

Letters to the Editor

When analyses are invalidated by erroneous assumptions

To the Editor:

In a recent publication in the “International Journal of Technology Assessment in Health Care” (7), Kildemoes and Kristiansen claim to address “Cost-effectiveness of interventions to reduce the thrombolytic delay for acute myocardial infarction.” Their study is based on a “Master of Public Health Assessment” thesis published by Kildemoes in the year 2001 (6). Three years ago, the author was informed that several of her assumptions were incorrect. In this letter, we will address six of the erroneous assumptions made by Kildemoes and Kristiansen.

§1. Kildemoes and Kristiansen assume that 0 percent of patients are treated within 1 hour of symptom onset if a strategy of prehospital diagnosis with the use of telemedicine is implemented. Kildemoes and Kristiansen claim that the short transport distances make prehospital thrombolysis impossible in Denmark. Furthermore, Kildemoes assumes in her thesis that “due to short distances to hospital in Denmark, the prehospital diagnostic procedure with the use of telemedicine will not be completed in the majority of patients until arrival at the hospital.” These assumptions are in clear contrast to previous international and Danish findings. Data from studies in the Netherlands indicate that implementation of a prehospital strategy of diagnosis and thrombolysis results in a 1-hour reduction in treatment delay, and results in 25% of patients being treated within 1 hour of symptom onset (8;9). Notably, the transport time to hospital in the study region was comparable to Danish findings (15;16). Furthermore, previous Danish findings report that, even in urban areas, the majority of patients can be diagnosed before hospital admission with the use of telemedicine (15).

§2. When estimating the benefit of a reduction in treatment delay before initiation of thrombolysis, Kildemoes and Kristiansen used a curve by Boersma and colleagues. This curve describes an inverse relationship between treatment delay and the number of extra lives saved per 1,000 treated with thrombolysis instead of placebo (3). However, the Boersma curve was based on the assumption that thrombolysis is ini-

tiated promptly after admission or randomization in a study. More likely, 45–60 minutes elapse from admission to initiation of thrombolysis in regions not covered by a prehospital diagnostic strategy (18). Thus, a right-shifted Boersma-curve may be more appropriate to describe the relationship between mortality and time to initiation of thrombolysis (14). In addition, the trials giving rise to the Boersma curve were not designed to evaluate the benefit of thrombolysis according to different treatment delays. The trials were designed to estimate the benefit of thrombolysis compared with placebo. The only trials comparing the beneficial effect of thrombolysis according to different treatment delays are the trials comparing prehospital thrombolysis with in-hospital thrombolysis. Meta-analyses including these trials report that a reduction in treatment delay from 2.7 hours to 1.7 hours, achieved by initiating thrombolysis before hospital admission rather than at the hospital, results in 15–22 extra lives saved per 1,000 treated (3;11;17). Similar results are obtained by a modified Boersma curve (14). In Denmark, the median treatment delay among patients diagnosed and treated with reperfusion therapy after hospital admission is close to 2.7 hours (12). If 75 percent ($n = 3,000$) of the latter patients can be diagnosed and treated before hospital admission, then 45–66 extra lives could be saved per year in Denmark, that is, seven to nine times the number expected by Kildemoes and Kristiansen.

§3. In their study, Kildemoes and Kristiansen do not specify in detail the cost of a prehospital diagnostic strategy with the use of telemedicine. However, detailed information is available in her original thesis. To establish a prehospital diagnosis of acute myocardial infarction (AMI) with the use of telemedicine, it is necessary that ambulances have the equipment for electrocardiogram (ECG) acquisition and transmission. For a physician at the hospital to evaluate the ECGs, the transmitted ECGs must be received at a hospital-based “receiving station.”

The first major miscalculation in the thesis by Kildemoes was to introduce 500 extra receiving stations in the model, that is, one receiving station for each ambulance, equal to an extra cost of 34,400,000 DKK. In fact, five receiving stations are sufficient to cover the country of Denmark.

In her thesis, Kildemoes stated that all ambulance staff was to receive additional training in acquiring and transmitting ECGs. The extra cost was estimated at 62,447,400

DKK. Kildemoes ignored the fact that a Departmental order was given in Denmark in the year 2000 by the National Board of Health to improve the prehospital management of patients. Thus, as a part of their basic education, all ambulance staff are scheduled to receive additional training in prehospital management of acute patients, irrespective of whether a prehospital diagnostic strategy is implemented or not. During this extra education, the ambulance staff will automatically obtain skills in acquiring and transmitting ECGs.

Kildemoes and Kristiansen assume that all ambulances need to be equipped with new defibrillators to acquire and transmit ECGs, with an additional cost of 85,520,000 DKK. In fact, more than 90 percent of ambulances in Denmark have defibrillators suitable for ECG acquisition. To transmit the ECGs, only an extra communication module is necessary in the ambulances, corresponding to an extra cost of 13,907,500 DKK.

