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RISKAP, A COMPUTER CODE FOR ANALYSIS OF INCREASED RISK TO ARBITRARY POPULATIONS

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CONTENTS

INTRODUCTION

The computer code RISKAP is used to estimate risk to a population exposed to radioactivity. Risk is measured in terms of the expected number of premature deaths resulting from radiogenic cancers, the number of years of life lost as a result of these deaths, and the average number of years of life lost per premature death. In the special case that the population consists of a single birth cohort, the decrease in life expectancy of the cohort is also computed.

RISKAP is related to two other computer codes, CAIRD[1,2] (developed by the Environmental Protection Agency) and SPAHR[3,4] (developed at Argonne National Laboratory). CAIRD is designed to estimate the number of premature deaths and years of life lost for a hypothetical cohort of persons, all simultaneously liveborn and all subject to the same competing risks throughout life. A limitation of the CAIRD code is that it cannot be applied to an arbitrary population or for an indefinite length of time after the beginning of exposure. This limitation was overcome by the SPAHR code, which applies to a population with arbitrary age structure and fertility rates. SPAHR allows detailed, site-specific demographic considerations but, in effect, is accessible only to the specialist because of the large amount of time required to become fully conversant with the code. In fact, the potential SPAHR user is confronted with five volumes of documentation covering nearly 300 pages (demographic model, introductory guide, interactive package guide, user's guide, and programmer's guide).[4]

The computer code RISKAP was designed to overcome the limitations of the CAIRD code while being readily usable by anyone familiar with the rudiments of Fortran IV. The user defines a population by specifying its size and age distribution at reference time 0, its subsequent age-specific mortality rates assuming no radiogenic deaths, and its subsequent birth rates. Radiation doses that may vary with age and time, beginning at time 0 or later, are also assigned by the user. These doses are used to compute an annual, age-specific risk of premature cancer death, based on a dose-response function selected by the user. Calculations of premature radiation deaths, deaths from all causes, and

the new age distribution of the population are performed for one-year intervals. The population is tracked over any specified period.

For many applications it is reasonable to assume that competing risks (as defined by mortality rates for all nonradiogenic causes of death) do not change a great deal during the period of radiogenic risk. It is sometimes the case, however, that observed or anticipated changes in non-radiogenic risks during the period of interest have significant impact on the estimate of the number of incremental (radiogenic) deaths. In particular, if the assumption is made that the risk of incurring a certain radiogenic health effect is related to its natural incidence, then changes with time in the incidence of that health effect could be large enough over a few years to alter estimates of premature deaths substantially. A case in point is lung cancer, whose incidence has changed dramatically in some populations during the last few decades. To handle such situations, the code has been designed to allow the use of time-dependent mortality rates. The birth rate is also allowed to vary with time.

The dose-response function or "risk function" for a radiation exposure is usually expressed in terms of a latency period in which no radiogenic cancers are expected to occur, followed by a so-called "plateau" period in which the risk of radiogenic cancer persists. It is usually assumed that the risk is uniformly distributed across the plateau period (as the name suggests).[1] Recent evidence has indicated that the length of the latency and plateau periods as well as the level of risk during the plateau period may vary substantially with the age at which exposure occurred, and the risk may be expressed nonuniformly during the plateau period (Fig. 1).[5,6] For this reason RISKAP has been designed to accommodate latency and plateau periods that vary with age at exposure and risk functions that vary with age at exposure as well as time after exposure.

Estimates of risk at low doses depend strongly on the mathematical form of the dose-response function used. The general form commonly used in current models is a sum of linear and quadratic terms (in which one term or the other may be absent), sometimes multiplied by an exponential factor that accounts for reduced risk at very high doses due to a cell-killing effect.[5] The version of RISKAP listed in this report allows the

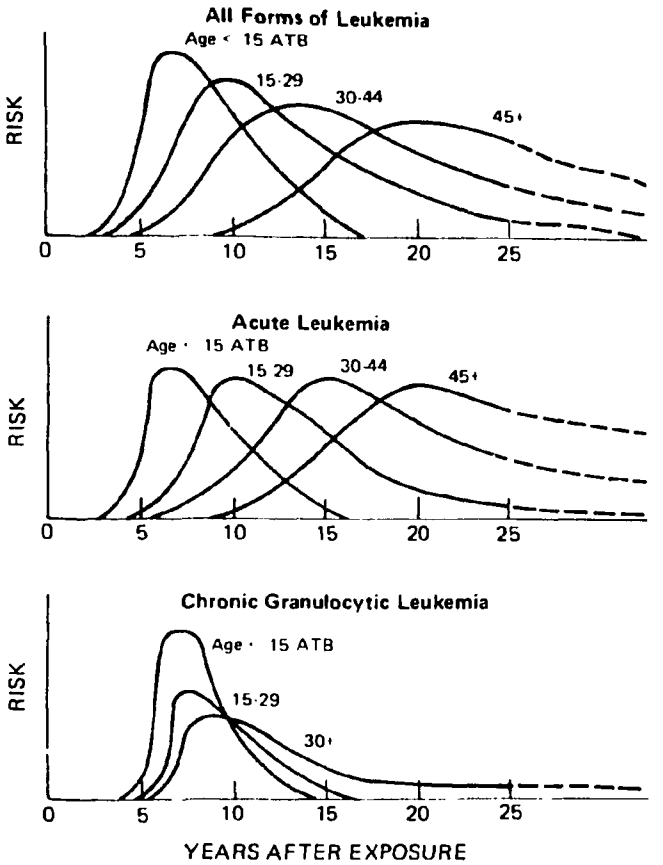

Fig. 1. The atomic bomb survivor data indicate that the latency and plateau periods for leukemia may vary with age at exposure, and the risk may be expressed nonuniformly during the plateau period.[5,6] (ATB means "at time of bombing".)

use of a linear, quadratic, or linear-quadratic dose-response function, although the code is structured so that the user may include an exponential factor or substitute any preferred dose-response function by editing a few lines that define the function.

DESCRIPTION OF THE CODE

COMPONENTS OF THE CODE AND INPUT REQUIREMENTS

The computational portion of RISKAP consists of the main program (MAIN) and a subroutine called RSCALL. These are given in Listing 1 and Listing 2, respectively, in the following pages. RSCALL, which is called by MAIN once for each year considered in the calculation, computes the age-specific incremental risks of death associated with the given radiation exposure. All other computations are performed in MAIN.

