

Safety in numbers 1: Essential numerical and scientific principles underpinning medication dose calculation

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ABSTRACT

Registered nurses spend up to 40% of their professional clinical practice engaged in the art and science of medication dosage calculation problem-solving (MDC-PS). In advancing this patient safety critical discipline it is our position that as a profession we must first situate MDC-PS within the context of the wider features of the nursing numeracy, medicines management and clinical pharmacokinetic domains that inform its practice. This paper focuses on the essential relationship between numeracy, healthcare numeracy, medicines management, pharmacokinetics and MDC-PS. We present a taxonomy of generic numerical competencies for the pre-registration curriculum, with examples of essential medication dosage calculation requirements mapped to each skills domain. This is followed by a review of the symbols and measurement units that represent essential components of calculation competence in healthcare and medicines management practice. Finally we outline the fundamental pharmacokinetic knowledge that explains how the body deals with medication and we illustrate through clinical correlations why numeric and scientific knowledge and skills must be mastered to ensure safe dosage calculation and medicines management practice. The findings inform nurse education practice via advancing our understanding of a number of issues, including a unified taxonomy of generic numerical competencies mapped to the 42 revised UK Nursing and Midwifery Council (NMC) Essential Skills Clusters (NMC, 2010a; NMC, 2010b).

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Introduction and background

The potency of medication used in 21st century healthcare practice requires registered nurses to have an up to date knowledge of evidence-based interventions and the ability to effectively and accurately apply numeracy as part of their medicines management and wider clinical practice. From a regulation perspective, the UK Nursing and Midwifery Council (NMC, 2010a) Essential Skills Clusters (ESC) and Advice and Supporting Information for Implementing NMC Standards for Pre-Registration Nursing Education (NMC, 2010b) includes reference to a wide range of generic and field-specific numerical concepts and competencies that must be mastered to practice as a registered nurse. The medication dosage calculation problem-solving (MDC-PS) component of the Medicines Management ESC was informed by a NHS Education for Scotland commissioned programme of research (see Sabin et al., 2013).

Throughout this *Safety in Numbers* series we will explore the construct of conceptual competence (understanding the medication dosage problem to be solved), calculation competence (computation of an accurate numerical value for the dose to be administered) and technical measurement competence (accurate measurement of the medication dose and/or rate of administration). The mastery and integration of these competencies is necessary to demonstrate the essential knowledge and skills that underpin safe MDC-PS practice. This paper commences the explication of the essential applied numerical knowledge and skills and wider pharmacological principles required to meet the MDC-PS requirements of professional nursing practice. Within this context we aim to:

- a. Provide a definition of numeracy.
- b. Articulate the relationship between numeracy, healthcare numeracy, medicines management and medication dosage calculation.
- c. Present a unified taxonomy of generic numerical competencies and examples of representative medication dosage calculation computation requirements mapped to the 42 NMC ESC.

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- d. Review the esoteric symbols and measurement units that represent important components of calculation competence in healthcare and medicines management practice.
- e. Outline the fundamental pharmacokinetic knowledge that explains how the body deals with medication; and illustrates through clinical correlations why numeric and scientific knowledge and skills must be mastered to ensure safe medicines management practice.

What is numeracy?

The Oxford English Dictionary (OED) defines being numerate as being 'familiar with the basic principles of mathematics'.

This definition of numeracy provides a foundation for understanding the concept and fundamental basis of numeracy. However it provides little scope for considering numeracy in context, nor does it define any of the boundaries that should be considered when an educator assists a student in developing numeracy skills. In order to consider numeracy in its educational context a more rounded and functional definition of numeracy has been provided by Coben (2000, p. 35).

To be numerate means to be competent, confident, and comfortable with one's judgements on whether to use mathematics in a particular situation and if so, what mathematics to use, how to do it, what degree of accuracy is appropriate, and what the answer means in relation to the context.

In order to develop and maintain calculation competence this definition adds important detail for the educator. The definition illustrates the importance of the type of mathematics to be used in a given context. A numerate structural engineer and numerate nurse both fall within the boundaries of the OED definition. However the definition provided by Coben (2000) specifies situational and contextual comfort, competence and confidence. This highlights how the numerate engineer requires a different set of numeracy skills than the numerate nurse or healthcare professional. The important features to consider in developing calculation competence is the context in which the calculations are used (Das, 1988) and, secondly, in defining the boundaries of numeracy within which the healthcare professional uses those calculations.

Defining medication calculation competence and its boundaries in medication dosage calculation problem-solving (MDC-PS)

We have previously defined medication calculation-competence as 'the need to undertake appropriate arithmetical operations and computations to calculate a numerical value that falls within an appropriate degree of accuracy for the required dose or rate (Coben et al., 2010)'. This definition situates calculation competence as a keystone in developing MDC-PS within nursing practice. The concept of MDC-PS competence has been extended by Sabin et al. (2008) and Coben et al. (2010) through the use of illustrative set theory (see Fig. 1). This provides the context within which MDC-PS and calculation competence lies in the broader arena of numeracy, healthcare numeracy and medicines management. Within this series we draw on the Audit Commission definition of medicines management as encompassing 'the entire way that medicines are selected, procured, delivered, prescribed, administered and reviewed to optimize the contribution that medicines make to producing informed and desired outcomes of patient care' (Audit Commission, 2001, p. 5).

These definitions illustrate two key education tenets that lie at the core of supporting calculation competence development in professional practice: First, that of defining the context in which calculation competence is centred and the importance of situated cognition, i.e., the learning and application of knowledge and skills

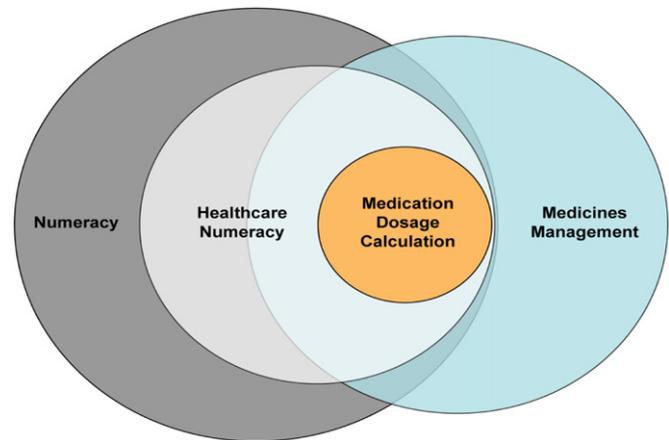


Fig. 1. An illustration of how competence in healthcare numeracy is a subset of Coben's wider definition of numeracy and medication dosage calculation is a subset of both healthcare numeracy and of a wider competency in medicines management. (Sabin et al., 2008).

situated in the context of real life situations and practice environments (Brown et al., 1989; Lave and Wenger, 1990; Weeks et al., 2013b); and second, the importance of supporting the construction of accurate schemata (internal cognitive representations of our world) that reflect the ability to understand and use arithmetical operations, computations and symbols to competently solve authentic medication dosage problems. In essence, this requires the bridging of the theory-practice and knowledge-performance gap and to commence our advancement of this premise we now present a taxonomy of essential nursing numeracy skills.

