Use of DLW to support analysis of daily energy requirements

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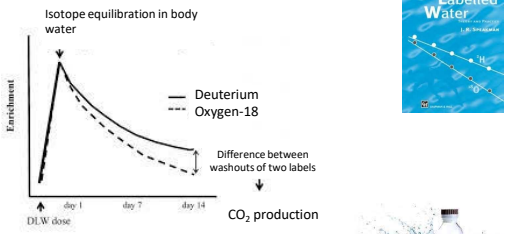
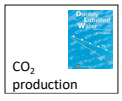
Committee to review DRIs : National Academies of the USA

Doubly-labelled water



Daily requirements for energy

Energy intake

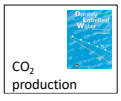


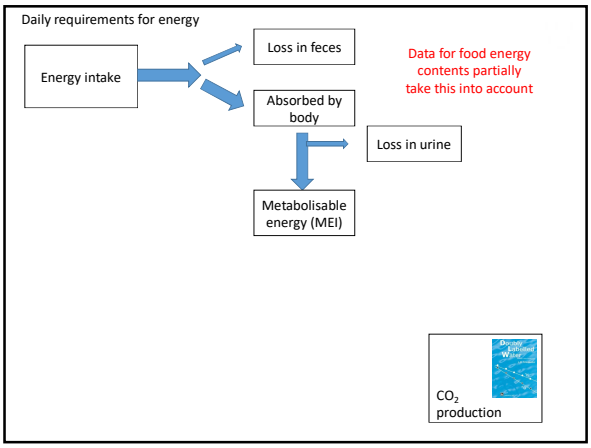
Daily requirements for energy

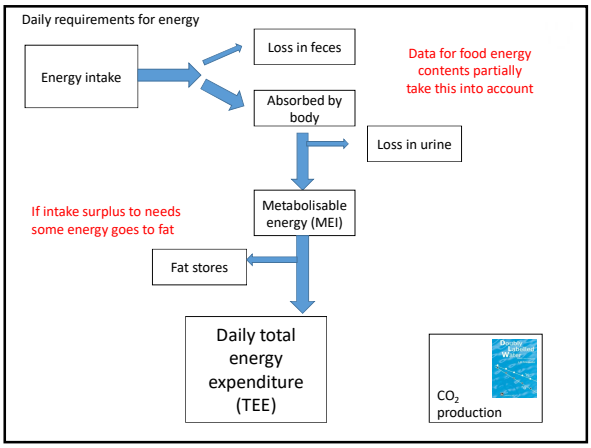
Energy intake

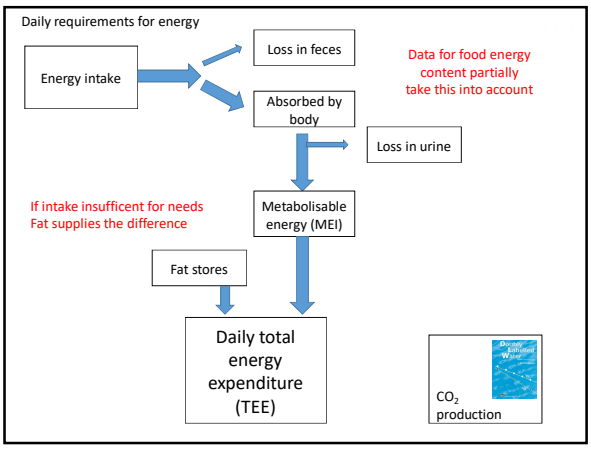
Loss in feces

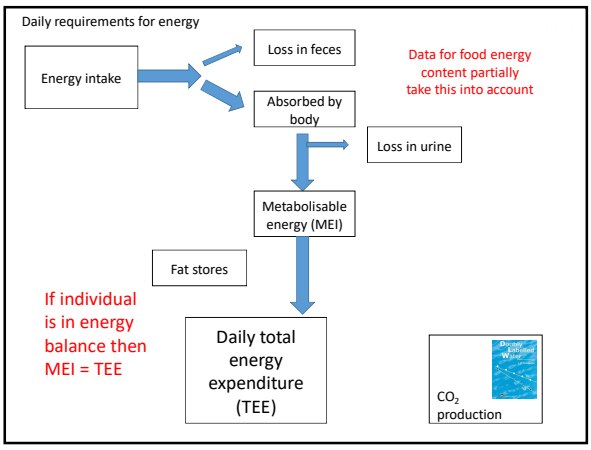
Absorbed by body



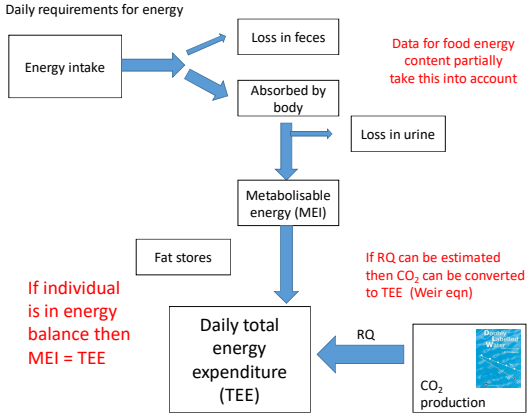

Daily requirements for energy
Energy intake
Loss in feces
Absorbed by body
Loss in urine
Metabolisable energy (MEI)
Data for food energy contents partially take this into account
CO_2 production


Daily requirements for energy
Energy intake
Loss in feces
Absorbed by body
Loss in urine
Metabolisable energy (MEI)
Fat stores
Daily total energy expenditure (TEE)
If intake surplus to needs some energy goes to fat
Data for food energy contents partially take this into account
CO_2 production

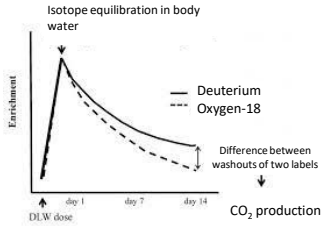

Daily requirements for energy
Energy intake
Loss in feces
Absorbed by body
Loss in urine
Metabolisable energy (MEI)
Fat stores
Daily total energy expenditure (TEE)
If intake insufficent for needs Fat supplies the difference
Data for food energy content partially take this into account
CO_2 production

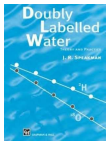

Daily requirements for energy