The method of entering data into the code is left to the user, although detailed suggestions are provided in the illustrative examples described later. The reason for not specifying input procedures is that the most efficient method of input may vary substantially from one application to another. Some exposure scenarios require relatively little input data, and all data may be specified in data statements or read from a data file. For other scenarios (for example, those that require time-dependent as well as age-dependent data) it may be most efficient to "call" values that have been interpolated or otherwise pre-processed from a smaller set of values input into subroutines. In the illustrative examples we provide a set of subroutines that may be used as prototypes for most applications. The user should keep in mind that such subroutines are optional; in every application all data may be entered in the form of data statements or read from data files, for example.

SUMMARY OF INPUT REQUIREMENTS

Values of the following variables must be entered in some manner into the code by the user at the points indicated in Listing 1 and Listing 2. Unless otherwise indicated, variable names beginning with I through N are integers and all others are real.

The following data must be input into MAIN in some manner (perhaps read by MAIN or called by MAIN from "input subroutines"):

NYEARS - the number of years considered in the calculation, starting at some reference time 0. NYEARS may be any positive integer, but the dimensions of BIRTH, ALLPRE, and SUMYLL (in MAIN) and FETDOS (in RSCALL), and the second dimension of DOSE (in RSCALL) must be reset to

Listing 1. The main program (MAIN) of the computer code RISKAP.

```
      REAL LX(110),ENTRE(110),BIRTH(200),Q(110),Q1(110),                (1)
     $ ALLPRE(200),PMATUR(110),RISK(110),INCMOR(110),
     $ ENTEMP(110),EXPECT(110),YRSLST(110),SUMYLL(200),
     $ REFMOR(110),CUMDTH(10),TOTYRS(10),AVERAG(10),LXSUM(110)
C INPUT DATA NYEARS,IREL,NOCAN,ICOHRT HERE.                           (2)
      TOTDTH=0.0                                                      (3)
      TOTYLL=0.0
      AVGYLL=0.0
      DO 9000 JCAN=1,NOCAN                                            (4)
      TOTYRS(JCAN)=0.0                                                (5)
      CUMDTH(JCAN)=0.0
      AVERAG(JCAN)=0.0
C INPUT INITIAL POPULATION SIZE (POPSIZ) AND AGE DISTRIBUTION         (6)
C (ENTRE(110)) HERE.  IF BIRTH RATE (BIRTH(NYEARS)) AND AGE-
C DEPENDENT PROBABILITY OF DEATH (Q1(110)) DO NOT CHANGE WITH
C THE YEAR N, THEY MAY BE INPUT HERE ALSO.
      PZERO=POPSIZ
      JCANN=JCAN
        DO 5000 N=1,NYEARS                                            (7)
        ALLPRE(N)=0.0
        IF (N .EQ. 1) GO TO 1000
        ENTRE(1)=BIRTH(N-1)*POPSIZ                                    (8)
          DO 500 I=2,110
 500      ENTRE(I)=ENTEMP(I-1)*(1.0-Q(I-1)-RISK(I-1))
 1000   NN=N
        CALL RSCALL(NYEARS,JCANN,IREL,NN,INCMOR)                      (9)
C IF BIRTH RATE (BIRTH(NYEARS)) AND AGE-DEPENDENT PROBABILITIES       (10)
C OF DEATH (Q1(110)) CHANGE WITH THE YEAR N, INPUT THEM HERE.
        POPSIZ=0.0
          DO 2000 I=1,110
          REFMOR(I)=Q1(I)/(1.0-0.5*Q1(I))
          Q(I)=REFMOR(I)/(1.0+0.5*(REFMOR(I)+INCMOR(I)))              (11)
          RISK(I)=INCMOR(I)/(1.0+0.5*(REFMOR(I)+INCMOR(I)))
          PMATUR(I)=RISK(I)*ENTRE(I)                                  (12)
          ALLPRE(N)=ALLPRE(N)+PMATUR(I)
          POPSIZ=POPSIZ+ENTRE(I)                                      (13)
 2000     ENTEMP(I)=ENTRE(I)
        LX(1)=1.0
          DO 2200 I=1,109
 2200     LX(I+1)=LX(I)*(1.0-Q1(I))                                   (14)
        LXSUM(110)=LX(110)/2.0
        EXPECT(110)=0.5
          DO 2500 I=2,110
          LXSUM(111-I)=LXSUM(112-I)+(LX(112-I)+LX(111-I))/2.0
 2500     EXPECT(111-I)=LXSUM(111-I)/LX(111-I)                        (15)
        SUMYLL(N)=0.0
          DO 3000 I=1,109
 3000     YRSLST(I)=PMATUR(I)*(EXPECT(I)+EXPECT(I+1))/2.0             (16)
          YRSLST(110)=PMATUR(110)/4.0
          DO 3200 I=1,110
 3200     SUMYLL(N)=SUMYLL(N)+YRSLST(I)                               (17)
```

```
          CUMDTH(JCAN)=CUMDTH(JCAN)+ALLPRE(N)
 5000     TOTYRS(JCAN)=TOTYRS(JCAN)+SUMYLL(N)                    (18)
        IF (CUMDTH(JCAN) .NE. 0.0) AVERAG(JCAN)=
     $    TOTYRS(JCAN)/CUMDTH(JCAN)
        TOTDTH=TOTDTH+CUMDTH(JCAN)                              (19)
        TOTYLL=TOTYLL+TOTYRS(JCAN)
 9000 CONTINUE                                                  (20)
      IF (TOTDTH .NE. 0.0) AVGYLL=TOTYLL/TOTDTH                 (21)
      IF (ICOHRT .EQ. 1) DLIFEX=TOTYLL/PZERO
C PRINT TOTAL NUMBER OF PREMATURE DEATHS (TOTDTH), TOTAL YEARS OF
C LIFE LOST (TOTYLL), AVERAGE YEARS OF LIFE LOST PER PREMATURE DEATH
C (AVGYLL), AND, IF POPULATION IS A SINGLE COHORT ONLY, DECREASE IN
C LIFE EXPECTANCY (DLIFEX).
      STOP
      END
```

