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OBESITY AND WEIGHT CYCLING

Use SAS® Software for Epidemiological Studies

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ABSTRACT

Epidemic of obesity is a serious problem. According to CDC statistics for the United States population about 35.7% of adults and approximately 17% of children and adolescents (2-19 years old) were obese in 2009-2010. Numerous epidemiological studies demonstrated that obesity is a risk factor for multiple diseases like cancer and cardiovascular. The various weight loss and weight control programs were conducted in recent years and demonstrated effectiveness for the short period of time, yet, the majority of participants re-gained weight sooner or later. Such process of loss and re-gain weight is called weight cycling, and the prevalence of weight cyclers is growing in the United States.

The phenomenon of weight cycling is less studied. Some research for association of weight cycling and morbidity and mortality was conducted in 90th of last century and demonstrated controversial results. National Task Force on the Prevention and Treatment of Obesity summarized the forty three (43) English-language articles that evaluated the effects of weight cycling on humans or animals in studies done from 1966 through 1994. Authors concluded that most studies demonstrated the association between body weight cycling and mortality and morbidity. Nevertheless, the biggest problem to drive solid conclusion was the lack of standardized definition of weight cycling, and research slowed down in this area.

This paper provides a brief review of proposed methodological approaches for weight cycling. The most critical key elements of weight cycling like the magnitude of gain/loss, duration and the frequencies-number of cycles are suggested for unified algorithm. User-friendly SAS® V9.12 macro that is flexible in choosing parameters and transparent in each step of calculation determines weight cyclers. The author is convinced that this paper and proposed algorithm supported by SAS® macro can expedite the research of harm and/or benefit of weight cycling on the health of million people.

INTRODUCTION

Obesity was known in historical time. Obese people can be seen in ancient art works and crafts. Some portraits of obese people are dated as old as 20,000 years ago. The Hippocrates viewed obesity as special kind of inflammation.[10] Soranus of Ephesus (2nd century AD) believed that obesity was an acute and chronic disease.[9] "Extra consumption" as the cause of obesity was stated in Plutarch's, Aristotle's, Hippocrates' and Galen's manuscripts.[8,910,11] Ancient doctors believed that the best treatment for obesity was eliminating "the extras". They prescribed "Mediterranean Diet" and active lifestyle (physical exercises, walk, massages, baths and sweating, etc.) that are the basic treatments for overweight and obese in modern world.[8,9,10,11]

The ancient doctors underscored the burden of obesity. During the last half-century the researches collected and analyzed data that scientifically evidenced that overweight and obesity are risk factors for many chronic diseases including NIDDM (noninsulin-dependent diabetes mellitus), coronary heart diseases (CHD), hypertension, gallbladder disease, nonalcoholic fatty liver disease, psychosocial problems, and some types of cancer.[14] Obesity is associated with increased risk of disability, and even all-cause mortality.[14] Nevertheless, some studies demonstrated that overweight and obese individuals have better short and long-term prognosis for hypertension, heart failure, coronary heart disease, and cancer. The fact is now known as "obesity paradox". The latest meta-analysis was performed by the researchers from the Centers of Disease Control and Prevention (CDC) led by Katherine Flegal analyzed data from 97 studies involving up to 2.9 million participants and more than 270000 deaths.[3] The objective was to investigate the relationship between BMI and all-cause mortality. The data suggested that "overweight" people (BMI of 25 to 30 kg/m^2) had significantly lower death rate with hazard ratio HR=0.94 (95% CI, 0.91-0.96). People with "grade 1 obesity" (BMI from 30 to 35 kg/m^2) had a lower death rate from all causes compared to participants of "normal" BMI. However, participants with "grade 2", and "grade 3 obesity" (BMI greater than 35 kg/m^2) had a significantly greater all-cause mortality rate.[3]

In addition, some studies evidenced that weight change independent of weight status is a risk factor for multiple diseases. The association between variability in body weight and health end points was studied in Framingham Heart Study where participants were followed for 32 years (since 1948). Subjects with highly variable body weight had significantly increased total mortality, mortality from coronary heart disease, and morbidity due to coronary heart disease independent of obesity and the trend of body weight over time.[6] In the large prospective US study 55,983 men and 66,655 women were followed in the Cancer Prevention Study II Nutrition Cohort from 1992 to 2008, and association between weight cycling and death was investigated. The low numbers of cycles (1-4) was slightly protective for mortality in men and women, and high number of cycles (≥20) was not associated with all-causes of death. [7]

The results demonstrated that relationships between weight and mortality and morbidity are extremely complex. Additional research is needed to bring new insights into "weight paradox" phenomena. If being overweight might be protective for survival, then weight loss programs should have selective population. Moreover, fast and uncontrolled weight loss can induce the development of some health complications like gallbladder disease, and have negative impact on morbidity and mortality from cardiovascular diseases and cancer. The author wants to underscore the importance of studies to examine the risks and/or benefits of weight loss and weight gain in overweight and obese; and the careful weight reduction approach should be taken for overweight and obese as prevention and treatment of diseases. In addition, various weight loss programs end up with consequent weight regains. The risk and/or benefits of so-called "weight fluctuation" or "weight cycling" is least known; and the research is this area was hampered because of multiple methodological issues.