Energy intake
Loss in feces
Absorbed by body
Loss in urine
Metabolisable energy (MEI)
Fat stores
Daily total energy expenditure (TEE)
If individual is in energy balance then MEI = TEE
Data for food energy content partially take this into account
CO_2 production

Daily requirements for energy



Doubly-labelled water





Unfortunately its expensive to use so most studies too small to address big issues like dietary requirements for energy

DLW database was formed by some of the world leaders using this method
Aim was to pool data to get a large enough sample to answer big issues.

I played a major role in organizing compilation of this database and am the current chair of the database management committee

IAEA

www.dlwdatabase.org

Pooling data across DLW studies is not straightforward

In the 1990s there was some debate about the best equation to use
To convert mass spec isotope data into estimates of TEE
(Total energy expenditure)
Key variable in equation is the **dilution space ratio (DSR)**

Eg	DSR
Schoeller et al 1988	1.0342
Speakman et al 1993	1.0493
Racette et al 1994	1.0346

No clear consensus was reached on the best equation.
So individual labs continued to use what they thought was best

The equations differ by about 3-10% (depends on elimination ratio of the isotopes)
Many studies don't say what equation they used!

By getting the baseline data on the equation components for all individuals
We were in a position to recalculate all the estimates to a single standard equation.

Question was which one to choose??

