

FOURTH AND FINAL RESEARCH CO-ORDINATION MEETING FOR THE COORDINATED RESEARCH PROJECT ON "COMPARATIVE INTERNATIONAL STUDIES OF OSTEOPOROSIS USING ISOTOPIC TECHNIQUES"

SUMMARY REPORT



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INTRODUCTION

Osteoporosis is a skeletal disease characterized by low density and general deterioration of bone tissue. Bone fragility induces fractures that represent the major clinical aspect of the disease. The number of hip fractures worldwide due to osteoporosis is expected to rise three-fold by the middle of the next century, from 1.7 million in 1990 to 6.3 million by 2050. Annual direct medical costs to treat the 2.3 million osteoporosis fractures in Europe and in the United States of America add up to US\$ 27 000 million.

There are three major fractures due to osteoporosis: of the hip, vertebrae and distal radius. These fractures should not be considered as an unavoidable price to pay for a longer life. Early detection is the key. By measuring bone mineral density (BMD) it is easy to identify those at risk and to suggest the preventive course of action.

There are a number of important risk factors for bone density, including low body weight, history of fracture, smoking, high alcohol intake, use of steroids and physical inactivity. Bone density in later life is dependent on the maximum bone mass ("peak" bone mass (PBM)) attained in early adulthood, as well as the subsequent rate of loss. The incidence of osteoporosis, as indicated by markers such as the frequency of occurrence of hip and vertebral fractures, varies significantly from one country to another. It is difficult to compare bone mass measurements between one country and another due to methodological problems.

In 1994, the International Atomic Energy Agency started the five-year Co-ordinated Research Project (CRP) on Comparative International Studies of Osteoporosis Using Isotope Techniques.

The objectives of this study were:

- To harmonize the techniques of measuring BMD within the participating countries and to obtain data that can be compared between the different study groups (countries)
- To determine whether early adult PBM varies between populations over the age range from 15 to 50 years. In other words, to determine the age of peak bone mass in selected populations from developing countries.
- To explore environmental and nutritional contributions to any determined differences.

Further information about the purpose and scope of the CRP may be found in the report of the Advisory Group Meeting (AGM) held in 1992¹ and other reports of this CRP².

¹ NAHRES-14: Comparative international studies of osteoporosis using isotope techniques. Report of an IAEA Advisory Group Meeting, Vienna, October 1992.

The fourth Research Co-ordination Meeting (RCM) for participants of the CRP, which is the subject of the present report, was held at the University of Sheffield Medical School; WHO Collaborating Center for Metabolic Bone Diseases in Sheffield, UK from 28 Feb. to 3 Mar 2000. The list of participants is given in Appendix 1 and the agenda in Appendix 2. The following report summarizes the main conclusions of the meeting.

PROGRESS TO-DATE

Since the last RCM held in 1998, the CRP participants have gathered up more data on BMD. Indeed 3488 subjects (15-50 years) have been recruited for the purpose of this project and have been stratified equally by sex and age into six –year age bands. Most of the participants have also completed collecting data on dietary intake, medical history, physical exercise, and lifestyle, as suggested in the WHO questionnaire. Some participants have analyzed trace elements in a number of bone samples as well.

One of the most important purposes of this CRP is to obtain “harmonized “ data on BMD that is comparable from one study group to another. To ensure this quality insurance, the densitometers in each center were cross calibrated using a European Spine Phantom (ESP). Furthermore, day-to-day control of DEXA machines was managed by each individual center.

Further information on the methodology is presented in Dr. McCloskey and Dr. Bostock’s report in Appendix 3 and also in the individual country’s report. Information on project performance indicators (status as of date of this meeting) is summarized in Appendix 4.

Central evaluations of the data of BMD and associated factors have been done by the UK Center (Dr. McCloskey) as decided in the previous RCMs. This evaluation so far has been done for at least 10 centers (Brazil, Canada, Beijing and Shanghai (China), Chile, the Philippines, Moscow, Obninsk (Russia), Singapore, Turkey). A review of the available information and conclusions that may be drawn from it is given in Appendix 3. Fluorine was determined in bone samples from Turkey and Russia. Fluorine was determined in the iliac crest bones of patients and in ribs collected from post-mortem investigations by particle-induced gamma-ray emission based on the $^{19}\text{F}(p,p'\gamma)^{19}\text{F}$ reaction, using 2.0/2.5 MeV protons. The results indicate that for 68% of the human samples the F concentration is in the range 500-1999 $\mu\text{g g}^{-1}$. For comparison purposes fluorine was also determined in some animal bones; in some animal tissues lateral profiles of fluorine were measured. Details are given in Appendix 5.