Weight cycling does not have formal definition. Researchers describe the phenomena as repeated loss and regain of body weight, and all investigators pointed out that "diet" is a cause of weight cycling. Weight cycling was also referred to as "yo-yo dieting" or "crash dieting". Weight cycling is a process of going on a diet to lose weight, going off the diet and gaining weight back again, then repeating the same over and over. Why weight cycling became the most critical in recent years? The global epidemic of obesity was formally announced in the WHO Expert Technical Report published in Geneva, 2000 under the title "WHO TRS 894 Obesity: Preventing and Managing the Global Epidemic".[2] Statistics demonstrated almost 8% increase in BMI in the US population from 1976-1980 to 1988-1994, with a similar increase from 1988-1994 to 1999-2000.[12] The enormous amount of weight loss/control programs was initiated. The results from those programs reported that majority of participants re-gained the initial weight. But the link between weight cycling and human health in short and long-term is not clear.

EPIDEMIOLOGICAL CONCERN

In 1994, National Task Force on the Prevention and Treatment of Obesity had an objective to address concerns about the effects of weight cycling on public health, and to provide guidance on the risk-to-benefit ratio of attempts at weight loss. [4] Experts used original reports from MEDLINE, and psychological abstracts searches for publication from 1966 through 1994 on topic of weight cycling, yo-yo dieting, and weight fluctuation. Forty-three English articles in humans and animals were reviewed by expects. The major concerns about weight cycling were summarized: (1) the effect on metabolism and future weight loss; (2) the effect on morbidity and mortality; and (3) the effect on psychological well-being.[4]

(1) WEIGHT CYCLING AND METABOLISM

The adverse effects of weight cycling on body composition, resting metabolic rate, body fat distribution, and even futures successful weight loss were investigated for decades. Nevertheless, some studies demonstrated the beneficial effect of body fat and adipose tissue emphasizing that stored body fat is important for survival in starvation, as well as for reproduction features. Recent studies brought attention about two types of fat: white adipose tissue (white fat), and brown adipose tissue (brown fat). In 2009, Cypress et. al. published a study about importance of brown fat in adult humans.[13] People with more brown fat are not obese, because brown fat regulates body temperature and burns extra calories to keep the body weight stable.[13] To determine if brown fat could be used to treat obesity, and how weight cycling relates to it is under recent agenda.

(2) MORBIDITY AND MORTALITY

Experts are not sure if weight cycling associates with health outcomes. Some studies suggest a link to high blood pressure, high cholesterol, gallbladder disease, and some types of cancer. Weight cycling appeared to be associated with increased risk of mortality. Yet, the mechanisms how weight fluctuation can increase morbidity and mortality has not been demonstrated. The controversial results between studies revealed the complexity and limitations of the research.

(3) PSYCHOLOGICAL WELL-BEING

Weight cycling may affect psychological well-being and self-esteem. People who went through weight loss diet and then re-gained weight feel like failure. Yet, usually people with pre-existing depressed condition related to the body weight start dieting. Unfortunately not enough research has been done in this area especially with complication to separate the psychological effects of weight cycling from pre-existing psychological factors.

The controversial results from conducted studies revealed multiple methodological problems in this research area. Intentional weight loss should be separated from non-intentional since the last one might be the consequences of hidden disease. It is not clear how much time it takes for particular disease to be developed, and where confounding with weight is under effect. But the most important limitation is lack of standardized definition of weight cycling. Conducted studies cannot be compared, nor pooled together because of differences in methodological approaches to weight cycling definition. The significance of this paper is to underscore the importance of developing the criteria how to separate weight cyclers from non-cyclers. The goal is to determine the clinically meaningful components of weight cycling that should serve as starting point towards unified definition; and develop an algorithm based on those components while accommodating the flexibility of cut-offs until further clarity in this area of research.

METHODOLOGICAL APPROACHES FOR WEIGHT CYCLING

Earlier studies measured weight cycling by various approaches including the standard deviation of weight, coefficient of variation (standard deviation divided by the mean) in body weight, regression analysis, individual variability about the slope, the number of diets combined with mean lifetime weight loss of a specified magnitude, and the number of cycles. Nevertheless, those measures couldn't reflect single large changes versus frequent small fluctuations, nor the duration or the magnitudes of variability. Cutter et. al. reviewed the various measures and demonstrated the superiority of cycles measure over the most others. [5] Authors proposed cycles measure and "runs test" as a viable definition of weight cycling and a tool for evaluation the critical amount of weight fluctuation in relationship to health risk. [5] Many researches started using this approach. Nevertheless, different algorithms defining a cycle, and variety of chosen cut offs didn't bring investigators closer to the standard definition of weight cycling. The major questions are: (1) what are the best measurements of body weight; (2) when those assessments should be taken to become relevant for health; (3) what patterns of weight change and/or fluctuation are healthier than others?

