Possible Hormetic Relationship Between Age And Death Rates In Early Years Of Life

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Abstract

A hormetic dose-response relationship is nonlinear where adverse responses typically occur in the lowest and highest dose ranges, while optimum responses occur between these extremes. Typically, dose variables in this context are substances such as vitamins, or stressors such as radiation or exercise. Age is theorized in this study to also be a "dose" variable, having a possible hormetic effect on death rates early in life. The study compared consecutive yearly ages up to age 84 (the "dose" variable) to all-cause crude death rates (response variable). At the youngest age (lowest "dose"), < 1 years old, the death rate was relatively high, followed by a decreased death rate for each passing year to around age seven. Beginning around age 10, death rates tended to increase with each passing year through the remainder of years, as expected. Thus, age and death rates show a dose-response relationship that appears hormetic in the early years of life (e.g., age 0 to 7). Implications of the study may pertain to investigating possible mechanisms for this relationship and understanding of the relationship may lead to innovative health care interventions that could promote longevity. The body has an innate (inborn) striving to maintain and heal itself, and the study shows an example of this striving in the form of what appears to be a hormetic dose-response regarding death rates and early years of life.

INTRODUCTION

Hormesis is a term applied to nonlinear dose-response relationships. As an example, vitamin deficiency (where dose is too low) and toxicity (where dose is too high) both result in adverse responses. However, the ideal (moderate) dose, in between low and high, is necessary for a beneficial response (healthy living). Such a relationship forms a J or U-shaped curve (Figure 1). (1) Radiation is another example of a nonlinear hormetic dose-response relationship. (2) Here, cancer rates may actually be higher in the lowest radiation level range than they are in a slightly higher level of low level radiation range. Of course at sufficiently high doses, cancer rates increase essentially in a linear fashion. A third example of a hormetic dose variable is exercise intensity. Here, a sedentary level of intensity corresponds with a higher risk of upper respiratory tract infection (URTI) compared to a moderate exercise intensity, as perhaps expected. (3) What may be unexpected, as with the other examples of hormesis, the moderate amount of exercise intensity corresponds to the lowest risk of URTI

compared to the sedentary and intense levels of exercise. (3)

It may be common knowledge that death rates tend to increase with each passing year of life, that is to say, death rates for example are higher at age 30 compared to age 29. However, in going through some death rate data by age group this writer happened to notice a J-shape relationship, where increasing age in the first years of life was correlated with decreasing death rates. At first this seemed counter-intuitive since death rates, as previously mentioned, in general tend to increase with age. A one or maybe two-year consecutive decrease in death rates seems not too far-fetched, e.g., from age 1 to 2, but a trend (to age 7 or so) seemed odd to this investigator. A curve (for age versus death rates) would seem to appear as a nonlinear, hormetic type response. A literature search on this nonlinear finding did not reveal any particularly relevant articles. One article was obtained on hormesis and aging in the context of cellular activity and stress, where it was observed that: "Hormesis in aging is, therefore, defined as the life supporting beneficial effects resulting from the cellular

responses to single or multiple rounds of mild stress." (4) No articles were found that discussed decreasing death rates in the first years of life. One study, on asthma death rates came close to the topic of the present study, and looked at the relationship between age and death rates in a general sense. Here, no trend in asthma death rates was observed for any age group. (5) Another study that looked to also be relevant, as evidenced by its title, pertained to the introduction of mild stresses as a means of promoting longevity. (6) The present preliminary study however simply looks at age itself as a dose variable, comparing it to death rates, using an ecological / observational design. The focus of the study is on comparing the first seven or so years of life to later years. This information is not necessarily hidden, as upon close inspection, actuarial tables would indicate. (7) However, the observation of a pattern – of decreasing death rates with increasing years of age - in the early years of life – is what appears to be new, which this study explores.

In the context of hormesis, the dose variable in the present study, age, is theorized to be detrimental in the lowest and highest "doses" (ages) while beneficial for ages somewhere in-between. Thus, age was compared to death rates in the present study for the purpose of identifying trends of death rates from one age (in years) to the next. The results of the study may lead to innovative health care innovations that could promote longevity.