Listing 2. The subroutine RSCALL.

```
      SUBROUTINE RSCALL(NYEARS,JCAN,IREL,NN,INCMOR)
      REAL A1MTRX(110,110),A2MTRX(110,110),DOSE(110,200),
     $ INCMOR(110),EXMORT(110),FETDOS(200),
     $ B1MTRX(110),B2MTRX(110)
      INTEGER LATNCY(110),PLATO(110),FLTNCY,FPLATO
      INTEGER DOSAGE,RSKAGE
      RSFUNC(A1,A2,D)=A1*D+A2*(D*D)                                    (1)
C INPUT POSTNATAL DOSES DOSE(I,J) AND PRENATAL DOSES FETDOS(J) HERE.
C INPUT FETAL RISK COEFFICIENTS (B1MTRX AND B2MTRX), FETAL
C LATENCY (FLTNCY), AND FETAL PLATEAU (FPLATO) HERE.                   (2)
C INPUT POSTNATAL RISK COEFFICIENTS (A1MTRX AND A2MTRX), LA.. ..CY
C PERIODS (LATNCY), AND PLATEAU PERIODS (PLATO) HERE.
C INPUT ABBREVIATED CANCER MORTALITY RATES (EXMORT) HERE.              (3)
      IF (IREL .EQ. 1) GO TO 50
      DO 25 I=1,110
 25   EXMORT(I)=1.0                                                    (4)
 50   CONTINUE
      DO 200 I=1,110                                                   (5)
      RSMORT=0.0
      RSKAGE=I
      B1=EXMORT(RSKAGE)*B1MTRX(RSKAGE)
      B2=EXMORT(RSKAGE)*B2MTRX(RSKAGE)                                   (5a)
      D1=0.0
      IF (RSKAGE .LT. NN) D1=FETDOS(NN-RSKAGE)
      IF (RSKAGE .LE. FPLATO+FLTNCY .AND. RSKAGE .GT. FLTNCY)            (5b)
     $ RSMORT=RSFUNC(B1,B2,D1)
      JSTART=MAX0(1,1+I-NN)
        DO 100 J=JSTART,I
        DOSAGE=J
        IF (RSKAGE .GE. DOSAGE+NN) GO TO 100
        A1=EXMORT(RSKAGE)*A1MTRX(DOSAGE,RSKAGE)
        A2=EXMORT(RSKAGE)*A2MTRX(DOSAGE,RSKAGE)                          (5a')
        D=DOSE(DOSAGE,NN+DOSAGE-RSKAGE)
        IF (RSKAGE .EQ. DOSAGE+LATNCY(DOSAGE)+PLATO(DOSAGE))
     $  RSMORT=RSMORT+RSFUNC(A1,A2,D)*0.5                                (5c)
        IF (RSKAGE .GT. DOSAGE+LATNCY(DOSAGE) .AND.
     $  RSKAGE .LT. DOSAGE+LATNCY(DOSAGE)+PLATO(DOSAGE))
     $  RSMORT=RSMORT+RSFUNC(A1,A2,D)
        IF (RSKAGE .EQ. DOSAGE+LATNCY(DOSAGE))
     $  RSMORT=RSMORT+RSFUNC(A1,A2,D)*0.5
 100    CONTINUE
      INCMOR(I)=RSMORT/(1.0+0.5*RSMORT)                                (6)
 200  CONTINUE
      RETURN
      END
```

NYEARS or greater if NYEARS exceeds the present arbitrary limit of 200. The user may choose to truncate the calculation at some point beyond which estimates are not expected to increase substantially, or NYEARS may be set conservatively as 110 plus the last year in which a dose was incurred.

IREL - a switch from relative to absolute risk. IREL is 1 for relative risk and 0 for absolute risk.

NOCAN - the number of cancer types considered. It is now limited arbitrarily to 10 but may be raised provided the dimensions of CUMDTH, TOTYRS, and AVERAG are raised accordingly.

ICOHRT - a switch set equal to 1 when the population consists of a single cohort and otherwise set equal to 0. This allows the decrease in life expectancy to be computed for the cohort. (This is not computed for a general population because there is some ambiguity in its interpretation in the general case.)

POPSIZ - the initial population size.

ENTRE(I), I=1,2,...,110 - the number of persons entering year of life I at time 0. For each year N>1, ENTRE(I) is recalculated by the code. For simplicity it is assumed that all persons have birthdays on the first day of the year.

BIRTH(J), J=1,2,...,NYEARS - the birth rate during year J. (All births for year J are assigned to the first day of year J+1.)

Q1(I), I=1,2,...,110 - the age-specific probabilities of dying from all causes in an equivalent but unexposed population. A new set of values Q1(I) may be entered for each year N if desired. If the values Q1(I) are assumed to be independent of time, then the single set of values Q1(I) may be entered before the loop on N begins.

The following data must be input into subroutine RSCALL in some manner (perhaps read by RSCALL or called by RSCALL from "input subroutines"):

DOSE(I,J), I =1,2,...,110, J=1,2,...,NYEARS - the radiation dose received in year J by persons in year of life I.

FETDOS(J), J=1,2,...,NYEARS - the fetal dose received in year J.

FLTNCY (integer-valued) - the length of the latency period associated with a fetal irradiation.

FPLATO (integer-valued) - the length of the plateau period associated with a fetal irradiation.

A1MTRX(I,J) and B1MTRX(J), I=1,2,...,110, J=1,2,...,110 - the linear risk coefficients for postnatal and prenatal exposures, respectively, for irradiation in year of life I or as a fetus, and associated with year of life J. Values for J < I are irrelevant and may be set equal to zero.

A2MTRX(I,J) and B2MTRX(J), I=1,2,...,110, J=1,2,...,110 - the quadratic risk coefficients for postnatal and prenatal exposures, respectively, for irradiation in year of life I or as a fetus, and associated with year of life J. Values for J < I are irrelevant and may be set equal to zero.

LATNCY(I), I=1,2,...,110 - the length of the latency period associated with irradiation received in year of life I.

PLATO(I) (integer-valued), I=1,2,...,110 - the plateau period associated with irradiation received in year of life I.

EXMORT(I), I=1,2,...,110 - age-specific mortality rates for the given cancer type, to be used with the relative risk hypothesis.

