Assessment of Postneonatal Growth in VLBW Infants: Selection of Growth References and Age Adjustment for Prematurity

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A B S T R A C T

Objectives: To assess growth outcomes of VLBW infants using different growth references and to validate the practice of age adjustment for prematurity in the growth assessment for VLBW infants.
Methods: Longitudinal growth data of 514 VLBW infants from 4 to 36 months of adjusted age were analyzed separately based on chronological and adjusted age and by comparison with three growth references.
Results: More infants were labelled as having "subnormal growth" assessed on chronological age than on adjusted age throughout the first three years of life. The proportions of subnormal growth determined using a Canadian and the WHO reference for breastfed infants were similar; they were different from those obtained using the NCHS/WHO reference.
Conclusions: Our findings suggested that the interpretations of growth in VLBW infants vary substantially depending on which reference is used. The age adjustment for prematurity makes substantial difference in identifying subnormal growth in VLBW infants. The adjustment should be carried out throughout the first three years of life.

A B R É G É

Objectifs : Évaluer la croissance d'enfants de très petit poids de naissance en utilisant différentes courbes de croissance standards et valider la pratique qui consiste à corriger l'âge pour le degré de prématurité lors de l'évaluation de la croissance chez ces enfants.
Méthodes : Les données sur la croissance longitudinale de 514 enfants de très petit poids de naissance obtenues de 4 à 36 mois corrigés ont été analysées séparément en se basant sur l'âge chronologique et corrigé et par comparaison en utilisant trois différentes courbes de croissance standards.
Résultats : Durant les trois premières années de vie, plus d'enfants ont été étiquetés comme ayant "une croissance subnormale" lorsque l'on se basait sur l'âge chronologique que lorsqu'on se basait sur l'âge corrigé. La proportion d'enfants à croissance subnormale déterminée en utilisant des courbes de croissance canadienne et celle de l'OMS était la même pour les enfants allaités. Elle était toutefois différente de celle obtenue en utilisant les courbes de croissance SCNS/OMS.
Conclusions : Nos résultats suggèrent que la correction de l'âge pour le degré de prématurité crée une différence importante dans l'identification de la croissance subnormale parmi les enfants de très petit poids de naissance. Cette correction devrait être appliquée durant les trois premières années de vie. L'interprétation de la croissance des enfants de très petit poids de naissance varie de manière importante, dépendant de la courbe de croissance utilisée.

Very low birthweight (VLBW) infants are at high risk for subnormal growth during the first few years of life.[1-10] The accurate assessment and interpretation of their growth is an important part of optimal care. Growth charts are an important tool in the surveillance of infants' growth,[11,12] and several growth references are available to health professionals and parents. The NCHS/WHO growth reference is most widely used, but a WHO expert committee pointed out concerns regarding the NCHS/WHO reference and recommended the development of a new reference for infants.[13] Based on data from seven studies in six developed countries, a growth reference for breastfed infants has been developed.[13,14] In addition, Guo et al.[15] developed a growth reference based on a longitudinal study of Canadian infants. Finally, using data from eight centers in the US, Casey et al. reported growth curves specific to preterm infants.[2] These systems are all helpful, but the question arises as to which growth references are most appropriate for assessing longitudinal growth of VLBW infants in Canada.

Recent studies assessing the growth of preterm infants have utilized age adjusted for prematurity.[1-10,16] Although this is a common practice, there are few studies to assess the necessary period of age adjustment and what difference the age adjustment makes in evaluation of growth outcomes.

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The purposes of this study were to compare the growth outcomes of VLBW infants assessed by using different growth references for normal term infants and to validate the practice of age adjustment for prematurity.