METHODS

Crude death rates per 100,000 by age were obtained for all years available (1999-2013) at the data base used – CDC Wonder (8) for: a) all-causes, b) all ages (< 1 through and including 84), and c) five group (cohort) categories based on combinations of race and gender, as follows: 1) White non-Hispanic female ("white female"), 2) white non-Hispanic male ("white male"), 3) black non-Hispanic female ("black female"), 4) black non-Hispanic male ("black male"), and 5) all races, both genders ("all"). In this way, a rather comprehensive view can be gleaned regarding the relationship between age and death rates. Three approaches were used to assess the data, as follows:

A death rate corresponding to a given age was compared to the death rate corresponding to its immediately prior age. For example, the death rate at age 1 was compared to the death rate at age <1; and the death rate at age 2 was compared to the death rate at age 1; and so on. Thus, all death rates were compared consecutively by age (the older age death rate minus the previous younger age death rate). In

this way, negative results of this subtraction more easily differentiated increased death rates from decreased death rates in table format.

Scatter plot charts were constructed for age versus death rates for the five cohorts in Excel 2003 (Microsoft Corp., Redmond, WA). When all ages and their corresponding death rates are shown in a chart for any of the cohorts, the death rate variability appears nonexistent (flat) in years 0 to around 50 due to the high death rates in older ages (example shown in Figure 2). As a remedy for obtaining a closer look at the age-mortality relationship in the first years of life, so that death rate variability could be better assessed in the scatter plot, ages were limited to those (early) years which had similar mortality rates – except for age 0 which is also unusually high and similarly flattens the death rate variability in a chart. A marker for age 0's mortality was manually positioned (by the author) in the upper left hand corner of the charts as a larger circle, after the statistical software automatically scaled the other death rates. Thus, the death rate for age 0 is "off the chart" relative to the scale of the other death rates for a given cohort. Charts are provided for years 1-15 since this age (15) was part of a clear trend upward for the death rates from which death rates for the younger years could be visually compared in the charts. Figures 2-4 graphs were constructed by the author in Excel (Microsoft Corp, Redmond, WA).

RESULTS

After age 10 or so, death rates tended to increase with each passing year of life (Figure 3a-e; Table 1) as might be expected. For ages 0 to around age seven, death rates decreased with each passing year (Figure 3a-e; Table 1) as might be unexpected. Between age seven and 10 the death rates remained relatively constant, with no clear trend either way (Figure 3a-e; Table 1). Thus, for the ages charted, 0 to 15, U or J-shaped dose-response curves are observed for the 5 cohorts (Figure 3a-e). That is to say, higher death rates were associated with the lowest and highest ages within this age group (0-15), while a trend for decreasing death rates was observed for ages in-between this lowest and highest (e.g., age 0 to 7). No other time frame for ages showed a clear trend of consecutive death rate decreases, as evidenced by the minus signs in Table 1 under the "diff" columns.

DISCUSSION

These findings show that age can be likened to a dose variable, such as a vitamin, e.g., vitamin A. In the lowest dose (vitamin A deficiency) and highest dose (vitamin A toxicity), adverse responses are observed; whereas in the

moderate amounts (between the extremes of too low and too high), a normal (beneficial) response is observed. So too with age in this study: Higher death rates were observed at the lowest age (<1 year) and at the higher ages (of 10 and beyond), while a decreased death rate trend was observed each passing year for ages in between (e.g., from age 0 to 7). Consequently, it appears that age can join the list of dose variables that are associated with hormetic responses, in this rather narrow range of years (0 to age 7 or so).

Causes of death for single years do not appear to be available in the literature but are available for age groups. These groupings may provide limited and inferred understanding for single-year death rates causes. In 2007, the rate of accidental deaths per 100,000 was as follows: 9.6 in ages 1-4, 5.5 in ages 5-14, and then 37.4 for ages 15-24. (9) Figure 4 is provided for these data and show a J type (hormesis) relationship. Figure 4 also shows a similar finding for heart disease. (9) These changing rates are similar (but not exactly overlapping) to the changing death rates in ages 1-15 in the present study: high accidental death rates in the earlier years (ages 1-4), then decreased in the next age category (ages 5-14), and then increased again after that (ages 15-24, charts not shown in the present study).

Other possible explanations for the study's findings could be other causes of death whose rates similarly might change with age. The question then becomes, what factors are related to the changing death rates in the various death rate categories? Here, the author opines that age may be one such factor. Later years of life corresponded to increased death rates with each passing year, as expected, with very few exceptions. In these exceptions, where a decreased death rate was observed, the decrease was an isolated event (year) rather than multiple consecutive years for the decrease. The only time this latter condition was observed, that is a clear trend of decreasing death rates with each passing year was for the first seven years or so of life.