In her original thesis, Kildemoes ended up with a total cost of 351,913,149 DKK when implementing a 5-year strategy of prehospital diagnosis with the use of telemedicine. If selling the 500 extra receiving stations, if you accept that ambulance staff as a part of their basic education obtain skills in acquiring and transmitting ECGs, and if you accept that a nationwide strategy of transmitting ECGs only necessitate that ambulances are equipped with a communication module, then the actual extra cost of a 5-year strategy of telemedicine is at maximum 183,453,249 DKK or less than two thirds of the amount mentioned in the study by Kildemoes and Kristiansen and only half that mentioned in the thesis by Kildemoes.

§4. Kildemoes assumes that media campaigns have a long-lasting effect. This is not consistent with previous findings. Most trials studying the effect of media campaigns have concluded that, if any effect at all, it is of short duration. It is surprising that Kildemoes and Kristiansen ignore the result of the largest study so far addressing this issue. Thus, the REACT trial, performed in twenty cities in ten states in the United States, and with a more prolonged intervention phase than the trial by Blohm and colleges (2), documented no effect of a media campaign on treatment delay, no effect whatsoever (10).

§5. Kildemoes and Kristiansen conclude that “programs aimed at reducing delay of thrombolysis in patients with AMI are likely to have a limited impact on AMI fatality.” This statement indicates that they are unaware of the fact that implementation of prehospital thrombolysis instead of hospital thrombolysis is reported to result in 15–22 extra lives saved per 1,000 treated (3;11;17). In comparison, when introducing treatment with thrombolysis instead of placebo in the 1980s, this strategy resulted in 10 extra lives saved per 1,000 treated (5).

§6. Kildemoes and Kristiansen ignore that primary percutaneous coronary intervention (primary PCI) is accepted as the preferred reperfusion strategy in most regions in Denmark

after the publication of the DANAMI-2 trial (1). A recent study has documented that a prehospital diagnostic strategy results in an 81-minute earlier initiation of primary PCI if combined with direct referral of patients to an interventional center (13). If combining these findings with estimates of the beneficial effect of primary PCI according to treatment delay (4), and with current mortality rates among patients treated with reperfusion therapy (12), then a widespread implementation of a prehospital diagnostic strategy with referral of patients directly to an interventional center would result in 14–20 extra lives saved per 1,000 treated. Assuming that 75% ($n = 3,000$) of patients are eligible for prehospital diagnosis, then 42–60 extra lives would be saved per year in Denmark.

Kildemoes and Kristiansen also ignore the significance of earlier initiation of reperfusion therapy on comorbidity. In addition to the lives saved by earlier initiation of therapy, one would also expect an improved outcome among the remaining patients, that is, improved left ventricular function, less need of medication, fewer readmissions with heart failure, fewer reinfarctions, and so on.

In summary, the number of lives saved by earlier initiation of thrombolysis or primary PCI may be seven to nine times higher than reported by Kildemoes and Kristiansen, and the costs when implementing a strategy of prehospital diagnosis with the use of telemedicine may be less than two thirds of that reported by Kildemoes and Kristiansen. Thus, Kildemoes and Kristiansen may overestimate the cost per life year gained after implementation of a prehospital diagnostic strategy by at least a factor of eleven to fourteen. There is no substantial evidence indicating that the cost-effectiveness analysis by Kildemoes and Kristiansen reflects real-life. With this viewpoint, it is hoped that we have corrected some of the erroneous assumptions made by Kildemoes and Kristiansen. We hope that any pessimism caused by their study will be replaced by optimism and inspire the readers to establish a prehospital diagnostic strategy to reduce treatment delay in patients with AMI. Reappraisal of a prehospital diagnostic strategy may, in fact, be one of the new successes in modern cardiology resulting in improved patient outcome. Hopefully, proper cost-effectiveness analyses will address this issue in the future.