These data constitute a data stream for a given cancer type. Some or all of the variables FLTNCY, FPLATO, A1MTRX, A2MTRX, B1MTRX, B2MTRX, LATNCY, PLATO, and EXMORT will depend on the cancer type, and new values of those variables must be inserted into the data stream for each cancer type. For all other variables the input for each new cancer type will be a repetition of that for the preceding one. If the user wishes to apply the absolute risk hypothesis for some cancer types and the relative risk hypothesis for others in the same computer run, then IREL must be entered within the DO 9000 loop, before the call to RSCALL.

DESCRIPTION OF MAIN

The following paragraphs give a step-by-step explanation of MAIN. The numbering of the steps corresponds to the numbers typed in parentheses on Listing 1.

(1) At present, each matrix is dimensioned with one of three values: 110 for matrices indexed over the years of life of members of the population; 200 for matrices indexed over the period of years considered in the calculation; or 10 for matrices indexed over the number of cancer types considered. The number of years considered in the calculation or the number of cancer types considered may be changed to any positive integer simply by redimensioning the appropriate variables, but the maximum number of years lived by any member of the population cannot be altered without changing several statements in the code.

(2) Input data NYEARS, IREL, NOCAN, and ICOHRT are entered.

(3) The primary indices of risk calculated by RISKAP are the total number of premature deaths (TOTDTH) during years 1 through NYEARS and the total number of years of life lost (TOTYLL). These parameters are initialized to 0.0 before computations begin, as is the average number of years of life lost per premature death (AVGYLL).

(4) A "do loop" is established to calculate, for each cancer type, JCAN = 1 to NOCAN, the cumulative number of deaths during years 1 to NYEARS (CUMDTH(JCAN)), the total years of life lost (TOTYRS(JCAN)), and the average years of life lost per premature death (AVERAG(JCAN)).

(5) CUMDTH(JCAN), TOTYRS(JCAN), and AVERAG(JCAN) are initialized to 0.

(6) Input data POPSIZ and ENTRE(I), I=1,2,...,110, are entered. The initial value of POPSIZ is saved as PZERO.

(7) Within the loop for cancer type JCAN, a "do loop" is established to calculate for each year N from 1 to NYEARS the total number of premature deaths and years of life lost during year N.

(8) For each year N > 1, new values of ENTRE(I) must be calculated for each year of life I. The number entering the first year of life is the

population size POPSIZ at the beginning of the preceding year times the birth rate for the preceding year (BIRTH(N-1)). For I > 1, the number of persons entering year of life I is the number of persons who entered year of life I-1, minus those who died of natural causes (estimated as Q(I-1)*ENTRE(I-1)) and those who died from the incremental radiation doses (RISK(I-1)*ENTRE(I-1)). (The matrices Q and RISK are described later.) These computations are skipped the first year, since the values of ENTRE(I) at time 0 have been entered by the user.

(9) A call is made to subroutine RSCALL to supply age-specific incremental mortality rates INCMOR(I) associated with all incremental radiation doses delivered through year N. Subroutine RSCALL is described later.

(10) Input data BIRTH(N) and Q1(I), I=1,2,...,110, are entered. They may be entered earlier (step (6)) if they do not vary with time.

(11) Since the values Q1(I) express risk of death for those entering the I-th year of life, they are not compatible for addition to the incremental mortality rates INCMOR(I), because mortality rates express risk to an average number of people alive during the age interval. As in CAIRD, the values Q1(I) are converted to mortality rates REFMOR(I):

$$\text{REFMOR}(I) = Q1(I)/(1.0-0.5*Q1(I)).$$

The values INCMOR(I) and REFMOR(I) are added to obtain the total mortality rate, and the components are converted to probabilities of death; RISK(I) is associated with the incremental radiation doses and Q(I) is associated with all other causes of death:

$$\text{RISK}(I) = \text{INCMOR}(I)/(1.0+0.5*(\text{REFMOR}(I)+\text{INCMOR}(I))),$$

$$Q(I) = \text{REFMOR}(I)/(1.0+0.5*(\text{REFMOR}(I)+\text{INCMOR}(I))).$$

The total probability of death during the I-th year of life in year N is the sum Q(I)+RISK(I), as indicated in the DO 500 loop.

(12) PMATUR(I), the number of premature deaths of persons in their I-th year of life in year N, is

$$\text{PMATUR}(I) = \text{RISK}(I)*\text{ENTRE}(I),$$

and the total of all premature deaths during year N, ALLPRE(N), is the sum over I of PMATUR(I).

(13) The population size in year N is calculated as the sum over I of ENTRE(I), and the values ENTRE(I) are stored temporarily as ENTEMP(I).

(14) For calculation of the years of life lost due to the premature deaths, we require an estimate of the probability LX(I) of living to the beginning of the I-th year of life, I = 1,2,...,110. The values LX(I) are recalculated each year N, based on possibly new values Q1(I) supplied as input. The calculation is an iterative procedure:

$$LX(1) = 1.0$$

$$LX(I+1) = LX(I)*(1.0-Q1(I)).$$

Note that the probabilities LX(I) are based on information available in year N and do not anticipate changes in mortality rates in future years. Calculations are made from the viewpoint of an observer (demographer) in year N rather than from the viewpoint of an observer living at a time past NYEARS and already having information for years 1 through NYEARS. Both observers would see the same number of premature deaths in year N, but their estimates of the number of years of life lost by those dying prematurely in year N may be different if there are subsequent changes in the mortality rates for all causes. The "observer in year N" approach is computationally efficient and should yield a close estimate of the years of life lost as determined by the later observer, unless there are unusually large changes in mortality rates after year N.

(15) Based on the mortality rates for the present year N, the life expectancy EXPECT(I) of a person entering his/her I-th year of life at the beginning of year N is approximately

$$(0.5*[LX(I)+LX(I+1)] +0.5*[LX(I+1)+LX(I+2)] + \ldots + 0.5*[LX(109)+LX(110)] + 0.5*LX(110))/LX(I)$$

$$=(LX(110) + LX(109) + \ldots + LX(I+1) + 0.5 * LX(I))/LX(I).$$

(16) The number of years of life lost by persons dying prematurely in their I-th year of life (YRSLST(I)) in year N due to incremental

radiation doses is estimated as

$$YRSLST(I) = PMATUR(I) * (EXPECT(I)+EXPECT(I+1))/2 .$$

(17) The total years of life lost (SUMYLL(N)) in year N due to all premature deaths from incremental radiation doses is the sum over I of YRSLST(I).