METHODS

Study population

The study population was selected from the Alberta Children's Hospital Perinatal Follow-Up Program.[2] Eligibility was restricted to infants who were born between January 1977 and May 1992 and survived to discharge from the Neonatal Intensive Care Unit (NICU). To be consistent with the current cut off point in the Follow-Up Program, we used birthweight "1250 grams or less" instead of the conventional "less than 1500 grams" to define VLBW infants. One thousand and seven (1,007) infants met the above criteria and were routinely followed up at 4±1, 8±1, 12±1, 18±3, and 36±6 months adjusted age. Of the 1,007 infants, 514 had growth data for length and weight available on 4 or 5 visits; the other 493 infants were excluded due to having missed more than one measurement within the indicated time ranges. Of the 514 infants, 476 were examined at 4±1, 490 at 8±1, 441 at 12±1, 483 at 18±3 and 447 at 36±6 months adjusted age. The characteristics of the population studied are displayed in Table I. The 493 infants not included differed slightly from the study sample in that they had higher birthweight and gestational age, and less bronchopulmonary dysplasia and cerebral palsy in follow-up.

Measures and definitions

Weight and length were measured in a standardized fashion by trained volunteers using a calibrated infant scale and infant measurement board.[18] Birthweight was measured by clinical staff to the nearest 10 grams. Gestational age was assessed based on a best estimate derived from the maternal last menstrual period and antenatal ultrasound examinations. The postconception age was calculated as the time from estimated conception date. Adjusted ages for prematurity were generated by subtracting the time between the actual and expected date of a 40-week full-term birth from the chronological age of the infant.

Analyses

The postnatal growth in length and weight recorded according to adjusted age were expressed in standard deviation scores (SDS) or Z-scores,[13] relative to: NCHS/WHO reference,[19,20] Canadian reference[15] and WHO reference for breastfed infants.[14] The Z-scores relative to the NCHS/WHO growth reference were calculated using Epi Info 6.[21] The calculation of Z-scores relative to the Canadian reference[15] and WHO reference for breastfed infants[14] were based on the published reference data.

For population-based assessment, there are two ways of expressing anthropometry-based results using Z-scores: the prevalence-based and the mean Z-score-based reportings. For clinical purposes, the Z-score of a growth measurement ≤ -2 is considered abnormal at any particular age; such subnormal growth was also described as "low length for age" or "stunted" and "low weight for age" or "underweight" for length and weight, respectively, by WHO.[13] Prevalence of "subnormal growth" identified using different growth references was compared using a chi-square test. For the mean Z-score-based reporting, the population growth level of VLBW infants was expressed by calculating mean and standard deviation of Z-scores. Mean Z-scores based on both adjusted age and chronological age were compared using a t-test. Our goal was to study VLBW infants in relation to references for normal term infants, so comparisons of growth of study infants with the preterm infants growth reference[2] were not reported here.

TABLE I
Characteristics of the Study Sample

Total Number of Infants	**514**	
Continuous Variables	Mean	SD
Birthweight	954.6	185.9
Gestational age (weeks)	27.7	2.3
Maternal age (years)	27.6	5.2
Maternal school	13.1	2.4
Total hospital stay (days)	87.3	35.9
Categorical Variables		Prevalence %
Male		48.1
Apgar score < 6		
at 1 minutes		73.6
at 5 minutes		20.6
Race Caucasian		88.5
Low socioeconomic category		
Blishen index* ≤ 40		47.2
Maternal education <12 years		16.6
Primarily breastfed during NICU stay		61.1
Primarily breastfed at 4 months adjusted age		12.3
Bronchopulmonary dysplasia at discharge		32.7
Necrotizing enterocolitis		15.0
Neonatal sepsis		17.2
Cerebral palsy diagnosed in follow-up		7.7

* Blishen et al.[17]

TABLE II
Difference in Estimated Z-score by Adjusted and Chronological Age

Age Group	No.	Length		Weight	
		Difference*	**95% CI****	**Difference***	**95% CI****
4	476	1.93	1.89, 1.97	1.58	1.54, 1.61
8	490	1.33	1.30, 1.37	0.90	0.88, 0.92
12	441	1.04	1.02, 1.06	0.49	0.48, 0.51
18	483	0.73	0.71, 0.75	0.37	0.36, 0.38
36	447	0.49	0.47, 0.51	0.25	0.24, 0.26

* Difference = Z-score estimated by using adjusted age minus Z-score estimated by using chronological age
** P value based on t-test <0.001 for each of the comparisons.