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REFERENCES

1. Andersen HR, Nielsen TT, Rasmussen K, et al. A comparison of coronary angioplasty with fibrinolytic therapy in acute myocardial infarction. *N Engl J Med.* 2003;349:733-742.
2. Blohm M, Herlitz J, Hartford M, et al. Consequences of a media campaign focusing on delay in acute myocardial infarction. *Am J Cardiol.* 1992;69:411-413.
3. Boersma E, Maas ACP, Deckers JW, Simoons ML. Early thrombolytic treatment in acute myocardial infarction: Reappraisal of the golden hour. *Lancet.* 1996;348:771-775.
4. De Luca G, Suryapranata H, Ottervanger JP, et al. Time delay to treatment and mortality in primary angioplasty for acute myocardial infarction: Every minute of delay counts. *Circulation.* 2004;109:1223-1225.
5. Fibrinolytic Therapy Trialists' (FTT) Collaborative Group. Indications for fibrinolytic therapy in suspected acute myocardial infarction: Collaborative overview of early mortality and morbidity results from all randomised trials of more than 1000 patients. *Lancet.* 1994;343:311-322.
6. Kildemoes HW. Reduktion of forsinkelsen i trombolisebehandlingen af patienter med akut myokardie infarkt. En sundhedsøkonomisk model-analyse. *DSI Institut for Sundhedsvæsen DSI rapport 2001 07.*
7. Kildemoes HW, Kristiansen IS. Cost-effectiveness of interventions to reduce the thrombolytic delay for acute myocardial infarction. *Int J Technol Assess Health Care.* 2004;20:368-374.
8. Lamfers EJP, Hooghoudt TEH. Winst van prehospital trombolise bij de behandeling van het acute myocarinfarct. *Ned Tijdschr Geneesk.* 2000;144:514-518.
9. Lamfers EJP, Schut A, Hooghoudt TEH, et al. Prehospital thrombolysis with reteplase: The Nijmegen/Rotterdam study. *Am Heart J.* 2003;146:479-483.
10. Luepker RV, Raczynski JM, Osganian S, et al. Effect of a community intervention on patient delay and emergency medical service use in acute coronary heart disease: The Rapid Early Action for Coronary Treatment (REACT) Trial. *JAMA.* 2000;284:60-67.
11. Morrison LJ, Verbeek PR, McDonald AC et al. Mortality and prehospital thrombolysis for acute myocardial infarction: A meta-analysis. *JAMA* 2000;283:2686-92.
12. Terkelsen CJ, Lassen JF, Nørgaard BL, et al. Mortality rates in patients with ST-elevation vs. non-ST-elevation acute myocardial infarction: Observations from an unselected cohort. *Eur Heart J.* 2005;26:18-26.
13. Terkelsen CJ, Lassen JF, Nørgaard BL, et al. Reduction of treatment delay in patients with ST-elevation myocardial infarction: Impact of prehospital diagnosis and direct referral to primary percutaneous coronary intervention. *Eur Heart J.* 2005;26:770-777.
14. Terkelsen CJ, Lassen JF, Nørgaard BL, et al. Are we underestimating the full potential of early thrombolytic treatment in patients with acute myocardial infarction? *Heart.* 2003;89:483-484.
15. Terkelsen CJ, Nørgaard BL, Lassen JF, et al. Telemedicine used for remote prehospital diagnosing in patients suspected of acute myocardial infarction. *J Intern Med.* 2002;252:412-420.
16. Terkelsen CJ, Nørgaard BL, Lassen JF, et al. [Prehospital diagnosis and reduction of treatment delay in patients with acute ST-elevation myocardial infarction]. *Ugeskr Laeger.* 2003;165:4001-4005.
17. The European Myocardial Infarction Project Group. Pre-hospital thrombolytic therapy in patients with suspected acute myocardial infarction. *N Engl J Med.* 1993;329:383-389.
18. The GUSTO I investigators. An international randomized trial comparing four thrombolytic strategies for acute myocardial infarction. *N Engl J Med.* 1993;329:673-682.

Response to an optimistic viewpoint

To the Editor:

We appreciate the interests in our work and observe that we agree that earlier thrombolysis for AMI can reduce the AMI case fatality. The question is how much and at what price. There are no data available to directly address this issue, and we developed a simulation model to quantify costs and health consequences of less thrombolytic delay by using public awareness campaigns, telemedicine, or a combination of the two. Inevitably, such a model needs to be based on several uncertain parameter values. We performed a range of sensitivity analyses so readers of the analysis could see the effect of replacing our base case values with others that the reader might consider more appropriate. Due to space restrictions, we had to omit a table with sensitivity analyses that would have addressed several of the concerns Terkelsen and coworkers have.

Ad §1. With reference to a Dutch study (10), Terkelsen and coworkers claim that 25% of the AMI population will have prehospital thrombolytic within the first hour after onset of symptoms. We argue that prehospital thrombolytic therapy does not seem very realistic or relevant in Denmark for at least two reasons:

- 1) The delay between calling an ambulance and the patient arriving at the nearest hospital rarely exceed 30 minutes in Denmark (total prehospital delay) and, in an urban setting, less.
- 2) The time elapsing from the ambulance arriving to the patient until the prehospital diagnostic procedure and preparation of the thrombolytic infusion (streptokinase/anistreplase) is accomplished would exceed the period spent in the ambulance (20 minutes). Data from the Dutch study (10) and a Swedish study (2) support this assumption. In the Dutch study, the time elapsed from arrival of the ambulance until start of thrombolytic infusion was 27 minutes (10). In the Swedish study, it is claimed that prehospital thrombolytic therapy is recommended when the prehospital delay exceeds 30 minutes (2).

Based on two earlier studies of prehospital telemedicine AMI diagnostics where door-to-needle delay (hospital delay) was reduced by approximately 30 minutes (6;7), we assumed that hospital delay as base case would be reduced from 60 minutes to 30 minutes. In a Danish feasibility study of prehospital telemedicine diagnostics (16), hospital delay was reduced from 81 minutes to 38 minutes, and it was estimated

that the prehospital diagnostic procedure itself will last 13 minutes. Thus the study does demonstrate the feasibility of prehospital telemedicine diagnostics but *not* the feasibility of prehospital thrombolysis in Denmark.

We *explicitly* based our analysis of the telemedicine strategy on reduction of hospital delay. Even with a minimum of patient delay and a total prehospital delay of 20–30 minutes, no patients would be treated within the first hour if the hospital delay is reduced 60 minutes to 30 minutes.