Black males showed a noticeably higher death rate in their graph compared not only to black females, but compared to the other cohorts too. One possible explanation for this is that for black males, homicide occurs at a substantially higher rate in black male teenagers compared to whites (Figure 5). (10)

A limitation to the study is its (ecological) design, where exposures and outcomes at the individual level are unknown. However, this design can also be considered a strength to the extent that large "sample sizes" are included (e.g., entire populations). In addition, ecological studies help to form the framework for future studies that use other research designs. Another limitation is that the population was based on one country - the U.S. Thus, results may be less generalize-able to populations in other countries. However, it would seem that some generalize-ability might be possible to other countries when comparing the same race and gender.

CONCLUSION

This study showed a nonlinear, possibly hormetic type dose-response relationship between age in early years of life and corresponding death rates. The death rates decreased with each passing year from age < 1 years old to around age seven. This is the opposite of what occurs later in life, where death rates tended to increase with increasing years of age. Thus, it appears that the body has a remarkable ability to resist increasing death rates in each passing year in the first seven years or so of life. Future research is needed to verify these findings. If the results are repeatable, an investigation of possible underlying mechanisms would be a reasonable next step, and may lead to innovative health care innovations that could promote longevity.

Figure 1

Hormetic models may show a J or U-shaped dose-response relationships as shown in the figure. Higher responses are observed at the lower and higher ends of dose while decreased responses are observed in-between. Adapted from Reference #1.
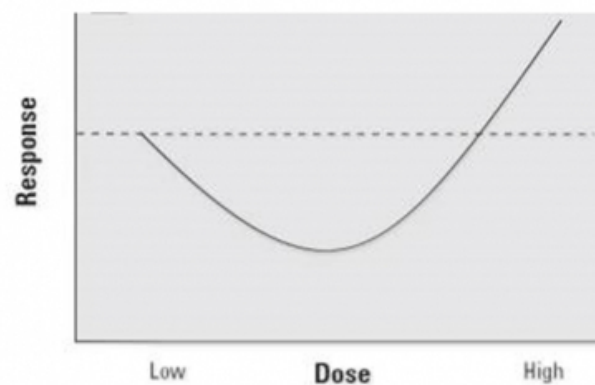
Figure 2

A representative chart for all ages, white females for death rates per 100,000. Due to the large difference of death rates (in the thousands by age 80 versus 15 around age seven), the death rate variation appears flat in the younger years due to the data being compressed (due to scaling limitations of the chart software). This is the typical appearance of the other cohorts in the study where all ages were also included (other cohort charts not shown). The first data point, for age 0 (< 1 year old, lower left corner) is noticeably higher in the chart compared to subsequent data points because it (the first point) is substantially larger than the subsequent points (death rate of 505.6 at age 0 versus 38.6 at age 1, as shown in Table 1).
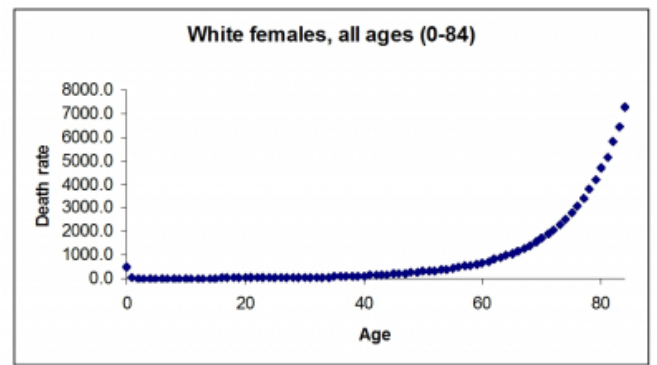

