Recent (2016-2019) Interesting and Important Clinical Trials, Guideline Changes, & Journal Articles
Question Case #1

75 y/o Asian Male
- No CVD, CKD, stroke
- Normal BMI, active, good diet
- Normal PE & baseline labs except for BP 150/80 – 160/80 (both arms & repeated X 3)
  His BP at home is similar
Question Case #1

You would recommend:

1. It’s normal for age. No Rx.
2. Put him on 1 gm Na$^+$ diet and check in 3 months.
3. Start beta-blocker
4. Start CCB, thiazide or ACD-I
2017 Guideline for the Prevention, Detection, Evaluation, and Management of HTN in Adults

A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

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J Am Col Cardiol. Sep 2017, 23976.
### Categories of BP in Adults*

<table>
<thead>
<tr>
<th>BP Category</th>
<th>SBP</th>
<th>DBP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt;120 mm Hg</td>
<td>&lt;80 mm Hg</td>
</tr>
<tr>
<td>Elevated</td>
<td>120-129 mm Hg</td>
<td>&lt;80 mm Hg</td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 1</td>
<td>130–139 mm Hg</td>
<td>80–89 mm Hg</td>
</tr>
<tr>
<td>Stage 2</td>
<td>≥140 mm Hg</td>
<td>≥90 mm Hg</td>
</tr>
</tbody>
</table>

*Individuals with SBP and DBP in 2 categories should be designated to the higher BP category.

Table 6

### Corresponding Values of Systolic BP/Diastolic BP for Clinic, Home (HBPM), Daytime, Nighttime, and 24-Hour Ambulatory (ABPM) Measurements.

<table>
<thead>
<tr>
<th>Clinic</th>
<th>HBPM</th>
<th>Daytime ABPM</th>
<th>Nighttime ABPM</th>
<th>24-Hour ABPM</th>
</tr>
</thead>
<tbody>
<tr>
<td>120/80</td>
<td>120/80</td>
<td>120/80</td>
<td>100/65</td>
<td>115/75</td>
</tr>
<tr>
<td>130/80</td>
<td>130/80</td>
<td>130/80</td>
<td>110/65</td>
<td>125/75</td>
</tr>
<tr>
<td>140/90</td>
<td>135/85</td>
<td>135/85</td>
<td>120/70</td>
<td>130/80</td>
</tr>
<tr>
<td>160/100</td>
<td>145/90</td>
<td>145/90</td>
<td>140/85</td>
<td>145/90</td>
</tr>
</tbody>
</table>
## BP Thresholds for and Goals of Pharmacologic Therapy in Patients with Hypertension According to Clinical Conditions

<table>
<thead>
<tr>
<th>Clinical Condition(s)</th>
<th>BP Threshold mm Hg</th>
<th>BP Goal mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>General</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinical CVD or 10 year ASCVD risk ≥ 10%</td>
<td>≥130/80</td>
<td>&lt;130/80</td>
</tr>
<tr>
<td>No clinical CVD and 10 year ASCVD risk &lt;10%</td>
<td>≥140/90</td>
<td>&lt;130/80</td>
</tr>
<tr>
<td>Older persons (≥65 years of age; non-institutionalized, ambulatory, community-living adults)</td>
<td>≥130 (SBP)</td>
<td>&lt;130 (SBP)</td>
</tr>
<tr>
<td><strong>Specific Comorbidities</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>≥130/80</td>
<td>&lt;130/80</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>≥130/80</td>
<td>&lt;130/80</td>
</tr>
<tr>
<td>Chronic kidney disease post-renal transplantation</td>
<td>≥130/80</td>
<td>&lt;130/80</td>
</tr>
<tr>
<td>Heart failure</td>
<td>≥130/80</td>
<td>&lt;130/80</td>
</tr>
<tr>
<td>Stable ischemic heart disease</td>
<td>≥130/80</td>
<td>&lt;130/80</td>
</tr>
<tr>
<td>Secondary stroke prevention</td>
<td>≥140/90</td>
<td>&lt;130/80</td>
</tr>
<tr>
<td>Peripheral arterial disease</td>
<td>≥130/80</td>
<td>&lt;130/80</td>
</tr>
</tbody>
</table>
Blood Pressure (BP) Thresholds and Recommendations for Treatment and Follow-Up

BP Thresholds and Recommendations for Treatment and Follow-up

- Normal BP (BP <120/80 mm Hg)
  - Promote optimal lifestyle habits
  - Reassess in 1 y (Class Ia)

- Elevated BP (BP 120-129/<80 mm Hg)
  - Nonpharmacologic therapy (Class I)
  - Reassess in 3-6 mo (Class I)

- Stage 1 Hypertension (BP 130-139/80-89 mm Hg)
  - Clinical ASCVD or estimated 10 y CVD risk ≥10%*
  - No
  - Reassess in 3-6 mo (Class I)
  - Nonpharmacologic therapy (Class I)

- Stage 2 Hypertension (BP ≥140/90 mm Hg)
  - Nonpharmacologic therapy and BP-lowering medication (Class I)
  - Reassess in 1 mo (Class I)

- BP goal not met
  - Assess and optimize adherence to therapy
  - Reassess in 3-6 mo (Class I)

* Using the ACC/AHA Pooled Cohort Equations. Note that patients with DM or CKD are automatically placed in the high-risk category. For initiation of RAS inhibitor or diuretic therapy, assess blood tests for electrolytes and renal function 2 to 4 weeks after initiating therapy.

† Consider initiation of pharmacologic therapy for stage 2 hypertension with 2 or more antihypertensive agents of different classes. Patients with stage 2 hypertension and BP >160/100 mm Hg should be promptly treated, carefully monitored, and subject to upward medication dose adjustment as necessary to control BP. Reassessment includes BP measurement, detection of orthostatic hypotension in selected patients (e.g., older or with postural symptoms), identification of white coat hypertension or a white coat effect, documentation of adherence, monitoring of the response to therapy, reinforcement of the importance of adherence, reinforcement of the importance of treatment, and assistance with treatment to achieve BP target.
Question Case #1

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SPRINT Clinical Trial

The NEW ENGLAND JOURNAL of MEDICINE

A Randomized Trial of Intensive versus Standard Blood-Pressure Control

The SPRINT Research Group

ABSTRACT

BACKGROUND
The most appropriate targets for systolic blood pressure to reduce cardiovascular morbidity and mortality among persons without diabetes remain uncertain.

METHODS
We randomly assigned 9361 persons with a systolic blood pressure of 130 mm Hg or higher and an increased cardiovascular risk, but without diabetes, to a systolic blood-pressure target of less than 120 mm Hg (intensive treatment) or a target of less than 140 mm Hg (standard treatment). The primary composite outcome was

The members of the writing committee (Jackson T. Wright, Jr., M.D., Ph.D., Jeff D. Williamson, M.D., M.H.S., Paul K. Whelton, M.D., Joni K. Snyder, R.N., B.S.N., M.A., Kaycee M. Sink, M.D., M.A.S., Michael V. Rocco, M.D., M.S.C.E., David M. Rebourssin, Ph.D., Mahboob Rahman, M.D., Suzanne Oparil, M.D., Cora E. Lewis, M.D., M.S.P.H., Paul L. Kimmel, M.D., Karen C. Johnson, M.D.)
Figure 2. Systolic Blood Pressure in the Two Treatment Groups over the Course of the Trial.
The systolic blood-pressure target in the intensive-treatment group was less than 120 mm Hg, and the target in the standard-treatment group was less than 140 mm Hg. The mean number of medications is the number of blood-pressure medications administered at the exit of each visit. I bars represent 95% confidence intervals.
SPRINT Clinical Trial

## Table 1. Serious Adverse Events, Conditions of Interest, and Mentioned Clinical Events.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Intensive Treatment (N=4447)</th>
<th>Standard Treatment (N=4455)</th>
<th>Hazard Ratio</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Serious adverse event</strong></td>
<td>1790 (38.3)</td>
<td>1796 (37.3)</td>
<td>1.04</td>
<td>0.25</td>
</tr>
<tr>
<td><strong>Conditions of interest</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serious adverse event only</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypotension</td>
<td>138 (3.0)</td>
<td>64 (1.4)</td>
<td>1.47</td>
<td>0.001</td>
</tr>
<tr>
<td>Syncope</td>
<td>107 (2.3)</td>
<td>80 (1.8)</td>
<td>1.33</td>
<td>0.05</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>87 (1.9)</td>
<td>79 (1.8)</td>
<td>1.18</td>
<td>0.38</td>
</tr>
<tr>
<td>Electrolyte abnormality</td>
<td>144 (3.2)</td>
<td>107 (2.4)</td>
<td>1.35</td>
<td>0.02</td>
</tr>
<tr>
<td>Injuries†</td>
<td>105 (2.2)</td>
<td>110 (2.5)</td>
<td>0.95</td>
<td>0.71</td>
</tr>
<tr>
<td>Acute kidney injury or acute renal failure‡</td>
<td>193 (4.2)</td>
<td>117 (3.0)</td>
<td>1.66</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Emergency department visit or serious adverse event</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypotension</td>
<td>138 (3.0)</td>
<td>64 (1.4)</td>
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<td>117 (3.0)</td>
<td>1.66</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

### Adverse laboratory measurements

<table>
<thead>
<tr>
<th>Variable</th>
<th>Intensive Treatment (N=4447)</th>
<th>Standard Treatment (N=4455)</th>
<th>Hazard Ratio</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum sodium &lt;130 mmol/liter</td>
<td>180 (3.2)</td>
<td>193 (3.0)</td>
<td>1.00</td>
<td>0.37</td>
</tr>
<tr>
<td>Serum potassium &lt;0.5 mmol/liter</td>
<td>6 (0.1)</td>
<td>12 (0.3)</td>
<td>0.22</td>
<td>0.15</td>
</tr>
<tr>
<td>Serum potassium &lt;3.0 mmol/liter</td>
<td>214 (4.2)</td>
<td>259 (5.8)</td>
<td>1.00</td>
<td>0.14</td>
</tr>
<tr>
<td>Serum potassium &gt;5.0 mmol/liter</td>
<td>54 (1.2)</td>
<td>40 (0.9)</td>
<td>1.00</td>
<td>0.32</td>
</tr>
</tbody>
</table>

### Other clinical events

<table>
<thead>
<tr>
<th>Variable</th>
<th>Intensive Treatment (N=4447)</th>
<th>Standard Treatment (N=4455)</th>
<th>Hazard Ratio</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute kidney injury or acute renal failure‡</td>
<td>204 (4.4)</td>
<td>120 (2.6)</td>
<td>1.71</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

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* A serious adverse event was defined as an event that was fatal or life-threatening, that required or prolonged hospitalization, or that was judged by the investigator to represent a clinically significant hazard or harm to the patient that might require medical or surgical intervention to prevent one of the other events listed above.

† Acute kidney injury or acute renal failure were defined if the diagnosis was listed in the hospital discharge summary and was believed by the clinical office to be one of the causes of admission or continued hospitalization. A few cases of acute kidney injury were noted in an emergency department if the patient presented for one of the other conditions of interest.

‡ Adverse laboratory measures were detected as routine or unscheduled tests; routine laboratory tests were performed at 1 month, then quarterly during the first year, then every 6 months.

§ Orthostatic hypotension was defined as a drop in systolic blood pressure of at least 20 mm Hg or in diastolic blood pressure of at least 10 mm Hg at 1 minute after the participant stood up, as compared with the value obtained when the participant was seated. Standing blood pressures were measured at screening, baseline, 1 month, 6 months, 12 months, and yearly thereafter. Participants were asked if they felt dizzy at the time the orthostatic measure was taken.

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Question Case #2

70 y/o retired cardiologist comes to you for ↑ BP at home
- His BP at your office (X3 visits over 2 months) was always 120/80 or better
- His BP at home is always >140/80
- EKG – normal
- Echo – borderline LVH. Normal EF
Question Case #2

What will you do?

