

# The Hunger Games as the Key to Happily Ever After?

Jacques A. Deere <sup>1,\*</sup>, Aziz Aboobaker <sup>1</sup> and Roberto Salguero-Gómez <sup>1,2,3</sup>

<sup>1</sup> Department of Zoology, 11a Mansfield Rd, University of Oxford, Oxford, OX1 3SZ, United Kingdom; aziz.aboobaker@zoo.ox.ac.uk (A.A.); rob.salguero@zoo.ox.ac.uk (R.S.-G.)

<sup>2</sup> Centre for Biodiversity and Conservation Science, University of Queensland, St Lucia 4071QLD, Australia.

<sup>3</sup> Evolutionary Demography Laboratory, Max Plank Institute for Demographic Research, Rostock 18057, Germany.

\* Correspondence: jacques.deere@zoo.ox.ac.uk

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## Methods

To determine the generality of the predicted beneficial effects of CR on longevity, we conducted a literature search of peer-review publications via ISI Web of Science. We used the search terms “calorie” AND “restriction” AND “longevity” and covered the period from 1900 to March 2020. In many cases (~31%), the papers from the review that provided results on experiments comparing calorie restricted diets to non-calorie restricted diets did not provide enough detail on the study outcomes other than mean values in a table or a figure. Additionally, there were studies that stated significant differences between calorie restricted and non-calorie restricted diets but did not provide significance values or confidence intervals. Thus, we were unable to perform a meta-analysis on this literature review.

For each study in the literature review, outcomes of calorie restriction on longevity were identified as ‘positive’, ‘negative’, ‘no effect’, or ‘variable’: ‘positive’ describes outcomes that extends longevity; ‘negative’ outcomes shorten longevity; ‘no effect’ outcomes describe no extension or shortening of longevity; ‘variable’ describes both extension and shortening of longevity within studies (here the general effect is unclear). We define short-lived species as species with a mean life expectancy of less than five years. Within our review, all invertebrate species have a mean life expectancy of less than one year. Only two short-lived species live longer than one year: *Mus musculus* and *Rattus norvegicus*. To obtain mean life expectancy values for these two species, we searched the PANTHERA database<sup>1</sup>. In the case of *Mus musculus*, the only datum available was for maximum longevity (6 years). However, for *Rattus norvegicus* no data were available. As such, we identified the maximum longevity of these two species in our literature review (4.2 years for *Mus musculus*, 4.1 years for *Rattus norvegicus*) and identified short-lived species as those with a mean life expectancy of less than 5 years. We identified the effect size of the outcomes of each study in two ways: (1) where studies explicitly stated effect sizes, we used those values; (2) for studies that did not explicitly state effect sizes, we calculated effect size from the data or figures presented in those studies. Where effect size was given within a study, this was in percentage change in longevity of the CR treatment compared to the non-CR treatment. As such, in the case of studies that did not report effect size, we calculated the percentage change in longevity of the CR treatment compared to the non-CR treatment from the data or figure presented within a study where possible. In the case of five studies on yeast, where present, the effect size was in orders of magnitude as in these cases the longevity under CR treatments increased in orders of magnitude.

To determine if there were significantly more studies where the outcomes show a positive effect of calorie restriction on longevity (lifespan extension), we analysed our data using a chi-square test on studies investigating effects of CR without interaction effects. For studies focused on the

interaction of CR with other variables, we conducted a separate chi-square test to determine if there were significantly more studies showing positive effects on longevity. In both tests, where studies were not identified as having positive outcomes on longevity ('positive'), they were grouped into a single category (*i.e.*, 'negative', 'no effect' and 'variable' were combined) for the analyses. Data analyses were performed in R version 3.6.3<sup>2</sup>.

**Supplementary Table 1. Summary of studies from the literature search.**

Studies investigating the effect of calorie restriction on longevity, result of a literature search in ISI Web of Science between YYYY and 2020. Life history pace indicates either fast-living (short-lived) or slow-living (long-lived) species. In the case of response to calorie restriction *variable* indicates positive and negative effects within studies whilst *no effect* indicates no positive or negative effect. Effect size is given in percentage (%) or orders of magnitude ( $10^n$ ). CR = calorie restriction, Ref. = reference, NA = information not provided by the study. <sup>a</sup> Indicates studies that stated effects sizes. Where studies did not contain an estimated effect size, we calculated effect size from the studies' available data and figures when possible.