Figure 3a

a-e. Age versus all-cause mortality per 100,000 for ages 0-15, for the five cohorts. The large round marker in the upper left region of the charts was manually positioned by the author and represents the unusually high, off-the-scale death rate (in the hundreds per 100,000) for age < 1 years old (indicated as age 0 on the horizontal axis). Actual death rate values for this (age 0), along with the other ages can be found in Table 1. For all charts, decreasing death rates are observed with increasing years from age 0 to around age 7, where it becomes flat, and then shows increasing death rates with increasing years for remaining years, including beyond age 15 (please see Table 1 for further numerical information). a. White females
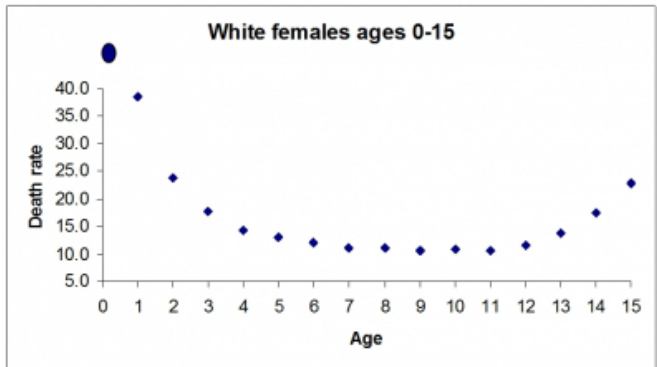
Figure 3b