(18) The cumulative number of premature deaths through the present year for cancer JCAN (CUMDTH(JCAN)) and the total years of life lost due to those premature deaths (TOTYRS(JCAN)) are the sums through the present year of ALLPRE(N) and SUMYLL(N), respectively. Calculations are repeated for the next year N.

(19) The total number of premature deaths and the total years of life lost from all types of cancer are the sums of CUMDTH(JCAN) and TOTYRS(JCAN), respectively.

(20) All calculations are repeated for the next cancer, JCAN.

(21) The average years of life lost, if any, due to premature deaths from all cancer types (AVGYLL) is TOTYLL divided by TOTDTH. If a single cohort is being considered, the decrease in life expectancy is estimated as the total years of life lost by the cohort, divided by the original size of the cohort.

DESCRIPTION OF THE SUBROUTINE RSCALL

For each year N, this subroutine calculates the age-specific incremental mortality rate INCMOR(I), I=1,2,...,110, based on all incremental radiation doses received through year N. The various steps in RSCALL are explained in the following paragraphs. The numbering of these steps corresponds to the numbers typed in parentheses on Listing 2.

(1) RSFUNC is the dose-response function. At present the code is designed to treat linear (A2=0), quadratic (A1=0), or linear-quadratic risk as a function of dose D. Essentially any type of dose-response function can be employed, however, by altering this function statement and the related risk coefficients defined in RSCALL.

(2) If N=1 (the first time RSCALL is called by MAIN) input data FLTNCY, FPLATO, FETDOS(J), DOSE(I,J), A1MTRX(I,J), A2MTRX(I,J), B1MTRX(J), B2MTRX(J), LATNCY(I), and PLATO(I) (I=1,2,...,110, J=1,2,...,NYEARS) are entered.

(3) Input data EXMORT(I), I=1,2,...,110 are entered. If the matrix EXMORT varies with time it is reentered for each N; otherwise it is entered only for N=1. Entry of EXMORT is necessary only if IREL=1.

(4) If the absolute risk hypothesis is to be used, the multiplicative factors EXMORT(I) are set equal to 1.0.

(5) The age-dependent incremental mortality rates INCMOR(I) for year N=NN are calculated in the DO 200 loop. For fixed I, the incremental risk RSMORT is calculated and later converted to INCMOR(I). For each previous year of life of those persons now in year of life I, the dose, latency period, and plateau period are checked to see if there is a resulting incremental risk to be incurred in year N.

(5a,5a') Arguments of the function RSFUNC are indexed. For fetal exposures ((5a) on the listing) the index is the year of life in which corresponding risk is incurred (RSKAGE). For postnatal exposures (5a') indexing is in terms of the present year N, the years of life DOSAGE at which doses have been incurred, and the years of life of members of the population at which risk corresponding to those doses are experienced (RSKAGE). If a different type of dose-response function is substituted in step (1), these arguments must be changed accordingly.

(5b) Risk from fetal exposure will be experienced in years of life numerically greater than the fetal latency period and no greater than the latency plus plateau periods. A person in year of life I in year N would have received the fetal dose, if any, in year N-I.

(5c) For a given dose experienced at postnatal age DOSAGE, there is a latency period LATNCY(DOSAGE), and risk is experienced over a plateau period PLATO(DOSAGE). If RSKAGE equals DOSAGE plus the latency period, the incremental mortality rate for that year is multiplied by 0.5 to reflect the fact that times in year of life

RSKAGE are, as an integral, LATENCY(DOSAGE) years later than half the times in year of life DOSAGE; for the same reason, the factor 0.5 is used for the year of life at the end of the plateau period. This factor is not used in conjunction with fetal doses; it is assumed, in effect, that fetal doses are received near the end of pregnancy. The factor 0.5, as well as the latency and plateau periods, could have been omitted from subroutine RSCALL and simply incorporated in the risk coefficients. The present approach is taken because current risk factors usually are expressed in terms of a latency period, a plateau period, and a constant risk value for years during the plateau period.

(6) The incremental risk for year N and year of life I is converted to a mortality rate before being sent to the main program.

ILLUSTRATIVE EXAMPLES

EXAMPLE 1.

We consider the case of a cohort of 100,000 persons continually exposed throughout its lifetime to radon daughters in air at a continuous level of 0.05 working levels. We estimate the risk of dying prematurely from lung cancer caused by this exposure, using the relative risk model. It is assumed that continuous exposure to this concentration of radon daughters would result in dose rates of 2.25 rem/y to persons of age 0-5 y, 2.73 rem/y to persons of age 5-15 y, and 1.82 rem/y to persons of age 15-110 y (K. F. Eckerman and D. J. Crawford, private communication).

In order to compare our estimates with those made by CAIRD, we will use mortality rates for lung cancer and for all causes based on the 1969-1971 U. S. population data.[1] We assume a latency period of 5 years and a plateau period of 30 years for all ages at exposure, and the risk factor during the plateau is assumed to be 0.2%/rem for all ages at exposure.

For the given exposure scenario it may be most efficient to read input from data files or enter them as data statements, since none of the input data vary as N varies from 1 to NYEARS. With more complex scenarios in mind, however, we will set up "input subroutines" that may serve as prototypes for a wide variety of cases.

Since we are considering the lifespan of a cohort (as defined in CAIRD), we require NYEARS=110. Since we are using the relative risk hypothesis, estimating deaths from only one type of cancer, and considering a cohort that begins its first year of life at time 0, we require IREL=1, NOCAN=1, and ICOHRT=1. These may be defined, for example, in a DATA statement in MAIN:

```
DATA NYEARS,IREL,NOCAN,ICOHRT/110,1,1,1/
```

The initial population size, POPSIZ, is 100,000. The number of persons entering year of life I at time 0 is 100,000.0 for I=1 and 0.0 for all other I. We define these values in a subroutine, AGEDST, given in Listing 3. These data are called in MAIN by the statement

```
CALL AGEDST(POPSIZ,ENTRE).
```