As described in the study (9), the magnitude of the reduction in hospital delay was tested in the sensitivity analysis. If hospital delay is totally eliminated (corresponding to a delay reduction of 1 hour), the reduction in case fatality more than doubles. This estimate is mainly explained by the fact that some patients in this situation will be treated during the first hour after onset of symptoms. However, based on a Danish study (13), we estimated that only approximately 7% of Danish AMI population (i.e., of all AMI patients arriving *alive* at the hospital) arrive at the hospital within the first hour after symptom debut and that only a fraction of those arrive by ambulance. Thirty-four percent arrive at the hospital within the first 2 hours (12). Thus if the hospital delay is eliminated as a consequence of the telemedicine strategy, approximately 7 percent of the Danish AMI population could be treated within the first hour—if all arrived by ambulance and if thrombolytic therapy were beneficial for all. If a greater proportion of patients were transported by ambulance shortly after onset of symptoms, the health benefit of the telemedicine strategy would increase!

In the Dutch study mentioned by Terkelsen and colleagues, 21 percent of the included AMI patients who were treated with prehospital thrombolytic *infusion* (as opposed to those treated with bolus injection) were treated within the first hour. The delay from *arrival* of the ambulance to treatment was 27 minutes. In Danish routine practice, however, it is unlikely that 21 percent of the AMI population have a patient delay of less than 33 minutes—and that all of them would be transported by ambulance and also would benefit from thrombolytic therapy.

Our arguments about prehospital thrombolytic therapy is supported by Stern and Arntz (14), who state that “As is evidenced by several studies, most benefit in terms of myocardial salvage and short- and long-term mortality is achieved with initiation of therapy within the first 60–90 minutes after onset of symptoms. Nearly exclusively, prehospital initiation of thrombolysis makes it possible to take advantage of this early time window. Since it has been shown that prehospital diagnosis of an acute myocardial infarction is reliable and out-of-hospital initiation of therapy has no additional specific risk, patients seen within the first 60–90 minutes after onset of symptoms or for whom a relevant time gain of more than 90 minutes can be expected are ideal candidates for, and therefore should receive, prehospital thrombolysis.”

Ad. §2. While an early meta-analysis concluded that the effect of thrombolysis on mortality declines linearly with increasing delay from onset of symptoms (1), Boersma and colleagues argue that the decline is exponential (i.e., much greater effect with small delays) (3). Boersma and colleagues reanalyzed the data, including also analysis of prehospital versus in-hospital thrombolytic therapy (randomization of delay). We adopted Boersma’s functional form, which is in line with the opinion of Terkelsen and colleagues (as far as we understand their arguments) (15).

The crucial issue is then what proportion of unselected Danish AMI patients will have early thrombolysis (defined as the first 1–2 hours after onset of symptoms) within a telemedicine strategy. The real weakness of our analysis rather lies in the fact that we divided patients into time categories rather than treating time continuously. This strategy may have caused some underestimation of the beneficial effect of treatment during the golden hour(s). Our method, however, cannot bias the result by a factor of seven to nine. If Terkelsen and coworkers assume that prehospital thrombolysis reduces the case fatality by 15–22 per 1,000 treated—independently of the *distribution of patient delay* in Danish routine practice and of the time gained by pre-hospital thrombolytic therapy—they might overestimate the effect of prehospital thrombolysis in Denmark considerably.

Ad. §3. Due to space limitation, we were not allowed to present detailed cost data in the paper. These data, however, were based on the original Danish report (8) but were revised based on published comments to the report about the resources needed for the telemedicine strategy. We had discussions with the Danish ambulance operator (Falck) to get reliable data, and we observe that Terkelsen and coworkers disagree with the ambulance operator on several points.

To improve the prehospital management of patients, the Danish ambulance staff (not paramedics) needs upgrading, but this upgrading does not necessarily include prehospital telemedicine diagnostic tools. As proposed by Falck and described in the study (9), we tested the consequences of excluding upgrading costs in the sensitivity analysis. Due to space limitations, we could not present the sensitivity analysis in detail.

The defibrillators should be excluded from the base case analysis, only if new defibrillators are not required due to the introduction of the telemedicine system. But outdated equipment is not as easily sold as Terkelsen and coworkers propose. Excluding defibrillators, the total costs would be 272,225,000 DKK, corresponding to 89% of the base case estimate.

Terkelsen and coworkers claim that the costs of a 5-year telemedicine strategy would be 183,453,249 DKK, corresponding to 60% of our base case estimate. From experience with a Norwegian telemedicine project (4), we know that the real costs of telemedicine may increase by a factor of two

to three compared with estimates from telemedicine enthusiasts.

Ad. §4. As explicitly stated in the study, the evidence on the effect of public campaigns is conflicting (9). We applied data from the Swedish study because of cultural similarities between Sweden and Denmark, comparable precampaign patient delay and very detailed descriptions and documentation of the campaign: importantly, the *distributions of patient delay* before and after the campaign. In the REACT trial (11), such detailed information was not available; moreover, both the intervention group and the comparison group experienced reduction in median delay times—this finding might be explained by diffusion of information from the intervention group to the comparison group and not merely by a secular trend.