MEASUREMENTS: In Geneva, 1995, WHO Expert Committee published technical report where anthropometric indicators and indices were defined, and the principles of applied biostatistics and epidemiology were outlined for their wide use.[1] It was recommended to combine two basic measurements: weight and height into the Body Mass Index (weight/height^2), or Ponderal Index (weight/height^3) for adults.[1] Body Mass Index (BMI) that also known as Quetelet's Index is the weight in kilograms divided by the square of the height in meters (kg/m^2) became a common index of weight-for-height classification in adults. Change in BMI or percent change BMI from baseline became another popular measure in many studies.
Even if the amount of extra fat is the same among some individuals, there might be substantial difference how extra fat is distributed in the bodies. Differences in distributions effect the risk associated with obesity and even predict what kind of obesity-related disease is highly probable. Therefore, waist circumference was proposed to be considered as another simple measure. In the United States the following cut offs are commonly used to be considered at risk of obesity-related disease: >35 inches for women, and >40 inches for men. Yet, the global grading system on waist circumference has not been developed.
Body composition (underwater measuring), anatomical distribution of fat (magnetic resonance imaging), energy intake (prospective dietary record), and energy expenditure (doubly labeled water) are other choices for measuring status of obesity that were proposed.[2] But high cost and difficulties of measuring any of them (comparing to BMI) limited their applications.

TIME: How often assessments should be performed: daily, monthly, semi-annually, annually, etc.? The measurements should correlate with biological effect of weight fluctuation.

PATTERNS: The weight patterns of change and fluctuation include the following components: 1) direction: loss or gain (down-up or up-down for cycling); 2) magnitude; 3) duration of time (or span of fluctuation); 4) number of cycles where each cycle is characterized by 1)-2)-3). Moreover, all these components should have meaningful clinical interpretations. For example, most people that started dieting fluctuate in weight, but what magnitude of fluctuation is clinically helpful or damaging: 10 pounds or 20 pounds? Moreover, lose and gain of 10 lb during 6 months might have different health impact comparing the same loss during three years.

Summarizing, it became clear that definition of weight changes and weight cycling should be clinically relevant measurements. Embracing the approach to define weight cycling by decomposing it into important multiple parameters, the next question will be to establish the clinical relevance of the components that will define the weight cyclers.