1. Keep reassuring him
2. Start him on anti-anxiety medication
3. Start him on BP meds
<table>
<thead>
<tr>
<th></th>
<th>BP at Office</th>
<th>BP at Home</th>
</tr>
</thead>
<tbody>
<tr>
<td>White coat hypertension</td>
<td>Not controlled</td>
<td>Controlled</td>
</tr>
<tr>
<td>Masked hypertension</td>
<td>Controlled</td>
<td>Not controlled</td>
</tr>
</tbody>
</table>
Detection of White Coat Hypertension or Masked Hypertension in Patients Not on Drug Therapy

Office BP:
- ≥130/80 mm Hg but <160/100 mm Hg after 3 mo trial of lifestyle modification and suspect white coat hypertension

Daytime ABPM or HBPM
BP <130/80 mm Hg

Yes → White Coat Hypertension
- Lifestyle modification
- Annual ABPM or HBPM to detect progression
  (Class Ila)

No → Hypertension
- Continue lifestyle modification and start antihypertensive drug therapy
  (Class Ila)

Office BP:
- 120–129/<80 mm Hg after 3 mo trial of lifestyle modification and suspect masked hypertension

Daytime ABPM or HBPM
BP ≥ 130/80 mm Hg

Yes → Masked Hypertension
- Continue lifestyle modification and start antihypertensive drug therapy
  (Class Ila)

No → Elevated BP
- Lifestyle modification
- Annual ABPM or HBPM to detect MH or progression
  (Class Ila)
Relationship between Clinic and Ambulatory Blood-Pressure Measurements and Mortality


ABSTRACT

BACKGROUND
Evidence for the influence of ambulatory blood pressure on prognosis derives mainly from population-based studies and a few relatively small clinical investigations. This study examined the associations of blood pressure measured in the clinic (clinical blood pressure) and 24-hour ambulatory blood pressure with all-cause and cardiovascular mortality in a large cohort of patients in primary care.

METHODS
We analyzed data from a registry-based, multicenter, national cohort that included 63,910 adults recruited from 2004 through 2014 in Spain. Clinic and 24-hour ambulatory blood-pressure data were examined in the following categories: sustained hyper-

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. Banegas at the Department of Preventive Medicine and Public Health, Universidad Autónoma de Madrid, id:

Reprint: 2018 Massachusetts Medical Society

DOI: 10.1056/NEJMoA1712231
Relationship between Clinic & Ambulatory BP Measurements and Mortality

<table>
<thead>
<tr>
<th>Table 3. Association of Hypertension Phenotypes with All-Cause and Cardiovascular Mortality in Cox Regression Models. *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality and Blood-Pressure Phenotype</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>---------------------------</td>
</tr>
<tr>
<td><strong>All-cause mortality</strong></td>
</tr>
<tr>
<td>Normotension</td>
</tr>
<tr>
<td>Controlled hypertension</td>
</tr>
<tr>
<td>White-coat hypertension</td>
</tr>
<tr>
<td>White-coat uncontrolled hypertension</td>
</tr>
<tr>
<td>Masked hypertension</td>
</tr>
<tr>
<td>Masked uncontrolled hypertension</td>
</tr>
<tr>
<td>Sustained hypertension</td>
</tr>
<tr>
<td>Sustained uncontrolled hypertension</td>
</tr>
<tr>
<td><strong>Cardiovascular mortality</strong></td>
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<tr>
<td>Sustained hypertension</td>
</tr>
<tr>
<td>Sustained uncontrolled hypertension</td>
</tr>
</tbody>
</table>

*Hazard ratios were estimated for each blood-pressure phenotype, with normotension as reference. Hypertension phenotypes were defined in untreated patients as follows: normotension was normal clinic blood pressure (systolic <140 mm Hg and diastolic <90 mm Hg) and normal 24-hour pressure (systolic <120 mm Hg and diastolic <80 mm Hg); white-coat hypertension was defined as elevated clinic blood pressure (systolic ≥140 mm Hg or diastolic ≥90 mm Hg) and normal 24-hour pressure; masked hypertension was defined as normal clinic blood pressure and elevated 24-hour pressure (systolic ≥135 mm Hg or diastolic ≥85 mm Hg); and sustained hypertension was defined as elevated clinic and 24-hour blood pressures. In treated patients, the corresponding terms were controlled hypertension, white-coat uncontrolled hypertension, masked uncontrolled hypertension, and sustained uncontrolled hypertension, respectively, and were defined with the same blood-pressure cut-off points as those used for untreated patients.

1 Model 3 was adjusted for age, sex, smoking status, body-mass index, and status with respect to diabetes, dyslipidemia, previous cardiovascular disease, and number of antihypertensive drugs used.
2 Model 2 was additionally adjusted for clinic systolic and diastolic blood pressures.

Question Case #2

70 y/o retired cardiologist comes to you for ↑ BP at home
No CAD, stroke, heart failure, DM or renal problem.
Asymptomatic. Exercises 5X/week. Strict diet.
- His BP at your office (X3 visits over 2 months) was always 120/80 or better
- His BP at home is always >140/80
- EKG – normal
- Echo – borderline LVH. Normal EF
Question Case #2

What will you do?

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Question Case #2

What will you do?

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Hypertension

- Hypertension is defined as high blood pressure
- Blood pressure increases with age
  - At birth normal SBP 60-75 and DBP 30-45 mm Hg
  - 17 year old boy average 117/68 mm Hg
- Previously Hypertension was defined SBP > 140 or DBP > 90 mm Hg but ACC/AHA 2017 Guidelines have changed definition and goals for treatment
Question Case #3

A 75 y/o “retired” cardiologist comes to you for HTN. He has no CAD, stroke, heart failure or renal problems.

He argues with you about the benefits of drug therapy, especially reducing cardiovascular mortality.

You show him the evidence-based risk reduction by pharmacological therapy.
Question Case #3

Which one is correct based on previous RT?

<table>
<thead>
<tr>
<th></th>
<th>Heart Failure</th>
<th>Stroke</th>
<th>Coronary Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>↓ 50%</td>
<td>↓ 40%</td>
<td>↓ 20%</td>
</tr>
<tr>
<td>2.</td>
<td>↓ 30%</td>
<td>↓ 30%</td>
<td>↓ 50%</td>
</tr>
<tr>
<td>3.</td>
<td>↓ 20%</td>
<td>↓ 20%</td>
<td>↓ 20%</td>
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Question Case #3

Which one is correct based on previous RT?

Risk Reduction by Event

<table>
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</tr>
<tr>
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<tr>
<td>3.</td>
<td>↓ 20%</td>
<td>↓ 20%</td>
<td>↓ 20%</td>
</tr>
</tbody>
</table>
The trial was difficult to interpret at best and, in at least one important respect, unethical.

The trial adopted an unprecedented and novel method to measure blood pressure, making it impossible to compare with previous trials. In all the major recent hypertension trials, blood pressure had been measured three separate times with an automatic monitor in the presence of a healthcare professional.

In SPRINT, however, the healthcare professionals were trained to leave the room before the measurements started.
Welcome to dabl® Educational Trust

Services Offered

Validation Status of Devices
The most comprehensive and up-to-date list of tables on the validation status of all makes of BP devices - click for details

ESH-IP 2010 Online Service
The dabl® Educational Trust ESH-IP 2010 Online system offers a service whereby a validation study for a blood pressure device can be recorded and managed. The system calculates the results according to the ESH-IP 2010 protocol and allows the scientific paper to be generated.

Device Equivalence
Equivalence procedure for device manufacturers allowing manufacturers to submit devices for consideration for validation equivalence - click for details

ESH International Protocol Revision 2010
The International Protocol for the validation of blood pressure measuring devices in adults was revised by the European Society of Hypertension in 2010. A number of modifications in the revised protocol acknowledge that device accuracy has improved with technological advancements, and the passing criteria have been raised to ensure that only the best devices are recommended for clinical use. It superseded the original protocol for new studies that began since 1st July 2010 and it will supersede it for publications from 1st July 2011. Any doubts, using the original protocol, that are currently being completed must be published before that date.
<table>
<thead>
<tr>
<th>Model</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omron M3 IT (HEM-7131U-E)</td>
<td>Equivalent to M5 AC (HEM-7322-E)</td>
</tr>
<tr>
<td>Omron M3W (HEM-7202-E)</td>
<td>Single validation</td>
</tr>
<tr>
<td>Omron M4-1 (HEM-752-E)</td>
<td>Equivalent to 70SIT (HEM-759-E)</td>
</tr>
<tr>
<td>Omron M5-1 (HEM-757-E)</td>
<td>Two validations</td>
</tr>
<tr>
<td>Omron M6 (HEM-7001-E)</td>
<td>Four validations</td>
</tr>
<tr>
<td>Omron M6 (HEM-7211-E)</td>
<td>Single validation + Equivalent to 70SIT (HEM-759-E)</td>
</tr>
<tr>
<td>Omron M6 (HEM-7211-ES)</td>
<td>Equivalent to 70SIT (HEM-759-E)</td>
</tr>
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<td>Omron M6 AC (HEM-7322-E)</td>
<td>Single validation</td>
</tr>
<tr>
<td>Omron M6 Comfort (HEM-7000-E)</td>
<td>Single validation + Equivalent to M7 (HEM-780-E)</td>
</tr>
<tr>
<td>Omron M6 Comfort (HEM-7221-E)</td>
<td>Equivalent to M7 (HEM-780-E) and M5 Comfort (HEM-7000-E)</td>
</tr>
<tr>
<td>Omron M6 Comfort (HEM-7221-E)</td>
<td>Single validation + Equivalent to M6 Comfort (HEM-7000-E)</td>
</tr>
<tr>
<td>Omron M6 Comfort (HEM-7222-E)</td>
<td>Equivalent to M6 Comfort (HEM-7221-E)</td>
</tr>
<tr>
<td>Omron M6 Comfort IT (HEM-7322U-E)</td>
<td>Single validation</td>
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<tr>
<td>Omron M6W (HEM-7213-E)</td>
<td>Equivalent to M6 Comfort (HEM-7321-E)</td>
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<tr>
<td>Omron M7 (HEM-780-E)</td>
<td>Four validations</td>
</tr>
<tr>
<td>M7 Intelli IT (HEM-7322IT-E)</td>
<td>Equivalent to Omron M6 Comfort (HEM-7321-E)</td>
</tr>
<tr>
<td>Omron M10-IT (HEM-7000IT-E)</td>
<td>Equivalent to M7 (HEM-780-E) and M5 Comfort (HEM-7000-E)</td>
</tr>
<tr>
<td>Omron MX2 Basic (HEM-742-Z2)</td>
<td>Equivalent to M2 Compact (HEM-7102-E)</td>
</tr>
<tr>
<td>Omron MX8 Plus (HEM-742-E)</td>
<td>Single validation</td>
</tr>
<tr>
<td>Omron DEM-1 (HEM-7051-C12)</td>
<td>Equivalent to M3 Intelligence (HEM-7051-E)</td>
</tr>
<tr>
<td>Oregon Scientific BPU 320</td>
<td>Single validation</td>
</tr>
<tr>
<td>Panasonic R4W3108</td>
<td>Single validation</td>
</tr>
<tr>
<td>Panasonic EW2109</td>
<td>Single validation</td>
</tr>
<tr>
<td>Fansco PD-000811</td>
<td>Single validation</td>
</tr>
<tr>
<td>Philips DL8760</td>
<td>Single validation</td>
</tr>
</tbody>
</table>
Sphygmomanometers for Clinical Use

The following tables are lists of currently available Mercury, Aneroid and Non-Mercury Manual Sphygmomanometers, Automated Devices for Clinical Use and Finger Devices for Clinical Measurement. Discontinued devices are shown on a separate table. A complete list of all devices is available on our Device Index.

Manual Devices

<table>
<thead>
<tr>
<th>Device</th>
<th>Mode</th>
<th>AAMI</th>
<th>ESH 2002</th>
<th>ESH 2010</th>
<th>Circumstance</th>
<th>Recommendation</th>
<th>Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td>A&amp;D UM-101</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Without use of &quot;Mark&quot; button</td>
<td>Recommended</td>
<td>7</td>
</tr>
<tr>
<td>A&amp;D UM-102</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>With use of &quot;Mark&quot; button</td>
<td>Not Recommended</td>
<td>7</td>
</tr>
<tr>
<td>Accoson Greenlight 300</td>
<td>Electronic Display</td>
<td></td>
<td></td>
<td></td>
<td>A&amp;D UM-101 Equivalence, Without use of &quot;Mark&quot; button</td>
<td>Recommended</td>
<td>E127</td>
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<tr>
<td>Heine Gamma G7</td>
<td>Aneroid</td>
<td></td>
<td></td>
<td></td>
<td>At rest</td>
<td>Recommended</td>
<td>1</td>
</tr>
<tr>
<td>Heine Gamma XXL-LP</td>
<td>Aneroid</td>
<td></td>
<td></td>
<td></td>
<td>At rest</td>
<td>Recommended</td>
<td>6</td>
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</tbody>
</table>
### Automated Devices for Clinical Use

For a complete list of devices see our Device Index and for discontinued devices see our Discontinued Devices Index.