Different approach
Use the database to redefine DSR and then derive a new equation

Speakman, J.R et al (2021)
A standard calculation methodology for human doubly labeled water studies.
Cell reports medicine **2:** 100203
DOI: 10.1016/j.xcrm.2021.100203

Average dilution space ratio for adults (1.036)
New equation

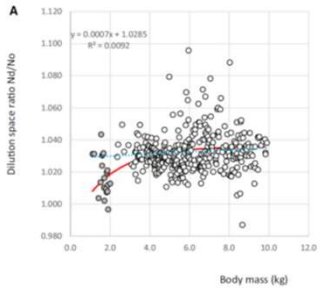
$$rCO_2 = [(N/2.078) * (1.007 * k_o - 1.043 * k_d) - (0.0246 * N * 1.05(1.007 * k_o - 1.043 * k_d))] * 22.26,$$

Went back over validation studies

N = 61 individuals

Average discrepancies	%	PRECISION
Coward and Prentice (1985)	-12.9	9.94
Schoeller et al 1988	+2.74	7.97
Speakman et al 1993	-4.72	7.51
Racette et al (1994)	+0.6	7.74
New equation	-0.4	7.67

DSR depends on age
Cant use this equation in infants



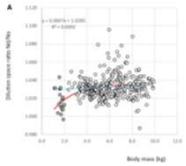
Allows derivation of more general equation

$$rCO_2 = [(N/2.078) * (1.007 * k_o - (DSR * 1.007 * k_d))] - [0.0246 * N * 1.05(1.007 * k_o - (DSR * 1.007 * k_d))] * 22.26,$$

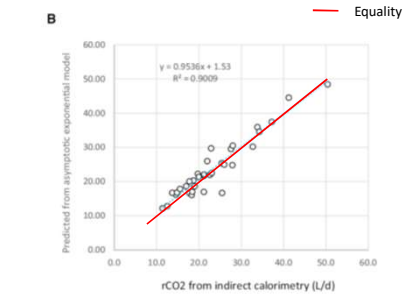
$$DSR = 1.036 - 0.05 * \exp(-0.5249 * BM),$$

Gives space for future developments
as we understand more about
factors that influence DSR

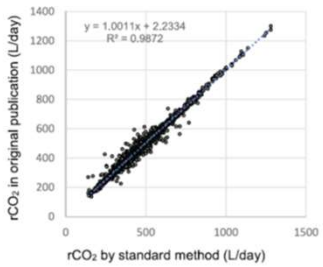
(work in progress: WW Wong)



Validation studies of babies



Recalculated all data in database with new standard
Comparison of new equation for TEE against published values



What data are in the database? (Nov 2021)

7646 measurements (v 3.4)
32 countries
128 studies

Youngest 8 days
Oldest 101 years
51% between 18 and 65

Breakdown by country (v3.6 n = 7668 Jan 2022)

Americas	USA	4741	(61.8%)
	Jamaica	72	
	Ecuador	59	
	Chile	6	
	Bolivia	46	(subsistance agriculturalists)
Europe	Sweden	106	
	Portugal	167	
	Norway	32	
	Netherlands	863	
	Greece	20	
	GB	489	
	France	10	
	Finland	66	
	Spain	31	
	Denmark	39	
	Germany	84	
	Belgium	71	
Total Europe		1978	(25.8%)
Europe + USA			(87.6%)

Breakdown by country… (continued)

Africa	South Africa	96	
	Tanzania	51	(Hunter gatherers)
	Seychelles	72	
	Rwanda	8	
	Nigeria	122	
	Mauritius	51	
	Morocco	23	
	Kenya	40	
	Ghana	69	
Total		532	(6.8%)
Asia	Thailand	42	
	Nepal	5	
	Japan	159	
	China	22	
	Australia	6	
Total		234	(3.0%)

Special groups

High activity groups

Professional athletes	40	
Not athlete unusual activity	8	
Amateur athlete	179	
Total	227	(2.9%)

Disease

D9	circulatory system	6
D6	nervous system	22
D5	mental disorder	18
D4	endocrine disorder incl. T2D	60
D17	Prader-willi	47
	Cystic fibrosis	40
D10	COPD	80
D1	infectious disease	10
Total	283	(3.0%)

