The major aim of therapy is the prevention of fractures. The properties of all ideal therapeutic agents include the following: the medication is well tolerated and safe with minimal side effects; it has oral and intravenous bioavailability; it has been proven to increase bone mass, improve bone quality and reduce fractures at all sites including the hip. It should be pointed out at the outset that there are considerable variations in both quality and credibility in results from randomized trials dealing with the efficacy of different treatment schedules. When results of these clinical trials are assessed and compared, questions and problems arise with respect to the following criteria:

- Duration of the study
- Number and age of the patients
- Definition of exclusion criteria
- Primary aim of the study
- Fracture incidence versus fracture rate
- Fractures prior to start of study
- Definition of “fracture”
- Definition of “control group”

It is now possible to evaluate results of studies and reports of experiences in an objective and balanced fashion (“evidence-based medicine”) especially with reference to:

- Meta-analysis of randomized controlled studies
- Individual randomized controlled studies
- Studies based on observations
- Results of basic research
- Results and reports of clinical experience
- Results based on recommended guidelines, such as those issued by the National Institute for Health and Clinical Excellence (NICE) in the UK

With the continuing worldwide acceptance of evidence-based methodology, the classification of levels of evidence and the grading of recommendations are becoming better and more widely known and form the basis of an effective and rational treatment of osteoporosis:

- Levels of evidence:
  - Ia From meta-analysis of randomized controlled trials (RCTs)
  - Ib From at least one large RCT
  - IIA From at least one well-designed controlled study without randomization
  - IIb From at least one other type of well-designed quasi-experimental study
  - III From well designed non-experimental descriptive studies
  - IV From expert committee reports or opinions

11.1 Evidence-Based Strategies for the Therapy of Osteoporosis

Status of vitamin D and calcium
Risk profiles of the participants
Method and accuracy of bone density measurements
Differences in statistics used for analysis

...
Grading of recommendations:
- A Levels Ia and Ib
- B Levels IIa, IIb and III
- C Level IV

When this rigorous approach of evidence-based medicine is adopted, the most conclusive evidence for reducing fracture risk ("A class" recommendation) has been shown for the following antiresorptive and osteoanabolic drugs (Figs. 11.1 and 11.2; Table 11.1):
- Supplements with calcium and vitamin D
- Therapy with alendronate, risedronate, ibandronate and zoledronate
- Therapy with PTH and teriparatide

**Fig. 11.1.** Changes in bone remodelling and bone density under antiresorptive and osteoanabolic drugs

**Fig. 11.2.** Physiological factors, therapeutic agents and their influence on bone remodelling and bone mass. Physiological (black) and pharmacological (red) stimulators and inhibitors of bone formation and resorption are listed. The relative impact, where known, is represented by the thickness of the arrows. BMP, bone morphogenetic proteins; SOST, sclerostin; LRPS, low density lipoprotein (LDL)-receptor-related protein; PTH, parathyroid hormone; SERM, selective oestrogen-receptor modulator (modified from Harada and Rodan [2003])