A taxonomy for nursing numeracy and essential medication dosage calculation skills

Hutton developed a taxonomy of numeracy skills required by practising nurses in the UK (Hutton, 1998). She substantially developed the inventories produced by Pirie (1987) and Roberts (1990), and reflected the major changes that had occurred in both clinical practice and nurse education since their initial reporting. One critical contribution of Hutton's study was to identify the nursing mathematics that was either specific to, or generally used within the four current UK branches or fields of nursing, i.e., child, adult, mental health and learning disability (and that form the core curricula of essential international general nursing programmes, e.g., USA Pre-Licensure KSA's: Quality and Safety Education for Nurses, 2011). This represented a substantial development of Pirie's inventory, which while being a seminal piece of work at the time, provided a rather general overview of nursing mathematics. Hutton interviewed clinical nursing staff and students from all four branches of nursing and relevant clinical settings, to identify their perceptions of the mathematics used in those areas. These findings were then confirmed and enhanced by the processes of observation and shadowing of clinical staff and students in clinical practice. Here we report how Hutton extended her original research into a unified taxonomy of generic numerical competencies mapped to the 42 revised NMC Essential Skills Clusters (NMC, 2010a). The taxonomy in Table 1 illustrates the numeracy skill required, examples of where the skill is utilised in nursing practice and the specific branch or field of nursing practice where the numeracy skill is relevant. An addendum by Weeks and Young provides examples of the minimum level of essential medication dosage & intra-venous infusion calculation skills required at the point of registration and that act as a foundation for development of more complex skills.

Table 1
Taxonomy of essential numeracy skills required by nurses mapped against NMC (2010a) essential skills clusters.

Numeracy skill	Examples	Branch/field of practice most commonly using the skill	Essential skills clusters (NMC, 2010a, b)		Examples of essential medication dosage & intravenous infusion calculation skills
			For entry to branch/field	For entry to register	
Estimation	All medication dosage & IV infusion rate calculations	All C = Child A = Adult MH = Mental Health LD = Learning Disability	Is competent in basic medicines calculations (33i)	Makes a comprehensive assessment of patients/clients' needs in relation to nutrition, identifying, documenting and communicating level of risk (28v) Accurately calculates medicines frequently encountered within branch (33ii) Safely manages drug administration and monitors effects (36iii)	Dose of medication or rate of infusion may be estimated to provide a frame of reference or "ball park" figure prior to computing & checking the calculation for accuracy, e.g.: Prescribed dose: 200 mg Dispensed: 250 mg/10 mL Estimate: >5 mL & <10 mL Accurate computation: 8 mL Prescribed dose 8 mg 5 mg + 2 mg + 1 mg tablets
Addition of whole numbers	Fluid balance Addition of tablet doses of varying formulations	All	Accurately monitors dietary and fluid intake and completes relevant documentation (27ii) Accurately monitors and records fluid intake and output (29ii)	Documents progress against prescription and markers for hydration (32iii)	
Subtraction of whole numbers	Fluid balance	All	Accurately monitors dietary and fluid intake and completes relevant documentation (27ii) Accurately monitors and records fluid intake and output (29ii)	Documents progress against prescription and markers for hydration (32iii)	
Multiplication of whole numbers	Conversion of units, drip rate calculation	All	Is competent in basic medicines calculations (33i)	Monitors and assesses patients/clients receiving intravenous fluids (32ii) Accurately calculates medicines frequently encountered within branch (33ii) Safely manages drug administration and monitors effects (36iii)	25 × 1 50 × 2 250 × 5 1000 × 20 450 × 15
Division of whole numbers	Conversion of units, drip rate calculation	All	Is competent in basic medicines calculations (33i)	Monitors and assesses patients/clients receiving intravenous fluids (32ii) Accurately calculates medicines frequently encountered within branch (33ii) Safely manages drug administration and monitors effects (36iii)	1000/8 1000/6 1000/12 450/3 450/4 125/4 167/3
Use of fractions	Drip rate calculations, enteral feeding, conversion to SI units	All	Is competent in basic medicines calculations (33i)	... administers enteral feeds safely and maintains equipment in accordance with local policy (31iv) Monitors and assesses patients/clients receiving intravenous fluids (32ii) Accurately calculates medicines frequently encountered within branch (33ii) Safely manages drug administration and monitors effects (36iii)	½ expressed as decimal equivalent ¼ expressed as decimal equivalent 1/3 expressed as decimal equivalent 5/10 expressed as decimal equivalent 125/250 expressed as decimal equivalent 2/5 expressed as decimal equivalent 200/250 expressed as decimal equivalent 12.5/25 expressed as decimal equivalent 6.25/12.5 expressed as decimal equivalent
Use of decimals	Conversion of units, infusion pumps	All	Is competent in basic medicines calculations (33i)	Monitors and assesses patients/clients receiving intravenous fluids (32ii) Accurately calculates medicines frequently encountered within branch (33ii) Safely manages drug administration and monitors effects (36iii)	12.5 × 2 6.25 × 5
Système International d' Unités (S.I.) Units	Prescriptions, haematology & biochemistry blood results, patients' weight measurement & conversion	All	Is competent in basic medicines calculations (33i)	Monitors and assesses patients/clients receiving intravenous fluids (32ii) Safely manages drug administration and monitors effects (36iii) Applies knowledge of basic pharmacology, how medicines act and interact in the systems of the body, and their therapeutic action... (36ii)	Understand the magnitude difference between SI unit mass (weight) expressed in: Litres (L) Millilitres (mL) Kilograms (Kg) Grams (g) Milligrams (mg) Micrograms Nanograms Understand the difference between SI

Table 1 (continued)