b. White males
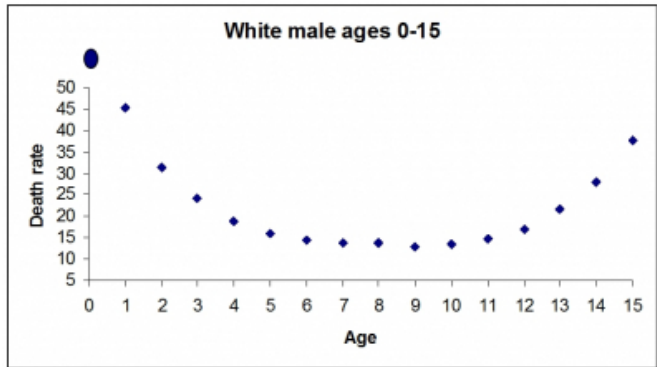
Figure 3c

c. Black females
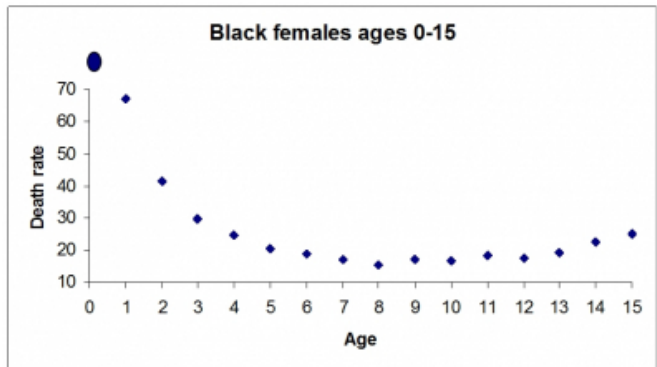
Figure 3d

d. Black males
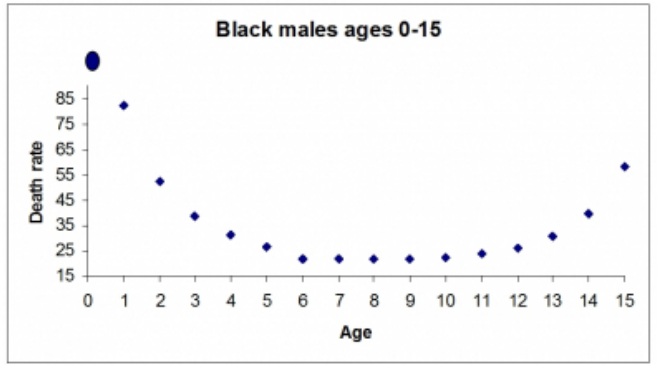
Figure 3e

e. All races, both genders
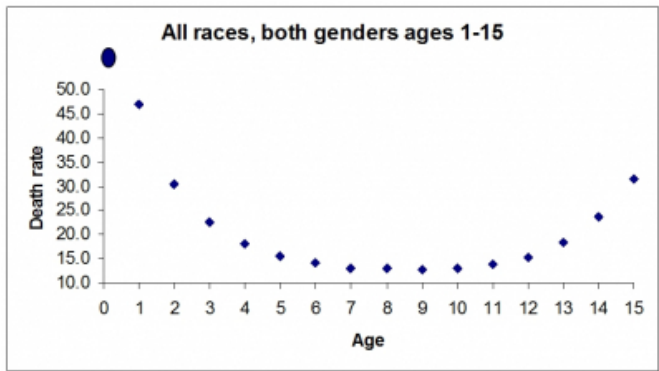
Figure 5

Graph showing homicide rates for children ages 12-19, U.S., 1999-2006. From reference #10.
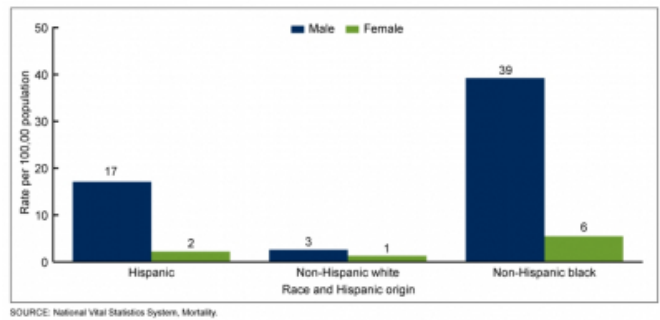
Figure 4a

Figure 4 a-b. Charts constructed by author based on crude death rates per 100,000 for accidents (upper chart) and heart disease (lower chart) for early years of life. 9 A J type relationship is observed for both causes of death, similar to the U shaped relationships in Figure 3. a. Death rates due to accidents by age groups

Figure 4b

b. Death rates due to heart disease by age groups

Table 1

All-cause crude death rates (per 100,000) by cohort and age (in years) for ages <1 to 84. F = female. M = male. All = all races, both genders. diff = death rate difference between older age and preceding younger age (e.g., age 2 minus age 1). Only ages <1 to around 7 showed multiple (at least seven) consecutive decreased death rates with each passing year.