For this study, evaluation prior to publication was using the National Educational Fast Track validation Service.

#### Device Information

<table>
<thead>
<tr>
<th>Device</th>
<th>Mode</th>
<th>AAMI</th>
<th>BHS</th>
<th>ESH 2002</th>
<th>ESH 2010</th>
<th>Circumstance</th>
<th>Recommendation</th>
<th>Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omron 723 CIC (HEM-725CIC)</td>
<td>Osc</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Ad Hoc Protocol.</td>
<td>None</td>
<td>26</td>
</tr>
<tr>
<td>Omron 907 (HEM-907-E)</td>
<td>Aus &amp; Osc</td>
<td>Pass</td>
<td></td>
<td></td>
<td></td>
<td>Data analysed according to IP proposal only, Osc mode only</td>
<td>Questionable</td>
<td>19</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>At rest, Osc mode only, AAMI only, Recruitment violation</td>
<td>Questionable</td>
<td>11</td>
</tr>
<tr>
<td>Omron HBP-1100</td>
<td>Osc</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Elderly Population. Mode not stated.</td>
<td>Recommended</td>
<td>27</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>In ESRD before and after haemodialysis, Osc mode only</td>
<td>Not Recommended</td>
<td>26</td>
</tr>
</tbody>
</table>

**References:**

1. Page 26
2. Page 19
3. Page 11
4. Page 27
5. Page 26
Corresponding Values of SBP/DBP for Clinic, HBPM, Daytime, Nighttime, and 24-Hour ABPM Measurements

<table>
<thead>
<tr>
<th>Clinic</th>
<th>HBPM</th>
<th>Daytime ABPM</th>
<th>Nighttime ABPM</th>
<th>24-Hour ABPM</th>
</tr>
</thead>
<tbody>
<tr>
<td>120/80</td>
<td>120/80</td>
<td>120/80</td>
<td>100/65</td>
<td>115/75</td>
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<tr>
<td>130/80</td>
<td>130/80</td>
<td>130/80</td>
<td>110/65</td>
<td>125/75</td>
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<tr>
<td>140/90</td>
<td>135/85</td>
<td>135/85</td>
<td>120/70</td>
<td>130/80</td>
</tr>
<tr>
<td>160/100</td>
<td>145/90</td>
<td>145/90</td>
<td>140/85</td>
<td>145/90</td>
</tr>
</tbody>
</table>

ABPM indicates ambulatory blood pressure monitoring; BP, blood pressure; DBP diastolic blood pressure; HBPM, home blood pressure monitoring; and SBP, systolic blood pressure.
First Take Away Points

• Office BP measurements helpful but
• Home BP measurements crucial
• Need to check equipment and probably calibrate to auscultatory standard
• Need multiple measurements
  - After confirming BP measurements, I recommend to my patients checking morning and evening blood pressures at least 5 days prior to office visit and recording all BP
  - Averaging BP measurements on day to day basis
Second Take Away Points

• High blood pressure is a risk factor for heart disease, stroke and kidney disease

• Systolic blood pressure increases as you age

• Even in ages >80 years old, medication treatment has been shown to improve outcomes with 20-30% decrease in stroke or cardiac related death

• Life style changes should be pursued in all patients with hypertension
Question Case #4

68 y/o female with paroxysmal AF; (+) for HTN & DM
- Asymptomatic
- Now appears to be in persistent AF
  (asymptomatic, rate-controlled with BB)
Question Case #4

Which statement is correct?

1. Need to control the rhythm for prevention of stroke
2. Amiodarone to control the rhythm, which can lead to lower mortality
3. AF ablation would improve prognosis
4. No additional meds (except for anticoagulation) is necessary
AF: Rate versus Rhythm Control

• Rate control
  - May AF patients minimally symptomatic
  - Avoids AAD toxicities
  - Simpler and less costly

• Rhythm control
  - Hemodynamic benefits of NSR
    ▪ Left atrial contribution to ventricular filling
    ▪ Regular rhythm
  - Risk of tachymyopathy in AF with poorly controlled rate
  - ? Reduce risk of stroke and mortality
AFFIRM study: Rate vs Rhythm Control

N=4060 (1/3 first episode) with AF and ≥ 1 CVA risk factor (CHADS₂ or LA>5 cm)
Age 69.7 yrs
F-U 3.5 yrs

Cumulative Mortality (%)

Time (years)

- All-cause mortality: 17.5% in rhythm control, 15.1% in rate control
- Stroke: 7.3% in rhythm control vs. 5.7% in rate control
- Caveats: Older patients, able to tolerate rate control, AAD use, f-u period

P=.058

NEJM 2002; 347:1825
**Rate control: Medical**

- Beta-blockers generally first-line
- Diltiazem and verapamil alternatives (except systolic CHF)
- Digoxin second-line
  - CHF with LV dysfunction, or as second agent
  - Generally not useful for paroxysmal AF
- **Target of therapy**
  - Minimize symptoms, no tachymyopathy
  - 70-90 bpm at rest, acceptable exercise tolerance

RACE-II trial (Van Gelder IC, et al. *NEJM* 2010; 362: 1363) suggests even more “lenient” rate control (up to 110 bpm at rest) OK in medium term

- **But** resting rate in follow-up 75 bpm in “strict” rate control group and 86 bpm in “lenient” group
Rhythm control: Cardioversion

- **Chemical – most effective if AF < 7 days**
  - Ibutilide, dofetilide, flecainide, propafenone (Class I)
  - Amiodarone (Class IIa)

- **Electrical – DCCV**
  - 200-360J synchronized, biphasic waveform
  - Ibutilide pre-treatment may facilitate

- **Anticoagulate 3 weeks pre- and 4 weeks post-CV if AF >48 hours or unknown duration**
  - TEE alternative to 3 weeks pre-CV
  - Same whether chemical, electrical, or ablative CV
  - For NOACs, verify compliance with patient
Antiarrhythmic Drugs for Maintenance of Sinus Rhythm in AF (2014)

- No structural heart disease
  - Dofetilide
  - Dronedarone
  - Flecaïnide
  - Propafenone
  - Sotalol
  - Amiodarone
  - Catheter ablation
- Substantial LVH (>1.5 cm)
  - Dronedarone
  - Amiodarone
  - Catheter ablation
- Coronary artery disease
  - Dofetilide
  - Dronedarone
  - Sotalol
  - Amiodarone
  - Catheter ablation
- Heart failure
  - Amiodarone
  - Dofetilide
  - Catheter ablation

Based on January CT, et al. JACC 2014

- Tailor AA drug to patient’s clinical situation and risk tolerance
- Changes 2011 -> 2014
  - Dofetilide moved up, dronedarone added to amiodarone for LVH
  - Amiodarone advised only when other AADs have failed or contraindicated
  - Enhanced role for catheter ablation
Question Case #4

68 y/o female with paroxysmal AF; (+) for HTN & DM
- Asymptomatic
- Now appears to be in persistent AF
  (asymptomatic, rate-controlled with BB)
Question Case #4

Which statement is correct?

1. Need to control the rhythm for prevention of stroke
2. Amiodarone to control the rhythm, which can lead to lower mortality
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Question Case #4

Which statement is correct?

1. Need to control the rhythm for prevention of stroke
2. Amiodarone to control the rhythm, which can lead to lower mortality
3. AF ablation would improve prognosis
4. No additional meds (except for anticoagulation) is necessary
Question Case #5

55 y/o male with symptomatic paroxysmal AF; (+) for HTN & DM
- Failed on Flecainide and Sotalol
- Referred for ablation
Question Case #5

Which statement concerning AF ablation is True?

1. Major complication rate is <0.5%
2. Efficacy of over 90%
3. Anticoagulation may be stopped after 3 months if there is no AF on rhythm recorder
4. The procedure is equally effective in men and women
Catheter Ablation for AF
2014 AF Guidelines

• Class I
  - Symptomatic paroxysmal AF refractory to or with intolerance of at least 1 class I or III AAD (LOE A)

• Class IIa
  - Patients with symptomatic persistent AF refractory to or with intolerance of at least 1 class I or III AAD (LOE A)
  - Selected patients with recurrent symptomatic paroxysmal AF prior to trial of AAD after weighing risks/benefits (LOE B)

• Class III
  - Patient who cannot be anticoagulated
  - Sole intent of obviating need for OAC
Paroxysmal AF:
Role of Pulmonary Vein Ectopy

- 45 patients with PAF
  - PAF at least every other day
  - >700 APBs/ 24 hr
  - Mean LA size 39 mm
  - Mean age 54 yo

Catheter Ablation of Atrial Fibrillation
Meta-Analysis of Four Randomized Clinical Trials

Efficacy: 162 / 214 = 76% (ABL) vs. 41/218 = 19% (AAD)

Catheter Ablation for AF
Key Points

• Reasonable for symptomatic AF refractory to one or more antiarrhythmic drugs

• Electrical isolation of PVs is a key component
  - Autonomic denervation
  - Ablation of complex electrogram sites
  - Ablation of non—PV triggers

• 60-80% success in control of AF symptoms
Catheter Ablation for AF
Key Points (con’t)

• Patient selection:
  - Paroxysmal better than persistent
  - Shorter duration persistent AF (<1 year)
  - Small LA size (< 5cm)
  - Younger patients (<75 y/o)
  - No/minimal structural heart disease
  - Fewer comorbidities (CHF, COPD, OSA, prior CVA)
Indications for Catheter Ablations

Indications for Catheter Ablation of Symptomatic Atrial Fibrillation

Symptomatic AF

- Paroxysmal AF
  - IIa
  - AA Drugs
  - Catheter Ablation
- Persistent AF
  - IIa
  - AA Drugs
  - Catheter Ablation
- Long-standing Persistent AF
  - IIb
  - AA Drugs
  - Catheter Ablation
Purpose of CABANA

Compare Ablation to state-of-the-art drug therapy for patients with new onset / undertreated AF

*Primary Endpoint*
- All-cause mortality, disabling stroke, serious bleeding, or cardiac arrest

*Major Secondary Endpoints*
- All-cause mortality
- Death (all-cause) or cardiovascular hospitalization
Patient Randomization

Subjects
2204

Ablation Therapy
1108

- Ablated
  1006 (90.8%)
  repeat ablation 215 (19.4%)

- Not ablated
  102 (9.2%)

Completed FU
1002 (90.4%) 48.9 mo

Drug Therapy
1096

- Drug Treated
  1092 (99.6%)
    rhythm control 953 (87.2%)
    rate control only 126 (11.5%)

- Cross Over Ablated
  301 (27.5%)

Completed FU
966 (88%) 48.2 mo

* Withdrew <3 years
## Patient Demographics

<table>
<thead>
<tr>
<th></th>
<th>Ablation (N=1108)</th>
<th>Drug Therapy (N=1096)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, Median (Q1, Q3)</td>
<td>68 (62, 72)</td>
<td>67 (62, 72)</td>
</tr>
<tr>
<td>&lt;65 yrs</td>
<td>33.8%</td>
<td>35.7%</td>
</tr>
<tr>
<td>65 - 74</td>
<td>52.1%</td>
<td>50.5%</td>
</tr>
<tr>
<td>≥75</td>
<td>14.1%</td>
<td>13.9%</td>
</tr>
<tr>
<td>Sex (Female)</td>
<td>37.3%</td>
<td>37.0%</td>
</tr>
<tr>
<td>Minority</td>
<td>10.2%</td>
<td>10.2%</td>
</tr>
<tr>
<td>BMI, Median (Q1, Q3)</td>
<td>30 (27, 84)</td>
<td>30 (26, 35)</td>
</tr>
<tr>
<td>Condition</td>
<td>Ablation</td>
<td>Drug Therapy</td>
</tr>
<tr>
<td>-----------------------------------</td>
<td>----------</td>
<td>--------------</td>
</tr>
<tr>
<td>Sleep Apnea</td>
<td>23.6%</td>
<td>22.5%</td>
</tr>
<tr>
<td>Cardiomyopathy</td>
<td>8.9%</td>
<td>11.2%</td>
</tr>
<tr>
<td>Congestive Heart Failure</td>
<td>15.7%</td>
<td>14.9%</td>
</tr>
<tr>
<td>NYHA Class</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Class I</td>
<td>13.9%</td>
<td>11.6%</td>
</tr>
<tr>
<td>Class II/III</td>
<td>34.3%</td>
<td>36.7%</td>
</tr>
<tr>
<td>Prior CVA or TIA</td>
<td>10.6%</td>
<td>9.4%</td>
</tr>
</tbody>
</table>
## Arrhythmia History in CABANA