Study	Scientific name	Common name	Treatment	Life history pace	CR response	Study length	Study length units	Interaction	Effect size (min)	Effect size (max)	p-value	Longevity measure	Manuscript type	Date	Ref.
1	<i>Rattus norvegicus</i>	Rat	Normal/ad libitum diet and 70% CR diet	Fast	positive	38	months	n	NA	17.0%	0.01	median	Experiment	2020	3
2	<i>Danio rerio</i>	Zebrafish	Normal/ad libitum diet, 25% CR diet and 50% CR diet	Fast	positive	260	days	n	NA	43.0%	0.001	mean	Experiment	2020	4
3	<i>Saccharomyces cerevisiae</i>	Yeast	Normal diet (2% glucose) and CR diet (0.5% glucose); two culture methods (bottle-ageing & microplate-ageing)	Fast	variable	6	days	n	10.0%	42.0%	<0.05	mean	Experiment	2019	5
4	<i>Mus musculus</i>	Mouse	Normal/ad libitum diet and CR diet	Fast	positive	1400	days	n	19.0%	37.5%	0.001	median	Experiment	2019	6 <sup>a</sup>
5	<i>Caenorhabditis elegans</i>	Nematode	Normal/ad libitum diet and CR diet	Fast	positive	31	days	n	NA	25.4%	0.001	median	Experiment	2019	7 <sup>a</sup>

6	<i>Saccharomyces cerevisiae</i>	Yeast	4% glucose diet, 2% glucose diet and 0.5% glucose diet	Fast	positive	270	hours	n	13.0%	41.0%	0.01	mean	Experiment	2019	8 <sup>a</sup>
7	<i>Tetranychus urticae</i>	Spider mite	Normal/ad libitum diet, 33% intermittent fasting, 50% intermittent fasting, 67% intermittent fasting	Fast	variable	60	days	y	0.0%	29.0%	0.001	mean	Experiment	2019	9
8	<i>Mus musculus</i>	Mouse	Normal/ad libitum diet, 30% CR diet and single-meal feeding	Fast	positive	126	weeks	n	NA	28.0%	0.001	median	Experiment	2019	10 <sup>a</sup>
9	<i>Mus musculus</i>	Mouse	Normal/ad libitum diet, 20% CR, 30% CR and one treatment switched from CR to ad libitum	Fast	positive	85	weeks	y	12.0%	24.0%	0.001	median	Experiment	2018	11
Study	Scientific name	Common name	Treatment	Life history speed	CR response	Study length	Study length units	Interaction	Effect size (min)	Effect size (max)	p-value	Longevity measure	Manuscript type	Date	Ref.
10	<i>Microcebus murinus</i>	Grey mouse lemur	Normal/ad libitum diet and 30% CR diet	Slow	positive	13	years	n	NA	50.0%	0.03	median	Experiment	2018	12 <sup>a</sup>
11	<i>Caenorhabditis elegans</i>	Nematode	Normal/ad libitum diet and CR diet(s);	Fast	positive	60	days	n	NA	80.0%	NA	mean	Meta-analysis	2018	13 <sup>a</sup>

			extent of CR varied over studies in meta-analysis													
12	<i>Drosophila melanogaster</i>	Fruit fly	Normal/ad libitum diet and CR diet(s); extent of CR varied over studies in meta-analysis	Fast	positive	60	days	n	NA	100.0%	NA	mean	Meta-analysis	2018	13 <sup>a</sup>	
13	<i>Musca domestica</i>	House fly	Normal/ad libitum diet and diets increasing in CR; Caloric content: Sucrose>Xylitol>Sorbitol>Mannitol>Truvia>Water	Fast	negative	14	days	n	NA	70.0%	0.001	mean	Experiment	2017	14	
14	<i>Bombyx mori</i>	Silkworm	Normal/ad libitum diet and reduced daily feeding diet (16 hours)	Fast	no effect	1800	hours	n	NA	0.0%	>0.05	mean	Experiment	2017	15	
15	<i>Saccharomyces cerevisiae</i>	Yeast	Normal diet (2% glucose) and CR diet (0.4% glucose)	Fast	positive	25	days	n	NA	170.0%	NA	mean	Experiment	2017	16	
16	<i>Saccharomyces cerevisiae</i>	Yeast	Normal diet (2% glucose) and CR diet (0.5% glucose)	Fast	positive	15	days	n	45.0%	50.0%	0.001	mean	Experiment	2017	17 <sup>a</sup>	

