Kaare Harald Bønaa - CURRICULUM VITAE

Kaare Harald Bønaa, MD, PhD
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Bønaa is professor in cardiovascular epidemiology and senior consultant in interventional cardiology. He has extensive experience in executive leader roles for large population surveys and multicentre randomized trials. Bønaa initiated and was the principal investigator for 3 randomized trials that were all successfully completed and published in the NEJM with editorial comments. His PhD thesis is based on 5 articles published in influential journals in medicine and biology such as the NEJM, ATVB, and Circulation. Bønaa contributed to the development and clinical documentation of the drug Omacor™, the first therapeutic drug for humans developed in Norway, and he has world-wide patents together with industry researchers. Bønaa has published more than 100 original scientific papers in high-ranked scientific journals such as NEJM, Lancet, BMJ, JAMA, and Circulation. The NORVIT paper[14] from 2006 is the most cited Norwegian scientific paper during the first 5 years after publication, and was by May 2017 cited in more than 1100 peer reviewed articles.

EDUCATION

2004:	Completed clinical training in interventional cardiology
2003:	Board Certification in Cardiology (Norwegian Medical Association)
2002:	Board Certification in Internal Medicine (Norwegian medical Association)
1992:	Ph.D., University of Tromsø, Tromsø. Thesis: "Relationship between hemodynamics and blood lipids in population surveys, and effects of n-3 fatty acids"
1986-92:	Nine advanced courses in clinical research methods, statistics, epidemiology
1980:	MD, University of Tromsø.

CURRENT POSITIONS

Professor in Cardiovascular Epidemiology, Faculty of Medicine and Health Science, Norwegian University of Science and Technology, Trondheim (since 2010).
Consultant in Cardiology, St. Olav University Hospital, Trondheim, Norway (since 2010).
Professor in Cardiovascular Epidemiology, University of Tromsø – The Arctic University of Norway (since 1999).
Head, the Norwegian Myocardial Infarction Register (since 2016).

PREVIOUS POSITIONS

2006-10:	Consultant in interventional cardiology, University Hospital of North Norway, Tromsø.
2008-09:	Professor in cardiology, University of Tromsø.
2004-06:	Consultant in interventional cardiology, St. Olav University Hospital, Trondheim
1997-00:	Head, Dept. of Clinical Research, University Hospital of North Norway, Tromsø
1993-04:	Fellow in internal medicine and cardiology.
1992-98:	Senior researcher in cardiovascular medicine, University of Tromsø.

RESEARCH PRIZES / HONORS

2012:	Highly Cited Paper Award. European Society of Cardiology
2010:	Grant from The Tromsø Research Foundation for "Outstanding Research"
2010:	First Prize winner, the Norwegian Society of Epidemiology for best scientific paper
2006:	First Prize winner, the Norwegian Society of Epidemiology for best scientific paper
2006:	NORVIT trial awarded as "One of 10 Ground-breaking Studies in the Practice of Cardiovascular Medicine – Circulation Editors Choices 2005-2006" at the American Heart Association Annual Scientific Congress 2006.
2004:	Scientific Award (Storsteins Prize) given by the Norwegian Society of Cardiology.
2000:	Awarded the Norwegian Research Council Top Research Program in medicine.
1993:	Awarded the Malthes prize for the best Ph.D. thesis in medicine in Norway 1992-93.
1989:	Young Investigators Award - the World Congress in Preventive Cardiology.

COMMISSIONS OF TRUST (selected)

2016-	Head, the Norwegian Myocardial infarction Registry

2012-16 Board member, The National Cardiovascular Registry
1993-99 Principle investigator, The Tromsø Heart Study
1997-01 Head, program for applied clinical research, Research Council of Norway
2005-13 Board member on several national research councils

EXPERIENCE AS MANAGER / PRINCIPLE INVESTIGATOR OF RANDOMIZED CLINICAL TRIALS AND RESEARCH PROGRAMMES

2017- The Norwegian trial of Exercise after myocardial infarction
2008- The Norwegian Coronary Stent Trial (published in *N Engl J Med* 2016)
1998-05: The Norwegian Vitamin Trial (published in *N Engl J* Med 2006
1993-99: The Tromsø Heart Study (publications in *Lancet*, *BMJ*, *N Engl J Med*, *Circulation*)
1987-89: The Omega-3 hypertension trial (published in *N Engl J Med* 1992)

REVIEWER

for The New England Journal of Medicine, Circulation. The Lancet, JAMA, BMJ, Tidsskrift for den norske legeforening.

