Appendix 1 Literature search strategies

Sources searched for systematic reviews and other evidence-based reports:

1. The Cochrane Library (CDSR). Issue 3, 2002.
2. Database of Abstracts of Reviews of Effects(DARE). NHS Centre for Reviews & Dissemination, October 2002.
3. HTA Database, NHS Centre for Reviews & Dissemination, October 2002.
4. Medion database of diagnostic met-analyses and reviews. University of Maastricht, October 2000 .
   URL:http://www.hag.unimaas.nl/Internationalisering/onderzoek/Cochrane/database%20Frank%20Buntinx/welcome_on_the_webpage_of_medion.htm
5. National Guideline Clearinghouse URL: http://www.guideline.gov/index.asp
6. Scottish Intercollegiate Guidelines Network URL:
   http://www.show.scot.nhs.uk/sign/index.html
7. Trip database URL: http://www.tripdatabase.com/
8. Agency for Healthcare Research and Quality URL: http://www.ahrq.gov/
9. American College of Cardiology URL: http://www.acc.org/index.htm
10. American Society of Nuclear Cardiology URL: http://www.asnc.org/
11. British Cardiac Society URL: http://www.bcs.com/resources/links.html
12. British Nuclear Cardiology Society URL: http://www.bncs.org.uk/
13. Global Cardiology Network URL: http://www.globalcardiology.org/index.html
14. European Society of Cardiology URL: http://www.escardio.org/
15. Royal College of Physicians URL: http://www.rcplondon.ac.uk/

Ovid Multifile Search: Medline 1966- Oct 2002, Embase 1980- 2002 (week44), Premedline 5th November 2002*

1. myocardial ischemia/
2. coronary disease/
3. exp chest pain/
4. myocardial infarction/
5. exp heart infarction/
6. coronary arteriosclerosis/
7. exp coronary stenosis/
8. coronary thrombosis/
9. coronary artery constriction/
10. exp angina pectoris/
11. heart muscle perfusion/
12. (myocardi$ adj3 perfusion).tw.
13. coronary heart disease?.tw.
14. (isch?emi$ adj3 (heart or coronary or myocardial)).tw.
15. angina.tw.
16 . chest pain?.tw.
17. ((myocardial or coronary) adj3 (infarct$ or thrombosis or stenosis or restenosis or arteriosclerosis)).tw.
18. or/1-17
19. Tomography, Emission-Computed, Single-Photon/
20. (spect or spet).tw.
21. single photon emission computed tomography.tw.
22. scintigraph$.tw.

23. or/19-22
24 . 18 and 23
25. 23 and (heart or coronary or myocardi$).tw.
26 . ((exercise or stress) adj3 test?).tw.
27 . 18 and imag$.tw.
28. thallium.rw.
29. technetium tc 99m.rw.
30. 29 and (sestamibi or tetrofosmin).tw.
31. (26 or 27) and (28 or 30)
32. methoxy isobutyl isonitrile technetium tc 99m/
33.tetrofosmin tc 99m/
34. thallium 201/
35. thallium chloride tl 201/
36. (26 or 27) and (32 or 33 or 34 or 35)
37. 24 or 25 or 31 or 36
38. electrocardiography/
39. electrocardiograph$.tw.
40. (ecg or ekg).tw.
41. or/38-40
42. exercise test/
43. (exercise or stress or stressor or treadmill or bicycl$ or cycling).tw.
44. dipyridamole/
45. adenosine/
46. adenosine triphosphate/
47. dobutamine/
48. or/42-47
49. 41 and 48
50. exp coronary angiography/
51. ((coronary or myocardi$) adj3 (angiograph$ or angiogram$ or arteriograph$)).tw.
52. or/50-51
53. "sensitivity and specificity"/
54. roc curve/
55. predictive value of tests/
56. false positive reactions/
57. false negative reactions/
58. diagnostic accuracy/
59. diagnostic error/
60. diagnostic value/
61. differential diagnosis/
62. early diagnosis/
63. prediction/
64. prognosis/
65. risk assessment/
66. recurrence risk/
67. (ri or di or du).fs.
68. sensitivity.tw.
69. specificity.tw.
70. roc.tw.
71. (predictive adj4 value$).tw.
72. (prognosis or prognostic).tw.
73. (risk adj3 stratif$).tw.
74. (false adj3 (positive$ or negative$)).tw.
75. likelihood ratio$.tw.