<table>
<thead>
<tr>
<th>AF Type</th>
<th>Ablation</th>
<th>Drug Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paroxysmal</td>
<td>42.4%</td>
<td>43.5%</td>
</tr>
<tr>
<td>Persistent</td>
<td>47.3%</td>
<td>47.3%</td>
</tr>
<tr>
<td>Longstanding Persistent</td>
<td>10.3%</td>
<td>9.2%</td>
</tr>
<tr>
<td>Years since onset of AF [Median (Q1,Q3)]</td>
<td>1.1 (0.3, 4.1)</td>
<td>1.1 (0.3, 3.9)</td>
</tr>
</tbody>
</table>

### CCS Severity of AF

<table>
<thead>
<tr>
<th>Class</th>
<th>Ablation</th>
<th>Drug Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class 0-1</td>
<td>34.6%</td>
<td>26.7%</td>
</tr>
<tr>
<td>Class 2</td>
<td>31.8%</td>
<td>32.4%</td>
</tr>
<tr>
<td>Class 3-4</td>
<td>43.5%</td>
<td>41.0%</td>
</tr>
</tbody>
</table>

Prior hospitalization for AF: 40.6% 38.8%
Primary Endpoint (Death, Disabling Stroke, Serious Bleeding, or Cardiac Arrest) (ITT)

Ablation vs. Drug
Hazard ratio: 0.86 (95% CI, 0.65–1.15)
P=0.303

Event rate (%) vs. Months since randomization

Number at risk

<table>
<thead>
<tr>
<th>Drug</th>
<th>1096</th>
<th>1036</th>
<th>1006</th>
<th>970</th>
<th>880</th>
<th>763</th>
<th>652</th>
<th>578</th>
<th>499</th>
<th>418</th>
<th>312</th>
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</thead>
<tbody>
<tr>
<td>Ablation</td>
<td>1108</td>
<td>1045</td>
<td>1021</td>
<td>996</td>
<td>915</td>
<td>793</td>
<td>700</td>
<td>614</td>
<td>535</td>
<td>432</td>
<td>309</td>
</tr>
</tbody>
</table>
Estimates of All-Cause Mortality Risk (ITT)

Ablation vs. Drug
Hazard ratio: 0.85 (95% CI, 0.60–1.21)
P=0.377
## Primary and Secondary Outcomes as Randomized (ITT)

<table>
<thead>
<tr>
<th></th>
<th>Ablation (N = 1108)</th>
<th>Drug (N = 1096)</th>
<th>Hazard Ratio (95% CI)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary Outcome</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Composite:</td>
<td>89 (8.0%)</td>
<td>101 (9.2%)</td>
<td>0.86 (0.65, 1.15)</td>
<td>0.30</td>
</tr>
<tr>
<td>Death</td>
<td>58 (5.2%)</td>
<td>67 (6.1%)</td>
<td>0.85 (0.60, 1.21)</td>
<td>0.38</td>
</tr>
<tr>
<td>Disabling stroke</td>
<td>3 (0.3%)</td>
<td>7 (0.6%)</td>
<td>0.42 (0.11, 1.62)</td>
<td>0.19</td>
</tr>
<tr>
<td>Serious bleeding</td>
<td>36 (3.2%)</td>
<td>36 (3.3%)</td>
<td>0.98 (0.62, 1.56)</td>
<td>0.93</td>
</tr>
<tr>
<td>Cardiac arrest</td>
<td>7 (0.6%)</td>
<td>11 (1.0%)</td>
<td>0.62 (0.24, 1.61)</td>
<td>0.33</td>
</tr>
<tr>
<td><strong>Secondary Outcomes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>58 (5.2%)</td>
<td>67 (6.1%)</td>
<td>0.85 (0.60, 1.21)</td>
<td>0.38</td>
</tr>
<tr>
<td>Death or CV hospitalization</td>
<td>573 (51.7%)</td>
<td>637 (58.1%)</td>
<td>0.83 (0.74, 0.93)</td>
<td>0.001</td>
</tr>
<tr>
<td>Group</td>
<td>Interaction P-Value</td>
<td>N</td>
<td>Hazard Ratio</td>
<td>95% CI</td>
</tr>
<tr>
<td>--------------------------------</td>
<td>---------------------</td>
<td>-----</td>
<td>--------------</td>
<td>----------</td>
</tr>
<tr>
<td>All Subjects</td>
<td>0.074</td>
<td>2204</td>
<td>0.86</td>
<td>0.65, 1.15</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 65 years old</td>
<td>0.161</td>
<td>765</td>
<td>0.52</td>
<td>0.27, 1.00</td>
</tr>
<tr>
<td>65 and &lt; 75 years old</td>
<td>0.55</td>
<td>1130</td>
<td>0.84</td>
<td>0.57, 1.23</td>
</tr>
<tr>
<td>75 years old</td>
<td>0.161</td>
<td>306</td>
<td>1.46</td>
<td>0.80, 2.77</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>0.065</td>
<td>1385</td>
<td>0.74</td>
<td>0.52, 1.08</td>
</tr>
<tr>
<td>Female</td>
<td>225</td>
<td>819</td>
<td>1.14</td>
<td>0.70, 1.86</td>
</tr>
<tr>
<td>Minority status</td>
<td></td>
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</tr>
<tr>
<td>White</td>
<td>0.065</td>
<td>1879</td>
<td>0.96</td>
<td>0.71, 1.31</td>
</tr>
<tr>
<td>Minority*</td>
<td>0.925</td>
<td>225</td>
<td>0.43</td>
<td>0.20, 0.95</td>
</tr>
<tr>
<td>AF type</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paroxysmal</td>
<td>0.925</td>
<td>646</td>
<td>0.82</td>
<td>0.51, 1.31</td>
</tr>
<tr>
<td>Persistent</td>
<td>1.042</td>
<td>1042</td>
<td>0.87</td>
<td>0.59, 1.28</td>
</tr>
<tr>
<td>Long-standing persistent</td>
<td>0.718</td>
<td>215</td>
<td>1.01</td>
<td>0.36, 2.61</td>
</tr>
<tr>
<td>Years since onset of AF</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 1 year</td>
<td>0.734</td>
<td>1063</td>
<td>0.83</td>
<td>0.57, 1.21</td>
</tr>
<tr>
<td>≥ 1 year</td>
<td>1.122</td>
<td>1122</td>
<td>0.92</td>
<td>0.59, 1.42</td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>0.843</td>
<td>427</td>
<td>0.97</td>
<td>0.47, 2.01</td>
</tr>
<tr>
<td>Present</td>
<td>1.776</td>
<td>1776</td>
<td>0.85</td>
<td>0.62, 1.15</td>
</tr>
<tr>
<td>Hypertension with LVH</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Absent</td>
<td>1.176</td>
<td>587</td>
<td>0.94</td>
<td>0.61, 1.31</td>
</tr>
<tr>
<td>Present</td>
<td>1.176</td>
<td>1176</td>
<td>0.89</td>
<td>0.51, 1.78</td>
</tr>
<tr>
<td>Sleep apnea</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>0.339</td>
<td>1695</td>
<td>0.94</td>
<td>0.67, 1.32</td>
</tr>
<tr>
<td>Present</td>
<td>0.339</td>
<td>508</td>
<td>0.69</td>
<td>0.41, 1.17</td>
</tr>
<tr>
<td>BMI</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>&lt; 30</td>
<td>0.378</td>
<td>1064</td>
<td>0.74</td>
<td>0.49, 1.11</td>
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<tr>
<td>≥ 30</td>
<td>0.716</td>
<td>1106</td>
<td>0.96</td>
<td>0.64, 1.44</td>
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<tr>
<td>CHA2DS-VASc score</td>
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<tr>
<td>≤ 2</td>
<td>0.196</td>
<td>959</td>
<td>0.93</td>
<td>0.54, 1.58</td>
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<tr>
<td>≥ 2</td>
<td>1.245</td>
<td>1245</td>
<td>0.83</td>
<td>0.59, 1.16</td>
</tr>
<tr>
<td>History of congestive heart failure</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>0.147</td>
<td>1865</td>
<td>0.95</td>
<td>0.68, 1.32</td>
</tr>
<tr>
<td>Yes</td>
<td>0.147</td>
<td>337</td>
<td>0.61</td>
<td>0.35, 1.08</td>
</tr>
<tr>
<td>Baseline NYHA class</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No heart failure or Class I</td>
<td>0.44</td>
<td>1468</td>
<td>1.04</td>
<td>0.71, 1.52</td>
</tr>
<tr>
<td>≥ Class II</td>
<td>0.44</td>
<td>778</td>
<td>0.68</td>
<td>0.44, 1.05</td>
</tr>
</tbody>
</table>

*Minority=Hispanic or Latino or non-white race

Ablation Better | Drug Better
0.25 0.5 1 2 4
All-Cause Mortality or Cardiovascular Hospitalization (ITT)

Ablation vs. Drug
Hazard ratio: 0.83 (95% CI, 0.74–0.93)
P=0.002

Event rate (%)

Months since randomization

Drug
Ablation

Number at risk
Drug 1096 778 643 563 474 387 302 244 197 166 112
Ablation 1108 807 708 643 558 450 372 307 261 207 137
First Recurrence AF – Post Blanking* (ITT)

Ablation vs. Drug
Hazard ratio: 0.53 (95% CI, 0.46–0.61)
P<0.0001

Number at risk
- Drug: 629, 303, 251, 211, 180, 156, 130, 114, 93
- Ablation: 611, 430, 380, 327, 290, 239, 199, 162, 133

*Using CABANA Monitors
## Primary and Secondary Outcomes (Treatment Received)*

<table>
<thead>
<tr>
<th></th>
<th>Ablation (N = 1307)</th>
<th>Drug (N = 897)</th>
<th>Hazard Ratio (95% CI)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary Outcome</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>92 (7.0%)</td>
<td>98 (10.9%)</td>
<td>0.67 (0.50, 0.89)</td>
<td>0.006</td>
</tr>
<tr>
<td><strong>Secondary Outcomes</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>All-cause mortality</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>58 (4.4%)</td>
<td>67 (7.5%)</td>
<td>0.60 (0.42, 0.86)</td>
<td>0.005</td>
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</tr>
<tr>
<td>Death or CV hospitalization</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>538 (41.2%)</td>
<td>672 (74.9%)</td>
<td>0.83 (0.74, 0.94)</td>
<td>0.002</td>
<td></td>
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</tbody>
</table>

*pre-specified
Conclusion of the CABANA Trial

- Ablation did not produce a significant reduction in the primary endpoint and all-cause mortality.
- The results were affected by cross-overs in both directions and lower than expected event rates.
- Ablation significantly reduced mortality or CV hospitalization by 17% compared to drug therapy.
- There also was a significant 47% reduction in recurrent AF with ablation compared to drug therapy.
- A 33% reduction in the primary endpoint and 40% mortality risk reduction was present when patients actually underwent ablation (treatment received).
- Ablation is an acceptable treatment strategy for treating AF with low adverse event rates even in higher risk patients.
55 y/o male with symptomatic paroxysmal AF; (+) for HTN & DM
- Failed on Flecainide and Sotalol
- Referred for ablation
Question Case #5

Which statement concerning AF ablation is True?

1. Major complication rate is <0.5%
2. Efficacy of over 90%
3. Anticoagulation may be stopped after 3 months if there is no AF on rhythm recorder
4. The procedure is equally effective in men and women
Question Case #5

Which statement concerning AF ablation is True?

1. Major complication rate is <0.5%
2. Efficacy of over 90%
3. Anticoagulation may be stopped after 3 months if there is no AF on rhythm recorder
4. The procedure is equally effective in men and women
Question Case #6

75 y/o male
- HFrEF (non-ischemic, EF 40%)
- Persistent AF (rate 80/min at rest) for 6 months
- NYHA Class III on GDMT (BB, ACE-I, NOAC)
Question Case #6

What do you recommend?