Numeracy skill	Branch/field of practice most commonly using the skill	Essential skills clusters (NMC, 2010a, b)	For entry to branch/field	For entry to register	Examples of essential medication dosage & intravenous infusion calculation skills
Conversion between units	A, C, MH	Paediatric dosages, translation to imperial measures for patients/relatives e.g., birth weight	Takes and records accurate measurements of weight, height/length, body mass index, and other appropriate measures of nutritional status (28i) Is competent in basic medicines calculations (33i)	Accurately calculates medicines frequently encountered within branch (33ii) Safely manages drug administration and monitors effects (36iii)	units of mass and International Units (IU) of biological activity or effect (e.g. used in the measurement of Insulin) 1.0×1000 0.5×1000 0.25×1000 0.625×1000 $1/1000$ $500/1000$ $250/1000$ $62.5/1000$ Convert 220 pound to Kg Convert 6.6 pound to Kg 10% of 100 5% of 1000 0.5% of 1000
Understanding percentage	All	Distinguish between percentage expressions, e.g.: 5% Dextrose: grams/100 mL 98% oxygen saturation 2% management cuts	Administers medication safely under direct supervision, including orally and by injection in simulation and/or practice (38iii) Is competent in basic medicines calculations (33i)	Safely and effectively administers medicines via routes and methods commonly used within the branch and maintains accurate records (38iv)	Understand measurement unit dosing ratios, e.g., In mg/kg dosing e.g., a 10 mg/kg dose represents a ratio of 10 mg to be administered for every kg of the patient's body weight. Adrenaline (Epinephrine) 1 in 1000 = 1 mg/mL $\frac{\text{Prescribed Volume (mL)} \times \text{Drop Factor (drops per mL)}}{\text{Prescribed Duration (hours)} \times \text{Minutes per hour}}$ BSA: Square root of (height (cm) \times weight (kg)/3600)
Ratio	All	Preparation of solutions Medications dosage calculation	Is competent in basic medicines calculations (33i)	Accurately calculates medicines frequently encountered within branch (33ii) Safely manages drug administration and monitors effects (36iii)	Understand measurement unit dosing ratios, e.g., In mg/kg dosing e.g., a 10 mg/kg dose represents a ratio of 10 mg to be administered for every kg of the patient's body weight. Adrenaline (Epinephrine) 1 in 1000 = 1 mg/mL $\frac{\text{Prescribed Volume (mL)} \times \text{Drop Factor (drops per mL)}}{\text{Prescribed Duration (hours)} \times \text{Minutes per hour}}$ BSA: Square root of (height (cm) \times weight (kg)/3600)
Use of formulae	All	Dosage calculation Infusion rate calculation Body surface area (BSA) estimation BMI calculation Conversion tables (Imperial/SI units) Body mass index tables	Is competent in basic medicines calculations (33i)	Safely manages drug administration and monitors effects (36iii)	Understand measurement unit dosing ratios, e.g., In mg/kg dosing e.g., a 10 mg/kg dose represents a ratio of 10 mg to be administered for every kg of the patient's body weight. Adrenaline (Epinephrine) 1 in 1000 = 1 mg/mL $\frac{\text{Prescribed Volume (mL)} \times \text{Drop Factor (drops per mL)}}{\text{Prescribed Duration (hours)} \times \text{Minutes per hour}}$ BSA: Square root of (height (cm) \times weight (kg)/3600)
Use of tables	A, C	Conversion tables (Imperial/SI units) Body mass index tables	Takes and records accurate measurements of weight, height/length, body mass index, and other appropriate measures of nutritional status (28i) Measures and documents vital signs under supervision and responds appropriately to findings outside the normal range (9ix) Uses prescription charts correctly and maintains accurate records (38i)	Makes a comprehensive assessment of patients' clients' needs in relation to nutrition, identifying, documenting and communicating level of risk (28v)	Understanding a series of tables contained in the British National Formulary (or international equivalent) specifying important parameters such as ideal body weight and conversion of pounds and stones to Kg Understand nomogram dosing regimes
Use of charts/graphs	A, C, LD	Temperature charts, growth charts, prescription charts	Measures and documents vital signs under supervision and responds appropriately to findings outside the normal range (9ix) Uses prescription charts correctly and maintains accurate records (38i)	Measures, documents and interprets vital signs and acts appropriately on findings (9xxiii) Safely and effectively administers medicines via routes and methods commonly used within the branch and maintains accurate records (38iv)	Use of statistics such as <i>n</i> numbers: number needed to harm/treat and in understanding the frequency of the appearance of Adverse Drug Reactions
Appreciation of statistics	All	Evidence-based practice	Measures and documents vital signs under supervision and responds appropriately to findings outside the normal range (9ix) Uses prescription charts correctly and maintains accurate records (38i)	Questions, critically appraises and uses evidence to support an argument when medicines may or may not be an appropriate choice of treatment. (35iv) Orders, receives, stores and disposes of medicines safely... (37ii) Assisting clients with collecting benefits and pension if unable to do so themselves Measures, documents and interprets vital signs and acts appropriately on findings (9xxiii) Makes a comprehensive assessment of patients' clients' needs in relation to nutrition, identifying, documenting	Use of statistics such as <i>n</i> numbers: number needed to harm/treat and in understanding the frequency of the appearance of Adverse Drug Reactions
Budgeting		Stock control	Measures and documents vital signs under supervision and responds appropriately to findings outside the normal range (9ix) Uses prescription charts correctly and maintains accurate records (38i)	Orders, receives, stores and disposes of medicines safely... (37ii) Assisting clients with collecting benefits and pension if unable to do so themselves Measures, documents and interprets vital signs and acts appropriately on findings (9xxiii) Makes a comprehensive assessment of patients' clients' needs in relation to nutrition, identifying, documenting	Stock control of medicines and dressings in the clinical area
Basic bookkeeping	MH, LD	Helping clients with managing their money	Measures and documents vital signs under supervision and responds appropriately to findings outside the normal range (9ix) Uses prescription charts correctly and maintains accurate records (38i)	Orders, receives, stores and disposes of medicines safely... (37ii) Assisting clients with collecting benefits and pension if unable to do so themselves Measures, documents and interprets vital signs and acts appropriately on findings (9xxiii) Makes a comprehensive assessment of patients' clients' needs in relation to nutrition, identifying, documenting	Technical measurement of the calculated dose of medication or rate of IV infusion: Counting the number of tablets or capsules to be administered. Measuring the volume of medication
Measurement	All	Fluid balance, vital signs, preparing/drawing-up and dispensing medicines	Measures and documents vital signs under supervision and responds appropriately to findings outside the normal range (9ix) Uses prescription charts correctly and maintains accurate records (38i)	Orders, receives, stores and disposes of medicines safely... (37ii) Assisting clients with collecting benefits and pension if unable to do so themselves Measures, documents and interprets vital signs and acts appropriately on findings (9xxiii) Makes a comprehensive assessment of patients' clients' needs in relation to nutrition, identifying, documenting	Technical measurement of the calculated dose of medication or rate of IV infusion: Counting the number of tablets or capsules to be administered. Measuring the volume of medication

to be administered in milliliters in a medicine pot. Measuring the volume of medication to be administered in milliliters in a syringe & displacing all air bubbles. Setting the rate of an IV infusion of crystalloid solution via a volumetric pump (mL per hour). Setting the rate of an IV infusion of crystalloid solution via a manual flow meter (drops per minute).	and communicating level of risk (28v) Safely manages drug administration and monitors effects (36iii) Safely and effectively administers medicines via routes and methods commonly used within the branch and maintains accurate records (38iv)	Takes and records accurate measurements of weight, height/length, body mass index, and other appropriate measures of nutritional status (28i) Administers medication safely under direct supervision, including orally and by injection in simulation and/or practice (38iii) Accurately monitors and records fluid intake and output (29i)	A, C	Fluid balance, ophthalmics	Negative numbers
	Identifies signs of dehydration and acts to correct these (29v)				
	Applies knowledge of basic pharmacology, how medicines act and interact in the systems of the body, and their therapeutic action... (36ii)		A, C	Blood results	Recognition of indices

Following presentation of the taxonomy we explore the essential measurement units employed in MDC-PS; and Weeks et al. (2013a) further explore the principles of diagnostic assessment of essential calculation skills.