76. (logistic adj2 (regression or model$)).tw.
77. (regression adj2 analys$).tw.
78. (distinguish$ or differentiat$).tw.
79. (identif$ or detect$ or diagnos$ or accura$).tw.
80. reproducibility of results/
81. or/53-80
82. exp myocardial revascularization/
83. exp coronary artery surgery/
84 . atherectomy, coronary/
85. angioplasty, balloon/
86. revasculari?ation.tw.
87. angioplasty.tw.
88. coronary artery bypass.tw.
89. clinical pathways/
90. clinical protocols/
91. "referral and consultation"/
92. ((clinical or critical) adj3 (path? or pathway?)).tw.
93. protocol?.tw.
94. (referral or refer or referred).tw.
95. ((management or diagnos$ or investigat$) adj3 plan).tw.
96 . myocardial reperfusion/
97. reperfusion.tw.
98. exp morbidity/
99. exp mortality/
100. death,sudden,cardiac/
102. major adverse cardiac event?.tw.
103. "Outcome Assessment (Health Care)"/
104. myocardial infarction/
105. exp heart infarction/
106. exp angina, unstable/
107. (evaluat$ or assess$ or increment$ or compara$).tw.
108. or/82-107
109. 37 and 81
110. 49 and 81
111. 52 and 81
112. 109 and (110 or 111)
113. 37 and (49 or 52)
114. 108 and 113
115. 112 or 114
116. (animal/ or nonhuman/) not human/
117. 115 not 116
118.(editorial or letter).pt.
119. 117 not 118
120. limit 119 to yr=1980-2002

*** using textword terms only**

2 Biosis (Edina) 1985 – 16th December 2002

((al:spect or al: spet or al:scintigraph*
or
al:thallium or al:technetium or al:tetrofosmin
or
tal:computed tomography)
AND
(al:ecg or al:electrocardiogra* or al:angiogra*
or
al:stress test or al:exercise test)
AND
(al:myocardial or al:heart or al:coronary
or
al:chest pain or al:angina
or
al:ischemi* or al:ischaemi*))
AND
(al:diagnos* or al:detect*
or
al:sensitivity or al:specificity or al:roc
or
al:prognosis or al: prognositic or al:predict*
or
al:protocol* or al:pathway*
or
al:false positive or al:false negative or al:incremental
or
al:risk stratif* or al:risk assess*)

3 Science Citation Index (Web of Science) and WOS Proceedings 1981 – 8th January 2003

(spect or spet or scintigraph*
or
thallium or technetium or tetrofosmin
or
computed tomography)
AND
(ecg or electrocardiogra* or angiogra*
or
stress test or exercise test)
AND
(myocardial or heart or coronary
or
chest pain or angina
or
ischemi* or ischaemi*))

AND
(diagnos* or detect*
or
sensitivity or specificity or roc
or
prognosis or prognositic or predict*
or
protocol* or pathway*
or
false positive or false negative or incremental
or
risk stratif* or risk assess*)

4 HMIC (1979 – 2002)

(Spect or spet or scintoigraph* or thallium or technetium or terofosmin or computed tomography
and
ecg or ekg or electrocardiogra* or angiogra* or stress test or exercise test)
or
(ischemi* or ischaemi* or chest pain or angina or myocardial or heart or coronary
and
diagnostic imaging in DE)

5 HTA and DARE 4th October 2002

ECG or electrocardiograph* or angiogr*
Or
SPECT or scintigraphy or perfusion imag*
Or
Diagnos* and (coronary or myocardial or ischem* or ischaem*)

6 Medion (October 2002)

Spect; spet; scintigraph; coronary; perfusion in ti ,ab

7 Cochrane Library Issue 3,2002

1. Tomography, Emission-Computed, Single-Photon (MESH)
2. spect or spet or scintigraph$. or computed tomography
3. #1 or #2
4. Electrocardiography (MESH)
5. ECG or EKG or electrocardiograph*
6. Coronary Angiography (MESH)
7. Coronary near angio*
8. Coronary near arteriograph*
9. #4 or #5 or #6 or #7 or #8
10. #3 and #9

Medline (1966 – October 2002), Embase (1980 – October 2002 week 47)and Pre-Medline (5th November 2002)