SUPERVISION OF PhD STUDENTS

I have been the **main supervisor** for 9 PhD students. I am currently supervising 4 PhD students

OTHER PROFESSIONAL ACTIVITIES

Member of committees for the academic doctor degree: 6
Professor evaluations: 3
Chairman of the PhD evaluation Committee, the National Health Association
Chairman of the Applied Clinical Research Program, The Norwegian Research Council
Member of the Research funding committee: Southern Norway Health Authority
Member of the Research funding committee: St. Olavs Hospital
Member of EU Research funding committee

GRANTS

Since 1993 I have received NOK 35 million (USD 5 mill) from the Norwegian Research Council. Current funding amounts to about NOK 18 million (mainly to the NorStent trial). I have also received grants from Norwegian Cardiovascular Research Council, Norwegian Regional Health Authorities, Helse og Rehabilitering, Norwegian Red Cross, University of Tromsø, Tromsø Research Council, and from the EU as participant in international research collaborations. We have applied for NOK 150 mill for funding of a large RCT to examine long-term clinical effects of physical exercise. The response is not known (sept 2017).

PATENTS

In collaboration with researchers in the Norwegian company Norsk Hydro I contributed to the development of the drug Omacor©, and hold a United States Patent: Fatty Acid Composition Patent number; 5,656,667.

NATIONAL AND INTERNATIONAL RESEARCH COLLABORATION AND NETWORKING

National: I have ongoing research collaborations with researchers at the University of Tromsø and the University Hospital of North Norway in Tromsø (prof Njølstad and others: incidence and case fatality of acute myocardial infarction, temporal trends cardiovascular risk factor levels, interventional cardiology), and with researchers at the University of Bergen (prof Nygård and others: vitamin metabolism and risk of cardiovascular disease). As principal investigator of the Norwegian Vitamin Trial (NORVIT), published in The New England Journal of Medicine, I developed a well-functioning network for research collaboration among clinicians working in 37 Norwegian acute care hospitals. As principal investigator of the Norwegian Coronary Stent Trial (NORSTENT), also published in the New England Journal of Medicine, I developed a well-functioning research network consisting of academic researchers at Norwegian University Hospitals.

International: Prospective studies collaboration (prof R Collins, Oxford , UK), B-vitamin trialist collaboration (dr R. Clarke, Oxford, UK), Tethys Bioscience Inc,, Emeryville, CA (novel biomarkers for CVD). Prof M Valgimigli, Bern University, Switzerland, and academic researchers in Italy, Germany, USA, and France UK. (comparison of drug-eluting vs bare metal coronary stents).

Kaare Harald Bønaa - PERSONAL STATEMENT

My research started in 1986 when professor Knut Westlund introduced me to cardiovascular epidemiology. He emphaziced that biology should be at the core of epidemiologic investigations. Following my PhD dissertation at the University of Tromsø in 1992, I was elected principal investigator (PI) of the large, population based Tromsø Heart Study. *A main strategy as PI during 1993-1999 was to bring the clinical and the laboratory disciplines into large population based epidemiologic investigations to integrate search for causal effects with the study of intermediary mechanisms.* We used ultrasound to study carotid artery intima media thickness and atherosclerosis[9-11], heart structures and function (eccocardiography), and abdominal aortic diameters (screening for aneurysms)[12] in a study of more than 6500 persons from the general population. These studies generated data for many articles and PhDs. I was the founder and head of the Cardiovascular Research Group in Tromsø. This group was rated "Excellent" by the Research Council of Norway. In 1999 I qualified for Toppforskningsprogrammet (The Top Research Program) by the Research Council. Data from the Tromsø study has been used in more than 100 PhDs.

Throughout my career my ambition has been to conduct and publish high quality research in the international front, not necessarily to publish many papers. I initiated and was the principal investigator for three randomized trials that were all successfully completed and published in the New England Journal of Medicine with editorial comments[2,14,18]. I have published epidemiologic articles in Circulation[3,4,11], BMJ[1], and JAMA[15,19]. In total I have authored or co-authored 105 scientific papers published in peer reviewed journals.