The symbology of healthcare numeracy

Symbols are a ubiquitous and defining feature of mathematics. The symbols we call numbers are abstract representations of something very concrete and real to humans (Bellos, 2010). One challenge that children face during the formative years of mathematical development is that the numerals we use to represent numbers bear no resemblance to the quantities they purport to represent (Liston, 1994; Weeks et al., 2000, Weeks et al. 2001; Weeks et al., 2013b). For example, the symbolic representation ‘2’ does not resonate with what we naturally associate with two as a numerical quantity (Ojose, 2008). One of the skills learned by humans in mathematical development is the graduated shift from concrete/enactive to abstract/symbolic representation of quantification (see Fig. 2), and the semantic association of abstract symbols with real concrete quantifications that are a part of everyday life (Piaget, 1983; Bruner, 1975, Bruner, 1978).

Symbols are important beyond the representation of numbers in the context of numeracy. Algebra, for example, uses symbolic representation to represent numbers or unknown quantities. In science (and everyday life) symbols representing units, universally define recognised quantities such as mass, length and time. These units and their associated symbols were derived to measure the quantities that define the world in which we live. The majority of units used globally belong to the International System of Units, universally abbreviated SI (from the French *Le Système International d’Unités*) (National Institute of Standards & Technology [NIST], 2008). The system was initially conceived in the late 18th century and was developed as an attempt to unify and rationalise systems of measurement and highlights the introduction of metrification into scientific disciplines (NIST, 2008). The SI is founded on seven SI base units for seven base quantities (See Table 2).

These seven units are the basic set of tools with which one can define any other scientific measurement. The SI units for length (m) and time (s) are base defined standards and can be used to derive units of measurement such as speed (distance (m)/time(s)) and acceleration (distance (m)/time²(s²)). Dimensional analysis using the base units gives speed a derived SI unit of ms⁻¹ and acceleration a derived SI unit of ms⁻². In healthcare practice the first three base units are important because they are used in the calculations associated with medication, mass and volume and more complex calculations involving infusion rates and syringe pump measurements and rates of administration. The SI base unit of temperature (K) is not used in healthcare practice but the degree Celsius scale (°C) is derived from and defined by the SI unit (NIST, 2008). The mole is also an important unit used in biochemistry and pharmacology and can for example be found on infusion bag labelling and is used to define molar concentration and in biochemical concepts such as osmolarity.

In addition to the symbols derived to represent the SI units, the healthcare professional will encounter the SI unit prefixes. Table 3 illustrates twenty key prefixes used by the SI. The prefixes represent decimal fractions and multiples of the SI unit (or derived unit) in question. The key units differ by a factor of 10³ (1000), e.g., a microgram (µg) is 10³ (1000) times smaller than a milligram (mg). In medication dosage calculation, conversion of SI units is necessary, for example, when medicines are prescribed in micrograms and the medication is only available as a concentration in milligrams. The knowledge that these conversions are necessary highlight that the healthcare professional needs to understand the

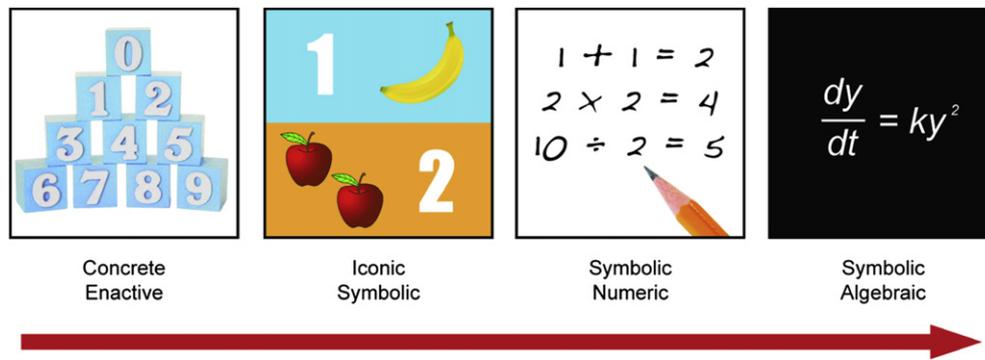


Fig. 2. Modes of representation in the construction of knowledge and quantification (Weeks et al., 2013b).

symbology of the SI unit and apply the knowledge as part of safe and effective medicines management practice.

Construction of accurate schemata for conversion between the SI units of grams, milligrams, micrograms and nanograms is critical in avoiding errors of magnitude of up to 1000 times the required dose. We illustrate in Fig. 3 a constructivist based 'slide-rule' tool designed to support nursing students' schema construction for dividing and multiplying by magnitudes of 1, 10, 100 and 1000 (see the animated process in the online paper). This construct lies in stark contrast to the commonly taught, 'rules without reason' (Mueller et al., 2010) process of 'moving the decimal point three places to the left or to the right', in the absence of additionally representing the 1000 fold magnitude shift of the numerical quantity.

Supplementary data related to this article can be found online at <http://dx.doi.org/10.1016/j.nepr.2012.10.012>.

In addition to the SI and derived SI units, the international unit (IU) is encountered in healthcare practice. The International Unit is a measurement of the amount of a substance based on its biological activity or effect. The traditional way of measuring the amount of a drug that is present in a medicinal product is by mass, e.g., mg or μg or by the amount of molecules it contains, e.g., molar solution. Many active drugs that originate from biological sources exist in a variety of forms. For example, Vitamin D is not one unitary substance; it is the name for a group of substances. The substance we know as vitamin D is made up of compounds such as ergocalciferol (Vitamin D₂), cholecalciferol (Vitamin D₃) and sitocalciferol (Vitamin D₄). The aim of having an international unit for these biological products is to be able to pharmacologically compare each form and produce a standard that produces the same biological effect. The World Health Organisation (WHO) committee on Biological Standardisation provides a reference preparation of given agents, sets the number of IUs contained in that preparation and then sets out an assay to compare other preparations to the reference preparation. Examples of this principle for Insulin and Vitamin A are illustrated in Table 4:

If a manufacturer wishes to produce an insulin preparation for use in humans or animals the potency of the insulin is not measured by the amount (mg or micrograms of insulin per mL) of

the suspension but by comparing the activity of the insulin with the biological standard in Table 4.