17	<i>Rattus norvegicus</i>	Rat	Normal/ad libitum diet, 60% CR diet and 90% CR diet	Fast	positive	32	months	n	15.0%	19.0%	0.001	mean	Experiment	2016	18 <sup>a</sup>
18	<i>Saccharomyces cerevisiae</i>	Yeast	Normal diet (2% glucose) and CR diet (0.1% glucose)	Fast	positive	14	days	n	NA	65.0%	0.005	mean	Experiment	2016	19
19	<i>Mus musculus</i>	Mouse	Normal/ad libitum diet and 30% CR diet	Fast	positive	1100	days	n	NA	50.0%	0.001	mean	Experiment	2016	20
20	<i>Saccharomyces cerevisiae</i>	Yeast	Normal diet (2% glucose) and CR diet (0.2% glucose)	Fast	positive	20	days	n	NA	30.0%	0.0001	mean	Experiment	2016	21
21	<i>Caenorhabditis elegans</i>	Nematode	Normal/ad libitum diet and 1% CR diet	Fast	positive	37	days	n	NA	40.0%	0.0001	mean	Experiment	2016	22 <sup>a</sup>
Study	Scientific name	Common name	Treatment	Life history speed	CR response	Study length	Study length units	Interaction	Effect size (min)	Effect size (max)	p-value	Longevity measure	Manuscript type	Date	Ref.
22	<i>Drosophila melanogaster</i>	Fruit fly	Multiple diets varying in protein and lipid content; total caloric content also varied through different concentrations	Fast	negative	40	days	y	NA	NA	0.01	mean	Experiment	2016	23
23	<i>Saccharomyces cerevisiae</i>	Yeast	Normal diet (2% glucose), CR	Fast	positive	70	days	n	22.0%	42.0%	0.0001	mean	Experiment	2015	24 <sup>a</sup>

			0.5% glucose diet and CR													
			0.05% glucose diet													
24	<i>Saccharomyces cerevisiae</i>	Yeast	Normal diet (2% glucose) and CR diet (0.5% glucose); two culture methods (bottle-ageing & microplate-ageing)	Fast	positive	100	hours	n	NA	10 <sup>3</sup>	0.001	mean	Experiment	2015	25	
25	<i>Saccharomyces cerevisiae</i>	Yeast	Normal diet (2% glucose), CR 0.5% glucose diet and CR 0.2% glucose diet; treatments either not moved or moved to new spatial location in same diet treatment after 15 generations	Fast	variable	40	generations	y	5.0%	30.0%	0.001	median	Experiment	2015	26 <sup>a</sup>	
26	<i>Saccharomyces cerevisiae</i>	Yeast	Normal diet (2% glucose) and CR diet (0.5% glucose)	Fast	positive	48	generations	n	NA	17.0%	NA	mean	Experiment	2014	27	
27	<i>Mus musculus</i>	Mouse	Normal/ad libitum diet, 5% CR diet and 40% CR diet	Fast	positive	1450	days	n	13.0%	32.0%	<0.05	median	Experiment	2014	28	

28	<i>Saccharomyces cerevisiae</i>	Yeast	Normal diet (2% glucose), CR 0.5% glucose diet and CR 0.05% glucose diet	Fast	no effect	50	buds	n	NA	0.0%	0.11	mean	Meta-analysis	2014	29 <sup>a</sup>
29	<i>Drosophila melanogaster</i>	Fruit fly	Normal/ad libitum diet and 2% CR diet	Fast	positive	500	minutes	n	NA	46.4%	0.0001	mean	Experiment	2014	30 <sup>a</sup>
30	<i>Mus musculus</i>	Mouse	Normal/ad libitum diet and 70% CR diet	Fast	positive	176	weeks	n	NA	20.3%	0.0001	mean	Experiment	2014	31 <sup>a</sup>
31	<i>Saccharomyces cerevisiae</i>	Yeast	Normal diet (2% glucose) and CR diet (0.4% glucose)	Fast	positive	30	days	n	NA	10 <sup>3</sup>	NA	mean	Experiment	2013	32
Study	Scientific name	Common name	Treatment	Life history speed	CR response	Study length	Study length units	Interaction	Effect size (min)	Effect size (max)	p-value	Longevity measure	Manuscript type	Date	Ref.
32	<i>Romalea microptera</i>	Lubber grasshopper	Normal/ad libitum diet and CR diet; CR based on the amount ovariectomized individuals ate on ad lib diet the week before	Fast	positive	120	days	n	NA	30.0%	0.0001	mean	Experiment	2013	33
33	<i>Saccharomyces cerevisiae</i>	Yeast	Normal diet (2% glucose) and CR diet (0.5% glucose)	Fast	positive	28	days	n	NA	60.0%	0.001	mean	Experiment	2013	34