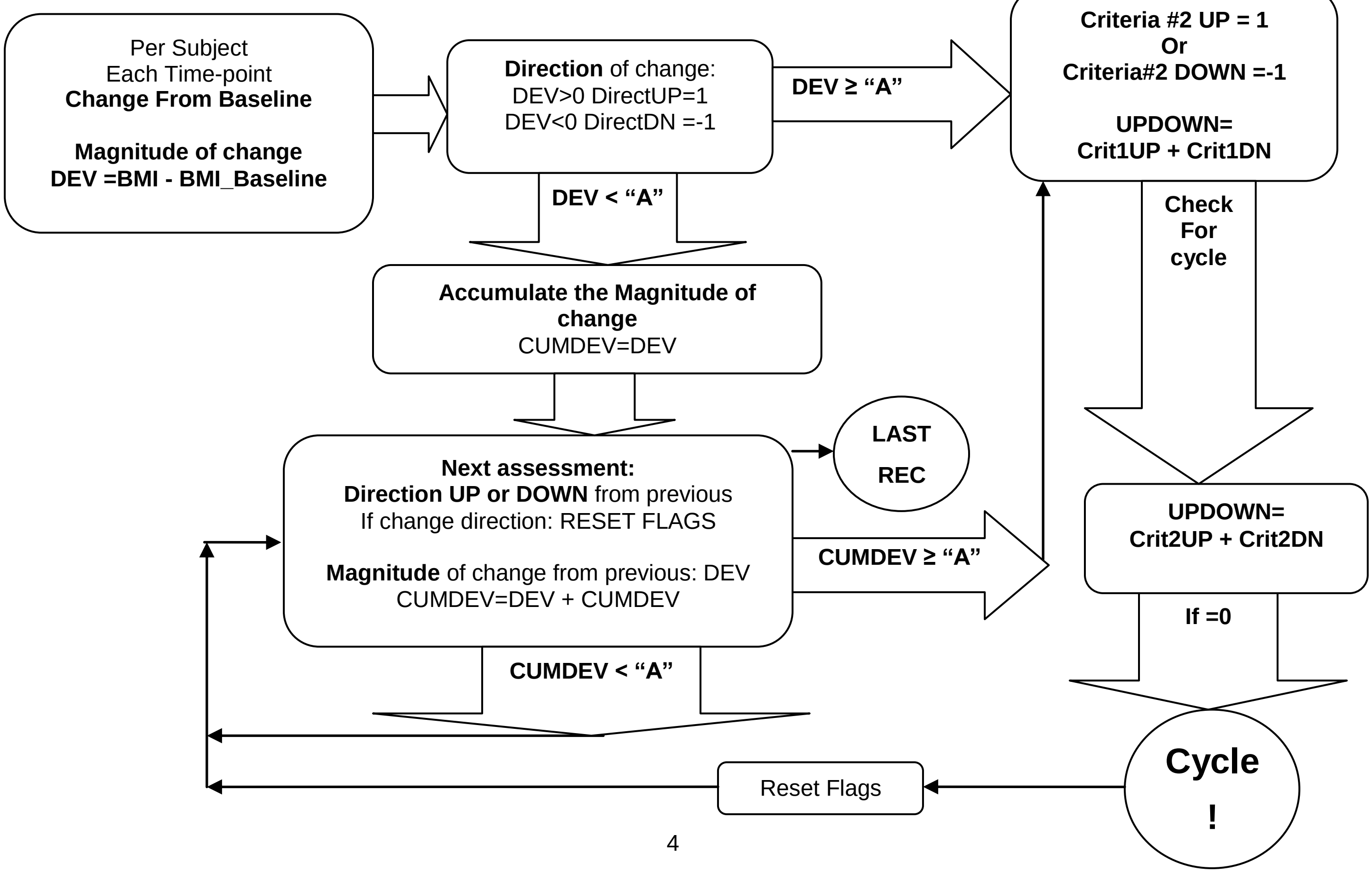
WEIGHT CHANGE CATEGORIES

Author suggests defining four groups for weight change: (1) stable weight; (2) weight gain; (3) weight loss; and (4) weight cycling. For example, if the baseline of weight assessment is 25 years old, then stable weight can be defined as the same weight at endpoint within (±) "A" units of measurement without the presence of weight cycling between the baseline and end point. Weight gain is the increase from baseline to end point for at least "A" units without presence of weight cycling. Weight loss is categorized as decrease from baseline to end point for at least "A" units without presence of weight cycling. If there is at least one cycle between the baseline and end point, than subject experienced weight cycling. The definition of four categories of weight change was summarized in Table 1: Definition OF Weight Change Categories.

Table 1: Definition OF Weight Change Categories

Categories	Criteria #1	Criteria #2
Stable Weight	Difference between end point and baseline within "A" units	No Cycles
Weight Gain	Increase from baseline to end point is ≥ "A" units	No Cycles
Weight Cycling	Capture Components for cycling *: Direction of each Cycle ("up-down" or "down-up" Duration of each Cycle Magnitude of each Cycle Number of Cycles	At least One Cycle: Weight loss is equal to or more than "A" units with gaining the same (or more) units (for example, BMI). Weight gain is equal to or more than "A" units with losing the same (or more) units (for example, BMI).
Weight Loss	Decrease from baseline to end point is ≥ "A" units	No cycles
Description of each cycle should be captured		

WEIGHT CYCLING ALGORITHM



MACRO WC (EXAMPLE FOR BMI)

```
%MACRO WC(sds= , delta= , num= );

* criteria #1 for delta unit BMI ****;
PROC SORT DATA=&sds; BY usubjid age; RUN;
DATA testcat1_&num;
 SET &sds;
 BY usubjid age;
 delta= &delta ;
   IF LAST.usubjid THEN DO;
         lastrec=1;
         bmi_last_first= bmi - bmi_first;
            IF bmi_last_first >= delta THEN crit1=2;                * gain ***;
               ELSE IF bmi_last_first <= delta*(-1) THEN crit1=3;    * loss ***;
                  ELSE IF abs(bmi_last_first) < delta THEN crit1=1;   * stable *;
      END;
RUN;

DATA testcat2_&num;
  SET testcat1_&num;
  BY usubjid age;
  RETAIN   devav oldbmi crit2up crit2dn cycle
              cumdevup cumdevdn directup directdn .;
*initialize all flags and find change in BMI from baseline ************;
IF first.haneseq THEN DO;
      dev=0;  cumdevup=0; cumdevdn=0;
      crit2up=.;  crit2dn=.; cycle=0 ; oldbmi=bmi;
      directup=.; directdn=.;
   END;
   ELSE DO; dev=bmi - oldbmi; oldbmi=bmi; END;
*define delta and flags for up-down ************;
IF dev >0 THEN DO; directup=1;
                   IF directdn=-1 THEN DO;    cumdevup=0; directdn=.;
                                                 IF crit2dn=. THEN cumdevdn= .;
                                          END;
                   cumdevup= cumdevup + dev;
                   IF abs(cumdevup) >delta THEN crit2up  =  1;
                END;
IF dev <0 THEN DO; directdn=-1;
                     IF directup= 1 THEN DO; cumdevdn=0; directup=.;
                                                IF crit2up=. THEN cumdevup=.;
                                          END;
                   cumdevdn= cumdevdn + dev;
                     IF abs(cumdevdn) >delta THEN crit2dn  = -1;
                END;
*check for cycle by adding flags for up-down ************;
updown=crit2up + crit2dn ; deltaupdn =abs(cumdevup + cumdevdn);

IF updown=0 THEN DO; *up-down are in selected magnitude (=delta) is CYCLE!***;
                   cycle=cycle +1;
                   IF dev>0 THEN DO; cumdevdn=0; crit2dn= .;  END;
                      IF dev<0 THEN DO; cumdevup=0; crit2up= .;  END;
                   END;
IF last.usubjid THEN DO; IF (cycle >= 1) THEN wcgroup=4;
                            ELSE IF crit1=1 THEN wcgroup=1;
                                  ELSE IF crit1=2 THEN wcgroup=2;
                                     ELSE IF crit1=3 THEN wcgroup=3;
                      END;
LABEL wcgroup="Weight Change Category";
RUN;
%MEND WC;
```

```
** call the Macro for cut off "A"=3 ***;
%WC(sds=myds , delta=3 , num= 1);

** call the Macro for cut off "A"=4 ***;
%WC(sds=myds , delta=4 , num= 2);

** call the Macro for cut off "A"=5 ***;
%WC(sds=myds , delta=5 , num= 3);
```