1. Add digoxin
2. Add Ivabradine
3. Cardioversion → Amiodarone
4. AF ablation
CASTLE - AF

Catheter Ablation for Atrial Fibrillation with Heart Failure

Nassir F. Marrouche, M.D., Johannes Brachmann, M.D., Dietrich Andresen, M.D., Jürgen Siebels, M.D., Lucas Boersma, M.D., Luc Jordaan, M.D., Béla Merkely, M.D., Eugene Pokushalov, M.D., Prashanthan Sanders, M.D., Jochen Proff, B.S., Heribert Schunkert, M.D., Hildegard Christ, M.D., Jürgen Vogt, M.D., and Dietmar Bänsch, M.D., for the CASTLE-AF Investigators

ABSTRACT

BACKGROUND
Mortality and morbidity are higher among patients with atrial fibrillation and heart failure than among those with heart failure alone. Catheter ablation for atrial fibrillation has been proposed as a means of improving outcomes among patients with heart failure who are otherwise receiving appropriate treatment.

METHODS
We randomly assigned patients with symptomatic paroxysmal or persistent atrial fibrillation who did not have a response to antiarrhythmic drugs, had unacceptable side effects, or were unwilling to take these drugs to undergo either catheter ablation (179 patients) or medical therapy (rate or rhythm control) (184 patients) from the Comprehensive Arrhythmia Research and Management Center, Division of Cardiovascular Medicine, School of Medicine, University of Utah Health, Salt Lake City (N.F.M.); Klinikum Coburg, Coburg (J.B.); Kardiologie an den Ev. Elisabeth-Kliniken (D.A.) and Boxtor (J.P.); Berlin, Klinik Roten Kruz, Frankfurt/Main (J.V.); Klinikum Links der Weser, Bremen (G.S.), Deutsches Herzzentrum München, Munich (H.S.), Institute of Medical Statistics and Computational Biology, Cologne (H.C.), and Klinikum Göttingen (D.B.).

CASTLE - AF

- HFrEF (31%)
- Mostly male (90%)
- Middle-aged (65)
- Symptomatic AF (70% persistent)
- Randomized to AF ablation or Medical Rx (rate control)

CASTLE - AF

Conclusion

Question Case #6

75 y/o male
- HFrEF (non-ischemic, EF 40%)
- Persistent AF (rate 80/min at rest) for 6 months
- NYHA Class III on GDMT (BB, ACE-I, NOAC)
Question Case #6

What do you recommend?

1. Add digoxin
2. Add Ivabradine
3. Cardioversion $\rightarrow$ Amiodarone
4. AF ablation
Question Case #6

What do you recommend?

1. Add digoxin
2. Add Ivabradine
3. Cardioversion → Amiodarone
4. AF ablation
CASTLE – AF Issues

• 3018 screened, 398 randomized over 8 years

• Inclusion criteria
  - Symptomatic AF, Failure or intolerance of AA, LVEF ≤ 35%, indication for ICD

• Exclusion criteria
  - Previous ablation for AF, ACS, contraindication for anticoagulation, Listed for heart transplant, uncontrolled HTN, ESRD, planned cardiac intervention, LA size >6

6.3.4. Catheter Ablation in HF

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIb</td>
<td>B-R</td>
<td>1. AF catheter ablation may be reasonable in selected patients with symptomatic AF and HF with reduced left ventricular (LV) ejection fraction (HFrEF) to potentially lower mortality rate and reduce hospitalization for HF (S6.3.4-1, S6.3.4-2). NEW: New evidence, including data on improved mortality rate, has been published for AF catheter ablation compared with medical therapy in patients with HF.</td>
</tr>
</tbody>
</table>

Referenced studies that support the new recommendation are summarized in Online Data Supplement 7.
CASTLE – AF
Issues

• Ablation group – 25% of time in AF
• Medical group – 60%

Meta-Analysis Digoxin Use Risk of Mortality

Digoxin and Mortality in Patients With Atrial Fibrillation

Renato D. Lopes, MD, PhD, MHS,§ Roberto Rordorf, MD,∥ Gaetano M. De Ferrari, MD,∥ Sergio Leonardi, MD, MHS,∥
Laine Thomas, PhD,§ Daniel M. Wojdyla, MS,∥ Peter Ridefelt, MD, PhD,∥ John H. Lawrence, MD,∥
Raffaele De Caterina, MD, PhD,∥ Dragos Vineanu, MD, PhD,§ Michael Hanna, MD,∥ Greg Flaker, MD,§
Sana M. Al-Khatib, MD, MHS,∥ Stefan H. Hohnloser, MD,∥ John H. Alexander, MD, MHS,∥
Christopher B. Granger, MD,∥ Lars Wallentin, MD, PhD,∥ for the ARISTOTLE Committees and Investigators

ABSTRACT

BACKGROUND Digoxin is widely used in patients with atrial fibrillation (AF).

OBJECTIVES The goal of this paper was to explore whether digoxin use was independently associated with increased mortality in patients with AF and if the association was modified by heart failure and/or serum digoxin concentration.

METHODS The association between digoxin use and mortality was assessed in 17,897 patients by using a propensity score-adjusted analysis and in new digoxin users during the trial versus propensity score-matched control participants. The authors investigated the independent association between serum digoxin concentration and mortality after multivariable adjustment.
# Digoxin & Mortality in Patients with Atrial Fibrillation


## Digoxin Use: New Users and Clinical Outcomes

<table>
<thead>
<tr>
<th></th>
<th>New Digoxin Users (n = 779)</th>
<th>Matched Control Participants† (n = 2,337)</th>
<th>HR (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>8.13 (79)</td>
<td>5.11 (151)</td>
<td>1.78 (1.37-2.31)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CV death</td>
<td>3.70 (36)</td>
<td>2.30 (68)</td>
<td>1.60 (1.07-2.38)</td>
<td>0.0218</td>
</tr>
<tr>
<td>Sudden cardiac death</td>
<td>1.34 (13)</td>
<td>0.61 (18)</td>
<td>2.14 (1.11-4.12)</td>
<td>0.0230</td>
</tr>
<tr>
<td>Non-CV death</td>
<td>3.19 (31)</td>
<td>1.93 (57)</td>
<td>1.67 (1.12-2.49)</td>
<td>0.0121</td>
</tr>
<tr>
<td>HF hospitalization‡</td>
<td>4.22 (33)</td>
<td>2.52 (62)</td>
<td>1.69 (1.15-2.49)</td>
<td>0.0083</td>
</tr>
</tbody>
</table>

*Rate per 100 patient-years of follow-up. †Each patient starting digoxin was matched to 3 control participants within the same region, setting where digoxin was initiated (during an HF hospitalization, during other hospitalization, or sensitivity), and HF status. ‡HF hospitalization for digoxin/control participants out of hospital.

Abbreviations as in Table 2.
Digoxin in Atrial Fibrillation?
Leave it Out of the Medicine Cabinet*

Mintu P. Turakhia, MD, MAS

Digoxin is a curious drug with an unusual history. The use of digitalis genus plants was first described in 1785 by British physician Dr. William Withering, for the treatment of edema ("dropsy") and other peculiar conditions (1). Following the advent of isolation of digoxin from the foxglove plant in the 1930s, the use of cardiac glycosides steadily soared to be a staple therapy of atrial fibrillation (AF) and heart failure for the past few decades. As of 2019, the World Health Organization still includes it on its Model List of Essential Medications to treat heart failure and arrhythmias (2). Digoxin is the harms of digoxin, including electrocardiogram findings of digoxin effect versus toxicity, indications for digoxin antigen-binding fragments, and vignettes of little old tea-drinking ladies presenting with nausea and bradycardia. Digoxin is cardiology’s “great masquerader”—our version of syphilis: it can conceivably cause almost any arrhythmia. And even when all appears well, a patient may report green-tinted vision or weight loss from intractable nausea. The observational association of harm in heart disease is historically well founded; 37 years ago, Moss et al. (3) reported an increase in cardiac mortality.

“Perhaps it’s time to leave foxglove in the garden and in the history books – and out of the medicine Cabinet.”

- Mintu P. Turakhia, MD
Question Case #7

48 y/o Asian female with Type II DM & HTN: asymptomatic

MEDS:  
- Metformin 1000 mg BID  
- Sitagliptin 100 mg daily  
- Lisinopril 10 mg daily  
- Amlodipine 10 mg daily

BP: 122/70  BMI: 22

Total Chol: 176  LDL-C: 92  HDL-C: 48  Triglycerides: 140  HbA1c: 6.5%
Question Case #7

Which of the following do you recommend?

1. ASA 81 mg daily
2. Omega-3 fatty acid 1000 mg daily
3. Increase Lisinopril to 20 mg daily
4. Start Simvastatin 20 mg daily
5. No additional medication
CARDS: Statins Lower CV Risk in Diabetic Patients

Rate reduction = 37% (95% CI: 17-52)
Absolute risk reduction = 3.2%  
p=0.001

n= 2838

Placebo
LDL-C 120 mg/dl

Atorvastatin
10 mg
LDL-C 81 mg/dl

Statin Initiation Recommendations to Reduce ASCVD Risk

Heart-healthy lifestyle habits are the foundation of ASCVD prevention
(See 2013 AHA/ACC Lifestyle Management Guideline)

Age ≥21 y and a candidate for statin therapy 

Clinical ASCVD

Yes

Age ≤75 y
High-intensity statin
(Moderate-intensity statin if not candidate for high-intensity statin)

Yes

Age >75 y OR if not candidate for high-intensity statin
Moderate-intensity statin

No

Yes

LDL-C ≥190 mg/dL
High-intensity statin
(Moderate-intensity statin if not candidate for high-intensity statin)

No

Yes

Diabetes
LDL-C 70-189 mg/dL
Age 40-75 y
Estimated 10-y ASCVD risk ≥7.5%†
High-intensity statin

Moderate-intensity statin

No

Yes

Definitions of High- and Moderate-Intensity Statin Therapy* (See Table 5)

High
Daily dose lowers LDL-C by approx. ≥50%

Moderate
Daily dose lowers LDL-C by approx. 30% to <50%

Regularly monitor adherence to lifestyle and drug therapy with lipid and safety assessments (See Fig 5)
Effects of Aspirin for Primary Prevention in Persons with Diabetes Mellitus

The ASCEND Study Collaborative Group

ABSTRACT

BACKGROUND
Diabetes mellitus is associated with an increased risk of cardiovascular events. Aspirin use reduces the risk of occlusive vascular events but increases the risk of bleeding; the balance of benefits and hazards for the prevention of first cardiovascular events in patients with diabetes is unclear.

METHODS
We randomly assigned adults who had diabetes but no evident cardiovascular dis-

The members of the writing committee (Louise Bowman, M.D., Marion Mafham, M.D., Karl Wallendszus, M.Sc., Will Stevens, Ph.D., Georgina Buck, M.Sc., Jill Barton, Kevin Murphy, Theingi Aung, M.D., Richard Haynes, D.M., Jolyon Cox, D.Phil., Aleksandra Murawska, M.Sc., Allen Young, Ph.D., Michael Lay, D.Phil., and the ASCEND Study Collaborative Group) wrote the manuscript. The members of the data monitoring committee included Jerson Benigni, Robert L. M.G. Cardona, and John P. B. Coughlin. The members of the data coordinating committee included Therese H. L. Healy, Karin Eggert, and John P. B. Coughlin. The statistical advice was provided by Richard J. B. Haynes, M.D., D.Phil., and Jolyon Cox, D.Phil.
## ASCEND Trial

![Graph](image)