Figs. 4 and 5 illustrate two examples of the fundamental differences in technical measurement and administration vehicle design for medications measured by SI unit (Prednisolone) and International Unit (IU) (Insulin). Understanding the essential differences in both the characterisation and the measurement of medications expressed in these unit forms is critical to avoiding dosing errors and patient fatalities.

It is our position that the combined use of virtual representations and diagnostic assessments such as that illustrated here, integrated with practice-based learning and competence assessments provide critical steps in constructing accurate schemata for understanding and competence in solving these variant dosage problems (See Weeks et al., 2013b; Weeks et al., 2013c; Sabin et al., 2013; Macdonald et al., 2013; Weeks et al., 2013d).

In summary, it is critical to the safe administration of medicines that nursing students construct accurate schemata and competence in the conceptual, calculation and technical measurement knowledge and skills that underpin medication dosage calculation problem-solving. Having articulated a taxonomy and the principle of a point of registration benchmark for the nursing mathematics and measurement units employed in solving essential medication dosage problems, we now turn to considering the fundamental pathways taken by medicines as they pass through the human body, illustrating how important the accuracy of calculation and dosing is in safe and efficacious medicines management.

Why is getting the medication dose right so important?

In addition to defining the conceptual, calculation and technical measurement competence mathematical influences required in getting the dose right, there are other important efficacy and safety considerations to be made when administering a medication to a patient. Some of these considerations extend beyond numeracy alone and need to be considered in the broader context of medicines management (Sabin et al., 2008).

Why is getting the dose correct so important? The question posed is fairly simple and the answer seemingly obvious. The outcomes associated with mis-prescribed, mis-calculated, mis-prepared or mis-administered doses of a drug (the active therapeutic agent contained in a medication) can range from, at the extremes, complete therapeutic failure due to under-dosing to overdose and consequent toxicity and fatality. The importance of accurate dosing should be recognised at every stage of the medicine's development and management chain of events. However, derivation of the data that is used by healthcare professionals in drug dosing in clinical practice is the result of complex scientific endeavour. The 'correct dose' is the result of several scientific and

Table 2
The seven base SI units.

Base quantity	Name	Symbol
Length	Meter	m
Mass	Kilogram	Kg
Time	Second	s
Electric current	Ampere	A
Thermodynamic temperature	Kelvin	K
Amount of substance	Mole	Mol
Luminous intensity	Candela	Cd

Table 3

The prefixes for the SI base units. The most commonly used are highlighted. The typical range used in healthcare practice are additionally italicised.

Factor	Name	Symbol	Factor	Name	Symbol
10^{24}	yotta	Y	<i>10^{-1}</i>	<i>deci</i>	<i>d</i>
10^{21}	zetta	Z	<i>10^{-2}</i>	<i>centi</i>	<i>c</i>
10^{18}	exa	E	<i>10^{-3}</i>	<i>milli</i>	<i>m</i>
10^{15}	peta	P	<i>10^{-6}</i>	<i>micro</i>	μ
10^{12}	tera	T	<i>10^{-9}</i>	<i>nano</i>	<i>n</i>
10^9	giga	G	10^{-12}	pico	p
10^6	mega	M	10^{-15}	femto	f
<i>10^3</i>	<i>kilo</i>	<i>k</i>	10^{-18}	atto	a
<i>10^2</i>	<i>hecto</i>	<i>h</i>	10^{-21}	zepto	z
<i>10^1</i>	<i>deka</i>	<i>da</i>	10^{-24}	yocto	y

mathematical considerations that oblige those who prescribe, dispense and administer medications to take the utmost care when performing practice duties that relate to the safe management of medicines.

A great deal of time and effort invested by the pharmaceutical industry goes into ensuring that the dose (or dose ranges) suggested by their data is the safest and most efficacious for the range

of patients for whom it is intended (Cobert, 2012). Getting the dose right for a diverse population of patients is a phenomenally complex facet of pharmaceutical science. However, some basic principles can be considered to underpin the science and have a bearing on how nurses and educators consider developing safe medication management principles. One key premise to consider in the broader context of medicines management is that in order for a drug to achieve its desired effect, a sufficient quantity of that drug (within a safe therapeutic range) must reach the drugs' site of action (e.g., the target human cell or a bacterium). This concentration must be maintained, within certain limits, for the desired period of treatment (Simonsen et al., 2006); i.e., the important endpoint of all drug dosing is to attain the correct concentration of drug at the site(s) of action so that the desired therapeutic effect is achieved.

What influences the concentration of drug that reaches the site of action?

Many factors can influence whether a drug reaches the site of action at the correct concentration. Key fundamental factors that the patient/healthcare professional are able to influence directly include concordance, prescribing and administering the correct drug to the correct patient; avoiding prescription and administration of drugs to which the patient is allergic or sensitive; taking/administering the correct dose of the drug; taking/administering the drug via the correct route; and taking/administering the drug at the correct dosing interval. Other factors, outside the direct control of the patient/healthcare professional can also influence the final

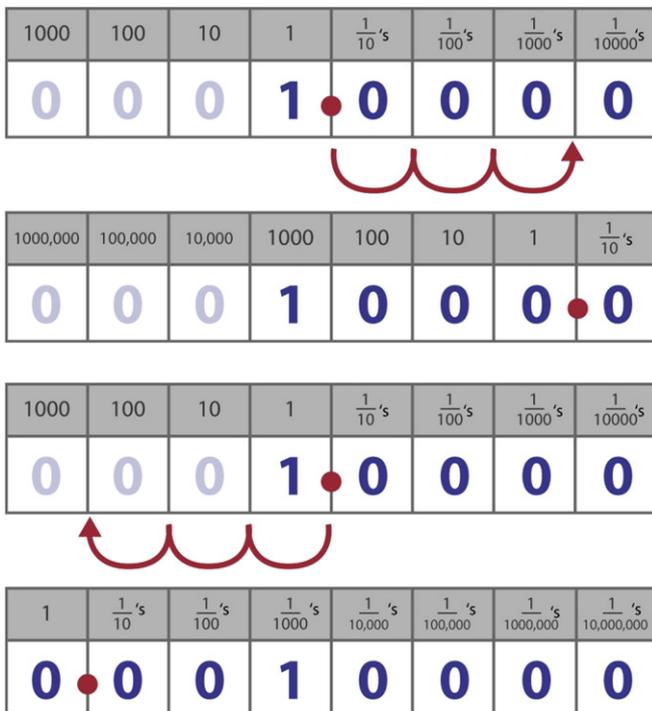


Fig. 3. A constructivist 'slide-rule' tool for supporting mathematical conversion of SI units.

Table 4
Illustrative biological units standards for medicinal products.