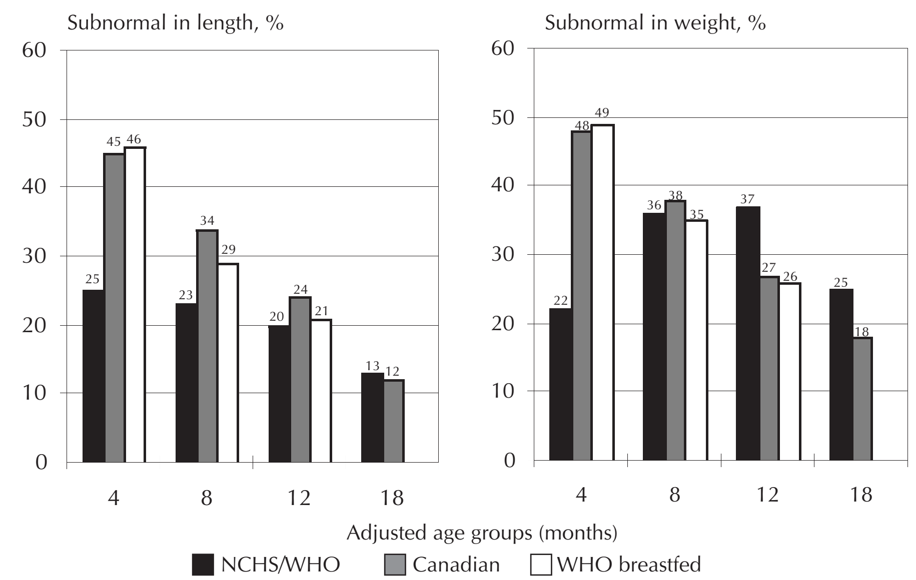

Figure 1. Prevalence of subnormal growth in VLBW infants estimated using different growth references

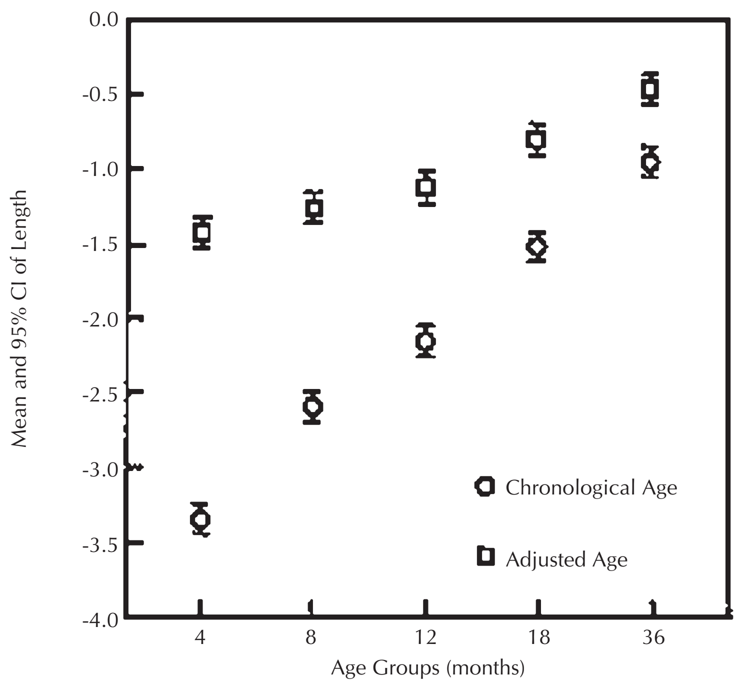

Figure 2. Mean Z-scores of body length estimated using adjusted and chronological age in VLBW infants, relative to the NCHS/WHO reference