Listing 3. Sample subroutines for entering and/or pre-processing data (optional).

```
      SUBROUTINE AGEDST(POPSIZ,ENTRE)
      DIMENSION ENTRE(110)
      POPSIZ=0.0
      DO 10 IAGE=1,110
      ENTRE(IAGE)=0.0
      IF (IAGE .EQ. 1) ENTRE(IAGE)=100000.0
      POPSIZ=POPSIZ+ENTRE(IAGE)
10    CONTINUE
      RETURN
      END


      SUBROUTINE MORTAL(NYEARS,N,Q,BIRTH)
      DIMENSION X(110),Q(110),BIRTH(110)
      DATA X/0.02002,0.00124,0.00086,0.00070,0.00057,0.00050,0.00047,
     $ 0.00050,0.00047,0.00035,0.00031,0.00030,0.00035,0.00046,0.00063,
     $ 0.00082,0.00101,0.00117,0.00128,0.00134,0.00140,0.00147,0.00152,
     $ 0.00153,0.00151,0.00147,0.00143,0.00142,0.00144,0.00149,0.00155,
     $ 0.00163,0.00172,0.00183,0.00195,0.00209,0.00225,0.00244,0.00266,
     $ 0.00290,0.00314,0.00341,0.00370,0.00404,0.00443,0.00484,0.00528,
     $ 0.00574,0.00624,0.00678,0.00738,0.00804,0.00876,0.00957,0.01043,
     $ 0.01136,0.01236,0.01341,0.01452,0.01570,0.01695,0.01829,0.01974,
     $ 0.02133,0.02306,0.02495,0.02699,0.02918,0.03152,0.03400,0.03661,
     $ 0.03943,0.04266,0.04644,0.05075,0.05552,0.06060,0.06596,0.07153,
     $ 0.07741,0.08394,0.09122,0.09892,0.10695,0.11548,0.12561,0.13748,
     $ 0.14979,0.16158,0.17292,0.18502,0.19888,0.21363,0.22870,0.24336,
     $ 0.25745,0.26959,0.28024,0.28977,0.29869,0.30696,0.31461,0.32167,
     $ 0.32817,0.33414,0.33960,0.34460,0.34917,0.35333,0.35712/
      DO 50 J=1,NYEARS
50    BIRTH(J)=0.0
      DO 100 I=1,110
100   Q(I)=X(I)
      RETURN
      END


      SUBROUTINE DOSES(NYEARS,DOSE,FETDOS)
      REAL DOSE(110,NYEARS),FETDOS(NYEARS)
      DO 15 J=1,NYEARS
      DO 15 I=1,110
      IF (I .LE. 5) DOSE(I,J)=2.25
      IF (I .GT. 5 .AND. I .LE. 15) DOSE(I,J)=2.73
      IF (I .GT. 15) DOSE(I,J)=1.82
15    CONTINUE
      DO 30 I=1,NYEARS
30    FETDOS(I)=0.0
      RETURN
      END
```

Listing 3 (Continued)

```
      SUBROUTINE POSNAT(N,JCAN,IREL,A1,A2,LATNCY,PLATO,EXMORT)
      REAL A1(110,110),A2(110,110),INCMOR(110),
     $ ABMORT(22),EXMORT(110),ABLUNG(22)
      INTEGER LATNCY(110),PLATO(110)
      INTEGER DOSAGE,RSKAGE
      DATA ABLUNG/0.000000028,0.000000019,0.000000044,0.000000060,
     $   .000000184,0.000000357,0.000001579,0.000005845,0.000015225,
     $ 0.000029732,0.000054034,0.000088539,0.000125791,0.000157406,
     $ 0.000176327,0.000157369,0.000128287,0.000106827,
     $ 0.000106827,0.000106827,0.000106827,0.000106827/
      DO 10 I=1,110
      LATNCY(I)=5
      PLATO(I)=30
 10   CONTINUE
      DO 20 I=1,110
      DO 20 J=1,110
      A1(I,J)=0.02
      A2(I,J)=0.
 20   CONTINUE
      IF (IREL .NE. 1) GO TO 45
      DO 40 J=1,22
      ABMORT(J)=ABLUNG(J)
 40   CONTINUE
      DO 50 J=1,22
      I=5*(J-1)+1
 25   EXMORT(I)=ABMORT(J)
      IF (I .EQ. 5*J) GO TO 50
      I=I+1
      GO TO 25
 50   CONTINUE
 45   CONTINUE
      RETURN
      END


      SUBROUTINE PRENAT(N,JCAN,IREL,B1,B2,FLTNCY,FPLATO)
      REAL B1(110),B2(110)
      INTEGER FLTNCY,FPLATO
      FLTNCY=0
      FPLATO=0
      DO 30 I=1,110
      B1(I)=0.0
      B2(I)=0.0
 30   CONTINUE
      RETURN
      END
```

The birth rate BIRTH(N) is 0.0 for each year N and age-specific probabilities of death Q1(I) are those taken from U. S. life tables for 1969-1971. BIRTH and Q1 are defined in a subroutine called MORTAL given in Listing 3. These data are called in MAIN by the statement

```
IF (N .EQ. 1) CALL MORTAL(NYEARS,NN,Q1,BIRTH),
```

after setting NN=N to avoid warning messages from some computer systems. In this example it suffices to call MORTAL only once since the values computed in MORTAL do not depend on the year.

For all J, DOSE(I,J) has the value 2.25 for I from 1 through 5, 2.73 for I from 6 through 15, and 1.82 for all remaining I. FETDOS(J) is 0.0 for all J. DOSE and FETDOS are defined in a subroutine called DOSES, given in Listing 3. These matrices are called in RSCALL by the statement

```
CALL DOSES(NYEARS,DOSE,FETDOS).
```

Since the fetal dose is 0.0, the values of the fetal risk coefficients B1MTRX(I) and B2MTRX(I), the fetal latency period FLTNCY, and the fetal plateau period FPLATO are irrelevant. However, we demonstrate how these values may be entered in general with the subroutine PRENAT, given in Listing 3. These data are called in RSCALL by the statement

```
CALL PRENAT(NN,JCAN,IREL,B1MTRX,B2MTRX,FLTNCY,FPLATO).
```

Note that if more than one cancer type were considered (NOCAN > 1), then conditional statements dependent on JCAN should be used in PRENAT to define B1MTRX, B2MTRX, FLTNCY, and FPLATO, since their values may change with cancer type.