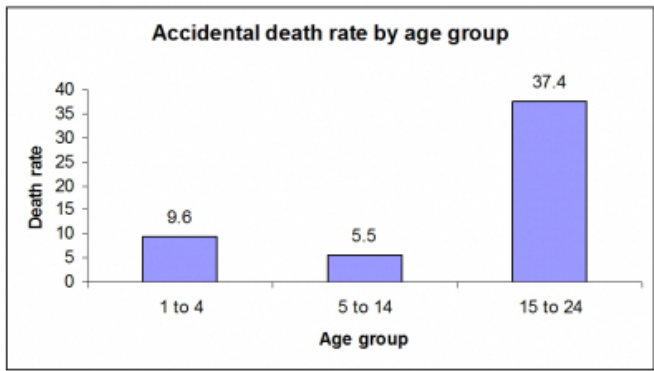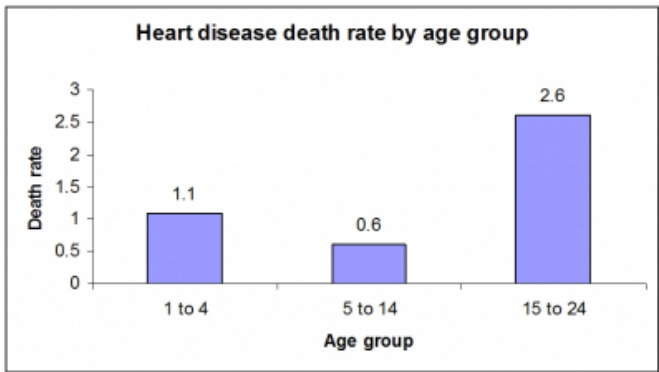| Age	White F	White F diff	White M	White M diff	Black F	Black F diff	Black M	Black M diff	All	All diff
< 1	505.6		626.4		1197.5		1456.1		676.2	
1	38.6	-467.0	45.3	-581.1	67.0	-1130.5	82.3	-1373.8	46.8	-629.4
2	23.9	-14.7	31.3	-14.0	41.4	-25.6	52.4	-29.9	30.4	-16.4
3	17.7	-6.2	24.1	-7.2	29.7	-11.7	38.8	-13.6	22.6	-7.8
4	14.2	-3.5	18.7	-5.4	24.7	-5.0	31.0	-7.8	18.2	-4.4
5	13.0	-1.2	16.0	-2.7	20.4	-4.3	26.8	-4.2	15.7	-2.5
6	12.0	-1.0	14.4	-1.6	18.7	-1.7	21.9	-4.9	14.1	-1.6
7	11.0	-1.0	13.8	-0.6	17.0	-1.7	21.6	-0.3	13.2	-0.9
8	11.2	0.2	13.8	0.0	15.3	-1.7	21.6	0.0	13.1	-0.1
9	10.6	-0.6	13.0	-0.8	17.2	1.9	21.8	0.2	12.9	-0.2
10	10.8	0.2	13.5	0.5	16.7	-0.5	22.5	0.7	13.1	0.2
11	10.7	-0.1	14.8	1.3	18.2	1.5	24.1	1.6	14.0	0.9
12	11.7	1.0	17.0	2.2	17.4	-0.8	26.0	1.9	15.3	1.3
13	13.9	2.2	21.7	4.7	19.4	2.0	30.7	4.7	18.5	3.2
14	17.6	3.7	27.9	6.2	22.4	3.0	39.8	9.1	23.8	5.3
15	22.9	5.3	37.7	9.8	25.0	2.6	58.1	18.3	31.5	7.7
16	34.3	11.4	58.5	20.8	29.7	4.7	82.0	23.9	46.1	14.6
17	38.4	4.1	74.0	15.5	36.9	7.2	114.3	32.3	58.1	12.0
18	42.9	4.5	99.2	25.2	45.9	9.0	159.0	44.7	75.0	16.9
19	43.2	0.3	111.9	12.7	50.7	4.8	183.9	24.9	82.6	7.6
20	43.6	0.4	116.5	4.6	56.6	5.9	198.0	14.1	85.8	3.2
21	46.6	3.0	130.8	14.3	63.2	6.6	212.6	14.6	93.1	7.3
22	45.6	-1.0	129.6	-1.2	65.8	2.6	226.2	13.6	93.5	0.4
23	47.1	1.5	130.3	0.7	71.2	5.4	231.0	4.8	93.8	0.3
24	49.1	2.0	130.6	0.3	76.5	5.3	237.4	6.4	94.7	0.9
25	49.8	0.7	129.9	-0.7	80.0	3.5	235.9	-1.5	93.9	-0.8
26	53.1	3.3	131.7	1.8	86.3	6.3	245.6	9.7	96.5	2.6
27	53.7	0.6	131.1	-0.6	91.6	5.3	247.9	2.3	96.6	0.1
28	57.7	4.0	131.7	0.6	97.6	6.0	248.4	0.5	98.2	1.6
29	61.5	3.8	135.3	3.6	108.1	10.5	258.7	10.3	102.2	4.0
30	64.4	2.9	134.9	-0.4	108.8	0.7	254.8	-3.9	102.9	0.7
31	67.7	3.3	142.0	7.1	116.7	7.9	260.0	5.2	108.1	5.2
32	72.1	4.4	143.2	1.2	131.2	14.5	261.4	1.4	111.3	3.2
33	76.1	4.0	150.1	6.9	141.1	9.9	272.3	10.9	116.9	5.6
34	82.4	6.3	155.7	5.6	150.6	9.5	287.2	14.9	123.4	6.5
35	89.3	6.9	165.5	9.8	163.4	12.8	291.2	4.0	131.0	7.6
36	96.6	7.3	172.2	6.7	175.4	12.0	307.8	16.6	138.5	7.5
37	104.4	7.8	185.9	13.7	189.5	14.1	329.8	22.0	149.6	11.1
38	113.1	8.7	199.7	13.8	210.8	21.3	348.5	18.7	161.2	11.6
39	124.6	11.5	212.1	12.4	229.2	18.4	366.5	18.0	173.5	12.3
40	134.9	10.3	230.9	18.8	248.7	19.5	386.0	19.5	188.2	14.7
41	146.1	11.2	250.8	19.9	269.6	20.9	418.5	32.5	204.4	16.2
42	159.1	13.0	270.2	19.4	295.8	26.2	454.2	35.7	221.9	17.5
43	175.1	16.0	293.9	23.7	325.2	29.4	493.3	39.1	242.6	20.7
44	191.8	16.7	320.1	26.2	348.8	23.6	539.3	46.0	264.6	22.0
45	206.6	14.8	345.8	25.7	381.2	32.4	582.8	43.5	286.1	21.5