<table>
<thead>
<tr>
<th>Type of Event</th>
<th>Aspirin (N=7740)</th>
<th>Placebo (N=7740)</th>
<th>Rate Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vascular Outcomes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonfatal myocardial infarction</td>
<td>191 (2.5)</td>
<td>195 (2.5)</td>
<td>0.98 (0.80–1.19)</td>
<td></td>
</tr>
<tr>
<td>Nonfatal presumed ischemic stroke</td>
<td>202 (2.6)</td>
<td>229 (3.0)</td>
<td>0.88 (0.73–1.06)</td>
<td></td>
</tr>
<tr>
<td>Vascular death excluding intracranial hemorrhage</td>
<td>197 (2.5)</td>
<td>217 (2.8)</td>
<td>0.91 (0.75–1.10)</td>
<td></td>
</tr>
<tr>
<td>Any serious vascular event excluding TIA</td>
<td>542 (7.0)</td>
<td>587 (7.6)</td>
<td>0.92 (0.82–1.03)</td>
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</tr>
<tr>
<td>TIA</td>
<td>168 (2.2)</td>
<td>197 (2.5)</td>
<td>0.85 (0.69–1.04)</td>
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</tr>
<tr>
<td>Any serious vascular event including TIA</td>
<td>658 (8.5)</td>
<td>743 (9.6)</td>
<td>0.88 (0.79–0.97)</td>
<td>0.01</td>
</tr>
<tr>
<td>Any arterial revascularization</td>
<td>340 (4.4)</td>
<td>384 (5.0)</td>
<td>0.88 (0.76–1.02)</td>
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</tr>
<tr>
<td>Any serious vascular event or revascularization</td>
<td>833 (10.8)</td>
<td>936 (12.1)</td>
<td>0.88 (0.80–0.97)</td>
<td></td>
</tr>
<tr>
<td>Major Bleeding</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intracranial hemorrhage</td>
<td>55 (0.7)</td>
<td>45 (0.6)</td>
<td>1.22 (0.82–1.81)</td>
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<tr>
<td>Sight-threatening bleeding in eye</td>
<td>57 (0.7)</td>
<td>64 (0.8)</td>
<td>0.89 (0.62–1.27)</td>
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</tr>
<tr>
<td>Serious gastrointestinal bleeding</td>
<td>137 (1.8)</td>
<td>101 (1.3)</td>
<td>1.36 (1.05–1.75)</td>
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<tr>
<td>Other major bleeding</td>
<td>74 (1.0)</td>
<td>43 (0.6)</td>
<td>1.70 (1.18–2.44)</td>
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</tr>
<tr>
<td>Any major bleeding</td>
<td>314 (4.1)</td>
<td>245 (3.2)</td>
<td>1.29 (1.09–1.52)</td>
<td>0.003</td>
</tr>
</tbody>
</table>

ASCEND Trial

The members of the writing committee (Louise Bowman, M.D., Marion Mafham, M.D., Karl Wallendszus, M.Sc., Will Stevens, Ph.D., Georgina Buck, M.Sc., Jill Barton, Kevin Murphy, Theingi Aung, M.D., Richard Haynes, D.M., Jolyon Cox, D.Phil., Aleksandra Murawska, M.Sc., Allen Young, Ph.D., Michael Lay, D.Phil., Fang

Effects of n–3 Fatty Acid Supplements in Diabetes Mellitus

The ASCEND Study Collaborative Group*

ABSTRACT

BACKGROUND
Increased intake of n–3 fatty acids has been associated with a reduced risk of cardiovascular disease in observational studies, but this finding has not been confirmed in randomized trials. It remains unclear whether n–3 (also called omega-3) fatty acid supplementation has cardiovascular benefit in patients with diabetes mellitus.

METHODS
We randomly assigned 15,480 patients with diabetes but without evidence of athr...
ASCEND Trial

ASCEND Trial

<table>
<thead>
<tr>
<th>Year of First Event</th>
<th>Fatty Acids (N=7740)</th>
<th>Placebo (N=7740)</th>
<th>Rate Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;3</td>
<td>236 (3.0)</td>
<td>234 (3.0)</td>
<td>1.01 (0.84–1.21)</td>
<td></td>
</tr>
<tr>
<td>3 to &lt;7</td>
<td>181 (2.5)</td>
<td>186 (2.5)</td>
<td>0.97 (0.79–1.20)</td>
<td></td>
</tr>
<tr>
<td>5 to &lt;7</td>
<td>167 (2.4)</td>
<td>184 (2.6)</td>
<td>0.91 (0.74–1.12)</td>
<td></td>
</tr>
<tr>
<td>≥7</td>
<td>105 (2.7)</td>
<td>108 (2.7)</td>
<td>0.98 (0.75–1.28)</td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>689 (8.9)</td>
<td>712 (9.2)</td>
<td>0.97 (0.87–1.08)</td>
<td>0.55</td>
</tr>
</tbody>
</table>

Test for trend across years $\chi^2=0.22$ (P=0.64)

Cardiovascular Risk Reduction with Icosapent Ethyl for Hypertriglyceridemia

Deepak L. Bhatt, M.D., M.P.H., P. Gabriel Steg, M.D., Michael Miller, M.D., Eliot A. Brinton, M.D., Terry A. Jacobson, M.D., Steven B. Ketchum, Ph.D., Ralph T. Doyle, Jr., B.A., Rebecca A. Juliano, Ph.D., Lixia Jiao, Ph.D., Craig Granowitz, M.D., Ph.D., Jean-Claude Tardif, M.D., and Christie M. Ballantyne, M.D., for the REDUCE-IT Investigators

ABSTRACT

BACKGROUND
Patients with elevated triglyceride levels are at increased risk for ischemic events. Icosapent ethyl, a highly purified eicosapentaenoic acid ethyl ester, lowers triglyceride levels, but data are needed to determine its effects on ischemic events.

METHODS
We performed a multicenter, randomized, double-blind, placebo-controlled trial involving patients with elevated triglyceride levels and established cardiovascular disease or with diabetes and other cardiovascular risk factors. Participants were randomized 1:1 to receive either 4.2 g daily of icosapent ethyl or placebo for 12 months. The primary end point was the incidence of major adverse cardiovascular events (death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke).

RESULTS
Among 8317 patients, the incidence of the primary end point was significantly lower in the icosapent ethyl group than in the placebo group (4.1% vs. 6.2%; hazard ratio, 0.658; 95% confidence interval, 0.517 to 0.843; P = 0.0023).

CONCLUSIONS
Among patients with elevated triglyceride levels and established cardiovascular disease, treatment with icosapent ethyl reduced the risk of major adverse cardiovascular events. (Funding: National Heart, Lung, and Blood Institute and the Ferring Pharmaceuticals Foundation."

From Brigham and Women’s Hospital Heart and Vascular Center and Harvard Medical School, Boston (D.L.B.); FACT (French Alliance for Cardiovascular Trials), Département Hospitalo-Universitaire F.I.R.E (Fibrose, inflammation, and Remodeling), Assistance Pubblique–Hôpitaux de Paris.

REDUCE IT Trial

Question Case #7

48 y/o Asian female with Type II DM & HTN: asymptomatic

MEDS:  Metformin 1000 mg BID
       Sitagliptin 100 mg daily
       Lisinopril 10 mg daily
       Amlodipine 10 mg daily

BP: 122/70  BMI: 22

Total Chol: 176  LDL-C: 92  HDL-C: 48  Triglycerides: 140
HbA1c: 6.5%
Question Case #7

Which of the following do you recommend?

1. ASA 81 mg daily
2. Omega-3 fatty acid 1000 mg daily
3. Increase Lisinopril to 20 mg daily
4. Start Simvastatin 20 mg daily
5. No additional medication
Question Case #7

Which of the following do you recommend?

1. ASA 81 mg daily
2. Omega-3 fatty acid 1000 mg daily
3. Increase Lisinopril to 20 mg daily
4. Start Simvastatin 20 mg daily
5. No additional medication
Question Case #8

65 y/o male with Type II DM, h/o LAD stenting 3 years ago, asymptomatic

MEDS: Metformin 1000 mg BID
      Glipizide 5 mg BID
      ASA 81 mg daily
      Lisinopril 20 mg daily
      Atorvastatin 40 mg daily

BP: 120/70  BMI: 22

Total Chol: 133   LDL: 40   HDL: 38  Triglycerides: 120
HbA1c: 8.5%
Question Case #8

Which is the best next step in management?

1. Increase Metformin to 1500 mg BID
2. Add Insulin
3. Add Sitagliptin
4. Add Empagliflozin
5. Go to gym and run on treadmill for 2 hours daily
Intensive Glucose Control Modestly Reduces MI: A Meta-analysis

Mortality

Non Fatal CVA

Non Fatal MI

14% RRR

Renal Glucose Handling

Glucose Filtration ~180g/day

Majority of glucose is reabsorbed by SGLT2 (90%)

Remaining glucose is reabsorbed by SGLT1 (10%)

Minimal to no glucose excretion

Wright EM. Am J Physiol Renal Physiol 2001; 280:F10–18;
Empagliflozin in Diabetics with CVD: EMPA-REG Outcome Trial

Primary Outcome
10.5 vs. 12.1%, ARR 1.6%

Median follow-up=3.1 yrs

Hazard ratio, 0.86 (95.02% CI, 0.74–0.99)
P=0.04 for superiority

No. at Risk
Empagliflozin
Placebo
4687
2333
4580
2256
4455
2194
4328
2112
3851
1875
4282
2102
2821
1380
2359
1161
1534
741
370
166

All Cause Mortality
5.7% vs. 8.3%, ARR 2.6%

Hazard ratio, 0.68 (95% CI, 0.57–0.82)
P<0.001

No. at Risk
Empagliflozin
Placebo
4687
2333
4651
2303
4608
2280
4556
2243
4128
2012
3079
1503
2617
1281
1722
825
414

Approved GLP1 Receptor Antagonists

<table>
<thead>
<tr>
<th>Exendin-4 based GLP-1R agonists</th>
<th>Acylated hGLP-1R agonists</th>
<th>Macromolecular hGLP-1R agonists</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exenatide</td>
<td>Liraglutide</td>
<td>Dulaglutide</td>
</tr>
<tr>
<td>Lixisenatide</td>
<td>Semaglutide</td>
<td>Albiglutide</td>
</tr>
</tbody>
</table>

GLP-1R, glucagon-like peptide-1 receptor; hGLP-1 RA, human GLP-1R; IgG4 Fc, immunoglobulin-G4 Fragment crystallisable.

†Insulin sensitivity and secretion
Delayed gastric emptying, †satiety
↓BP, Weight loss
GLP-1 RA in Patients with DM and CVD

<table>
<thead>
<tr>
<th></th>
<th>Lixisenatide</th>
<th>Liraglutide</th>
<th>Semaglutide</th>
<th>Exenatide</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>ELIXA</td>
<td>LEADER</td>
<td>SUSTAIN-6</td>
<td>EXSCEL</td>
</tr>
<tr>
<td>Primary composite MACE</td>
<td>0.81</td>
<td>0.01</td>
<td>0.02</td>
<td>0.06</td>
</tr>
<tr>
<td>Cardiovascular mortality</td>
<td>ns</td>
<td>0.007</td>
<td>ns</td>
<td>ns</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>ns</td>
<td>0.046</td>
<td>ns</td>
<td>ns</td>
</tr>
<tr>
<td>Stroke</td>
<td>ns</td>
<td>ns</td>
<td>0.04</td>
<td>ns</td>
</tr>
<tr>
<td>Unstable angina</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
</tr>
</tbody>
</table>

Hazard ratio (95% CI)

CI, confidence interval; MACE, major adverse cardiovascular event; ns, not significant.

### ADA Standard of Care 2018: Pharmacologic Therapy for T2DM

<table>
<thead>
<tr>
<th></th>
<th>ASCVD</th>
<th>CHF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin</td>
<td>Potential Benefit</td>
<td>Neutral</td>
</tr>
<tr>
<td>SGLT-2 Inh</td>
<td>Benefit: Canagliflozin Empagliflozin</td>
<td>Benefit: Canagliflozin Empagliflozin</td>
</tr>
<tr>
<td>GLP-1 RAs</td>
<td>Neutral: Lixisenatide Exenatide ER</td>
<td>Neutral</td>
</tr>
<tr>
<td></td>
<td>Benefit: Liraglutide</td>
<td></td>
</tr>
<tr>
<td>DPP-4 Inh</td>
<td>Neutral</td>
<td>Potential Risk: Saxagliptin Alogliptin</td>
</tr>
<tr>
<td>TZDs</td>
<td>Potential Benefit: Pioglitazone</td>
<td>Increased Risk</td>
</tr>
<tr>
<td>Sulfonylureas (2&lt;sup&gt;nd&lt;/sup&gt;)</td>
<td>Neutral</td>
<td>Neutral</td>
</tr>
<tr>
<td>Insulin</td>
<td>Neutral</td>
<td>Neutral</td>
</tr>
</tbody>
</table>
• In patients with type 2 diabetes and established ASCVD, antihyperglycemic therapy should begin with lifestyle management and metformin and subsequently incorporate an agent proven to reduce major adverse cardiovascular events and cardiovascular mortality (currently empagliflozin and liraglutide), after considering drug-specific and patient factors. (A)

• In patients with type 2 diabetes and established ASCVD, after lifestyle management and metformin, the antihyperglycemic agent canagliflozin may be considered to reduce major adverse cardiovascular events, based on drug-specific and patient factors. (C)
2018 ACC Expert Consensus Decision Pathway on Novel Therapies for Cardiovascular Risk Reduction in Patients With Type 2 Diabetes and Atherosclerotic Cardiovascular Disease

A Report of the American College of Cardiology Task Force on Expert Consensus Decision Pathways

Endorsed by the American Diabetes Association
Patient has T2D* and established clinical ASCVD.