EXAMPLE

DATA SETS FOR PROPOSED EXAMPLE:

The NHANES I Epidemiologic Follow-up Study (NHEFS) is a national longitudinal study that was jointly initiated by the National Center for Health Statistics and the National Institute on Aging in collaboration with other agencies of the Public Health Service (see http://www.cdc.gov/ nchs/nhanes/nhefs/ nhefspuf.htm). The NHEFS was designed to investigate the relationships between clinical, nutritional, and behavioral factors assessed in the first National Health and Nutrition Examination Survey (NHANES I) and subsequent morbidity, mortality, and hospital utilization, as well as changes in risk factors, functional limitation, and institutionalization. Currently the data sets cover approximately a 20-year interval from the first baseline evaluation to 1992. These subjects were followed-up in 1982, 1986, 1987, and 1992.

ASSESSMENTS OF WEIGHT:

Height and weight was measured in the very first examination in NHANES I, and two weight measurements were performed in one follow-up exam in1982. For all subsequent interviews subject was asked two questions: how much he/she weights now, and how current weight compares to 6 (in 1982, and 1986 interviews) or 12 (in 1987, and 1992 interviews) months ago. Questions about weight 6 or 12 months ago were categories as: the same, at least 10 pounds more, and at least 10 pounds less. Based on the answers, the weight at each time was calculated. Moreover, the recall of weight at 25, 40 and 65 years of age was asked if appropriate, and recorded.

For 1982 weight assessments, the exam weight measurements were taken. For 10267 subjects, only 323 were missing weight examination. They will be substituted by the survey questionnaire data.

All together, 12 assessments of weight were used for this study as presented in the table below. For this example, only subjects with weight assessment at 25 years of age, and having at least three weight assessments were included.

TIME OF ASSESSMENTS:

Age 25	**Age 40**	**Age 65**	**Exam 1971-74**	**Exam/Interview 1982-84 -6months**	**Exam/ Interview 1982-84**	**Interview 1986-6months**	**Interview 1986**	**Interview 1987-12months**	**Interview 1987**	**Interview 1992-12months**	**Interview 1992**
X	X	X	X	X	X	X	X	X	X	X	X

All assessments were ordered chronologically by subject's age, and participated in further calculations of BMI (by dividing a person's weight in kilograms by his or her height in meters squared), change of BMI from baseline, and weight status at baseline: 1=underweight (<18.5), 2=normal (18.5-24.9), 3=overweight (25-29.9), and 4=obese (≥30). Cancer is a health outcome for this example. The age of subject at first cancer diagnosis was calculated using the year of first cancer diagnosis from database. For this example, all weight assessments <u>right after</u> the cancer diagnosis were deleted (for example, a few records for subject 1099 that marked as grey in the MYDS data set presentation); and subjects with at least three assessments of weight were selected. The final total number of subjects for this example was 948, and the number of records 5873.

THE DATA SET (MYDS):

Unique Subject Identifier	Weight Status at Baseline	Number Time Points	Order	Age	Bmi	Bmi Baseline	Bmi Change Fr BL	Cancer Type	Age Cancer
1099	2	6	age1	25.0	22.1496	22.1496	0.0000	174	59
1099	2	6	age2	40.0	22.1496	22.1496	0.0000	174	59
1099	2	6	age3	48.0	27.0542	22.1496	4.9046	174	59
1099	2	6	age4	**65.0**	30.0602	22.1496	7.9106	174	**59**
1099	2	6	age7	**68.0**	29.7438	22.1496	7.5941	174	**59**
1099	2	6	age8	**69.0**	29.7438	22.1496	7.5941	174	**59**
2262	4	5	age1	25.0	38.4800	38.4800	0.0000	151	77
2262	4	5	age3	57.0	39.1672	38.4800	0.6871	151	77
2262	4	5	age8	70.0	34.8153	38.4800	-3.6648	151	77
2262	4	5	age11	75.0	26.2031	38.4800	-12.2770	151	77
2262	4	5	age12	76.0	28.0355	38.4800	-10.4446	151	77
…..									

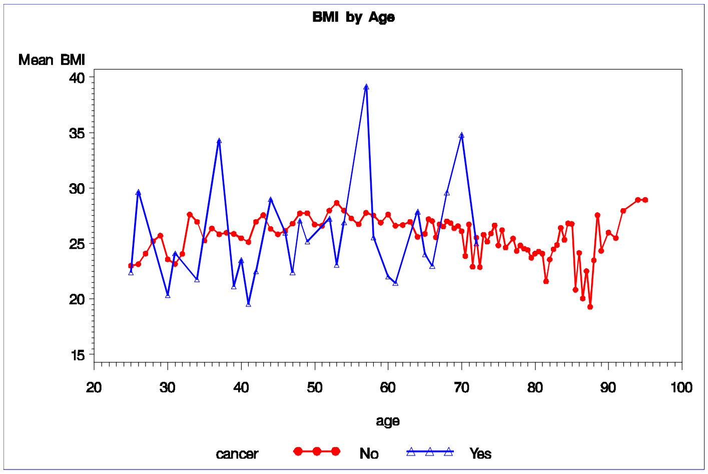
Define.doc (MYDS.sas7bdat)