34	<i>Mus musculus</i>	Mouse	Normal diet (92.5 kcal per week) or CR diet (74 kcal per week)	Fast	no effect	152	weeks	n	NA	0.0%	0.39	median	Experiment	2013	35 <sup>a</sup>
35	<i>Macaca mulatta</i>	Rhesus monkey	Normal diet and 30% CR diet. All animals were adults when CR initiated.	Slow	no effect	40	years	n	NA	0.0%	0.93	mean	Experiment	2012	36 <sup>a</sup>
36	<i>Bactrocera tryoni</i>	Queensland fruit fly	Multiple diets varying in protein and lipid content; total caloric content also varied through different concentrations	Fast	no effect	80	days	y	NA	0.0%	<0.05	mean	Experiment	2012	37 <sup>a</sup>
37	<i>Drosophila melanogaster</i>	Fruit fly	Normal diet and diets varying in sugar:protein content (high sugar:low protein, low sugar:high protein); total caloric concentration also varied through different	Fast	variable	85	days	y	26.3%	40.9%	0.001	mean	Experiment	2012	38 <sup>a</sup>

Study	Scientific name	Common name	Treatment	Life history speed	CR response	Study length	Study length units	Interaction	Effect size (min)	Effect size (max)	p-value	Longevity measure	Manuscript type	Date	Ref.
38	<i>Saccharomyces cerevisiae</i>	Yeast	Normal diet (2% glucose) and CR diet (0.5% glucose)	Fast	positive	52	days	n	NA	48.0%	0.001	mean	Experiment	2012	39
39	<i>Asobara tabida</i>	Parasitoid wasp	Ad lib diets varying in sucrose concentrations (0%, 20%, 40%, 80%, or 100%); 40% concentration diet varying in feeding frequency (once, weekly, twice weekly, daily or ad lib)	Fast	variable	40	days	y	10.0%	75.0%	0.001	mean	Experiment	2011	40
40	<i>Trichopria drosophilae</i>	Parasitoid wasp	Ad lib diets varying in sucrose concentrations (0%, 20%, 40%, 80% or 100%); 40% concentration	Fast	variable	90	days	y	9.0%	88.0%	0.001	mean	Experiment	2011	40

			diet varying in feeding frequency (once, weekly, twice weekly, daily or ad lib)													
41	<i>Drosophila melanogaster</i>	Fruit fly	Normal diet (15% yeast) and CR diet (5% yeast)	Fast	positive	60	days	y	23.0%	28.0%	0.0001	mean	Experiment	2011	41 <sup>a</sup>	
42	<i>Saccharomyces cerevisiae</i>	Yeast	Normal diet (2% dextrose) and CR diet (0.5% dextrose)	Fast	positive	43	days	n	NA	40.0%	0.001	mean	Experiment	2011	42	
43	<i>Brachionus plicatilis</i>	Rotifer	Normal/ad libitum diet (daily feeding) and CR diet (feeding every other day); two environments one non-stressed (no paraquat exposure) and one stressed (exposure to 10 mM paraquat). Experiment repeated with daughters from mothers on either AL or CR diet	Fast	positive	20	days	y	30.0%	50.0%	0.0001	mean	Experiment	2011	43 <sup>a</sup>	

44	<i>Podospora anserina</i>	Filamentous fungus	Normal diet (2% glucose), 0.2% glucose CR diet and 0.02% glucose CR diet	Fast	positive	100	days	n	50.0%	800.0%	NA	mean	Experiment	2010	44 <sup>a</sup>
Study	Scientific name	Common name	Treatment	Life history speed	CR response	Study length	Study length units	Interaction	Effect size (min)	Effect size (max)	p-value	Longevity measure	Manuscript type	Date	Ref.
45	<i>Saccharomyces cerevisiae</i>	Yeast	Normal diet (2% glucose), CR diet (0.5% glucose) and normal diet excluding amino acids	Fast	variable	43	generations	n	NA	64.0%	NA	mean	Experiment	2010	45
46	<i>Drosophila melanogaster</i>	Fruit fly	Normal/ad libitum diet and 50% CR diet	Fast	positive	75	days	n	NA	13.0%	0.01	mean	Experiment	2010	46
47	<i>Rattus norvegicus</i>	Rat	Normal/ad libitum diet and 70% CR diet	Fast	no effect	1065	days	n	NA	0.0%	0.06	mean	Experiment	2010	47 <sup>a</sup>
48	<i>Schizosaccharomyces pombe</i>	Fission yeast	Diets varying in glucose concentration (0.75%, 1%, 1.5%, 3% and 4%)	Fast	positive	7	days	n	NA	10 <sup>4</sup>	NA	mean	Experiment	2010	48
49	<i>Macaca mulatta</i>	Rhesus monkey	Normal diet and 30% CR diet. CR initiated gradually by 10% per month for three months to reach 30%. All animals	Slow	positive	32	years	n	NA	30.0%	0.03	mean	Experiment	2009	49