1. myocardial ischemia/
2. coronary disease/
3. exp chest pain/
4. myocardial infarction/
5. exp heart infarction/
6. coronary arteriosclerosis/
7. exp coronary stenosis/
8. coronary thrombosis/
9. coronary artery constriction/
10. exp angina pectoris/
11. heart muscle perfusion/
12. (myocardi$ adj3 perfusion).tw.
13. coronary heart disease?.tw.
14. (isch?emi$ adj3 (heart or coronary or myocardial)).tw.
15. angina.tw.
16. chest pain?.tw.
17. ((myocardial or coronary) adj3 (infarct$ or thrombosis or stenosis or restenosis or arteriosclerosis)).tw.
18. or/1-17
19. Tomography, Emission-Computed, Single-Photon/
20. (spect or spet).tw.
21. single photon emission computed tomography.tw.
22. scintigraph$.tw.
23. or/19-22
24. 18 and 23
25. 23 and (heart or coronary or myocardi$).tw.
26. ((exercise or stress) adj3 test?).tw.
27. 18 and imag$.tw.
28. thallium.rw.
29. technetium tc 99m.rw.
30. 29 and (sestamibi or tetrofosmin).tw.
31. (26 or 27) and (28 or 30)
32. methoxy isobutyl isonitrile technetium tc 99m/
33. tetrofosmin tc 99m/
34. thallium 201/
35. thallium chloride tl 201/
36. (26 or 27) and (32 or 33 or 34 or 35)
37. 24 or 25 or 31 or 36
38. *myocardial ischemia/di, du, ri use mesz
39. *myocardial ischemia/di
40. *coronary disease/di, du, ri use mesz
41. *coronary disease/di
42. exp *chest pain/di, du, ri use mesz
43. exp *chest pain/di
44. *myocardial infarction/di, du, ri use mesz
45. exp *heart infarction/di use emez
46. *coronary arteriosclerosis/di, du, ri use mesz
47. *coronary arteriosclerosis/di

48. exp *coronary stenosis/di, du, ri use mesz
49. exp *coronary stenosis/di
50. *coronary thrombosis/di, du, ri use mesz
51. *coronary thrombosis/di
52. *coronary artery constriction/di use emez
53. exp *angina pectoris/di, du, ri use mesz
54. exp *angina pectoris/di
55. *heart muscle perfusion/
56. or/38-55
57. economics/
58. exp "costs and cost analysis"/ use mesz
59. exp economics,hospital/ use mesz
60. exp models,economic/ use mesz
61. ec.fs. use mesz
62. exp economic evaluation/
63. exp hospital cost/
64. exp quality of life/
65. value of life/
66. cost of illness/
67. health status/
68. health status indicators/ use mesz
69. (qol or qaly?).tw.
70. (quality adj2 life).tw.
71. (health adj3 (indicator? or status or utilit$)).tw.
72. (cost? adj3 (analys?s or evaluat$ or effectiveness)).tw.
73. conomic adj3 (analys?s or evaluat$ or effectiveness)).tw.
74. or/57-73
75. 37 and 74
76. 56 and 74
77. 75 or 76
78. limit 77 to yr=1990-2002

NHS-EED (4th October 2002)

ECG or electrocardiograph*
Or
SPECT or scintigraphy or perfusion imag*
Or
Diagnos* and (coronary or myocardial or ischem* or ischaem

Appendix 2 Data extraction form

Administration details
Paper number: _____ Extractor initials: _____ Date information extracted: _____

Study identifier: _____
(Surname of first author + year of publication)

Number of trials included in this paper: _____
(if more than one, complete separate extraction forms
for each, and add letters A, B, C etc to the study identifier)

Paper numbers of other trials with which this may link: _____ _____ _____ _____

Type of study

Diagnostic ☐
Prognostic: ☐
- General ☐
- Pre-operative risk assessment ☐
- Post-revascularisation assessment ☐

Aim of study:

Study Design
RCT ☐ Controlled Clinical Trial ☐ Prospective Comparative Observational Study ☐ Retrospective Comparative Observational Study ☐ Other_____

Characteristics of the participants				
Inclusion criteria:				
Exclusion criteria:				
Did the participants have suspected ☐ or confirmed ☐ CAD?				
Comparators/ pathways (please tick) **1** **2** **3** **4** **(Other) 5**	**SPECT ☐** **Stress ECG/ SPECT ☐** **SPECT/CA ☐** **Stress ECG/ SPECT/CA ☐** **☐**	**Stress ECG ☐** **Stress ECG ☐** **CA ☐** **Stress ECG/CA** **☐**	**CA ☐**	**All**
Number of patients enrolled in trial				
No. of patients receiving intervention				
Number of patients lost to follow-up				
Age (mean, range)				
Gender	**M:** **F:**	**M:** **F:**	**M:** **F:**	**M:** **F:**
Ethnicity				
Number of patients with previous MI				
Number of patients with previous PTCA				
Number of patients with previous CABG				

