1. Rational

While the prevalence of osteoporosis and risk factors for low bone mineral density (BMD) has been well documented in Caucasian populations; and osteoporosis and fracture as its consequence is recognized as an important global public health problem, there is still a lack of data from Asia. Because bone loss occurs insidiously and is initially asymptomatic, osteoporosis is often diagnosed only after the first clinical fracture has occurred (Unnanuntana et al 2010; Vestergaard et al 2005). However, osteoporosis and fracture are preventable if we could have early diagnosis or indentify the high-risk factors and individuals.

Osteoporosis usually occurs as a natural consequence of aging especially after the age of 50 years. Vietnam has a rapid increase in aging population with about 9 millions women and men aged 50+ years in 2012, which is equal with the total population of Sweden, is the subject of concern.

Osteoporosis is also often considered as a consequence of industrialization, because the incidence of osteoporotic fractures is higher in industrialized countries than in developing countries (Lau et al 2001). Even, within a country, the incidence of fractures is higher in urban than in rural communities (Chevalley et al 2002; Madhok et al 1993; Mannius et al 1987; Sanders et al 2002). Due to recent economic development, Vietnam has undergone rapid urbanization and there is a clear separation between urban and rural areas. During this process, differences in life styles, dietary and working habits and also exposure to polluted air and environment have gradually developed between citizens living in different settings. Thus, studies on osteoporosis in emerging developing countries are important to provide more information on the evolution of the disease.

There was a lack of knowledge about prevalence of osteoporosis in Vietnam. Age and sex specific reference data on peak bone mass and risk factors to allow screening in these specific populations are also not available.

2. Objectives and Methodology

Therefore, the thesis was designed a) to clarify to what extent osteoporosis could be re-
garded as a major public health problem in Vietnam, b) to elucidate the prevalence of certain risk factors, such as vitamin D deficiency and other determinants of bone mass as a basis to indentify high-risk individuals among the Vietnamese women and men.

The clinical studies were designed as cross-sectional investigations using a multistage sampling scheme. Within the setting of northern Vietnam (latitude 21°N), districts were selected to represent urban and rural areas. In total 612 healthy women and 222 men aged 13-83 years were investigated. BMD was measured at the lumbar spine, femoral neck and total hip in all qualified subjects with dual energy X-ray absorptiometry (DXA). Serum concentrations of 25-hydroxy vitamin D (25(OH)D), parathyroid hormone, estrogen and testosterone were quantified by electrochemiluminescence immunoassay. Data on clinical history and lifestyle were collected by individual face-to-face interviews. An experimental study on the isoflavone content of different soymilk preparations also was performed by high pressure liquid chromatography.

3. Research results
The thesis has, for the first time, presented
• Reference values for peak BMD in Vietnamese women and men. These data allowed the calculation of T-scores and thus an accurate identification of osteoporosis. Among women, values for peak BMD in this study were found comparable to other Asian data but the prevalence of osteoporosis was higher and comparable to Caucasian populations. In men, the peak BMD was found somewhat lower than for other Asian and Caucasian populations, but the prevalence of osteoporosis was quite similar. As determined at the femoral neck, the prevalence of osteoporosis in women was 17-23% and for men 9%. Even more women (37-49%) may have a risk for lumbar compression and pain as a consequence of osteoporosis in the spine. These data clearly suggest that osteoporosis is an important public health problem in Vietnam.

• Significant predictors of BMD in men were age, BMI, and serum levels of estrogen. In postmenopausal women, age, weight and
residence (urban vs rural) were the most important predictors. Postmenopausal women living in urban areas experienced osteoporosis more than rural residents. For all women, also blood levels of estrogen and testosterone were significant determinants.

- Serum levels of 25(OH)D were significantly associated with bone mass in both women and men. The prevalence of vitamin D deficiency, even when using the low cut off value of < 20 ng/mL, was very high and estimated to 30% in women and 16% in men. Partly this finding might be explained by low exposure to sunlight (urban residency and winter season) especially in women younger than 30 years of age.

- The total isoflavone content of different soymilk preparations were low, around 60-80 mg/L and there were only 10-20% of bioactive aglycones. This is far below the reported threshold levels to exert significant effects on bone. Consumption of several liters of soymilk per day would be needed to achieve any protective effect.

### 4. Research impact

This work has important contributions to fill the gaps in the body of knowledge on osteoporosis in Vietnamese women and men.

For the first time, it has provide the valuable data of bone mineral density measured by DXA for both Hologic and Lunar densitometries, thus to improve the accuracy of osteoporosis diagnosis and for the clinical management of its consequences.

This is one of the largest studies of vitamin D status and sex steroid hormones in relation to BMD in the Asian population. The clinical material comprised both men and women with a wide age range from 13-83 randomly recruited from both rural and urban areas according to a rigorous selection scheme, which allowed the comparison of the relation between sex hormones, levels of vitamin D and BMD in different age groups. The results could probably be generalized for both urban and rural settings at least for the northern part of the country.

The aglycone content of commercial soy drinks were performed with HPLC, a high quality technique with high sensitivity. The conclusion that currently available commercial soymilk products contain low amounts of aglycone is unlikely to change. So, it seems that unless new products become available, a strategy to promote soy food intake would have only little influence to prevent osteoporosis.

### 5. Future potential

In the future these data will be useful as a valuable reference base to diagnose osteoporosis and for the clinical management of its consequences. The high prevalence of vitamin D deficiency should raise the
awareness of potentially important health issues such as osteoporosis but also about other serious diseases within the Vietnamese society.

Estrogen levels are essential for bone mass in both men and women. In the clinical setting, both sex steroid hormones, estrogen and testosterone should be investigated for both men and women with osteoporosis. To the general public, information on possible risks associated with reduced sex hormone levels e.g. from smoking should be given.

Rural citizens have better bone mass when compared with their urban counterparts. Thus, a healthy lifestyle as in some rural communities should be promoted e.g. the importance of healthy nutrition, moderate physical activity and a clean environment should be emphasized.

New products of soybean should be further invested to improve the aglycone content forwards to osteoporosis prevention.

Key words: Vietnamese men and women, peak bone mineral density, osteoporosis, vitamin D deficiency, estrogen, testosterone, soymilk, aglycone content.