Do clinical trials tell the whole story? Statins as a case in point

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In medicine, *efficacy* indicates the capacity for beneficial change (or therapeutic effect) of a given intervention (e.g. a drug, medical device, surgical procedure or a public health intervention). An efficacious intervention is at least as good as other available interventions, to which it has been compared. Such comparisons are typically made in explanatory randomized controlled trials (RCT), whose positive outcome may then constitute the basis for national or international guidelines. But RCTs are conducted in selected patient populations with defined characteristics (e.g. gender, age, race, pre-existing conditions) established before enrolment, with a very strict protocol. Because these trials present numerous exclusion criteria, the efficacy results may not reflect a drug's behaviour in an unselected population, particularly in terms of adherence to therapy, sex, age, race and polypharmacy. In actual clinical practice the situation can be completely different, and beneficial changes of a given intervention are referred to as *effectiveness*.

A good example of this is the use of statins in Italy.

We conducted a retrospective observational analysis between 2006 and 2011 on 3751 individuals starting statins for the first time with initial total cholesterol levels of 230 - 278 mg/dl (average cholesterol of 258 mg/dl reduction in total cholesterol was assessed two months after start of therapy. We also followed 10156 individuals with similar cholesterol levels (230 to 278 mg /dl, mean 255 mg/dl) but not treated with lipid-lowering drugs.

Subjects were stratified according to drug and prescribed dosage. Data were compared with those published in the STELLAR study.

Results at two months frequently deviated from those of the Stellar study. We also stratified subjects in homogeneous categories based on similar reductions in cholesterol obtained with a given statin and dose. Considering the variability of statins in terms of efficacy vs. effectiveness, does it still make sense to base Guidelines on efficacy studies only?