In this example the postnatal risk coefficients A1MTRX(I,J) are 0.002 for all I and J, the coefficients A2MTRX(I,J) are 0.0 for all I and J (no quadratic term), the latency periods LATNCY(I) are 5 years for all I, the plateau periods PLATO(I) are 30 years for all I, and the cancer-specific mortality rates EXMORT(I) are the lung cancer mortality rates for the U. S. for 1969-1971. These values are defined in a subroutine called POSNAT, given in Listing 3, and are called in RSCALL by the statement

CALL POSNAT(NN,JCAN,IREL,A1MTRX,A2MTRX,LATNCY,PLATO,EXMORT).

In POSNAT, the abbreviated lung cancer mortality data, given for five-year age intervals, are expanded to all ages in the same manner as in CAIRD. Alternatively, one may apply the interpolating subroutine INTERP given in Listing 4. This use of INTERP is demonstrated in a later example. Note that if multiple types of cancer are considered (NOCAN > 1), then conditional statements dependent on JCAN should be used in POSNAT to define A1MTRX, A2MTRX, LATNCY, PLATO, and EXMORT, since their values may change with cancer type. Also note that in this example it suffices to call POSNAT only once, when NN=1, since the values computed in POSNAT do not depend on the year.

Execution of RISKAP with the above input yields the following estimates:

Number of premature lung cancer deaths = 32.7,
Total years of life lost = 501,
Average years of life lost = 15.3,
Decrease in life expectancy (y) = 0.005.

These agree precisely with estimates obtained using CAIRD.

EXAMPLE 2.

We assume the same scenario as in Example 1, but in this example the plateau period is assumed to be the total lifetime for all ages at exposure, and the risk factor for exposure during the first 15 years of life is changed to 1%/rem (it remains at 0.2%/rem for higher ages at exposure). Input is the same as in Example 1, except two changes are made in subroutine POSNAT:

(a) the statement involving PLATO(I) is changed to

```
PLATO(I)=110
```

(b) the statement involving A1(I,J) is replaced by two statements:

```
IF (I .LE. 15) A1(I,J)=0.01
IF (I .GT. 15) A1(I,J)=0.002
```

With this new input the code yields the following estimates:

Listing 4. Sample pre-processing subroutines (optional).

```
      SUBROUTINE AGEDST(POPSIZ,ENTRE)
      DIMENSION ENTRE(110),NVALS(10),VALUES(10),SENBAK(110)
      DATA NVALS/1,15,35,50,70,80,85,90,100,110/
      DATA VALUES/0.014,0.02,0.012,0.012,0.007,0.0025,
     $ 0.0012,0.0006,0.00007,0.0/
      NPTS=10
      IEND=110
      CALL INTERP(NPTS,NVALS,VALUES,IEND,SENBAK)
      POPSIZ=0.0
      DO 10 IAGE=1,110
      ENTRE(IAGE)=SENBAK(IAGE)*100000.0
      POPSIZ=POPSIZ+ENTRE(IAGE)
 10   CONTINUE
      RETURN
      END


      SUBROUTINE INTERP(NPTS,NVALS,VALUES,IEND,SENBAK)
C NVALS(1) MUST BE 1 AND NVALS(NPTS) MUST BE IEND.
      INTEGER NVALS(NPTS)
      REAL VALUES(NPTS),SENBAK(110)
      IVAL=0
      DO 800 ISTEP=1,IEND
      IVAL=IVAL+1
      IF (IVAL .GE. NVALS(NPTS)) GO TO 500
      DO 200 KSTEP=1,NPTS
      IF (IVAL .GE. NVALS(KSTEP)) GO TO 200
      K=KSTEP-1
      GO TO 300
 200  CONTINUE
 300  CONTINUE
      L=K+1
      K1=NVALS(K)
      L1=NVALS(L)
      U=FLOAT(IVAL)-FLOAT(K1)
      V=FLOAT(L1)-FLOAT(IVAL)
      W=V/(U+V)
      Z=U/(U+V)
      GO TO 600
 500  K=NPTS
      L=NPTS
      W=1.0
      Z=0.0
 600  CONTINUE
      SENBAK(ISTEP)=W*VALUES(K)+Z*VALUES(L)
 800  CONTINUE
      RETURN
      END
```

Number of premature lung cancer deaths = 164,
Total years of life lost = 2415,
Average years of life lost = 14.7,
Decrease in life expectancy (y) = 0.024,

in agreement with CAIRD.

EXAMPLE 3.

We consider an exposure scenario similar to that in the two preceding examples, but instead of a single cohort we view a population whose initial age distribution is similar to that of the U. S. population in the early 1970's. This population is assumed to be exposed continuously to radon daughters in air at a concentration of 0.05 WL. We wish to estimate the lifetime risk of fatal lung cancer only to the population already existing at time 0, that is, persons born after time 0 are ignored. The age-dependent doses are assumed to be the same as in the preceding examples, and the (relative) risk factors of Example 2 are used. The age distribution of an initial population of 100,000 persons is defined by assigning fractions of the total population at time 0 in years of life 1, 15, 35, 50, 70, 80, 85, 90, 100, and 110 to be 0.014, 0.02, 0.012, 0.012, 0.007, 0.0025, 0.0012, 0.0006, 0.00007, and 0.0, respectively, and using linearly interpolated values for intermediate years of life.

The same input methods as in Example 2 may be used, except for three changes: (a) ICOHRT should be changed to 0 in MAIN since we are not considering a single cohort; (b) subroutine AGEDST is changed to describe the new age distribution (see Listing 4); (c) an interpolating subroutine INTERP (Listing 4) is also used to define the intermediate values of population fractions entered in a data statement in AGEDST.

With this input the code yields the following estimates:

Number of premature lung cancer deaths = 47.6
Total years of life lost = 647.4
Average years of life lost = 13.6.

Note that decrease in life expectancy is not calculated in this case since we are not considering a single cohort.

EXAMPLE 4.

The same situation as in Example 3 is considered, but in this case we include premature deaths to persons born after time 0. Again we consider premature deaths during the first 110 years after time 0. A birth rate of 0.014 is assumed for all years. The only change required from the input of Example 3 is in subroutine MORTAL, where the statement involving BIRTH(J) is changed to

```
BIRTH(J)=0.014.
```

The following estimates are obtained:

```
Number of premature lung cancer deaths = 152.7
                Total years of life lost = 2387
              Average years of life lost = 15.6.
```

Note that to consider the premature deaths over 10 years or 1000 years, for example, instead of 110 years, one need only assign NYEARS a value of 10 or 1000 in MAIN (in the latter case redimensioning some variables to 1000 as explained earlier).