Substance	Biological equivalence
Insulin	1 IU is biologically equivalent to 45.5 µg of pure crystalline insulin
Vitamin A	1 IU is equivalent to the standardised biological activity of 0.3 µg of retinol or 0.6 µg of beta carotene

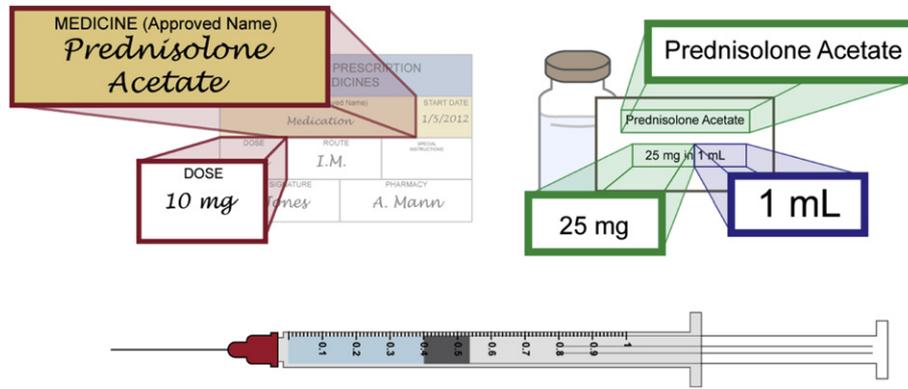


Fig. 4. Example of the conceptual, calculation and technical measurement features for a SI unit based medication dosage calculation problem (Prednisolone).

concentration at the site of action: genetics; age (especially the extremes of life); co–morbidity; concurrent illness, e.g., dehydration; and choice of pharmaceutical formulation. In order to better understand how some of these influences are exerted, clinical pharmacology should be studied and its influences on clinical practice considered. In particular an appreciation of the fundamental aspects of clinical pharmacokinetics informs the practicing healthcare professional of the science underpinning the safe and efficacious management of medicines. In this paper we focus on essential pharmacokinetic factors that the clinical nurse should consider when considering and calculating a dose of medication for administration to a patient.

Clinical pharmacokinetics

Clinical pharmacokinetics describes the influence that the human body has on drugs or foreign chemicals over a given time. The science of pharmacokinetics encompasses complex mathematical modelling of the movement of a drug through the body. When studying the subject for the first time, a more anatomical and less mathematical appreciation of pharmacokinetics can be made. The pharmacokinetics of a particular drug agent is best studied by considering four processes, known by the acronym ADME:

The four basic pharmacokinetic parameters (ADME)	
Absorption	A
Distribution	D
Metabolism	M
Excretion	E

When a healthcare professional studies the Summary of Product Characteristics (SPC) of a drug (e.g., <http://www.medicines.org.uk/emc/>) it can be seen that each SPC illustrates pharmacokinetic information using the ADME structure.

Absorption

Absorption describes the process of the drug agent moving from its site of administration into the general circulation. Key essential factors influencing absorption include:

- The rate and extent of absorption of drugs is governed by many factors including route of administration, formulation, stage of life, etc.
- Blood flow is an important factor in influencing the rate and extent of absorption of drugs.
- Dosing as per the manufacturers/prescribers instructions ensures that the plasma concentration of drugs is attained for the most efficacious result. Deviating from these instructions may have a similar effect to not getting the dose right.

The majority of drugs are administered via a licensed route to enter the general circulation and from there to their site of action. Intravenous drugs (IV) are the only group of drugs that do not undergo absorption. Drug entities must cross various barriers to get to the general circulation (Neal, 2012). Many drugs move by passive diffusion, i.e., movement from an area of high concentration to one of low concentration. Drugs administered via the oral route typically move from the small intestine, through the gut wall, through a blood vessel wall into the hepato-portal circulation, to the liver where they undergo ‘first pass effect metabolism’ and eventually

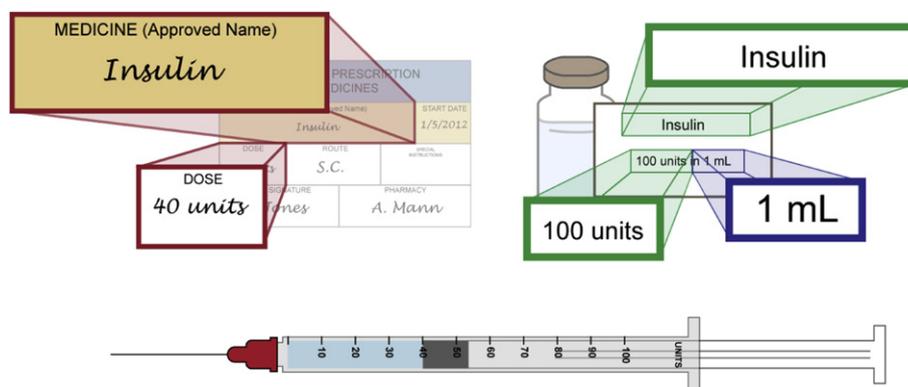


Fig. 5. Example of the conceptual, calculation and technical measurement features for an International Unit (IU) based medication dosage calculation problem (Insulin).

the systemic circulation. Some drugs utilise active transport mechanisms to reach the circulation, e.g., valaciclovir (Guo et al., 1999). Other drugs use both passive diffusion and active transport mechanisms, depending on factors such as their concentration in the gut, e.g., vitamin B₁ (Combs, 2008). Some of the factors that influence absorption from the GI tract are described in Clinical Correlation 1 (Table 5).

Distribution

Distribution of a drug around the body occurs when the drug reaches the general circulation. The drug must then enter the tissue or interstitial fluid to exert its pharmacological effect. Factors that influence drug distribution include:

- Blood flow
- Drug - plasma protein binding
- Blood brain/placental barrier
- Storage sites
- Disease states, e.g., hypoalbuminaemia

When a drug has been absorbed or introduced directly into the blood stream, it frequently needs to be transported and distributed to the site of action. The eminent pharmacologist, Paul Ehrlich coined the phrase “magic bullet” to describe the selective targeting of bacterium with antibiotics without the antibiotic affecting another organism. The majority of modern drug agents are not

Table 5
Clinical correlation 1: Factors that may influence the absorption of drugs in the gastrointestinal (GI) tract.