Ad. §5. It should be obvious from our study that we consider thrombolysis to be a real benefit to AMI patients, and earlier thrombolysis an even greater benefit. The question is whether further efforts to reduce delay are cost-effective. Our study results indicate that this may not be the case in a Danish setting (see §1). Hence, we conclude that programs aimed at reducing delay of thrombolysis in patients with AMI are likely to have limited impact on AMI fatality—in Denmark.

Ad. §6. We are well aware of PCI for AMI, and one of us (I.S.K.) recently has published a study on its cost-effectiveness (5). The study that Terkelsen and coworkers criticize (9), however, was designed to evaluate thrombolysis and not primary PCI. The study was designed and implemented at a time when PCI was not routine therapy, and thrombolytic *infusion* alone was a relevant strategy for AMI. The introduction of new types of thrombolytic agents has cost implications. Today, PCI is routine and frequently combined with prior thrombolysis.

Terkelsen and colleagues state that “a recent study (16) has documented that a prehospital diagnostic strategy results in 81 minutes earlier initiation of primary PCI if combined with direct referral of patients to an interventional center.” However, the earlier initiation of PCI is partly explained by the fact that prehospital diagnostic bypasses the local hospital, and the finding does not invalidate our arguments and analysis. In our study, we highlighted that telemedicine in combination with primary PCI might render the telemedicine strategy more cost-effective. A cost-effectiveness analysis of primary PCI with and without the use of telemedicine—in routine practice—would be of great interest.

The health and resource consequences of reducing thrombolysis delay depends on an array of assumptions about previous medical practice and what can be achieved through various strategies to reduce thrombolytic delay. Here, Terkelsen and coworkers appear to believe in one set of assumptions and we in another. They claim that telemedicine will achieve seven to nine times greater effect than our model would indicate; however, this statement seems to be based

on the assumption that prehospital thrombolysis will reduce the case fatality by 15–22 per 1,000 treated—independently of the distribution of patient delay in routine practice and the time gained by the strategy. They hope that our “pessimism” can be replaced by “optimism and inspire the readers to establish” new technologies. Our position is that science is brought forward by asking critical questions rather than excessive optimism. Finally, use of value-laden words such as “error,” “major miscalculation,” “ignore fact,” and so on is unlikely to facilitate exchange of viewpoints among researchers, especially when we are dealing with disagreement over assumptions rather than scientifically established truths.

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REFERENCES

1. Indications for fibrinolytic therapy in suspected acute myocardial infarction: Collaborative overview of early mortality and major morbidity results from all randomised trials of more than 1000 patients. Fibrinolytic Therapy Trialists' (FTT) Collaborative Group. *Lancet*. 1994;343:311-322.
2. Bengtsson JR, Karlsten R, Eriksson B. Prehospital thrombolysis: Lessons from Sweden and their application to the United Kingdom. *Emerg Med J*. 2002;19:578-583.
3. Boersma E, Maas AC, Deckers JW, Simoons ML. Early thrombolytic treatment in acute myocardial infarction: Reappraisal of the golden hour. *Lancet*. 1996;348:771-775.
4. Halvorsen PA, Kristiansen IS. Radiology services for remote communities: Cost minimisation study of telemedicine. *BMJ*. 1996;312:1333-1336.
5. Halvorsen S, Kristiansen IS, Linnestad K, et al. *Kostnader og nytte ved å erstatte trombolys med PCI ved akutt hjerteinfarkt*. Nasjonalt Kunnskapssenter for Helsetjenesten, editor. 3/2004. 2004. Norway, Nasjonalt Kunnskapssenter for Helsetjenesten. Report.
6. Karagounis L, Ipsen SK, Jessop MR, et al. Impact of field-transmitted electrocardiography on time to in-hospital