EXAMPLE 5.

The same situation as in Example 4 is considered, but we assume that the lung cancer mortality rates do not remain at the 1970 level. These rates are assumed to begin at the 1970 level but to increase at a rate of 2% per year, beginning in year 1. The only two changes in the input methods of Example 4 are (a) in subroutine POSNAT the statement involving ABLUNG(J) is changed to

```
ABMORT(J)=((1.02)**FLOAT(N))*ABLUNG(J)
```

where N is the present year in the calculation; and (b) in subroutine RSCALL, provisions must be made to call subroutine POSNAT for each year N since the values returned by POSNAT depend on N. The following estimates are obtained:

Number of premature lung cancer deaths = 767
Total years of life lost = 11725
Average years of life lost = 15.3

EXAMPLE 6.

In this and the following example we perform risk estimates similar to estimates made in the BEIR III report,[5] except that we do not consider male and female populations separately. We consider a population of initial size 1,000,000 and initial age distribution the same as in Examples 4 and 5. The population is assumed to receive external exposure to gamma radiation at a rate of 10 rad/yr for the first year and no exposure thereafter. Mortality rates for all causes are the same as those in the preceding examples. We wish to estimate the number of premature deaths in the population from all cancers except leukemia and bone cancer, based on absolute risk factors and a linear dose-response model discussed in the BEIR III report. Age-dependent risk functions are based on values given on p. 207 of that report but reflect average values for males and females. The risk factors used here are interpolated from the following average values:

Year of life:	1	10	15	27	42	51	110
Risk factors:	2.25	2.25	1.7	5.1	6.2	10.3	10.3

These factors, which are assumed to apply to both sexes, are in terms of premature cancer deaths per million persons per year per rad. The latency period is assumed to be 10 years for all ages at exposure, and a lifetime plateau period is assumed.

We can use the input of Example 4, with the following changes:

(a) In MAIN, IREL is assigned the value 0 (absolute risk);
(b) In subroutine AGEDST, the factor 100,000.0 is changed to 1,000,000.0;
(c) In subroutine DOSES, the statements involving D(I,J) are replaced by

```
DOSE(I,J)=0.0
IF (J .EQ. 1) DOSE(I,J)=10.0
```

(d) POSNAT is changed as indicated in Listing 5.

The following estimates are obtained:

Number of premature lung cancer deaths = 1278
Total years of life lost = 25530
Average years of life lost = 20.0

EXAMPLE 7.

The same population and exposure as in Example 6 are considered, but the quadratic dose response model of BEIR III is used (see p. 208 of Ref. 5). Again, risk factors used here are averages for males and females and are in terms of cancer deaths per million persons per year per "square rad"; these factors are interpolated from the following values:

Year of life:	1	10	15	27	42	51	110
Risk factors:	0.01474	0.01474	0.00931	0.02656	0.03521	0.04962	0.04962

The latency and plateau periods are the same as in Example 6.

The input for Example 6 may be used, with the following changes in subroutine POSNAT:

(a) the linear risk factors are replaced by the quadratic factors in the statement involving DATA VALUES;
(b) the statements involving A1(I,J) and A2(I,J) are replaced with the following:

```
A1(I,J)=0.0
A2(I,J)=SENBAK(I)/1000000.0
```

The following estimates are obtained:

Number of premature lung cancer deaths = 70.2
Total years of life lost = 1446
Average years of life lost = 20.6

SUMMARY

The computer code RISKAP is used to estimate risk to a population exposed to radioactivity. Risk is measured in terms of the expected number of premature deaths resulting from radiogenic cancers, the number of years of life lost as a result of these deaths, and the average number of years of life lost per premature death. In the special case that the population consists of a single birth cohort, the decrease in life expectancy of the cohort is also computed.

RISKAP was designed to overcome the lack of generality and/or the complexity and inaccessibility of previously developed risk analysis codes for cohorts or populations. The population may be assigned any initial size and age distribution and any subsequent time-dependent birth and mortality rates and may be tracked over any specified period of time. Radiation doses that are functions of age and time are assigned by the user. For a given cause of death, risk factors may be assigned individually to each pair (A,Y), where A is the age (in years) at exposure and Y is the number of years after exposure.

RISKAP is structured and documented to permit a user familiar with elementary FORTRAN IV to make minor editorial changes to describe special dose-response functions, populations, and exposure situations, many of which cannot be anticipated in the design of a "closed" computer code. The code is also structured to allow the user to alter the mode of data input and pre-processing to suit his/her preferences. These features are intended to enhance the flexibility, generality, and ease of application of RISKAP.

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Listing 5. A sample pre-processor subroutine (optional).

```
      SUBROUTINE POSNAT(N,JCAN,IREL,A1,A2,LATNCY,PLATO,EXMORT)
      REAL A1(110,110),A2(110,110),INCMOR(110),
     $ ABMORT(22),EXMORT(110),ABLUNG(22),VALUES(7),SENBAK(110)
      INTEGER LATNCY(110),PLATO(110)
      INTEGER DOSAGE,RSKAGE,NVALS(7)
      DATA NVALS/1,10,15,27,42,51,110/
      DATA VALUES/2.25,2.25,1.7,5.1,6.2,10.3,10.3/
      NPTS=7
      IEND=110
      CALL INTERP(NPTS,NVALS,VALUES,IEND,SENBAK)
      DO 10 I=1,110
      LATNCY(I)=10
      PLATO(I)=110
10    CONTINUE
      DO 20 I=1,110
      DO 20 J=1,110
      A1(I,J)=SENBAK(I)/1000000.0
      A2(I,J)=0.0
20    CONTINUE
      IF (IREL .NE. 1) GO TO 45
      DO 40 J=1,22
      ABMORT(J)=ABLUNG(J)
40    CONTINUE
      DO 50 J=1,22
      I=5*(J-1)+1
  25  EXMORT(I)=ABMORT(J)
      IF (I .EQ. 5*J) GO TO 50
      I=I+1
      GO TO 25
  50  CONTINUE
45    CONTINUE
      RETURN
      END
```