Factor	Explanation (examples)
Acid stability	Oral medication must be relatively acid stable to withstand the pH of the stomach. Acid labile drugs are unsuitable for oral administration (without special formulation). Example: flucloxacillin is acid stable while insulin is not; this highlights the necessity to administer medications via their prescribed/ordered route. Age: Stomach pH is less acidic in both the very young: typically premature babies to 3 year olds (due to immature parietal cells); and the elderly (due to reduced production of hydrochloric acid).
Surface area	The entire GI tract has a large surface area. Any condition that reduces the functional absorptive surface area, e.g., damage due to inflammatory bowel disease, or surgical removal of large segments of the bowel, may decrease the absorption of the drug. Age: In the elderly both the absorptive surface of the gut villi and the blood flow to the GI tract are reduced.
Gut motility	The majority of drug absorption occurs in the small intestine; any factor that speeds up or slows gut motility can influence absorption. For example, diarrhoea or the administration of the anti-emetic drug metoclopramide, which speeds up gastric emptying may influence the rate and extent of drug absorption. Age: Gastric emptying is reduced in both young children (due to irregular peristaltic movement) and the elderly (due to changes in smooth muscle tone and activity).
Lipid solubility	Lipophilic drugs will pass more easily from the gut into the cells of the gut and thence to the circulation.
Presence of Food	Food may hinder the absorption of drugs from the GI tract. For example, food will decrease the absorption of flucloxacillin from the gut and decrease its <i>bioavailability</i> (the amount of drug available to the circulation). This is the reason that flucloxacillin is administered half to 1 h before food or on an empty stomach. Calcium decreases the absorption of certain tetracyclines.
Other drugs	Antacid will increase stomach pH. This may influence the dissolution of the drug especially if it is enteric coated (EC). EC preparations are designed to dissolve further down the GI tract to avoid extensive contact with the stomach.

‘magic bullets’ and will travel indiscriminately in the circulation to their site of action and elsewhere in the body. This indiscriminate behaviour of drug agents leads to the most common adverse effects experienced by patients when using pharmacologically active agents.

Blood flow is an important factor in determining the exact distribution of a drug agent. Organs that are well perfused, e.g., the kidneys and heart will generally receive a plentiful supply of most drug agents. Tissues such as fat and bone, which are poorly perfused, will receive less of a drug in a given time and it may take a longer time period for the drug to reach an adequate concentration for therapeutic effect in those tissues.

Barriers to distribution

The human body possesses natural structures that protect vital organs from the influences of foreign chemicals. The brain, for obvious reasons, must be protected from poisons and other chemicals. The circulation of the brain possesses specific cellular formations (the blood–brain barrier) that prevent the passage of many chemicals from the general circulation to the brain (Neal, 2012). This protective mechanism is useful for survival, but a hindrance to pharmacological therapy. To exert their actions antidepressants, antipsychotics, hypnotics and centrally acting agents must pass into the central nervous system in adequate concentration. One key, common feature of these agents is that they are highly lipophilic. The placental barrier serves a similar purpose in protecting the developing foetus.

Protein binding

For drugs to cross from the circulation into organs and tissues they must be dissolved in tissue fluids or plasma. Fig. 6 provides a highly simplified illustration of how in pharmacokinetic terms, a drug, which is dissolved in plasma and is able to diffuse from the capillary into tissues where it can exert its effect on target cells is called *free drug*. Some drug agents, depending on their physico-chemical properties will bind to a greater or lesser extent to the protein components of plasma, e.g., albumin or α_1 -acid glycoprotein.

A delicate equilibrium is set up between bound and unbound drug and drug that diffuses from the circulation to the tissue and cells. The dose of drug that should be administered takes account of this binding and is part of the consideration made in getting the correct concentration. Errors in medication dosing and administration can affect this delicate balance and can result in issues such as increased prevalence of side effects and toxicity. Some of the factors that may influence the distribution of drugs are described in Clinical Correlation 2 (Table 6).

Competition at binding sites

The process of binding is usually competitive and some drugs will compete for binding sites with other drugs. If a highly protein bound drug is added to an existing therapy which includes another highly protein bound drug there will be competition for the binding to the plasma proteins. This results in changes in free drug concentration of the initial drug and may result in an increase in its actions.

Metabolism

Metabolism, in the pharmacological context, is concerned with the biochemical transformation of chemicals (including drugs) to detoxify them and hasten their excretion from the body. The fundamentals of metabolism include:

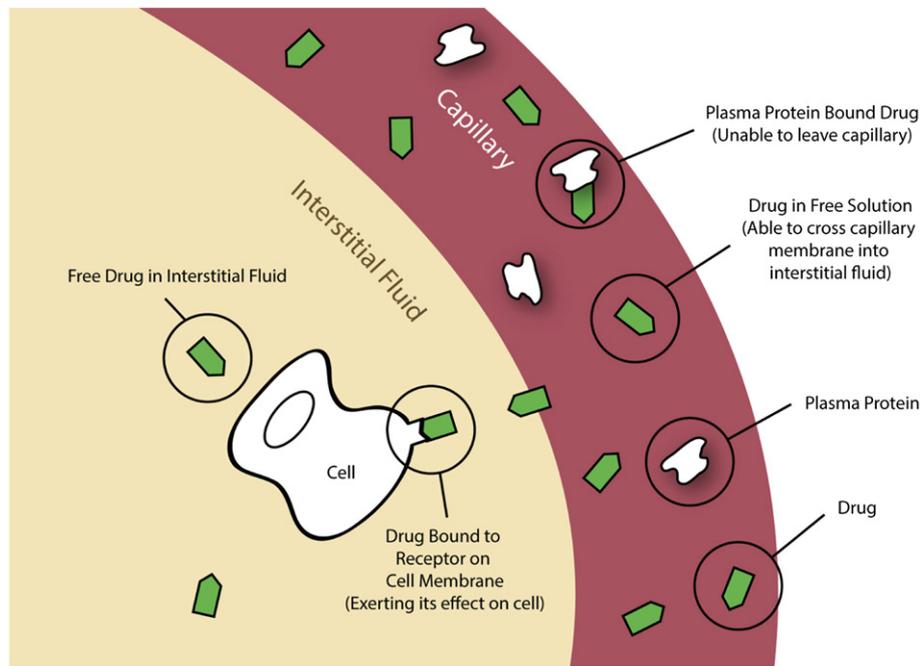


Fig. 6. Plasma binding of drugs, free drug and distribution of drugs to target cells.

- Altering the drug's chemical composition
- Removing/reducing pharmacological activity
- Generating more water-soluble metabolites (products of metabolism)
- Most metabolism occurs in the liver, catalysed by hepatic enzymes
- Other sites important in metabolic processing include the kidneys, intestinal mucosa, lungs, plasma & placenta

If the human body possessed no capacity to metabolise and excrete drug agents, a drug would never leave the body after its administration. A beta-blocker that was not metabolised or excreted would continually circulate around the body unchanged and exert its effect continuously. In health and with maturity the

Table 6

Clinical correlation 2: Factors that may influence the distribution of drugs.