Are all these characteristics approximately balanced amongst the groups receiving different tests?
If the trial does not consist wholly of patients with previous MI, are those patients with previous MI identifiable separately from the rest of the participants throughout the trial?
Source of participants:
Method of recruitment: (Consecutive etc)
Dates for recruitment:
Characteristics of the intervention
Location and country of trial centre(s):
Duration of trial:
Length of follow-up:
Make and model of SPECT equipment:
Sequence and time between tests:
Radionuclide used: **Thallium** ☐ **Technetium sestamibi** ☐ **Technetium tetrofosmin** ☐ **Dual isotope (give details)** ☐

SPECT stress induced by:

Exercise:

Treadmill ☐

Bicycle ☐

Pharmacalogically:

Adenosine ☐

Dipyridamole ☐

Dobutamine ☐

Combination of exercise/pharmacological means (give details)

ECG stress induced by:

Treadmill ☐

Bicycle ☐

Pharmacalogically:

Adenosine ☐

Dipyridamole ☐

Dobutamine ☐

Combination of exercise/pharmacological means (give details) ☐

Number of tests where patients reached at least 85% of their predicted maximal heart rate:

Stress ECG:

SPECT:

For diagnostic studies, was the reference test coronary angiography?
(If not, give details of the reference test used)

What was the definition of a positive test result?
Stress ECG:

SPECT:

What was the authors' definition of significant CAD?
(eg 50% stenosis, 70% stenosis etc)

Concomitant interventions (interventions given to all participants in addition to SPECT/ stress ECG/CA):

_____

_____

Outcomes (Diagnostic studies)			
Number of patients receiving test	**SPECT**	**Stress ECG**	**CA**
True positives			**Notes**
False positives			
True negatives			
False negatives			
Sensitivity			
Specificity			
Positive predictive value			
Negative predictive value			
Positive likelihood ratio			
Negative likelihood ratio			
Diagnostic accuracy			
Diagnostic odds ratio			

Outcomes (Prognostic studies.)				
Comparators/ pathways (please tick) (Other) 1 2	**SPECT** ☐ **----------** ☐	**Stress ECG** ☐ **----------** ☐	**CA** ☐ **----------** ☐	**All**
Mortality				
Cardiac mortality				
Non fatal MI				
Revasc – PTCA				
Revasc - CABG				
Occurrence of unstable angina				
Other major cardiac events				
Survival free of cardiac death				
Preservation of left ventricular function				
Post-operative complications				
Number of Cas performed				
Hospital admissions				
Quality of Life (e.g.SF 36)				

Type of multivariate regression used:

Reference characteristic/factor:

Characteristic/factor	Odds ratio	Hazard ratio	Standard error	P value

Other comments

Appendix 3 QUADAS checklist for diagnostic tests

Paper number: _____ Extractor initials: _____ Date study assessed:_____

Study identifier: _____

(Surname of first author + year of publication)

Item		Yes	No	Unclear
1.	Was the spectrum of patients representative of the patients who will receive the test in practice?			
2.	Were selection criteria clearly described?			
3.	Is the reference standard likely to correctly classify the target condition?			
4.	Is the time period between reference standard and index test short enough to be reasonably sure that the target condition did not change between the two tests?			
5.	Did the whole sample or a random selection of the sample, receive verification using a reference standard of diagnosis?			
6.	Did patients receive the same reference standard regardless of the index test result?			
7.	Was the reference standard independent of the index test (i.e. the index test did not form part of the reference standard)?			
8a.	Was the execution of the index test described in sufficient detail to permit replication of the test?			
8b.	Was the execution of the reference standard described in sufficient detail to permit its replication?			
9a.	Were the index test results interpreted without knowledge of the results of the reference standard?			
9b.	Were the reference standard results interpreted without knowledge of the results of the index test?			
10.	Were the same clinical data available when test results were interpreted as would be available when the test is used in practice?			
11.	Were uninterpretable/ intermediate test results reported?			
12.	Were withdrawals from the study explained?			

Appendix 4 Downs and Black quality assessment form

SPECT review

Quality assessment form – prognostic studies

Paper number: _____

Study identifier:

(surname of first author + year of publication)

_____

Assessor initials: _____

Date form completed: _____

Reporting

1. *Is the hypothesis/aim/objective of the study clearly described?*

Yes	
No	

2. *Are the main outcomes to be measured clearly described in the Introduction or Methods section?*

If the main outcomes are first mentioned in the Results section, the question should be answered no.