Address concurrently.

Guideline-directed medical therapy (lifestyle, antiplatelet, blood pressure, lipids) and glucose-lowering therapy (metformin).

Consider addition of an SGLT2 inhibitor or GLP-1RA with demonstrated CV outcome benefit.

Initiate clinician-patient discussion.

- No additional action taken at this time
- SGLT2 inhibitor selected
- GLP-1RA selected

*Most trials of SGLT2 and GLP-1RA required baseline A1C ≥7% (Example: EXSCEL Trial required HbA1c ≥ 6.5%), and most patients were already on metformin as first-line therapy if tolerated and not contraindicated

Abbreviations: ASCVD = atherosclerotic cardiovascular disease; CV = cardiovascular; GLP-1RA = glucagon-like peptide-1 receptor agonist; SGLT2 = sodium-glucose cotransporter-2; T2D = type 2 diabetes.

Question Case #8

65 y/o male with Type II DM, h/o LAD stenting 3 years ago, asymptomatic

MEDS: Metformin 1000 mg BID
Glipizide 5 mg BID
ASA 81 mg daily
Lisinopril 20 mg daily
Atorvastatin 40 mg daily

BP: 120/70  BMI: 22

Total Chol: 133  LDL: 40  HDL: 38  Triglycerides: 120
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Which is the best next step in management?

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5. Go to gym and run on treadmill for 2 hours daily
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2. Add Insulin
3. Add Sitagliptin
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5. Go to gym and run on treadmill for 2 hours daily
9. Pharmacologic Approaches to Glycemic Treatment: Standards of Medical Care in Diabetes—2019

The American Diabetes Association (ADA) “Standards of Medical Care in Diabetes” includes ADA’s current clinical practice recommendations and is intended to provide the components of diabetes care, general treatment goals and guidelines, and tools to evaluate quality of care. Members of the ADA Professional Practice Committee, a multidisciplinary expert committee, are responsible for updating the Standards of Care annually, or more frequently as warranted. For a detailed description of ADA standards, statements, and reports, as well as the evidence-grading system for ADA’s clinical practice recommendations, please refer to the Standards of Care Introduction. Readers who wish to comment on the Standards of Care are invited to do so at professional.diabetes.org/SOC.
Question Case #9

75 y/o female

- HTN, DM, ↑ Cholesterol
- Persistent AF (rate-controlled with BB)
- DOE for 3 months; mild edema for 1 month
- BP: 160/80  P: 80 irregular  R: 20  BMP: 30
- NV: 12 cm  Lungs: Clear
- Heart: “Not sure for extra heart sounds”
- Ext: 1+ edema
- CBC, BMP, TSH: all normal  BNP <100
75 y/o female

- CBC, BMP, TSH: all normal
- BNP <100
- CXR: “Cardiomegaly, clear lungs”
- Echo: Mild LVH, EF 70%, left atrial enlargement
  Trivial-to-mild MR, TR, AR, PR
  PASP – 60 mmHg “Pulmonary hypertension”
Question Case #9

This patient has:

1. Pulmonary arterial hypertension
2. Hypertrophic cardiomyopathy
3. Heart failure with preserved EF (HFpEF)
4. Tachycardia-induced cardiomyopathy
### Framingham Criteria for Clinical Diagnosis of Congestive Heart Failure

<table>
<thead>
<tr>
<th>Major Criteria</th>
<th>Minor Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>PND</td>
<td>Peripheral edema</td>
</tr>
<tr>
<td>Orthopnea</td>
<td>Night cough</td>
</tr>
<tr>
<td>Elevated JVP</td>
<td>DOE</td>
</tr>
<tr>
<td>Rales</td>
<td>Hepatomegaly</td>
</tr>
<tr>
<td>S3</td>
<td>Pleural effusion</td>
</tr>
<tr>
<td>CXR cardiomegaly</td>
<td>HR &gt;120/min</td>
</tr>
<tr>
<td>CXR pulm edema</td>
<td>Wgt loss ≥4.5 kg in 5 days with diuretic</td>
</tr>
</tbody>
</table>

Validated CHF if 2 major or 1 major and 2 minor are present concurrently
## HFpEF vs HFrEF

### Symptoms and Signs

**Table 2. Presenting Symptoms and Signs of Heart Failure.**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Reduced Ejection Fraction (≤40%) (N=1570)</th>
<th>Preserved Ejection Fraction (≥50%) (N=880)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symptoms</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute pulmonary edema</td>
<td>332 (21.1)</td>
<td>132 (17.3)</td>
<td>0.02</td>
</tr>
<tr>
<td>Dyspnea or shortness of breath</td>
<td>1511 (96.1)</td>
<td>833 (94.9)</td>
<td>0.11</td>
</tr>
<tr>
<td>Chest pain</td>
<td>399 (25.4)</td>
<td>212 (24.1)</td>
<td>0.47</td>
</tr>
<tr>
<td>Orthopnea</td>
<td>729 (46.4)</td>
<td>374 (42.5)</td>
<td>0.06</td>
</tr>
<tr>
<td>Syncope</td>
<td>27 (1.7)</td>
<td>10 (1.1)</td>
<td>0.26</td>
</tr>
<tr>
<td>Paroxysmal nocturnal dyspnea</td>
<td>473 (50.1)</td>
<td>210 (23.0)</td>
<td>0.007</td>
</tr>
<tr>
<td><strong>Signs</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bilateral ankle edema</td>
<td>888 (56.4)</td>
<td>581 (66.0)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Wheezing</td>
<td>302 (19.3)</td>
<td>173 (19.7)</td>
<td>0.80</td>
</tr>
<tr>
<td>Neck vein distension</td>
<td>962 (61.2)</td>
<td>506 (57.5)</td>
<td>0.07</td>
</tr>
<tr>
<td>Crackles or rales on lung examination</td>
<td>1324 (84.3)</td>
<td>743 (84.4)</td>
<td>0.95</td>
</tr>
<tr>
<td>Hepatomegaly</td>
<td>119 (7.6)</td>
<td>69 (7.8)</td>
<td>0.82</td>
</tr>
<tr>
<td>Hepatomegaly</td>
<td>81 (5.2)</td>
<td>38 (4.3)</td>
<td>0.35</td>
</tr>
<tr>
<td>Presence of S3</td>
<td>196 (12.3)</td>
<td>74 (8.4)</td>
<td>0.002</td>
</tr>
<tr>
<td>Presence of S4</td>
<td>80 (5.1)</td>
<td>33 (3.8)</td>
<td>0.13</td>
</tr>
<tr>
<td>Chest radiographic signs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonary edema</td>
<td>814 (51.1)</td>
<td>414 (47.0)</td>
<td>0.02</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>736 (45.4)</td>
<td>360 (40.3)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

### HFpEF with Normal BNP (30%)

<table>
<thead>
<tr>
<th></th>
<th>BNP $\leq$100</th>
<th>BNP $&gt;$100</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>BNP (pg/ml)</td>
<td>37</td>
<td>379</td>
<td></td>
</tr>
<tr>
<td>DOE</td>
<td>93%</td>
<td>90%</td>
<td>0.52</td>
</tr>
<tr>
<td>Orthopnea</td>
<td>48%</td>
<td>48%</td>
<td>0.99</td>
</tr>
<tr>
<td>NYHA III/IV</td>
<td>43%</td>
<td>50%</td>
<td>0.63</td>
</tr>
<tr>
<td>Age</td>
<td>62</td>
<td>66</td>
<td>0.04</td>
</tr>
<tr>
<td>CAD</td>
<td>28%</td>
<td>45%</td>
<td>0.049</td>
</tr>
<tr>
<td>AF</td>
<td>11%</td>
<td>39%</td>
<td>0.001</td>
</tr>
<tr>
<td>Est GFR</td>
<td>70</td>
<td>53</td>
<td>0.001</td>
</tr>
<tr>
<td>Obese</td>
<td>70%</td>
<td>47%</td>
<td>0.009</td>
</tr>
<tr>
<td>PCWP</td>
<td>25</td>
<td>27</td>
<td>0.42</td>
</tr>
</tbody>
</table>

Question Case #9

75 y/o female
- HTN, DM, ↑ Cholesterol
- Persistent AF (rate-controlled with BB)
- DOE for 3 months; mild edema for 1 month
- BP: 160/80 P: 80 irregular R: 20 BMP: 30
- NV: 12 cm Lungs: Clear
- Heart: “Not sure for extra heart sounds”
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- CBC, BMP, TSH: all normal BNP <100
Question Case #9

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- CXR: “Cardiomegaly, clear lungs”
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3. Heart failure with preserved EF (HFpEF)
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Heart Failure with Preserved Ejection Fraction

Margaret M. Redfield, M.D.

This Journal feature begins with a case vignette highlighting a common clinical problem. Evidence supporting various strategies is then presented, followed by a review of formal guidelines, when they exist. The article ends with the author's clinical recommendations.

A 73-year-old woman with a history of dyspnea on exertion presents for a follow-up visit after hospitalization for acute worsening of dyspnea and orthopnea. On admission to the hospital, the patient had atrial fibrillation with a ventricular rate of 120 beats per minute, and chest radiography revealed pulmonary venous hypertension. Despite anticoagulation, rate control with a beta-blocker, and administration of loop diuretics during the hospitalization, she continues to have fatigue and exertional dyspnea. On physical examination, the body-mass index (BMI; the weight in kilograms divided by the square of the height in meters) is 35, pulse 76 beats per minute, and blood pressure 160/70 mm Hg. There is jugular venous distention and lower-extremity edema but no third heart sound, murmurs, or rales. The serum creatinine level is 1.4 mg per deciliter (124 μmol per liter), estimated glomerular filtration rate (GFR) 37 ml per minute per 1.73 m² of body-surface area, and N-terminal pro–brain natriuretic peptide (NT-proBNP) level 300 pg per milliliter (age-specific and sex-specific normal range, 10 to 218 pg per milliliter). Echocardiography reveals an ejection fraction of 70%, a normal left ventricular cavity dimension and wall thickness, and left atrial enlargement. Doppler echocardiography shows elevated left atrial pressure (E/e’ ratio, 22) and an estimated pulmonary-artery systolic pressure of 52 mm Hg. How should this patient’s condition be managed?
Pre-Discussion Question

Which of the following statement is true?

1. HFpEF (Heart Failure with Preserved Ejection Fraction/Diastolic Heart Failure) has better 5-year survival than HFrEF (Heart Failure with Reduced Ejection Fraction/Systolic Heart Failure)
2. HFpEF should be treated with ACE-I and BB to improve prognosis
3. Number of patients with HFrEF far exceeds those with HFpEF
4. BNP (NT-proBNP) tends to be lower in HFpEF than HFrEF
HFpEF Mortality is High and Comparable to HFrEF

Causes of Death in HFpEF Compendium of Comorbidities

Pre-Discussion Question

Which of the following statement is true?

1. HFpEF (Heart Failure with Preserved Ejection Fraction/Diastolic Heart Failure) has better 5-year survival than HFrEF (Heart Failure with Reduced Ejection Fraction/Systolic Heart Failure)
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4. BNP (NT-proBNP) tends to be lower in HFpEF than HFrEF
Clinical Trials in HFpEF
No Clear Benefit of Neurohormonal Blockade

<table>
<thead>
<tr>
<th>Therapy</th>
<th>CHARM-PEF</th>
<th>iPRESERVE</th>
<th>PEP-CHF</th>
<th>SENIORS (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>&gt;18 (67)</td>
<td>≥60 (72)</td>
<td>≥70 (76)</td>
<td>≥70 (76)</td>
</tr>
<tr>
<td>EF (%)</td>
<td>≥40 (54)</td>
<td>≥45 (59)</td>
<td>≥40 (65)</td>
<td>≥35</td>
</tr>
<tr>
<td>Patients (n)</td>
<td>3,023</td>
<td>4,128</td>
<td>850</td>
<td>752</td>
</tr>
<tr>
<td>Female (%)</td>
<td>40%</td>
<td>60%</td>
<td>55%</td>
<td>38%</td>
</tr>
<tr>
<td>Death/HF Hospitalization</td>
<td>0.89 (0.77-1.03)</td>
<td>0.95 (0.86-1.05)</td>
<td>0.92 (0.70-1.21)</td>
<td>0.82 (0.63-1.05)</td>
</tr>
</tbody>
</table>
TOPCAT
No Difference in 1° Endpoint or All Cause Mortality

TOPCAT

FIGURE 1 Geographic disparities in the TOPCAT trial's results for the primary endpoint (cardiovascular death and heart failure hospitalization).}

Kaplan-Meier cumulative frequency of cardiovascular death and heart failure hospitalization in the TOPCAT (Treatment of Preserved Cardiac Function Heart Failure With an Aldosterone Antagonist) trial of spironolactone versus placebo by the Americas (solid lines) and Russia and the Republic of Georgia (dashed lines). Reprinted with permission from Pfeffer et al. (13). HR = hazard ratio.