Variable	Label	Type	Code	Comments
USUBJID	**Unique Subject Identifier**	Char		Subject Number
OBESE	**Weight Status at Baseline**	Num	1="Underweight <18.5" 2="Normal 18.5-24.9" 3="Overweight 25-29.9" 4="Obese ≥30";	Weight Status at Baseline
TIME	**Number of Time Points**	Num		Number of BMI assessments that contributed to the particular subject
ORDER	**Order:** chronological order of age	Char		Chronological order of AGE where BMI assessments were present for selected population
AGE	**AGE**	Num		Subject's age at particular BMI assessment
BMI	**BMI** at each time point	Num		BMI calculated as weight/height^2
BMI_FIRST	**BMI at baseline**	Num		BMI calculated as weight/height^2 at AGE=25 y.o.
BMI_LAST_FIRST	**Change in BMI**	Num	BMI_LAST_FIRST= BMI-BMI_FIRST	Change in BMI from baseline
CANCERTYPE	**Cancer Type**	Num		Cancer type ICD-9-CM Cancer Code
AGE_CANCER	**Age Cancer**	Num		Subject's age once cancer was diagnosed

The mean BMI values across age for project population presented in Figure 1. It summarized the mean BMI at every age point for two groups: cancer-free (dot-line), and cancer-subjects (triangle-line), where weight assessments only before cancer diagnosis were taken.

It is noticeable from the figure that higher variability in BMI was present in triangle line (cancer subjects). As the next step, the weight categories as (1) stable, (2) weight gain, (3) weight loss, and (4) weight cycling were calculated using the presented MACRO WC (example for BMI).

Figure 1: Average BMI by Age for Cancer and Cancer-free subjects



CALCULATION OF WEIGHT CHANGE CATEGORY (TESTCAT2 DATA SET):

Subject #	Num	Age	Age cancer	Bmi	Dev	Direct up	Direct Dn	crit2up	crit2dn	Cum devup	Cum devdn	Delta updn	Up down	Cycle Crit2	Crit1	Weight Change Group
201	1	25		24.8903	0.0000	.	.	.	.	0.0000	0.0000	0.0000		0		
201	2	27		32.8100	7.9197	1	.	1	.	7.9197	0.0000	7.9197		0		
201	3	40		34.8116	2.0017	1	.	1	.	9.9213	0.0000	9.9213		0		
201	4	42		59.1798	24.3682	1	.	1	.	34.2895	0.0000	34.2895		0		
201	5	43		57.4392	-1.7406	.	-1	1	.	34.2895	-1.7406			0		
201	6	47		46.9957	-10.4435	.	-1	.	-1	0.0000	-12.1841	**22.1054**	0	1		
201	7	48		46.9957	0.0000	.	-1	.	-1	0.0000	-12.1841	12.1841		**1**	**2**	**4**
550	1	25		25.0454	0.0000	.	.	.	.	0.0000	0.0000	0.0000		0		
550	2	67		25.1349	0.0894	1	.	.	.	0.0894	0.0000	0.0894		0		
550	3	81		26.8344	1.6995	1	.	.	.	1.7890	0.0000	1.7890		0		
550	4	82		26.8344	0.0000	1	.	.	.	1.7890	0.0000	1.7890		0		
550	5	83		26.8344	0.0000	1	.	.	.	1.7890	0.0000	1.7890		0		
550	6	87		26.2977	-0.5367	.	-1	.	.	0.0000	-0.5367	0.5367		0		
550	7	88		26.2977	0.0000	.	-1	.	.	0.0000	-0.5367	0.5367		**0**	**1**	**1**
963	1	25		23.8104	0.0000	.	.	.	.	0.0000	0.0000	0.0000		0		
963	2	40		25.4103	1.5999	1	.	.	.	1.5999	0.0000	1.5999		0		
963	3	41		22.5869	-2.8234	.	-1	.	.	0.0000	-2.8234	2.8234		0		
963	4	42		22.5869	0.0000	.	-1	.	.	0.0000	-2.8234	2.8234		0		
963	5	45		27.2925	4.7056	1	.	1	.	4.7056	0.0000	4.7056		0		
963	6	46		27.2925	0.0000	1	.	1	.	4.7056	0.0000	4.7056		**0**	**2**	**2**
2262	1	25	77	38.4800	0.0000	.	.	.	.	0.0000	0.0000	0.0000		0		
2262	2	57	77	39.1672	0.6871	1	.	.	.	0.6871	0.0000	0.6871		0		
2262	3	70	77	34.8153	-4.3519	.	-1	.	-1	0.0000	-4.3519	4.3519		**0**	**3**	**3**

