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Invited Plenary Abstract
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Growth – choosing the right parents

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Osteoporosis is a skeletal disease characterised by low bone mass and micro-architectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture. The cumulative incidence of fracture from age 50 years is estimated at around 50% among white women and 20% among white men. Preventive strategies against osteoporotic fracture can be targeted throughout the life course. Thus, modification of physical activity and dietary calcium/vitamin D nutrition in the elderly and during midlife, should complement high risk approaches entailing appropriate measurement of bone mineral density and targeting of anti-resorptive and formation stimulating drugs. Prevention of osteoporotic fracture can also be directed earlier in the life course. Although most effort in fracture prevention has been directed at retarding the rate of age-related bone loss, and reducing the frequency and severity of trauma among elderly people, evidence is growing that peak bone mass is an important contributor to bone strength during later life. The normal patterns of skeletal growth have been well characterised in cross-sectional and longitudinal studies. It has been confirmed that boys have higher bone mineral content, but not volumetric bone density, than girls. Furthermore, there is a dissociation between the peak velocities for height gain and bone mineral accrual, in both genders. Puberty is the period during which volumetric density appears to increase in both axial and appendicular sites. Many factors influence the accumulation of bone mineral during childhood and adolescence, including heredity, gender, diet, physical activity, endocrine status and sporadic risk factors such as cigarette smoking. Measures to maximise bone mineral acquisition, particularly through encouraging physical activity and adequate dietary calcium intake, are likely to impact upon fracture risk in later generations.

Although there is evidence to suggest that peak bone mass is inherited, current genetic markers are able to explain only a small proportion of the variation in individual bone mass or fracture risk. Evidence has also begun to accrue that fracture risk might be modified by environmental influences during intrauterine or early postnatal life, which modify the trajectory of skeletal growth and mineral accrual. The relatively rapid rate of mineral gain during this period, coupled with the plasticity of skeletal development in utero, offer the possibility of profound interactions between the genome and early environment in this stage of the life course. There is a strong biological basis for such a model of disease pathogenesis. Experimentalists have repeatedly demonstrated that minor alterations to the diet of pregnant animals can produce lasting changes in the body build, physiology and metabolism of the offspring. This is one example of a ubiquitous phenomenon (developmental plasticity), which enables one genotype to give rise to a range of different physiological or morphological states in response to different prevailing environmental conditions during development. Its essence lies in the critical period during which a system is plastic and sensitive to the environment, followed by a loss of that plasticity and a fixed functional capacity.

The evidence that osteoporosis risk might be modified in this way stems from four groups of studies: (1) Epidemiological studies which confirm that subjects who are born light and whose growth falters in the first year of postnatal life, have significantly lower bone size and mineral content, at age 60 to 75 years; (2) Cohort studies demonstrating that subsequent lower trajectories of childhood growth are associated with an increased risk of hip fracture among such men and women; (3) Detailed physiological studies of candidate endocrine systems which might be programmed have shown that birthweight and growth in infancy alter the functional settings of the GH/IGF-1, and hypothalamic pituitary adrenal axes; (4) Studies characterising the nutrition, body build and lifestyle of pregnant women which relate these to the bone mass of their newborn offspring, have identified a number of important determinants of reduced fetal mineral accrual (maternal smoking, low maternal fat stores and maternal vitamin D deficiency, intense levels of weight-bearing physical activity in late

pregnancy). Follow-up studies of randomised controlled trials of vitamin D supplementation in infancy suggest persisting benefits in adolescence and young adulthood. These data suggest that undernutrition and other adverse influences arising in fetal life or immediately after birth have a permanent effect on body structure, physiology and metabolism, which might independently influence the later risk of osteoporotic fracture.