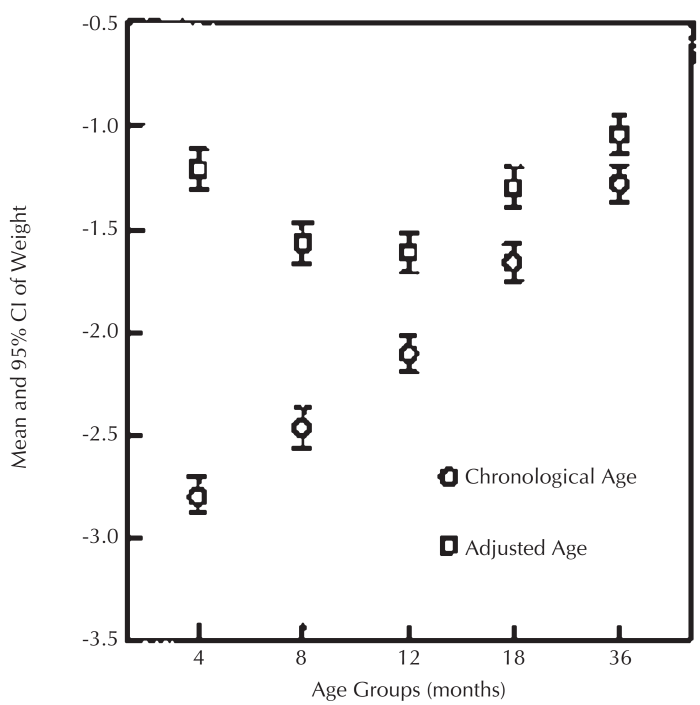

Figure 3. Mean Z-scores of body weight estimated using adjusted and chronological age in VLBW infants, relative to the NCHS/WHO reference

RESULTS

Prevalence of subnormal growth estimated by using different growth references

Since the Canadian growth reference data are only available until 18 months and WHO reference for breastfed infants until 12 months, the estimation of growth status using these references was not made after the above periods. There were no significant differences between estimated prevalence of subnormal growth determined using the Canadian reference and WHO reference for breastfed infants. The estimated prevalence of subnormal growth using the NCHS/WHO reference was lower than that estimated by either of the other two references at 4 months for weight and at 4 and 8 months for length (Figure 1), with statistical significance $p<0.05$ based on chi-square test. There were no statistically significant differences between the Canadian reference and NCHS/WHO reference at 12 and 18 months of adjusted age in estimated prevalence of subnormal growth in length. More infants were identified as underweight at 12 and 18 months of age using the NCHS/WHO reference than using the Canadian reference, with $p < 0.05$ based on chi-square test.

Mean Z-scores based on chronological age and adjusted age

The NCHS/WHO reference was used for comparing growth status of VLBW infants using chronological and adjusted age. Mean Z-scores and 95% confidence intervals based on chronological and adjusted age are presented in Figure 2 for length and Figure 3 for weight. The mean Z-scores based on adjusted age were always closer to zero, the average level of the reference population, than were scores based on chronological age. The adjusted estimate of Z-score was higher than the unadjusted estimate at every age group in both length and weight. Although the difference became smaller as infants grew older, it remained statistically significant up to 36 months adjusted age. (Table II)