46	226.0	19.4	380.2	34.4	411.2	30.0	636.9	54.1	313.6	27.5
47	243.7	17.7	411.0	30.8	441.9	30.7	698.7	61.8	339.9	26.3
48	262.1	18.4	444.7	33.7	485.6	43.7	764.0	65.3	368.7	28.8
49	284.7	22.6	483.2	38.5	523.7	38.1	826.0	62.0	399.7	31.0
50	308.0	23.3	522.4	39.2	568.9	45.2	905.5	79.5	433.2	33.5
51	332.7	24.7	563.5	41.1	603.5	34.6	984.7	79.2	467.1	33.9
52	358.3	25.6	606.6	43.1	646.8	43.3	1070.9	86.2	503.6	36.5
53	386.6	28.3	659.6	53.0	687.4	40.6	1145.8	74.9	543.4	39.8
54	416.5	29.9	701.3	41.7	747.0	59.6	1250.6	104.8	583.0	39.6
55	451.3	34.8	766.2	64.9	791.8	44.8	1368.0	117.4	632.6	49.6
56	489.6	38.3	819.0	52.8	840.5	48.7	1461.7	93.7	678.8	46.2
57	533.6	44.0	884.4	65.4	907.1	66.6	1575.9	114.2	733.3	54.5
58	576.6	43.0	958.3	73.9	988.8	81.7	1674.4	98.5	792.8	59.5
59	631.8	55.2	1035.7	77.4	1050.5	61.7	1819.3	144.9	858.7	65.9
60	691.8	60.0	1126.8	91.1	1125.4	74.9	1952.2	132.9	932.6	73.9
61	754.1	62.3	1201.7	74.9	1208.6	83.2	2048.3	96.1	999.8	67.2
62	823.3	69.2	1312.6	110.9	1318.3	109.7	2214.3	166.0	1089.7	89.9
63	913.2	89.9	1431.7	119.1	1391.9	73.6	2352.1	137.8	1188.1	98.4
64	998.3	85.1	1552.6	120.9	1516.4	124.5	2555.7	203.6	1292.1	104.0
65	1089.2	90.9	1674.3	121.7	1625.8	109.4	2668.9	113.2	1392.9	100.8
66	1187.4	98.2	1817.2	142.9	1735.7	109.9	2861.1	192.2	1509.3	116.4
67	1311.7	124.3	1992.5	175.3	1883.6	147.9	3053.7	192.6	1651.1	141.8
68	1423.9	112.2	2165.6	173.1	2034.1	150.5	3270.3	216.6	1791.6	140.5
69	1562.7	138.8	2374.1	208.5	2226.1	192.0	3536.6	266.3	1959.0	167.4
70	1731.6	168.9	2597.1	223.0	2388.8	162.7	3821.5	284.9	2143.9	184.9
71	1893.6	162.0	2833.0	235.9	2564.3	175.5	4059.3	237.8	2332.5	188.6
72	2093.8	200.2	3121.0	288.0	2797.9	233.6	4406.8	347.5	2565.2	232.7
73	2296.6	202.8	3426.7	305.7	2983.0	185.1	4709.3	302.5	2802.9	237.7
74	2532.1	235.5	3730.6	303.9	3273.0	290.0	5042.7	333.4	3062.0	259.1
75	2796.7	264.6	4124.2	393.6	3568.4	295.4	5537.1	494.4	3375.0	313.0
76	3085.6	288.9	4505.5	381.3	3848.4	280.0	5907.7	370.6	3686.3	311.3
77	3410.4	324.8	4963.7	458.2	4189.5	341.1	6406.2	498.5	4056.0	369.7
78	3776.7	366.3	5445.5	481.8	4562.5	373.0	6901.5	495.3	4450.7	394.7
79	4193.5	416.8	6018.3	572.8	4974.0	411.5	7446.8	545.3	4910.6	459.9
80	4673.8	480.3	6641.0	622.7	5428.7	454.7	8171.7	724.9	5426.8	516.2
81	5170.5	496.7	7344.7	703.7	5913.9	485.2	8637.3	465.6	5971.7	544.9
82	5813.4	642.9	8141.3	796.6	6515.5	601.6	9465.9	828.6	6641.2	669.5
83	6456.5	643.1	8976.3	835.0	7099.8	584.3	10149.3	683.4	7321.1	679.9
84	7265.4	808.9	10006.1	1029.8	7771.4	671.6	11021.4	872.1	8162.2	841.1

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