Research areas:

1. **Omega-3 fatty acids, and interrelations between blood lipid levels and hemodynamics.**
   We were the first to study the effects of highly purified omega-3 fatty acids on CVD risk factors, and found a significant blood pressure lowering effect in young patients with diastolic hypertension (NEJM 1990)[2]. During the work with my PhD I contributed to the development and clinical documentation of the drug Omacor ™, the first therapeutic drug for humans developed in Norway, and hold world-wide patents for Omacor™.[6] We found interrelations between blood lipid levels and blood pressure[3] and resting heart rate[4] and observed that dietary n-3 fatty acids improves left ventricular function[7], and suggested potential mechanisms for these relations in Circulation[3,4].
2. **Use of ultrasound to study subclinical atherosclerosis, heart structure, and aneurysms**
   We were among the first to use ultrasound in a large population – based surveys. We found that men had more plaques than women, and were the first to demonstrate that men have more soft and lipid-laden carotid artery plaques than women[9]. We observed that plaque morphology was a significant predictor for ischemic stroke (Circulation 2001)[11].
3. **Gender differences in cardiovascular risk factor levels and risk of coronary heart disease**.
   The sex differences in coronary heart disease is surely one of the most interesting of all epidemiologic questions, and has been focus for much of my research [9,11,13,19]. We recently published data in JAMA showing that there is a life-long gender gap in risk of incident myocardial infarction - with no evidence of any attenuation of the sex contrast around menopause[19]. It is noteworthy that the determinant(s) of this gender contrast still remains unknown (it is not caused by estrogen). I hypothesize that gender differences in plaque morphology, possibly related to testosterone and sex differences in atherogenic lipid levels, may contribute to the gender gap in risk for acute myocardial infarction, and published the hypothesis in 2002.[13]
4. **Determinants for trends in the incidence and case fatality of myocardial infarction.**
   We found a significant fall in incidence of myocardial infarction during the last 20 years, and showed that about 60 % of this reduction is associated with favourable trends in modifiable risk factors, and published our findings in Circulation in 2016.[17] Our data indicate that a large proportion of incidence variations across time and geographic areas are due to modifiable risk factors. This is good news for prevention.
5. **Multicentre randomized controlled clinical trials**
   In recent years I was PI for two large multicentre randomized controlled clinical trials in secondary prevention and interventional cardiology, and I have spent much time to secure the successful completion of these large projects. The NORVIT study (NEJM 2016)[14] tested the homocysteine-hypothesis by randomizing 3749 CHD patients to treatment with B-vitamins. There was no benefit, and we concluded that such treatment should not be recommended. The NORSTENT study (NEJM 2016)[18] compared long-term clinical effects of drug-eluting vs bare metal stents in 9013 patients. There were no significant differences in mortality, MI, or quality of life, during 6 years of follow-up. In-stent restenosis was lower after drug-eluting stent. We have suggested potential clinical implications of NORSTENT[20]. NORSTENT is referred to in recent international guidelines.

Kaare Harald Bønaa – 20 SELECTED PUBLICATIONS

1.Bønaa KH, Arnesen E, Thelle DS, Førde OH. Coffee and cholesterol: Is it all in the brewing? The Tromsø study. *Br Med J* 1988;297:1103-04

2.Bønaa KH, Bjerve KS, Straume B, Gram IT, Thelle D. Effect of eicosapentaenoic and docosahexaenoic acids on blood pressure in hypertension. A population-based intervention trial from the Tromsø study. *N Engl J Med* 1990;322:795-801.

3.Bønaa KH, Thelle D. Association between blood pressure and serum lipids in a population. The Tromsø study. *Circulation* 1991;83:1305-1314

4.*Bønaa KH*, Arnesen E. Association between heart rate and atherogenic blood lipid fractions in a population. The Tromsø Study. *Circulation* 1992; 86:394-405

5.Arnesen E, Refsum H, ***Bønaa KH***, Ueland PM, Førde OH, Nordrehaug JE. The Tromsø study: A population based prospective study of serum total homocysteine and coronary heart disease. *Int J Epidemiol* 1995;24:704-709.