- thrombolytic therapy in acute myocardial infarction. *Am J Cardiol.* 1990;66:786-791.
7. Kereiakes DJ, Gibler WB, Martin LH, Pieper KS, Anderson LC. Relative importance of emergency medical system transport and the prehospital electrocardiogram on reducing hospital time delay to therapy for acute myocardial infarction: A preliminary report from the Cincinnati Heart Project. *Am Heart J.* 1992;123(Pt 1):835-840.
 8. Kildemoes HW. *Reduktion af forsinkelsen i thrombolysebehandlingen af patienter med Akut Myokardie Infarkt.* En sundhedsøkonomisk model-analyse. DSI report 2001.07. 2001. Copenhagen, DSI Institut for Sundhedsvæsen. Report.
 9. Kildemoes HW, Kristiansen IS. Cost-effectiveness of interventions to reduce the thrombolytic delay for acute myocardial infarction. *Int J Technol Assess Health Care.* 2004;20:368-374.
 10. Lamfers EJ, Schut A, Hooghoudt TE, et al. Prehospital thrombolysis with reteplase: The Nijmegen/Rotterdam study. *Am Heart J.* 2003;146:479-483.
 11. Luepker RV, Raczynski JM, Osganian S, et al. Effect of a community intervention on patient delay and emergency medical service use in acute coronary heart disease: The Rapid Early Action for Coronary Treatment (REACT) Trial. *JAMA.* 2000;284:60-67.
 12. Ottesen MM, Kober L, Jorgensen S, Torp-Pedersen C. Determinants of delay between symptoms and hospital admission in 5978 patients with acute myocardial infarction. The TRACE Study Group. Trandolapril Cardiac Evaluation. *Eur Heart J.* 1996;17:429-437.
 13. Rasmussen CH, Munck A, Kragstrup J, Haghfelt T. Patient delay from onset of chest pain suggesting acute coronary syndrome to hospital admission. *Scand Cardiovasc J.* 2003;37:183-186.
 14. Stern R, Arntz HR. Prehospital thrombolysis in acute myocardial infarction. *Eur J Emerg Med.* 1998;5:471-479.
 15. Terkelsen CJ, Lassen JF, Norgaard BL, et al. Are we underestimating the full potential of early thrombolytic treatment in patients with acute myocardial infarction? *Heart.* 2003;89:483-484.
 16. Terkelsen CJ, Norgaard BL, Lassen JF, et al. Telemedicine used for remote prehospital diagnosing in patients suspected of acute myocardial infarction. *J Intern Med.* 2002;252:412-420.

Response to commentaries by Kildemoes and Kristiansen

To the Editor:

§1.1. Recent data documents that not a “majority” but only 40% of Danish patients arrive at the hospital within 30 minutes of ambulance call (7;8). §1.2. The Dutch study confirmed that, even in areas with 13 minutes transport time to the hospital, comparable to the Danish scenery, a prehospital thrombolytic strategy reduced treatment delay by nearly 1 hour (5). §1.3. We appreciate that the authors confirm our viewpoint, that is, quoting that “the mortality reduction more than doubles up,” “if hospital delay is totally eliminated (cor-

responding to a delay reduction of 1 hour).” In the future, patients should be diagnosed before hospital admission and either treated before hospital admission with thrombolysis or transferred directly to interventional center for primary PCI. In both settings, the delay at the local hospital, averaging 1 hour, would be eliminated (1;8). §2.0. Kildemoes and Kristiansen may have misunderstood our arguments regarding the Boersma formula. We recommend that they read our previous viewpoint (9). We have no reason to believe that distribution of patient delay in Denmark differs significantly from other countries. Moreover, we are surprised that the case fatality estimates implemented by Kildemoes and Kristiansen differs significantly from findings in a recent Danish Health Technology Assessment and findings in previous meta-analyses (2;4;6). §3.1. For 7 years, the present group of authors have worked with telemedicine in the prehospital evaluation of patients. Our close collaborators, the ambulance operators and the company delivering telemedicine equipment, have confirmed our cost data, whereas they disagree with the cost data implemented by Kildemoes and Kristiansen. §3.2. Equipment for twelve-lead ECG acquisition is necessary when implementing prehospital diagnosis, irrespective of whether the diagnoses are established by telemedicine, by paramedics, or by physicians. §5. A 1-hour reduction in treatment delay is achievable by a prehospital diagnostic strategy, both in the setting of prehospital thrombolysis and in the setting of prehospital referral to interventional centers for primary PCI (6;8). This reduction in treatment delay should have a major impact on AMI fatality (also in Denmark; 3;6).

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REFERENCES

1. Andersen HR, Nielsen TT, Rasmussen K, et al. A comparison of coronary angioplasty with fibrinolytic therapy in acute myocardial infarction. *N Engl J Med.* 2003;349:733-742.
2. Boissel J-P. The European Myocardial Infarction Project: An assessment of pre-hospital thrombolysis. *Int J Cardiol.* 1995;49(Suppl):S29-S37.
3. De Luca G, Suryapranata H, Ottervanger JP, Antman EM. Time delay to treatment and mortality in primary angioplasty for acute myocardial infarction: Every minute of delay counts. *Circulation.* 2004;109:1223-1225.
4. Kjølbj M, et al. MTV-enheden Aarhus Universitet. Telemedicinsk præhospital diagnostik af akutte hjertepatienter—et nyt IT-baseret koncept. En medicinsk teknologivurdering. Puljeprojekter 2002;2(3).
5. Lamfers EJP, Schut A, Hooghoudt TEH, et al. Prehospital thrombolysis with reteplase: The Nijmegen/Rotterdam study. *Am Heart J.* 2003;146:479-483.