2017 ACC/AHA/HFSA Focused Update Guidelines for Management of HF

Class IIa Recommendation (Level of evidence: B – R) for use of aldosterone antagonist in selected patients with HFpEF with:

• EF ≥ 45%
• Elevated BNP or HF admission within 1 year
• Estimated GFR ≥ 30 and creatinine < 2.5, K⁺ < 5.0

to decrease hospitalization

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More Patients Diagnosed and Admitted with HFpEF

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3. Number of patients with HFrEF far exceeds those with HFpEF
4. BNP (NT-proBNP) tends to be lower in HFpEF than HFrEF
CHART-2 Study

A Simple, Evidence-Based Approach to Help Guide Diagnosis of Heart Failure With Preserved Ejection Fraction

**BACKGROUND:** Diagnosis of heart failure with preserved ejection fraction (HFpEF) is challenging in euclidean patients with dyspnea, and no evidence-based criteria are available. We sought to develop and then validate noninvasive diagnostic criteria that could be used to estimate the likelihood that HFpEF is present among patients with unexplained dyspnea to guide further testing.

**METHODS:** Consecutive patients with unexplained dyspnea referred for invasive hemodynamic exercise testing were retrospectively evaluated. Diagnosis of HFpEF (case) or noncardiac dyspnea (control) was ascertained by invasive hemodynamic exercise testing. Logistic regression was performed to evaluate the ability of clinical findings to discriminate cases from controls. A scoring system was developed and then validated in a separate test cohort.
## H$_2$FPEF Score

<table>
<thead>
<tr>
<th>Clinical Variable</th>
<th>Values</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>H$_2$ Heavy</td>
<td>Body mass index &gt; 30 kg/m$^2$</td>
<td>2</td>
</tr>
<tr>
<td>Hypertensive</td>
<td>2 or more antihypertensive medicines</td>
<td>1</td>
</tr>
<tr>
<td>F Atrial Fibrillation</td>
<td>Paroxysmal or Persistent</td>
<td>3</td>
</tr>
<tr>
<td>P Pulmonary Hypertension</td>
<td>Doppler Echocardiographic estimated Pulmonary Artery Systolic Pressure &gt; 35 mmHg</td>
<td>1</td>
</tr>
<tr>
<td>E Elder</td>
<td>Age &gt; 60 years</td>
<td>1</td>
</tr>
<tr>
<td>F Filling Pressure</td>
<td>Doppler Echocardiographic E/e' &gt; 9</td>
<td>1</td>
</tr>
</tbody>
</table>

### H$_2$FPEF score

**Sum (0-9)**

**Total Points**

<table>
<thead>
<tr>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tr>
</tbody>
</table>

**Probability of HFpEF**

- 0.2
- 0.3
- 0.4
- 0.5
- 0.6
- 0.7
- 0.8
- 0.9
- 0.95

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Pulmonary HTN in HFpEF

PH suspected by history and exam

PH on echocardiography

1) Age > 60 years?
2) Comorbidities (DM, HTN, CAD, obesity)
3) Valvular heart disease?
4) LV systolic dysfunction?
5) Echo abnormalities (LAE, LVH, or significant DD)
6) BNP markedly elevated?

All no 1-2 yes ≥3 yes

PAH Probable PH from LHD PH from LHD
HFpEF - Key Points

• Signs and symptoms of HF with EF > 50%
• BNP can be normal or minimally ↑ (obesity)
• Always rule out CAD
• Think about amyloid – (Elderly + LVH – EKG with low voltage) → PYP scan
• Pulmonary Hypertension over the age of 60 – most commonly due to HFpEF
Question Case #10

75 y/o Asian Male
- Mild dyspnea with two flights of stairs
- Echo/Cath: Severe AS (AVA 0.8 cm², normal EF, normal coronaries)
- No other significant co-morbidity
- Told to undergo surgical AVR because he is “low-risk” for surgery (SAVR). He wants TAVR instead
Question Case #10

You will tell him:

1. TAVR is non-inferior to SAVR for “low-risk” patients, so go to see TAVR Center
2. At present, ACC/AHA guidelines recommend SAVR, so go ahead with surgery (SAVR)
3. Wait until next month (March-2019). The results of two pivotal trials will be presented at ACC meeting which will answer your question
Surgical AVR and TAVR Volumes in US

Source: The STS/ACC TVT Registry as of March 1, 2018. Provided by Michael J. Mack, MD, FACC.
## Prevalence

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>50-59</td>
<td>0.2%</td>
</tr>
<tr>
<td>60-69</td>
<td>1.3%</td>
</tr>
<tr>
<td>70-79</td>
<td>3.0%</td>
</tr>
<tr>
<td>80-89</td>
<td>9.8%</td>
</tr>
</tbody>
</table>

# Evaluation of Patients with AS

Understand the “Risks”

<table>
<thead>
<tr>
<th>RISK</th>
<th>AGE</th>
<th>STS</th>
<th>FRAILTY</th>
<th>OTHER</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>40 – 60</td>
<td>&lt; 3</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>Intermediate</td>
<td>70 – 80</td>
<td>3 – 8</td>
<td>None Moderate</td>
<td>Chest Radiation Lima</td>
</tr>
<tr>
<td>High</td>
<td>90</td>
<td>9 – 15</td>
<td>Moderate</td>
<td>Porcelain Aorta</td>
</tr>
<tr>
<td>Inoperable</td>
<td>&gt;90</td>
<td>&gt; 15</td>
<td>Severe</td>
<td></td>
</tr>
</tbody>
</table>
TAVR

• TAVR – Inoperable patients
  Lower mortality vs medical Rx

• TAVR – High risk patients
  Comparable mortality vs AVR

• TAVR – Intermediate risk patients
  Comparable mortality vs AVR
<table>
<thead>
<tr>
<th>RISK</th>
<th>RX</th>
</tr>
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<tr>
<td>Low</td>
<td>AVR</td>
</tr>
<tr>
<td>Intermediate</td>
<td>AVR</td>
</tr>
<tr>
<td>High</td>
<td>AVR vs TAVR</td>
</tr>
<tr>
<td>Inoperable</td>
<td>TAVR</td>
</tr>
<tr>
<td></td>
<td>Nothing (futile)</td>
</tr>
</tbody>
</table>
### Evaluation of Patients with AS Changing Paradigm (2017)

<table>
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<th>RX</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>AVR</td>
</tr>
<tr>
<td>Intermediate</td>
<td>AVR vs TVR</td>
</tr>
<tr>
<td>High</td>
<td>TAVR</td>
</tr>
</tbody>
</table>
| Inoperable   | TAVR
                Nothing (futile) |
Ongoing Randomized Trials
TAVR vs SAVR in the Low Risk Patient Pop.

- PARTNER 3 (SAPIEN 3 valve)
- NOTION 2 (CoreValve)
- Medtronic Transcatheter Aortic Valve Replacement in low risk patients
TAVR for Asymptomatic Patients
EARLY TAVR (Sapien 3 Valve)
Enrollment began July 20, 2017
Explosive Growth in TAVR

Does SAVR become obsolete?
Unanswered Concerns

• Paravalvular leak aortic regurgitation
• Heart block requiring PPM
• Lack of long term follow-up
• Bicuspid valve excluded
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Question Case #11

76-year old male. Well-controlled hypertension and hypercholesterolemia with meds.

Routine follow-up and asks you whether he should take Aspirin 81 mg daily, fish oil (1 gm daily of marine n-3 fatty oils) and Vitamin D (2,000 I.U. daily) for prevention of cardiovascular event.
Question Case #11

You tell him:

1. Take all three (10-100 dollars/month)
2. ASA & Vit D, not fish oil
3. ASA, Vit D, or fish oil
4. Vit D, not fish oil or ASA
5. None, Save money (10-100 dollars/Month)
Effect of Aspirin on All-Cause Mortality in the Healthy Elderly


ABSTRACT

BACKGROUND
In the primary analysis of the Aspirin in Reducing Events in the Elderly (ASPREE) trial, now published in the Journal, we report that the daily use of aspirin did not provide a benefit with regard to the primary end point of disability-free survival among older adults. A numerically higher rate of the secondary end point of death from any cause was observed with aspirin than with placebo.

METHODS
From 2010 through 2014, we enrolled community-dwelling persons in Australia and the United States who were 70 years of age or older (or ≥65 years of age among blacks and Hispanics in the United States) and did not have cardiovascular disease.

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. McNeil at the Department of Epidemiology and Preventive Medicine, Monash University, 553 St. Kilda Rd., Melbourne, VIC 3004, Australia, or at john.mcneil@monash.edu.

* A complete list of the ASPREE trial investigators is provided in the Supplementary Appendix, available at NEJM.org.

Effect of Aspirin on Cardiovascular Events and Bleeding in the Healthy Elderly


ABSTRACT

BACKGROUND
Aspirin is a well-established therapy for the secondary prevention of cardiovascular events. However, its role in the primary prevention of cardiovascular disease is unclear, especially in older persons, who have an increased risk.

METHODS
From 2010 through 2014, we enrolled community-dwelling men and women in Australia and the United States who were 70 years of age or older (or ≥65 years of age among blacks and Hispanics in the United States) and did not have cardiovascular disease, dementia, or disability. Participants were randomly assigned to receive 100 mg of enteric-coated aspirin or placebo. The primary end point was a...
Effect of Aspirin on Disability-free Survival in the Healthy Elderly


ABSTRACT

BACKGROUND
Information on the use of aspirin to increase healthy independent life span in older persons is limited. Whether 5 years of daily low-dose aspirin therapy would extend disability-free life in healthy seniors is unclear.

METHODS
From 2010 through 2014, we enrolled community-dwelling persons in Australia and the United States who were 70 years of age or older (or ≥65 years of age among blacks and Hispanics in the United States) and did not have cardiovascular disease, dementia, or physical disability. Participants were randomly assigned to receive 100 mg per day of enteric-coated aspirin or placebo orally. The primary end point was a composite of death, disability, or institutionalization.

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Marine n–3 Fatty Acids and Prevention of Cardiovascular Disease and Cancer


ABSTRACT

BACKGROUND
Higher intake of marine n–3 (also called omega-3) fatty acids has been associated with reduced risks of cardiovascular disease and cancer in several observational studies. Whether supplementation with n–3 fatty acids has such effects in general populations at usual risk for these end points is unclear.

METHODS
We conducted a randomized, placebo-controlled trial, with a two-by-two factorial design, of vitamin D (at a dose of 2000 IU per day) and marine n–3 fatty acids (at a dose of 1 g per day) in the primary prevention of cardiovascular disease and cancer among men 50 years of age or older and women 55 years of age or older in the United States. Primary end points were major cardiovascular events (a composite of myocardial

From the Department of Medicine, Brigham and Women's Hospital and Harvard Medical School (J.E.M., N.R.C., I.M.L., W.C., S.S.B., S.M., H.G., C.M.A., D.G., T.C., D.D., G.F., C.R., V.B., E.L.G., W.C.W., J.E.B.), and the Departments of Epidemiology (J.E.M., N.R.C., I.M.L., W.C.W., J.E.B.) and Nutrition (E.L.G., W.C.W.) Harvard T.H. Chan School of Public Health — all in Boston. Address reprint requests to Dr. Manson at the Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA.
ORIGINAL ARTICLE

Vitamin D Supplements and Prevention of Cancer and Cardiovascular Disease


BACKGROUND

It is unclear whether supplementation with vitamin D reduces the risk of cancer or cardiovascular disease, and data from randomized trials are limited.

METHODS

We conducted a nationwide, randomized, placebo-controlled trial, with a two-by-two factorial design, of vitamin D$_3$ (cholecalciferol) at a dose of 2000 IU per day and marine n-3 (also called omega-3) fatty acids at a dose of 1 g per day for the prevention of cancer and cardiovascular disease among men 50 years of age or older and women 55 years of age or older in the United States. Primary end points were invasive cancer of any type and major cardiovascular events (a composite of myocardial infarction, stroke, or death from cardiovascular causes). Secondary end points

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