6.Breivik H, ***Bønaa KH,*** Børretzen B, Dahl KH, Krokan H. Fatty acid composition. *United States Patent* Number 5,656,667. Aug. 12, 1997

7.Grimsgaard S, ***Bønaa KH***, Hansen JB, Myhre ESP. Effects of highly purified eicosapentaenoic acid and docosahexaenoic acid on hemodynamics in humans. *Am J Clin Nutr* 1998; 68:52-59

8.Grimsgaard S, ***Bønaa KH***, Jacobsen BK, Bjerve KS. Plasma saturated and linoleic fatty acid are independently associated with blood pressure. *Hypertension* 1999; 34: 478-483

9.Joakimsen O, ***Bønaa KH***, Stensland-Bugge E, Jacobsen BK. Age and sex differences in the distribution and ultrasound morphology of carotid atherosclerosis. The Tromsø Study. *Arterioscl Thromb Vasc Biol* 1999; 19:3007-3013

10. Joakimsen O, ***Bønaa KH***, Mathiesen EB, Stensland-Bugge E, Arnesen E. Prediction of mortality by ultrasound screening of a general population for carotid stenosis. The Tromsø study. *Stroke* 2000;31:1871-1876

11. Mathiesen EB**, *Bønaa KH***, Joakimsen O. Echolucent plaques are associated with high risk of ischemic cerebrovascular events in carotid stenosis. The Tromsø Study. *Circulation* 2001;103:2171-2175

12. Singh K, ***Bønaa KH***, Jacobsen B, Bjørk L, Solberg S. Prevalence of and risk factors for abdominal aortic aneurysms in a population-based study.The Tromsø study. *Am J Epidemiol* 2001;154: 236-44

13.*Bønaa KH*. A new hypothesis explaining the gender difference in risk of coronary heart disease. *Tidsskr Nor Lægefor* 2002;122: 1783-7

14.*Bønaa KH*, Njølstad I, Ueland PM, Schirmer H, Tverdal Aa, Steigen T, Wang H, Nordrehaug JE, Arnesen E, Rasmussen K. Homocysteine lowering and cardiovascular events after acute myocardial infarction (with editorial comment). *N Engl J Med* 2006;354:1574-88

15. Ebbing M, ***Bønaa KH***, Nygård O, Arnesen E, Ueland PM, Nordrehaug JE, Rasmussen K, Njølstad I, Refsum H, Nilsen DW, Tverdal Aa, Meyer K, Vollset SE. Cancer incidence and mortality after treatment with folic acid and vitamin B_{12}. *JAMA* 2009;302:2119-26.

16. Vollset SE, Clarke R, Lewington S, Ebbing M, Halsey J, Lonn E, Armitage J, Manson JE, Hankey GJ, Spence JD, Galan P, ***Bønaa KH,*** Jamison R, Gaziano JM, Guarino P, Baron JA, Logan RFA, Giovannucci EL, Heijer Md, Ueland PM, Bennett D, Collins R, Peto R, for the B-Vitamin Treatment Trialists' Collaboration. Effects of folic acid supplemen-Tation on overall and site-specific cancer incidence during the randomized trials: meta-analyses of data on 50 000 individuals. *Lancet* 2013;381:1029-1036.

17. Mannsverk J, Wilsgaard T, Mathiesen EB, Løchen M-L, Rasmussen K, Thelle DS, Njølstad I, Hopstock LA, ***Bønaa KH***. Trends in modifiable risk factors are associated with incidence of hospitalized and non-hospitalized acute coronary Heart disease in a population. *Circulation* 2016;133:74-81

18.*Bønaa KH*, Mannsverk J, Wiseth R, Aaberge L, Myreng Y et al. Drug-eluting or bare-metal stents for coronary artery disease. *N Engl J Med* 2016;375:1242-52

19. Albrektsen G, Heuch I, Løchen M-L, Thelle DS, Wilsgaard T, Njølstad I, ***Bønaa KH***. Lifelong gender gap in risk of incident myocardial infarction. The Tromsø Study. *JAMA Intern Med* 2016;176:1673-79

20. Wiseth R, ***Bønaa KH***. Potential implications of NORSTENT (Norwegian Coronary Stent Trial). *Circulation* 2017;136:701-703.