Reporting data to the CRL

No changes were made to the previous recommendations. It was planned during this RCM, that the final report and any peer-reviewed publications of the study should be completed within the next 6 months. However, this has not been accomplished in that timeframe due to unforeseen difficulties in gathering data from all laboratories. This still requires a concerted effort by all the participants to complete the transfer of the data to Sheffield. Only then can the WHO collaborating center finalize the data analysis. All participants will be kept fully informed about the outcome of these evaluations, and nothing will be finalized or published without the full consent of all participants.

² NAHRES 28: The role of trace minerals in osteoporosis. Report of an IAEA Consultants Meeting, Vienna, December 1995; NAHRES 31,40, 51: Comparative international studies of osteoporosis using isotope techniques. Reports on the 1st, 2nd, 3rd RCMs, Vienna, Dec. 1994, San Diego, CA, USA, Oct, 1996, Sao Paulo, Brazil, 1998; NAHRES-39: Minor and Trace Elements in Human bones and Teeth (prepared by G.V. Iyengar and L. Tandon).

Bone analysis studies (not core-programme)

As previously discussed in the third RCM, collection and analysis of specimens of iliac crest obtained by biopsy has been done by some countries according to the technical protocol prepared by Dr. Aras during the last RCM.

GENERAL DISCUSSION

Only the main evaluation results are summarized here. Since a final report is in preparation, it will comprehensively present all the relevant discussions.

Main results from central evaluation

In summary, the main results that came out of the central evaluation are as follows:

- i. Significant differences were found in the mean ages of the subjects between the study centers (countries). This could reflect the local difficulties in successfully recruiting subjects across the full age range as specified in the protocol.
- ii. There were significant differences between the center's subjects in terms of height and weight with the lowest values observed in the South East Asian Centers.
- iii. At all centers, the standardized bone densities for the femoral neck (sfm BMD) showed small or occasionally significant correlations with height and weight.
- iv. Equipment brands (Lunar and different Hologic equipment) seemed to have a significant effect on mean bone density at the femoral neck in both sexes. However, following adjustment of Lunar and Hologic equipment, as has been done by the Ankara center, no significant difference between mean bone density measured by both dosimeters were detected.
- v. There were highly significant differences in mean bone density between centers. The highest values were observed at the Russian center and the lowest at Shanghai's. Adjusting for age, height and weight had very little impact on these differences.
- vi. Femoral neck BMD appears constant between the age of 25-45 years, but this will require confirmation by further statistical analysis.
- vii. Low femoral neck BMD is accompanied by low spinal BMD
- viii. The impact of family history, environmental factors and nutrition will be explored in subsequent analyses.

CONCLUSION

The Central Reference Laboratory (CRL) has already compiled an interesting amount of results. These are reflected in the final report written by Dr. Parr and Dr. Dey during the consultants meeting called for this purpose in November 2001 report to be released in late 2002.

TABLE 1. CALENDAR OF EVENTS OF THE CRP UP TO THE TIME OF THE PRESENT RCM

Date	Action
1992:Oct.	Advisory Group Meeting, Vienna, recommended the setting up of the CRP and defined its purpose and scope.
1994: May	CRP proposal approved by Agency's in-house committee
1994: Nov/Dec.	Research contract and research agreements awarded to 12 participants
1994: Dec	Author contract awarded to G.V. Iyengar, USA, for literature survey on elemental composition of bones
1994: Dec	First RCM, Vienna, Austria
1995: Dec	Consultants' meeting on "The role of trace minerals in osteoporosis", Vienna
1995:	Technical Contract awarded to UK (McCloskey) for QC and data evaluation services.
1996: Oct	Second RCM, San Diego, USA
1996: Oct	European Spine Phantom Circulated
1998: Aug	Third RCM, Sao Paulo, Brazil
2000: March	Fourth RCM, Sheffield, UK
Late 2002	Release of final report as IAEA TEC DOC

COUNTRY REPORTS

