BUN) compared to a reference level of the one or more additional biomarkers.

8.~~10.~~ The use of claim 7~~9~~, wherein the one or more additional biomarkers are selected from the group consisting of BNP, proBNP, and NT-proBNP.

9.~~11.~~ A method for selecting a subject for participation in a clinical study of a treatment for reducing the risk of developing hypertension, the method comprising:

determining a level of soluble ST2 in a biological sample from a healthy subject who does not have hypertension;

comparing the level of soluble ST2 in the biological sample to a reference level of soluble ST2, wherein the reference level of soluble ST2 is a level of soluble ST2 in a healthy subject who has a low risk of developing hypertension; and

selecting a subject having an elevated level of soluble ST2 in the biological sample compared to the reference level of soluble ST2 for participation in a clinical trial of a treatment for reducing the risk of developing hypertension.

~~12. The method of claim 11, wherein the reference level of soluble ST2 is a level of soluble ST2 in a healthy subject who has a low risk of developing hypertension.~~

10.~~13.~~ The method of claim 9~~11~~, wherein the biological sample comprises blood, serum, or plasma.

11.~~14.~~ The method of claim 9~~11~~, further comprising:

determining the level of one or more additional biomarkers selected from the group consisting of: atrial natriuretic peptide (ANP), proANP, N-terminal (NT)-proANP, brain natriuretic peptide (BNP), proBNP, NT-proBNP, cardiac troponin ~~cardiac troponin I~~, C-reactive protein, creatinine, and Blood Urea Nitrogen (BUN) in the biological sample;

comparing the level of the one or more additional biomarkers in the biological sample to a reference level of the one or more additional biomarkers; and

selecting a subject having an elevated level of the one or more additional biomarkers in the biological sample compared to the reference level of the one or more additional biomarkers for participation in a clinical trial of a treatment for reducing the risk of developing hypertension.

12.~~15.~~ The method of claim 11, wherein the one or more additional biomarkers are selected from the group consisting of BNP, proBNP, and NT-proBNP.

13.~~16.~~ A method for evaluating the risk of developing hypertension in a healthy subject who does not have hypertension, the method comprising:

determining a level of soluble ST2 in a biological sample from a subject;

comparing the level of soluble ST2 in a biological sample to a reference level of soluble ST2, wherein the reference level of soluble ST2 is a level of soluble ST2 in a healthy subject who has a low risk of developing hypertension; and

identifying a subject having an elevated level of soluble ST2 in the biological sample compared to the reference level of soluble ST2 as having an increased risk of developing hypertension, or identifying a subject having a decreased ~~low~~ level of soluble ST2 in the biological sample compared to the reference level of soluble ST2 as having a decreased risk of developing hypertension.

~~17. The method of claim 16, wherein the reference level of soluble ST2 is a level of soluble ST2 in a healthy subject who has a low risk of developing hypertension.~~

14.~~18.~~ The method of claim 13~~16~~, wherein the risk of developing hypertension is the risk of developing hypertension within three years.

15.~~19.~~ The method of claim 13~~16~~, wherein the biological sample comprises blood, serum, or plasma.

16.~~20.~~ The method of claim 13~~16~~, further comprising:

determining the level of one or more additional biomarkers selected from the group consisting of: atrial natriuretic peptide (ANP), proANP, N-terminal (NT)-proANP, brain natriuretic peptide (BNP), proBNP, NT-proBNP, cardiac troponin ~~cardiac troponin I~~, C-reactive protein, creatinine, and Blood Urea Nitrogen (BUN) in the biological sample;

comparing the level of the one or more additional biomarkers in the biological sample to a reference level of the one or more additional biomarkers; and

identifying a subject having an elevated level of the one or more additional biomarkers in the biological sample compared to the reference level of the one or more additional biomarkers as having an increased risk of developing hypertension.

17.~~21.~~ The method of claim 16~~20~~, wherein the one or more additional biomarkers are selected from the group consisting of BNP, proBNP, and NT-proBNP.

18.~~22.~~ The method of any one of claims 1-4 and 9-16~~1-5 and 11-20~~, or the use of any one of claims 5-8~~6-10~~, wherein the subject is human.

19.~~23.~~ A kit comprising an antibody that specifically binds to soluble ST2 for use in a method of any one of claims 1-4 and 9-16~~1-5 and 11-20~~, or use of any one of claims 5-8~~6-10~~, and optionally instructions for performing ~~any of the methods~~ a method of any one of claims 1-4 and 9-16~~1-5 and 11-20~~ or use of any one of claims 5-8~~6-10~~.

20.~~24.~~ The use of claim 5~~6~~, wherein the anti-hypertensive agent is selected from the group consisting of Diuretics, Beta-blockers, Angiotensin-converting enzyme inhibitors (ACE inhibitors), Angiotensin II receptor blockers (ARBs), Calcium channel blockers, Alpha-blockers, Centrally acting drugs, Vasodilators, and Renin inhibitors.