Reproductive status

Females

Pre puberty	248
RANR	396
Post menopausal	1289
Pregnant	131
Lactating	20
Unknown	2619

males

RA	391
Pre-puberty	583
Post pub sub 18	15
Unknown	1875

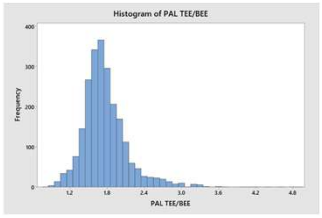
Published/unpublished status

Definitely unpublished	381	4.96%
Definitely published	**4464**	**58.2%**
Status unclear from submission	2823	36.8%

BEE data Db v3.5.4

There are 2292 BEE records alongside the TEE and so 2292 values of PAL

111 records have PAL > 2.5 (mostly athletes and/or unusual activity)
2089 are for adults
USA n = 686



Mean 1.77
Sd 0.39
Max 4.89
Min 0.73

PAL by country for adults in USA and Europe minus PAL > 2.5

Country	adults (18-65) Mean	sd	n	Elderly (65+) Mean	sd	n
USA	**1.73**	**0.30**	**268**	**1.70**	**0.26**	**418**
Belgium	1.99	0.17	19			
Germany	1.80	0.24	35			
Denmark	1.79	0.56	6	1.31	0.14	6
Finland	1.83	0.24	66			
GB	1.57	0.32	21			
Netherlands	1.75	0.22	479	1.62	0.21	82
Sweden				1.24	0.22	19
Europe	**1.76**	**0.24**	**630**	**1.53**	**0.26**	**107**

GLM	fat-free mass	F = 18.45	p = 0.0000185
	Age effect	F = 56.7	$p < 10^{-10}$
	USA/Eur	F = 17.1	$p = 6.04 \times 10^{-6}$
	Interaction	F = 33.74	$p = 1.49 \times 10^{-6}$

More detailed breakdown of total sample for USA (n = 4741)

By sex

Male = 1350 28.5%
Female = 3391 71.5%
Females over-represented

By age group

Descriptor	range (y)	Male n		Female n	
Infants	0 - 1.99	70		72	
Toddlers	2 – 4.99	98		89	
Children	5 – 12.99	95		154	
Adolescent	13 – 17.99	114		199	
Young total		377	42.3%	514	57.7%
Adult	18 – 64.99	681	29.1%	1656	70.8%
Elderly 1	65 – 74.99	123		713	
Elderly 2	75- 84.99	123		431	
Elderly 3	>85	45		75	
Elderly total		291	19.2%	1219	80.8%
Missing age data		1		2	

Male sample by Age and Ethnicity

N, % in red

Main points

1) Overall 21% have no ethnicity

2) No ethnicity % gets less with age

4) Hispanics Underrepresented Less so in young

5) African Americans overrepresented

	AA	AS	C	H	NA	O	All
Infant 0-2	0	2	19	17	25	9	72
	0	3	26	24	35	13	100
Toddler 2-5	12	1	18	9	48	1	89
	13	1	20	10	54	1	100
Child 5-12	29	14	61	19	31	0	154
	19	9	40	12	20	0	100
Adolescent 13-18	44	8	82	12	46	7	199
	22	4	41	6	23	4	100
Adult 18-65	476	31	426	7	112	8	681
	14	5	63	1	16	1	100
elderly 1 65-75	30	2	83	0	8	0	123
	24	2	67	0	7	0	100
elderly 2 75-85	53	0	50	0	20	0	123
	43	0	41	0	16	0	100
elderly 3 85+	4	0	36	0	4	1	45
	9	0	80	0	9	2	100
missing			1				1
All	245	35	698	60	283	29	1350
	18	3	52	4	**21**	2	100
Recalculated as % of known	23	4	66	5			
US census expectation	12	5	62	18			