Prevalence of subnormal growth based on chronological age and adjusted age

The prevalence of subnormal growth estimated by both adjusted and unadjusted

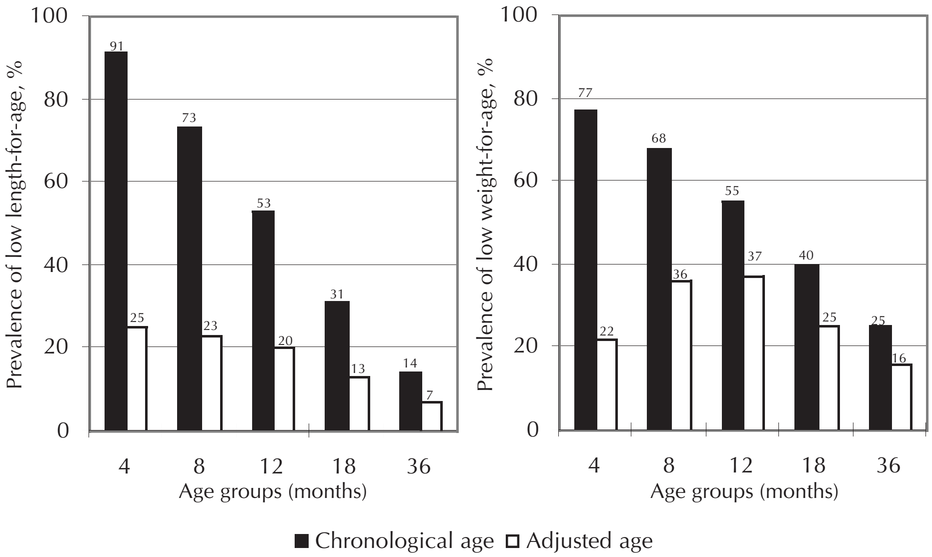

Figure 4. Prevalence of subnormal growth (≤-2 SD of median of the NCHS/WHO reference) in VLBW infants based on adjusted and chronological age

age is shown in Figure 4. A substantially higher proportion of infants were labelled as having "subnormal growth" (<-2SD of median) when assessed based on chronological rather than on adjusted age, especially in early age groups for both length and weight. The difference between adjusted and unadjusted prevalence of either stunted or underweight had statistical significance with p values < 0.001 at each growth group.

DISCUSSION

Growth references for growth assessment in VLBW infants

The differences in growth references from different populations have been realized in the literature.[12,13,15,22,23] However, the WHO working group pointed out that for practical purposes the differences are not considered large enough to invalidate the general use of the NCHS population both as a reference and a standard.[24] In our study, we obtained substantially different growth outcomes for the same sample of VLBW infants by using different references: Canadian reference and NCHS/WHO reference, especially for younger infants. At 4 months of age, over 20% of infants were classified as "subnormal" in growth for either length or weight using the Canadian reference and WHO reference for breastfed infants but as "normal" using the NCHS/WHO reference. Such discrepancies were caused by the differences in growth levels among the references. For example, the average weight in girls was 0.46 kg heavier and 0.44 cm taller in the Canadian reference than in the NCHS/WHO reference at 4 months of age.

The practical impact of using the NCHS/WHO reference and the WHO reference for breastfed infants on growth assessment was previously discussed using examples of growth data from developing countries and US and European formula-fed infants; different results in growth outcomes were obtained by using the different growth references.[13] In the present study, we did not find differences in growth outcomes of VLBW infants using the Canadian reference and WHO reference for breastfed infants, but both were different from the NCHS/WHO reference. We found that VLBW infants appear to have lagged further behind the NCHS/WHO reference in weight as they reached 12 months of age. Therefore, we question the appropriateness of using NCHS/WHO reference in the current clinical settings, especially since this pattern has also been found in normal birthweight infants when using NCHS/WHO reference.[13]

Which of the growth references should be used in assessing growth of VLBW infants in Canada? A definitive answer cannot be provided in this study, but it may depend on the purpose of growth assessment. If it is to compare the growth status between different populations, the NCHS/WHO reference makes the comparison simple. If the objective of assessment is to provide information for clinical or public health intervention, which is often the case for growth assessment of VLBW infants, we tend to recommend the Canadian reference or the WHO reference for breastfed infants. They may represent the current expected growth of normal term infants in the same social environmental context of population we assessed and with high breastfeeding rates.[25] Whatever the purpose of growth monitoring is, one should be cautious in that different growth outcomes may be obtained for the same infant if different growth references are used. An individual infant's growth should be plotted on a consistent growth reference whenever possible.