Yes	
No	

3. *Are the characteristics of the patients included in the study clearly described?*

In cohort studies and trials, inclusion and/or exclusion criteria should be given. In case-control studies, a case-definition and the source for controls should be given.

Yes	
No	

4. Are the interventions of interest clearly described?

Treatments and placebo (where relevant) that are to be compared should be clearly described.

Yes	
No	

5. *Are the distribution of principal confounders in each group of subjects to be compared clearly described?*

A list of principal confounders is provided.

Yes	
Partially	
No	

6. *Are the main findings of the study clearly described?*

Simple outcome data (including denominators and numerators) should be reported for all major findings so that the reader can check the major analyses and conclusions. (This question does not cover statistical tests which are considered below.)

Yes	
No	

7. *Does the study provide estimates of the random variability in the data for the main outcomes?*

In non normally distributed data the inter-quartile range of results should be reported. In normally distributed data the standard error, standard deviation or confidence intervals should be reported. If the distribution of the data is not described, it must be assumed that the estimates used were appropriate and the question should be answered yes.

Yes	
No	

8. *Have all important adverse events that may be a consequence of the intervention been reported?*

This should be answered yes if the study demonstrates that there was a comprehensive attempt to measure adverse events. (A list of possible adverse events is provided.)

Yes	
No	

9. *Have the characteristics of patients lost to follow-up been described?*

This should be answered yes where there were no losses to follow-up or where losses to follow-up were so small that findings would be unaffected by their inclusion. This should be answered no where a study does not report the number of patients lost to follow-up.

Yes	
No	

10. *Have actual probability values been reported (eg 0.035 rather than <0.05) for the main outcomes except where the probability value is less than 0.001?*

Yes	
No	

External validity

All the following criteria attempt to address the representativeness of the findings of the study and whether they may be generalised to the population from which the study subjects were derived.

11. *Were the subjects asked to participate in the study representative of the entire population from which they were recruited?*

The study must identify the source population for patients and describe how the patients were selected. Patients would be representative if they comprised the entire source population, an unselected sample of consecutive patients, or a random sample. Random sampling is only feasible where a list of all members of the relevant population exists. Where a study does not report the proportion of the source population from which the patients are derived, the question should be answered as unable to determine.

Yes	
No	
Unable to determine	

12. *Were those subjects who were prepared to participate representative of the entire population from which they were recruited?*

The proportion of those asked who agreed should be stated. Validation that the sample was representative would include demonstrating that the distribution of the main confounding factors was the same in the study sample and the source population.

Yes	
No	
Unable to determine	

13. *Were the staff, places, and facilities where the patients were treated, representative of the treatment the majority of patients received?*

For the question to be answered yes the study should demonstrate that the intervention was representative of that in use in the source population. The question should be answered no if, for example, the intervention was undertaken in a specialist centre unrepresentative of the hospitals most of the source population would attend.

Yes	
No	
Unable to determine	

Internal validity – bias

14. *Was an attempt made to blind study subjects to the intervention they have received?*

For studies where the patients would have no way of knowing which intervention they received, this should be answered yes.

Yes	
No	
Unable to determine	

15. *Was an attempt made to blind those measuring the main outcomes of the intervention?*

Yes	
No	
Unable to determine	

16. *If any of the results of the study were based on 'data dredging', was this made clear?*

Any analyses that had not been planned at the outset of the study should be clearly indicated. If no retrospective unplanned subgroup analyses were reported, then answer yes.

Yes	
No	
Unable to determine	

17. *In trials and cohort studies, do the analyses adjust for different lengths of follow-up of patients, or in case-control studies, is the time period between the intervention and outcome the same for cases and controls?*

Where follow-up was the same for all study patients the answer should be yes. If different lengths of follow-up were adjusted for by, for example, survival analysis the answer should be yes. Studies where differences in follow-up are ignored should be answered no.

Yes	
No	
Unable to determine	

18. *Were the statistical tests used to assess the main outcomes appropriate?*

The statistical tests used must be appropriate to the data. For example non-parametric methods should be used for small sample sizes. Where little statistical analysis has been undertaken but where there is no evidence of bias, the question should be answered yes. If the distribution of the data (normal or not) is not described it must be assumed that the estimates used were appropriate and the question should be answered yes.