Factor	Explanation (examples)
Total body water	Age: The <i>relative proportion</i> of total body water in infants is greater than in healthy young adults, however the <i>absolute volume</i> of total body water is much less and over dosage of drug will have a smaller volume of water to be distributed within than in the adult. This in part explains the critical requirement for accurate body weight dependent dosage calculation in children and ideal-body weight dependent dosage calculation in obese children. Similarly in the elderly the total body water volume is decreased as the lean body muscle mass (which stores a relatively high percentage of water) decreases and the stored fat (which is relatively anhydrous) to muscle ratio increases.
Protein binding	In disease states where there is either an increase or decrease in plasma protein, e.g., in cirrhosis of the liver (where there may be a decrease in plasma albumin production and concentration) the plasma-protein sites available for binding are reduced and there will be more 'free' unbound drug available to the body. Age: Protein binding is decreased in infants (due to reduced synthesis of protein by the <i>immature liver</i>) and in the elderly (due to decreased synthesis of protein by the <i>aging liver</i>). This in part explains the variation in dosing regimes observed in liver disease and in children.

body possesses efficient systems for biotransformation (metabolism) that serve many purposes. The most important, in the context of medicines, is to break down chemicals with the primary aim of making them less pharmacologically active, more water soluble and more easily excreted. The dose of drug administered is derived and prescribed such that the dosing and dosage interval are balanced against metabolism and excretion to maintain an appropriate plasma concentration. For example first pass metabolism in the liver or incomplete absorption can result in only a proportion of the administered drug reaching the systemic circulation: Flucloxacillin's oral bioavailability is approximately 79%. Only 395 mg of a 500 mg oral dose reaches the general circulation after oral dosing (Actavis, 2010).

Drug metabolism is divided into two phases:

Phase I

The reactions catalysed in Phase I of metabolism are simple chemical changes that are made to the drug such as oxidation, reduction and/or hydrolysis. The most common group of enzymes considered when studying Phase I metabolism are the cytochrome P450 isoenzyme family (CYP450). The primary aim of this phase is to make the drug pharmacologically inactive and more water-soluble and to prepare the metabolite for Phase II metabolism.

Phase II

If the metabolites of Phase I are not sufficiently hydrophilic then Phase II serves to conjugate (add) endogenous chemicals to the structure to enhance the drug's water solubility. Endogenous chemicals involved include glucuronates and sulphates. These more water-soluble compounds are more easily excreted.

Certain drugs only undergo Phase I metabolism; others only Phase II metabolism; and some drugs undergo very little or no metabolism. Some drugs undergo Phase II metabolism and then Phase I. Certain drugs, e.g., levodopa, are activated by the body when biotransformation takes place (Joint Formulary Committee, 2012). These drugs are known as *pro-drugs*. Certain drugs, e.g.,

Table 7
Clinical correlation 3: Factors that may influence the metabolism of drugs.

Factor	Explanation (examples)
Hepatic enzymes	Liver disease can damage and affect the capacity of the liver to synthesise hepatic enzymes and in liver disease the normal dosage range may need to be reduced. Age: Hepatic microsomal enzyme production is decreased in infants (due to reduced synthesis of enzyme by the <i>immature liver</i>) and in the elderly (due to decreased synthesis of enzyme by the <i>aging liver</i>). As the child's metabolic pathways mature and hepatic enzyme synthesis increases, the age and weight dependent medication dose will increase.

fluoxetine, are transformed into metabolites that are also active, and these metabolites are partially responsible for the therapeutic activity of the drug agent (Aurobindo, 2012).

The dosing of medication takes into account the metabolic pathways required for elimination of the agent. Accurate dosing is essential and inaccurate dosing, particularly in children and to an extent the elderly can result in significant toxicity and potential fatality. Some of the factors that may influence the metabolism of drugs are described in Clinical Correlation 3 (Table 7).

Excretion

Renal excretion is the process that eliminates most drugs and xenochemicals from the human body:

- Most drugs and metabolites are excreted by the kidneys
- In the glomerular filtrate, lipid-soluble drugs are readily reabsorbed in the renal tubules by passive diffusion
- Ionization of weak acids & bases depends on the pH of urine
- Manipulation of pH can increase renal excretion
- Declining renal function, e.g., with aging directly influences prescribing

The majority of drugs are excreted by the kidneys. The body has the capacity to excrete drugs through any path by which water leaves the body, e.g., drugs are excreted into tears, breast milk, sweat and even water vapour that is exhaled in breathing (Simonsen, 2006).

Drug agents are excreted either after undergoing metabolic processing or unchanged. To understand the process of renal excretion of drugs it is necessary to understand the physiology of the kidney and how the kidneys filter plasma. It is beyond the capacity of this paper to explore this, however, some basic principles apply.

Table 8
Clinical correlation 4: Factors that may influence the excretion of drugs.

Factor	Explanation (examples)
Renal disease or impaired renal function	Some patients' starting doses with impaired renal function may be lower and the interval between doses may differ from those in non-renal impaired patients.
Age	Glomerular filtration rate (GFR) and tubular secretion of drugs are decreased in infants and young children due to <i>immaturity</i> of the kidney. Drug dosing in children is sometimes tailored in considering the immaturity of the kidneys. The half life of a drug like Gentamicin varies from 11.5 h in small premature infants (weighing less than 1.5 kg) down to 3 h in infants greater than 6 months of age. In the case of gentamicin the half life in the six month old is comparable with that of an adult. Walker and Whittlesea, 2010. In the elderly, as GFR declines, it is often necessary to adjust (reduce) doses of drugs with narrow therapeutic indices such as digoxin and the aminoglycosides.

Very water soluble, unbound drugs will freely diffuse from the blood stream into the glomerulus of the kidney and be excreted (Neal, 2012). Drugs bound to plasma proteins will not pass from the blood stream after initial excretion. Certain drugs that have certain physico-chemical properties will be actively secreted by the kidneys. Some of the factors that may influence the excretion of drugs are described in Clinical Correlation 4 (Table 8).

Discussion & conclusion

This paper has illustrated the design of an essential skills nursing numeracy taxonomy, a consideration of the context of numeracy in nursing practice, measurement unit knowledge used in the calculation of dosage and rate computations and a brief review of the pharmacokinetic principles that illustrate the importance of accurate dosing.

This series highlights that the facilitation of teaching and learning in calculation competence requires considerations and demands from both the learner and facilitator whether the learning takes place in practice or in the classroom. The context and scientific background that underpins accurate dosing is highlighted in order that an appreciation of the complex nature of drug calculations is not underestimated by teachers and students alike.

The literature remains replete with reports of medication errors relating to a lack of calculation competence in healthcare practice. In addressing this problem we have commenced our advancement of this discipline with an approach centred on:

- a. A unified taxonomy of generic numerical competencies mapped to the 42 NMC (2010a) ESC and examples of a sub-set of embedded medication dosage calculation skills.
- b. An understanding of the measurement units used in medicines management and the critical requirement for understanding both appropriate conversion factors and appropriate use of measurement vehicles.
- c. An understanding of the basic science of pharmacokinetics and conditions when dose calculation and measurement must be altered.

In the final analysis it is our position that key to construction of MDC-PS competence is the need to dispense with reductionist approaches that focus on calculation skill development in isolation. Critical to solving this ubiquitous problem is the need to co-locate conceptual, calculation and technical measurement competence development and assessment within a competency model and education structure.

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Conflict of interest statement

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