Age adjustment for prematurity

The adjusting of age for prematurity is based on the idea that the expected postnatal growth before term for preterm infants is similar to the intrauterine growth of the fetus with the same "post-conception" age. If the postnatal environment was more favourable to infants' growth than the intrauterine environment was to the fetus, one would over-correct by calculating age starting from 40 weeks after conception. However, Brandt compared the postnatal growth of infants without intrauterine growth retardation with six intrauterine growth standards from different investigators and found that the postnatal growth was lower than all six intrauterine growth standards.[23] No reports have shown that the postnatal growth of preterm infants is better than the intrauterine growth of a fetus with the same post-conception age.

Empirical evidence is provided by this study for the differences seen if VLBW infants' postneonatal growth is assessed using adjusted and unadjusted or chronological age. The average growth levels estimated using adjusted age were higher than those estimated using chronological age at each age. Mean Z-scores of body weight plotted using adjusted versus chronological age result in very different types of curves.

When adjusted age is used, the Z-scores are -1.3 at 4 months, then decrease to -1.6 at 8 and 12 months. A possible explanation is that during the period from birth to near term, VLBW infants are hospitalized, and routinely receive intensive nutrition intervention (for example, parenteral nutrition, enriched expressed breastmilk or preterm infant formulas) aimed towards achieving growth near the level of reported intrauterine growth. However, the mean weight is significantly lower in VLBW infants than it is in term infants at 4, 8 and 12 months adjusted age. Therefore, as VLBW infants' age increases beyond the first few months of life, the relative good growth level achieved through the neonatal intensive nutritional intervention decreases, and the Z-scores depart further from 0. As the infants reach 18 and 36 months of age, their growth more closely approximates that of term infants and the differences between adjusted and chronological age diminish and hence the Z-scores again approach 0. Another possible explanation is that the reference values in the NCHS/WHO reference are lower than expected values for normal term infants at 4 and 8 months since the reversed U shape in the prevalence of subnormal growth was not found using the other two references.

Although adjusting age for prematurity seems intuitively correct and has been recommended for growth assessment for preterm infants,[26,27] few studies have explored the necessary period and the implication of the adjustment in VLBW infants discharged from contemporary Neonatal Intensive Care Units (NICU). Brandt[27] found that there was no significant difference between adjusted and unadjusted age for weight by 24 months of age and height by 3.5 years. However, the sample characteristics were different from those of the present study and from VLBW infants receiving current care techniques.

The differences become smaller as infants grow due to the decrease in growth rate with increasing age. This finding confirms that adjustment for prematurity is more important for younger infants than for older ones. The differences between adjusted and unadjusted Z-scores remained statistically significant at the end of the observation period of the present study for both length and weight, which suggests that the necessary period of age adjustment for prematurity is beyond 3 years of adjusted age, which is different from Brandt's 24 months of age for weight.[27] Similar to our findings, a recent study by Elliman et al.[28] demonstrates that the correction for gestational age continues to make a difference to the height Z-scores even to the age of 7 years in infants with birthweight 2000 grams or less.

The term "partial correction" for prematurity has appeared in the literature,[29] in which the calculated adjusted age is only a portion of the actual adjusted age. For example, one may only "half correct" for the difference between adjusted and chronological age, or calculate the adjusted age from sometime after birth but before 48 weeks gestation. However, the data in this study do not indicate a role for partial correction in assessing preterm infants' growth, although it may be useful in assessing other aspects of development.