Subject #	Num	Age	Age cancer	Bmi	Dev	Direct up	Direct Dn	crit2up	crit2dn	Cum devup	Cum devdn	Delta updn	Up down	Cycle Crit2	Crit1	Weight Change Group
9743	1	25	87	25.9603	0.0000	.	.	.	.	0.0000	0.0000	0.0000		0		
9743	2	40	87	23.7029	-2.2574	.	-1	.	.	0.0000	-2.2574	2.2574		0		
9743	3	65	87	27.0890	3.3861	1	.	1	.	3.3861	0.0000	3.3861		0		
9743	4	72	87	25.0009	-2.0881	.	-1	1	.	0.0000	-2.0881	2.0881		**0**	**1**	**1**
10083	1	25	73	19.5822	0.0000	.	.	.	.	0.0000	0.0000	0.0000		0		
10083	2	40	73	22.2151	2.6329	1	.	.	.	2.6329	0.0000	2.6329		0		
10083	3	54	73	26.9050	4.6899	1	.	1	.	7.3228	0.0000	7.3228		0		
10083	4	65	73	25.5063	-1.3987	.	-1	1	.	0.0000	-1.3987	1.3987		0		
10083	5	68	73	29.6202	4.1139	1	.	1	.	4.1139	0.0000	4.1139		**0**	**2**	**2**
13683	1	25		31.5096	0.0000	.	.	.	.	0.0000	0.0000	0.0000		0		
13683	2	40		27.8026	-3.7070	.	-1	.	-1	0.0000	-3.7070	3.7070		0		
13683	3	66		30.3048	2.5022	1	.	.	-1	2.5022	0.0000	2.5022		0		
13683	4	78		27.8026	-2.5022	.	-1	.	-1	0.0000	-2.5022	2.5022		0		
13683	5	79		27.9879	0.1854	1	.	.	-1	0.1854	0.0000	0.1854		0		
13683	6	80		27.9879	0.0000	1	.	.	-1	0.1854	0.0000	0.1854		0		
13683	7	84		22.0567	-5.9312	.	-1	.	-1	0.0000	-5.9312	5.9312		0		
13683	8	85		23.9102	1.8535	1	.	.	-1	1.8535	0.0000	1.8535		**0**	**3**	**3**
18338	1	25	70	15.7951	0.0000	.	.	.	.	0.0000	0.0000	0.0000		0		
18338	2	40	70	20.4407	4.6456	1	.	1	.	4.6456	0.0000	4.6456		0		
18338	3	58	70	25.3186	4.8779	1	.	1	.	9.5235	0.0000	9.5235		0		
18338	4	65	70	21.3699	-3.9488	.	-1	.	-1	9.5235	-3.9488	5.5747	0	**1**	**2**	**4**

Define.doc (TESTCAT2.sas7bdat)

Variable	Label	Type	Code	Comments
USUBJID	**Subject #**	Char		Unique Subject Identifier
NUM	**Number of assessments**	Num		Number of BMI assessments participated in this example
AGE	**AGE**	Num		Subject's age at particular BMI assessment
AGE_CANCER	**Age Cancer**	Num		Subject's age once cancer was diagnosed
BMI	**BMI** at each time point	Num		BMI calculated as weight/height^2
DEV	**Change BMI from previous time point**	Num	DEV=BMI-BMIOLD (previous record)	BMI change from previous time point
DIRECTUP	**Direction UP for BMI change** from previous assessment (=1 if "yes")	Num	If DEV >0 then DIRECTUP=1	Direction UP of BMI change from previous time point (=1 if "yes")
DIRECTDN	**Direction DOWN for BMI change BMI** from previous assessment (=-1 if "yes")	Num	If DEV < 0 then DIRECTDN=-1	Direction DOWN of BMI change from previous time point (=-1 if "yes")
CRIT2up	**Criteria #2 UP**	Num		Flag if magnitude of UP reached or above the cut off "A"

Variable	Label	Type	Code	Comments
CRIT2dn	**Criteria #2 Down**	Num		Flag if magnitude of DOWN reached or above the cut off “A”
CUMDEVUP	**Cumulative Magnitude for UP direction**	Num		Cumulative Magnitude for the same UP direction of BMI change
CUMDEVDN	**Cumulative Magnitude for DOWN direction**	Num		Cumulative Magnitude for the same DOWN direction of BMI change
DELTAUPDN	**Magnitude of Cycle**	Num		Magnitude of cycle
UPDOWN	**Flag when Direction Change Sign**	Num	Updown=crit2up+crit2dn	Direction Changed for UP-DOWN of magnitudes ≥ “A” (that might mean CYCLE)
CYCLE	**Number of Cycles**		If updown=0 then cycle=1	Number of cycles for specified cut off “A”
CRIT1	**Criteria #1 for weight groups**	Num		Criteria #1 to define weight change groups
WCGROUP	**Weight Change Group**	Num	1="Stable" 2="Weight Gain" 3="Weight Loss" 4="Weight Cycling";	Weight Change Groups defined for pre-specified level “A”
Direction, Cumulative Magnitude, Duration of each Cycle, and the Number of Cycles are calculated. Weight Change Groups are assigned based on criteria #1 and 2 from Table 1: Definition OF Weight Change Categories.				

The descriptive statistics for this example presented the number of Cancer Cases by Weight Change Groups (Table 2: Cancer Cases by Weight Change Categories.