Female sample by Age and Ethnicity

N, % in red
Main points

1) Overall 21% have no ethnicity

2) No ethnicity % gets less with age

4) Hispanics and Asian Americans Underrepresented Less so in young

5) African Americans overrepresented

	AA	AS	C	H	NA	O	All
Infant 0-2	1	1	17	16	19	16	70
	1	1	24	23	27	23	100
Toddler 2-5	25	0	14	14	45	0	98
	26	0	14	14	46	0	100
Child 5-12	19	0	22	18	36	0	95
	20	0	23	19	38	0	100
Adolescent 13-18	16	1	49	5	39	4	114
	14	1	43	4	34	4	100
Adult 18-65	476	33	844	44	229	30	1656
	29	2	51	3	14	2	100
elderly 1 65-75	112	6	509	50	33	3	713
	16	1	71	7	5	0	100
elderly 2 75-85	63	5	308	23	31	1	431
	15	1	71	5	7	0	100
elderly 3 85+	7	0	56	1	10	1	45
	9	0	75	1	13	0	100
missing	1	1					2
All	744	70	1897	175	453	52	3391
	18	3	52	4	**21**	2	100
Recalculated as % of known	25	2	65	6			
US census expectation	12	5	62	18			

Female sample By Ethnicity and BMI

ADULTS

N, % in red
Main points

UW = underweight
Norm = Normal
OW = overweight

O1,O2,O3 = Obesity classes 1-3

Miss = missing BMI

classification	UW	Norm	OW	O1	O2	O3	miss	All
BMI range	>18.5	18.5-25	25-30	30-35	35-40	>45		
AA	6	89	111	108	87	75		476
	1	19	23	23	18	16		100
AS	0	19	7	6	1	0		33
	0	58	21	18	3	0		100
C	5	336	259	114	72	57	1	843
	1	40	31	14	9	7		100
H	0	13	4	10	18	20		44
	0	30	9	23	18	20		100
NA	14	102	56	27	15	15		229
	6	45	24	12	7	7		100
O	0	14	7	0	2	7		30
	0	47	23	0	7	23		100
All	25	573	444	265	185	163	1	1655
	2	35	27	16	11	10		100

Female sample By Ethnicity and BMI

Elderly

N, % in red
Main points

UW = underweight
Norm = Normal
OW = overweight

O1,O2,O3 = Obesity classes 1-3

Miss = missing BMI

classification	UW	Norm	OW	O1	O2	O3	miss	All
BMI range	>18.5	18.5-25	25-30	30-35	35-40	>45		
AA	0	34	66	46	21	15		182
	0	19	36	25	12	8		100
AS	0	10	1	0	0	0		11
	0	91	9	0	0	0		100
C	13	337	285	155	62	18	3	870
	1	39	33	18	7	2		100
H	1	18	27	19	7	2		74
	1	24	36	26	9	3		100
NA	2	30	25	11	6	0		74
	3	41	34	15	8	0		100
O	0	1	1	2	1	0		5
	0	20	20	40	20	0		100
Elderly	16	430	405	233	97	35	3	1216
	1	35	33	19	8	3		100
Adults	25	573	444	265	185	163		1655
	2	35	27	16	11	10		100

Male sample By Ethnicity and BMI

ADULTS

N, % in red
Main points

UW = underweight
Norm = Normal
OW = overweight

O1,O2,O3 = Obesity classes 1-3

Miss = missing BMI

classification	UW	Norm	OW	O1	O2	O3	miss	All
BMI range	>18.5	18.5-25	25-30	30-35	35-40	>45		
AA	3	23	32	21	11	6	1	96
	3	24	33	22	11	6		100
AS	1	13	11	5	1	0		31
	3	42	35	16	3	0		100
C	1	117	218	59	23	8		426
	0	27	51	14	5	2		100
H	0	4	3	0	0	0		7
	0	57	43	0	0	0		100
NA	0	49	35	17	4	7		112
	0	44	31	15	4	6		100
O	0	2	5	0	0	1		8
	0	25	63	0	0	13		100
All males	5	208	304	102	39	22	1	680
	1	31	45	15	6	3		100
All females	25	573	444	265	185	163	1	1655
	2	35	27	16	11	10		100