Yes	
No	
Unable to determine	

19. *Was compliance with the intervention/s reliable?*

Where there was non compliance with the allocated treatment or where there was contamination of one group, the question should be answered no. For studies where the effect of any misclassification was likely to bias any association to the null, the question should be answered yes.

Yes	
No	
Unable to determine	

20. *Were the main outcome measures used accurate (valid and reliable)?*

For studies where the outcome measures are clearly described, the question should be answered yes. For studies which refer to other work or that demonstrate the outcome measures are accurate, the question should be answered yes.

Yes	
No	
Unable to determine	

Internal validity – confounding (selection bias)

21. *Were the patients in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited from the same population?*

For example, patients for all comparison groups should be selected from the same hospital. The question should be answered unable to determine for cohort and case-control studies where there is no information concerning the source of **patients included in the study.**

Yes	
No	
Unable to determine	

22. *Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same period of time?*

For a study which does not specify the time period over which patients were recruited, the question should be answered as unable to determine.

Yes	
No	
Unable to determine	

23. *Were study subjects randomised to intervention groups?*

Studies which state that subjects were randomised should be answered yes except where method of randomisation would not ensure random allocation. For example, alternate allocation would score no because it is predictable.

Yes	
No	
Unable to determine	

24. *Was the randomised intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable?*

All non randomised studies should be answered no. If assignment was concealed from patients but not from staff, it should be answered no.

Yes	
No	
Unable to determine	

25. *Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?*

This question should be answered no for trials if: the main conclusions of the study were based on analyses of treatment rather than intention to treat; the distribution of known confounders in the different treatment groups was not described; or the distribution of known confounders differed between the treatment groups but was not taken into account in the analyses. In non randomised studies if the effect of the main confounders was not investigated or confounding was demonstrated but no adjustment was made in the final analyses the question should be answered as no.

Yes	
No	
Unable to determine	

26. *Were losses of patients to follow-up taken into account?*

If the numbers of patients lost to follow-up are not reported, the question should be answered as unable to determine. If the proportion lost to follow-up was too small to determine main findings, the question should be answered yes.

Yes	
No	
Unable to determine	

Power

27. *Did the study have sufficient power to detect a clinically important effect where the probability value for a difference being due to chance is less than 5%?*

Sample sizes have been calculated to detect a difference of x% and y%.

	Size of *smallest* intervention group	
A	$<n_1$	0
B	n_1-n_2	1
C	n_3-n_4	2
D	n_5-n_6	3
E	n_7-n_8	4
F	n_8+	5

Appendix 5 List of principal confounders and possible adverse events SPECT studies.

Question 5 List of principal confounders

- Age
- Gender
- Previous myocardial infarction
- Previous PTCA
- Previous CABG
- Heart failure (only really a problem with thallium because of high lung uptake)
- Weight

Question 8 List of possible adverse events

- Coronary angiography:
  Mortality; nonfatal MI; cerebrovascular accident; infection (rare); allergic dye reaction (rare); local vascular injury at site of catheterization.

- Stress test:
- Dipyridamole:
  Mortality; nonfatal MI; ventricular tachycardia; pulmonary oedema; chest pain; headache; dizziness; ECG changes.

- Adenosine:
  Complete heart block; 2nd degree heart block; bronchospasm; refractory angina; flushing; headache.

- Dobutamine:
  Mortality; nonfatal MI; vent dysrhythmias; ventricular tachycardia; hypotension; headache; nausea; anxiety; chest pain; severe ischaemia.

Appendix 6 Formulae used for deriving estimated numbers of true positives, false positives, false negatives, and true negatives in diagnostic studies reporting sensitivity, specificity and accuracy values

1. Sensitivity, specificity, diagnostic accuracy and total number known

TN = [N(acc-sens)*spec]/(spec-sens)

TP = acc*N – TN

FP = (TN/spec) – TN

FN = (TP/sens) – TP

2. Sensitivity, specificity, positive predictive value, negative predictive value and total number known

TP = N/[(1/PPV) + (1/sens) – 1 + (NPV/sens*(1-NPV)) – (NPV/(1-NPV))]

FP = (TP/PPV) – TP

FN = (TP/sens) – TP

TN = [((TP/sens) – TP)*NPV]/(1-NPV)

Notation:

TP: true positives
FP: false positives
FN: false negatives
TN: true negatives
sens: sensitivity
spec: specificity
acc: diagnostic accuracy
PPV: positive predictive value
NPV: negative predictive value
N: total number (=TP+FP+FN+TN)