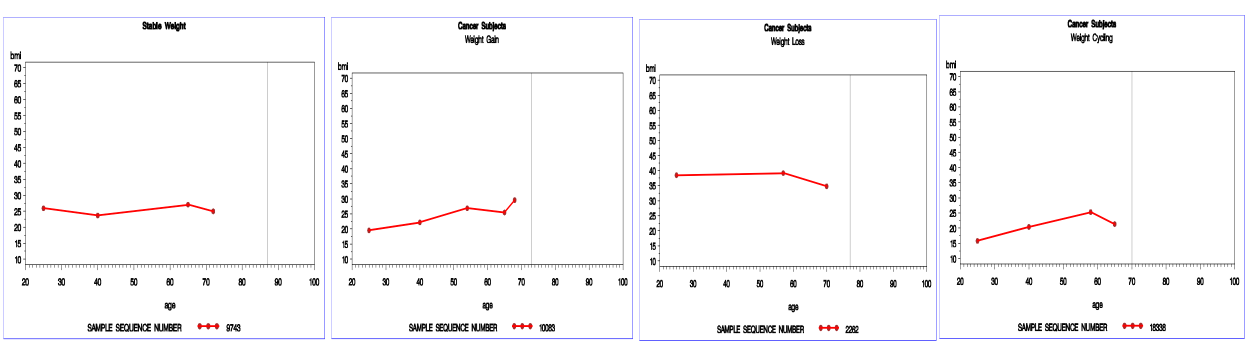
Table 2: Cancer Cases by Weight Change Categories

Weight Change Category	**Cancer**		
	No	**Yes**	**Total**
Stable	312 (95.41%)	15 (4.59%)	**327**
Weight Gain	364 (97.59%)	9 (2.41%)	**373**
Weight Loss	25 (96.15%)	1 (3.85%)	**26**
Weight Cycling	221 (99.55%)	1 (0.45%)	**222**
Total	922 (97.26%)	26 (2.74%)	**948 (100%)**

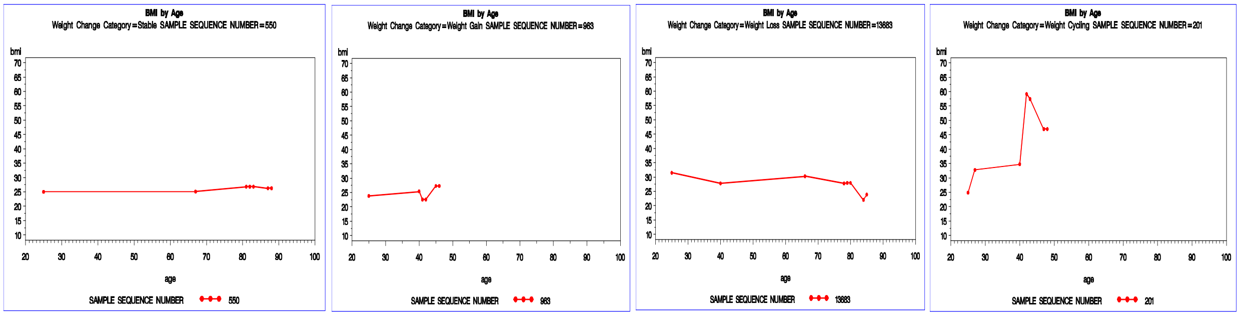
Randomly selected graphs for cancer and cancer-free subjects in each weight change group (for cut off “A” delta=3) are presented in Figure 2: Plots of Individual Subjects where solid vertical line is the age at cancer diagnosis.

Figure 2: Plots of Individual Subjects

Cancer Subjects (vertical line presents the age of first cancer diagnosis):



Cancer-Free Subjects:



DISCUSSION AND NEXT STEPS

Presented example used BMI as measurement of short and long-term weight changes. Nevertheless, the other measurements like weight circumference can be employed in the algorithm and the developed macro.

The example demonstrated how to calculate weight change relevant parameters: direction, duration, magnitude, and frequency, and link them to particular health outcome (cancer). For each cancer subject weight assessments right before the first cancer diagnosis were utilized in this example. Nevertheless, it might have taken up to 10 years for cancer development. This limitation should not be overlooked, and proper lag in time should be considered for development of health outcome under research.

The presented example used NHANES database where subjects were followed-up (from 1971) in 1982, 1986, 1987, and 1992 years. While planning the study, it should be taken in consideration what particular TIME POINTS are clinically relevant for weight assessments for investigated health outcome.

Having weight change and weight cycling components linked to health outcome of interest, the next step will be to demonstrate the clinical meaningfulness of parameters and chosen cut offs.

CONCLUSION

The definition of four weight change groups was presented in this paper. The step-by-step algorithm how assign subjects to weight change categories was outlined, and SAS® Macro was proposed with the flexibility of cut offs. Author wants to underscore that the most critical was the category of “weight cyclers”. Because there is no standardized definition of weight cycling endorsed, the best approach suggested was the algorithm to assign the status of “weight cycler” based on multiple clinically important components with a flexibility of cut offs. Suggested algorithm should expedite the further research with concurrent goal of clarification clinically relevant components and their thresholds. The example with cancer as health end point was presented using NHANES database. It demonstrated the feasibility of research, and highlighted the next steps. In time of obesity pandemic, the urgency of studies to examine the risks and/or benefits of weight changes on health outcomes is out of question. The knowledge from advanced research will serve as the basis for prevention and treatment of multiple obesity-related diseases. It will refine the weight control/loss programs, and help to maintain the healthiest weight.

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