6. Morrison LJ, Verbeek PR, McDonald AC, Sawadsky BV, Cook DJ. Mortality and prehospital thrombolysis for acute myocardial infarction: A meta-analysis. *JAMA*. 2000;283:2686-2692.
7. Terkelsen CJ, Lassen JF, Nørgaard BL, et al. Mortality rates in patients with ST-elevation vs. non-ST-elevation acute myocardial infarction: Observations from an unselected cohort. *Eur Heart J*. 2005;26:18-26.
8. Terkelsen CJ, Lassen JF, Nørgaard BL, et al. Reduction of treatment delay in patients with ST-elevation myocardial infarction: Impact of prehospital diagnosis and direct referral to primary percutaneous coronary intervention. *Eur Heart J*. 2005;26:770-777.
9. Terkelsen CJ, Lassen JF, Nørgaard BL, et al. Are we underestimating the full potential of early thrombolytic treatment in patients with acute myocardial infarction? *Heart*. 2003;89:483-484.

Health-care management and the culture of assessment: An urgent liaison?

To the Editor:

Effectiveness in health-care management has been defined as the relationship between what a manager achieves in terms of performance and what he or she is expected to achieve; that is, effectiveness is the extent to and means by which an organization carries out its defined functions (6). The implicit, albeit core functions of hospitals and primary care centers in providing patient access, professional and center responsiveness, effective and safe services, and improved health outcomes, have increasingly been blurred by other more explicit objectives, such as cost-containment and process reengineering. Indiscriminate cost-cutting and “reengineering mania” have become popular among health-care policy-makers all over the world. Such strategies have even been adopted by countries (including Spain) whose health-care expenditures have for decades ranked below the European average (9). However, the effects of these widespread trends have never been properly assessed. They seem to impose a common threat on professional job satisfaction, and in Europe, there are more impatient patients on the waiting list than ever (8)

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Given these pressures, why is the culture of assessment not yet an important ingredient in the social capital of health-care organizations? The members of the culture of assessment make critical thinking operational. This culture is part of an international, scientific, intellectual, and professional movement to encourage evidence-based decision-making in health care. Different labels are given to similar approaches in this movement, largely depending on sources of methodological specialization of the persons and groups involved. Hence, health services research (HSR), outcomes research (OR), health technology assessment (HTA), economic assessment, and evidence-based medicine (EBM), share similar conceptual bases and methodological tools to produce sound information for making better choices in health care (5). Critical attitudes and even critical skills are essential decision-making tools for recognizing valid information and protecting oneself from being seduced by rhetoric, indoctrinated by authority, or persuaded by enthusiasm.

Paradoxically, there are already a remarkable number of barriers and resistance to adopting a culture of assessment (4;10). Some managerial leaders often perceive the liaison between managers and researchers as useless, if not professionally dangerous. The underlying reasons for this attitude might be due a relative weight in the prevailing values held among the members of health-care organizations. These values may determine professional attitudes, which, in turn, inseparable from the corporate vision, influence executive decision making. These attitudes reflect a mainstream hierarchical construct where arbitrariness is an expression of power. In such a scenario, recommendations resulting from scientific evidence could contradict the opaque process of deliberation and its consequential decisions. In this case, the imposed culture is “obedience-based” rather than evidence-based. Furthermore, information coming from scientific evidence makes it difficult to practice medicine and management purely from obedience, or even to follow, without critics, the recommendation of charismatic leaders. In fact, a close relationship between health-care managers, clinicians, and researchers turns health-care organizations into learning (from assessment) organizations.

Nevertheless, a great array of values coexists in health-care organizations. Values will tend to imbue the atmosphere of a health corporation, rising and falling according to the influence of the people who hold them. Managers, clinicians, and researchers who are prone to organizational flexibility, that is, working in professional and scientific networks, are inclined to set priorities above and beyond cost-cutting. That sort of health professional prefers transparency in the process of decision-making and cooperation in planning as opposed to opacity and paternalism. Those managers, clinicians, and researchers who would prefer the former might consider the relationship between themselves helpful, even appealing. They could perceive a need to take advantage of

transdisciplinary work to overcome a hazardous relationship rather than tolerating and perpetuating an environment of mutual mistrust, suspicion, and aspersed illegitimacy.

To encourage a productive liaison between management and the culture of assessment, initiatives are emerging at different levels of health-care systems all over the world (1;2). In Catalonia (Spain), the leaders of the Catalan Institute of Health (CIH) represent a new generation of managers, clinicians, and researchers who are trying to foster a better understanding of each other's aims. In managing health-care public resources, there are different ways to respond to similar challenges and to evolve from an infertile liaison that limits opportunities to an association that serves as a lever of modernization for outdated public health-care organizations. A brief summary of our experience with some initiatives undertaken at CIH could illustrate this point.

FRAMEWORK TO PROMOTE THE CULTURE OF ASSESSMENT IN CATALONIA (SPAIN)

The CIH is the largest health-care provider in Catalonia (Spain). It has a budget of approximately 1,800 million Euros and a staff of over 32,000. It includes eight "high-tech" teaching-hospital centers and over 450 primary care units. In 2001, a framework to forward the culture of assessment was created.

Members of the corporation agreed upon a strategic vision and a set of five explicit initiatives to foster the Culture of Assessment. These initiatives included (i) introducing clinical governance (CG), (ii) setting up a committee for evaluation of new approved drugs (CEND), (iii) defining the corporate quality standard for drug prescription (QSDP), (iv) disseminating clinical practice guidelines (CPG), and (v) establishing and agreeing on a new payment system for nurses and physicians both. Simultaneously, and crucial for implementing these initiatives, a heavy investment was made in information and communication systems and technology.