As well as decreasing the likelihood of misclassification of VLBW infants as having subnormal postneonatal growth, age adjustment for prematurity may also influence our understanding of growth patterns of VLBW infants. Catch-up growth, which is indicated by a period of increase in average growth level[2,10] compared with reference data, or by a decrease in the prevalence of subnormal growth, [3,5,7-9,30] was obvious in VLBW infants using chronological age but not so using adjusted age. These findings are comparable to Karniski et al.'s results for premature infants with higher birthweight than our sample.[10]

CONCLUSION

Interpretation of growth in VLBW infants varies substantially depending on which reference is used. The NCHS/WHO reference makes comparisons between different individuals and different populations simple but increases the likelihood of misclassification of subnormal growth in VLBW infants. Misclassification of subnormal growth can indirectly lead to misuse of referrals, investigations or other health resources. For clinical or public health activities, the Canadian and WHO breastfed infants references result in less misclassification of growth and are more in keeping with the current Canadian context. Whichever growth curve is used, longitudinal monitoring of infant growth is a key component of pediatric care and public health practice.

Adjustment of age for prematurity is supported by these analyses, especially in early infancy, to avoid misclassification of subnormal growth and to promote understanding of normal VLBW infant growth patterns. Adjustment of age becomes less crucial as infants approach the third year of life.

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BOOK REVIEWS
RECENSION

Preventing Patient Falls

Janice M. Morse. Thousand Oaks, CA: Sage Publications, Inc., 1996; 152 pp.
Hardcover: $46 US; Softcover: $21.95 US

Falls are everyone's business. An individual can suffer serious physical (and psychological) harm, caregivers and families suffer increased burden of care, and hospital stays and costs are prolonged. Increasingly we recognize that many falls are not 'accidents' but are caused or exacerbated by numerous preventable factors.

In this easily readable book, Janice Morse starts by providing an excellent overview of the somewhat complex, multifactorial issues around patient falls. The author classifies falls into three different types which come with outlines of their prevention strategies. The core of the book, however, revolves around the use of Morse's own fall scale within the context of an interdisciplinary falls prevention program. An almost step-by-step approach to creating such a program is outlined together with heavy emphasis on evidence-based practices to back this up. Thus techniques for measurement of baseline data, types of variables to measure and ongoing program evaluation are discussed.

The Morse fall scale is a simple and effective way of assessing the risk of an individual's falling. It uses six easily measured variables (such as a history of falling, presence or absence of intravenous therapy, etc.) to provide a falls risk score. Accordingly, its use allows appropriate resources to be targeted more efficiently to those at high risk.

Discussion of the construction, reliability, validity, sensitivity and specificity of the scale is provided in detail in the appendices together with over 20 pages of references for further reading for those interested.

I disagree with Morse, in that this book is not just for nurses and administrators but would be appropriate and useful for any health care professional, particularly those involved with the high-risk populations in rehabilitation and long term care. Furthermore, the methodology described for the creation of a clinical scale and the implementation of an intervention program serves as a good example for individuals interested in community health and epidemiology.

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Evidence-based Health Care: How to Make Health Policy and Management Decisions

J.A. Muir Gray. Edinburgh: Churchill Livingstone, 1997; 270pp., $25.00 Cdn.

This book proposes a comprehensive approach to health care decision making, targeted at health care workers at all levels. It introduces the principles of epidemiology, defines and explains terms and gives practical examples of how these principles should be used as evidence for decision making. The clear writing style makes the book accessible to those without any formal training in epidemiology, economics or health administration. Throughout, key points are highlighted by use of clear diagrams and flow charts. As well, frequent checklists are provided and can be used as quick reference or revision aids. An innovative feature is the presence of various vignettes, which place the preceding topics in perspective and allow for reflection on their practical application.

The groundwork for the evidence-based decision making is laid in chapters one to three. Briefly, the author suggests an empirical approach be key to sound health care decision making. Some attention is given to the need for evidence-based decisions in clinical practice, policy making and management of health care services with specific examples for developing countries. The text then addresses significant epidemiological issues and offers strategies for each. In all scenarios, thorough literature synthesis, including methodological evaluation and data analysis, is emphasized. Additional user information is provided in an appendix on medical databases such as MEDLINE,

See Book Reviews, page 142