Male sample
By Ethnicity and BMI

Elderly

N, % in red
Main points

UW = underweight
Norm = Normal
OW = overweight

O1,O2,O3 =
Obesity classes 1-3

Miss = missing BMI

classification	UW	Norm	OW	O1	O2	O3	miss	All
BMI range	>18.5	18.5-25	25-30	30-35	35-40	>45		
AA	4	27	35	18	3	0		87
	5	31	40	21	3	0		100
AS	0	0	1	1	0	0		2
	0	0	50	50	0	0		100
C	0	48	78	33	6	1	3	166
	0	29	47	20	4	1		100
H	0	0	0	0	0	0		0
	0	0	0	0	0	0		
NA	0	14	12	5	1	0		32
	0	44	38	16	3	0		100
O	0	0	1	0	0	0		1
	0	0	100	0	0	0		100
Elderly males	4	89	127	57	10	1	3	680
	1	31	44	20	3	0		100
Elderly females	16	430	405	233	97	35		1216
	1	35	33	19	8	3		100

Male and females
By Ethnicity and BMI

Both age groups

N, % in red
Main points

UW = underweight
Norm = Normal
OW = overweight

O1,O2,O3 =
Obesity classes 1-3

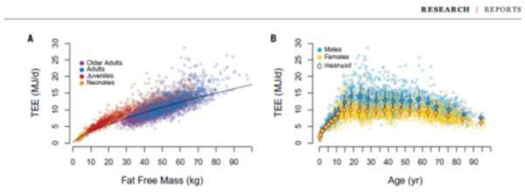
Miss = missing BMI

*Nhanes 2015-16

classification	UW	Norm	OW	O1	O2	O3	miss	All
BMI range	>18.5	18.5-25	25-30	30-35	35-40	>45		
Males	5	208	304	102	39	22	1	680
	1	31	45	15	6	3		100
Females	25	573	444	265	185	163	1	1655
	2	35	27	16	11	10		100
All adults (18-65)	30	781	748	367	224	185	2	2335
	1.4	33.4	32.0	15.7	9.6	7.9		
Elderly males	4	89	127	57	10	1	3	288
	1	31	44	20	3	0		100
Elderly females	16	430	405	233	97	35	3	1216
	1	35	33	19	8	3		100
All elderly (>65)	20	519	532	290	107	36	6	1504
	1.0	27.4	28.0	15.3	5.6	1.9		
ALL (>18)	50	1300	1280	657	331	221	8	3839
	1.3	33.9	33.3	17.1	8.6	5.7		100
				←	31.4	→		
Expectation*	1	28	31	22	10	8		100

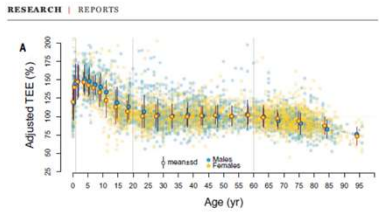
Analysis of data from existing database August 2021 Science Pontzer et al (2021)

Daily energy expenditure through the human lifecourse



Example publication ONE Science Pontzer et al (2021)

Daily energy expenditure through the human lifecourse



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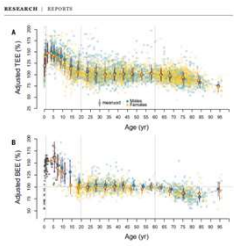
Daily energy expenditure through the human lifecourse



Key points

The life stages we thought might have changed TEE do not

Ie not puberty, not mid-life, not menopause

Expenditure almost stable between 20 and 60

Declines in older ages (>60)

On behalf of the DLW database management group

Thanks for your attention


John Speakman (chair)


Amy Luke


Herman Pontzer


Jennifer Rood


Hiroyuki Sagayama


Alexia Alford


Dale Schoeller


Klaas Westerterp


Bill Wong


Yosuke Yamada


Yaraslav Pynda

IAEA

www.dlwdatabase.org