The CG initiative was designed as a tool to promote the continuous improvement of quality of care. It was based on the use of quantitative and qualitative information, such as patient and professional surveys of expectations and satisfaction. A formal contract agreement was signed between clinicians and managers of the corporation; this agreement was inspired by the results of the above-mentioned surveys. Thus, particular compromises were made in health-care process policies, including patient access to care, organization and professional responsiveness, clinician coresponsibility in the allocation of resources, and the use of evidence-based information in the implementation of specific corporate strategies. Over 100 contracts have been signed since the CG launching.

Likewise the CEND was structured to assess and disseminate (largely among GPs) evidence-based information related to approved-for-commercialization drugs. The fastest-

growing component of Catalonian health-care spending is the introduction of new pharmaceutical drugs (centrally approved by the Spanish Ministry of Health in Madrid) into routine clinical practice. The CEND's comparative reports are available to all health professionals and the general population through the CIH corporate Web site (7).

Also through this Web site, sections pertaining to QSDP, an explicit set of quality indicators for drug prescriptions, are widely disseminated. This site allows clinicians to easily compare drugs and to use this information as a tool for quality self-assessment. The development, or adaptation and dissemination, of evidence-based "clinical practice guidelines," edited in different versions for clinicians and patients, was another mainstay of this set of initiatives.

Finally, all these initiatives were monitored. Data were used for the first time in Spain as indicators for implementing economic incentives to health-care professionals by means of a new payment system agreed upon by the labor unions (3). The main features of this new payment system were two-fold. First, a variable payment was introduced as part of salary and was linked to the achievement of measurable and mutually agreed-upon annual objectives. Key criteria for the planned change included patients' accessibility to care; patient and professional satisfaction; professional and center responsiveness; program and service effectiveness and safety; the use of both evidence-based CPG; and the quality standard for improvement in prescribing drugs. This variable payment accounted for a maximum of 15 to 20 percent of the total salary.

The second feature of the new system was the design of a career development program for both physicians and nurses to formally address how to enhance professional skills such as means to access, analyze, and use health related research. Formal evaluation processes are in place to determine the effectiveness of these approaches.

The hypotheses for action at CIH were founded on the values alluded to previously as well as several principles, the first being the acknowledgment that, in this era of information-based society, management and assessment need each other badly. The second principle was the opportunity to begin building and developing a common agenda in certain areas, such as priority-setting for health services research, health technology assessment and outcomes research, methods development, impact assessment, and public involvement. The third and final principle upon which intended actions must be based is that transparency and accountability are imperatives for all actors in open societies and organizations. The overall aim is to foster a behavior change in managers, clinicians, and researchers alike such that the paradigm of participation and top-down transference of information is transformed into a paradigm of bidirectional transacting information, knowledge, and values.

These are some initial principles and hypotheses, a tentative agenda for actions in the field, which with the contributions of others, can shape a new picture for the future.

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REFERENCES

1. Dash P, Gowman N, Traynor M. Increasing the impact of health services research. *BMJ*. 2003;327:1339-1341.
2. Denis JL, Lomas J. Convergent evolution: The academia and policy roots of collaborative research. *J Health Serv Res Policy*. 2003;8(Suppl 2):S2:1-S2:6.
3. Departament de Treball, Indústria, Comerç i Turisme Resolució. TIC/2809/2003, de 15 de maig, per la qual es disposa la inscripció i la publicació del contingut de l'Acord de la Mesa Sectorial de Negociació de Sanitat sobre les condicions de treball del personal de les institucions sanitàries de l'Institut Català

- de la Salut (ICS) (codi de conveni 7902012). (Pàg. 18188) DOGC núm. 3972-22/09/2003.
4. Granados A, Jonsson E, Banta HD, et al. EUR_ASSESS project subgroup report on dissemination and impact. *Int J Technol Assess Health Care*. 1997;13:220-286.
5. Granados A. Health technology assessment and clinical decision making: Which is the best evidence? *Int J Technol Assess Health Care*. 1999;15:585-592.
6. Hamlin RG. A study and comparative analysis of managerial and leadership effectiveness in the National Health Service: an empirical factor analytic study within a trust hospital. *Health Serv Manag Res*. 2002;15:245-263.
7. Institut Català de la Salut. Available at: <http://www.gencat.net/ics>.
8. McKee M, Healy J, Edwards N, Harrison A. Pressures for change. In: McKee M, Healy J, eds. *Hospitals in changing Europe*. World Health Organisation (WHO): European Observatory on Health Care Systems Series 2002: 36-58.
9. Organisation for Economic Co-operation and Development (OECD). *Health Data 2003*. Available at: <http://www.oecd.org>.
10. Sowden A, Watt IS, Wilson P, eds. *Getting evidence into practice*. Effective Health Care Series. York: NHS Centre for Reviews and Dissemination; 1999: 1-156.