			were adults when CR initiated but of varying ages (young to old)													
50	<i>Latrodectus hasselti</i>	Australian redback spider	Diets varying in caloric content; low diet one fly per week, mid diet of three flies three times per week, high diet of six flies three times per week; males fed in presence or absence of females	Fast	negative	20	days	y	33.0%	54.0%	0.007	mean	Experiment	2009	50	
51	<i>Mus musculus</i>	Mouse	Normal diet and CR diet; normal diet (litter size of 8 pups), CR for first 20 days of life and induced through changes in litter size (50% enlargement, 8 to 12 pups at birth)	Fast	positive	1100	days	n	NA	18.0%	0.0007	median	Experiment	2009	51 <sup>a</sup>	
Study	Scientific name	Common name	Treatment	Life history speed	CR response	Study length	Study length units	Interaction	Effect size (min)	Effect size (max)	p-value	Longevity measure	Manuscript type	Date	Ref.	

52	<i>Bactrocera tryoni</i>	Queensland fruit fly	Multiple diets varying in carbohydrate:protein ratios and concentrations; additional treatment with choice of separate sucrose and yeast diets at one of five concentrations	Fast	variable	92	days	y	20.0%	50.0%	NA	mean	Experiment	2009	52
53	<i>Saccharomyces cerevisiae</i>	Yeast	Diets varying in glucose concentration (0.2%, 0.5%, 1% and 2%)	Fast	positive	35	days	n	60.0%	90.0%	0.001	mean	Experiment	2009	53 <sup>a</sup>
54	<i>Saccharomyces cerevisiae</i>	Yeast	Normal diet (2% glucose) and CR diet (0.5% glucose)	Fast	positive	50	generations	n	NA	37.0%	0.04	mean	Experiment	2009	54
55	<i>Anastrepha ludens</i>	Tephritid fruit fly	Multiple diets varying in sugar:yeast ratios and three dilution levels	Fast	no effect	100	days	y	0.0%	60.0%	NA	mean	Experiment	2009	55
56	<i>Mus musculus</i>	Mouse	Normal/ad libitum diet and 30% CR diet	Fast	positive	50	months	n	12.0%	36.0%	0.0001	median	Experiment	2009	56
57	<i>Saccharomyces cerevisiae</i>	Yeast	Normal diet (2% glucose) and CR diet (0.5% glucose)	Fast	positive	24	days	n	10.0%	50.0%	NA	mean	Experiment	2009	57

58	<i>Caenorhabditis elegans</i>	Nematode	Diets varying in bacterial concentrations (gradient of concentrations)	Fast	positive	32	days	n	19.0%	40.0%	0.0001	mean	Experiment	2009	58
59	<i>Mus musculus</i>	Mouse	Normal/ad libitum diet (daily feeding) and CR diet (feeding every other day; approximately 10-15% reduction in daily food intake)	Fast	positive	1010	days	n	NA	16.0%	<0.008	median	Experiment	2009	59 <sup>a</sup>
60	<i>Caenorhabditis elegans</i>	Nematode	Normal/ad libitum diet (bacteria, 1.5 optical density) and CR diet (bacteria, 0.5 optical density)	Fast	positive	32	days	n	NA	39.0%	0.0001	median	Experiment	2009	60 <sup>a</sup>
61	<i>Mus musculus</i>	Mouse	Normal/ad libitum diet and 70% CR diet	Fast	positive	1388	days	n	NA	42.0%	0.01	mean	Experiment	2008	61
Study	Scientific name	Common name	Treatment	Life history speed	CR response	Study length	Study length units	Interaction	Effect size (min)	Effect size (max)	p-value	Longevity measure	Manuscript type	Date	Ref.
62	<i>Saccharomyces cerevisiae</i>	Yeast	Normal diet (2% glucose) and CR	Fast	positive	24	hours	n	13.0%	49.0%	NA	mean	Experiment	2008	62

			diet (0.5% glucose)													
63	<i>Anastrepha ludens</i>	Tephritid fruit fly	Multiple diets varying in sugar:yeast ratios and varying in CR regimes (percentages of ad lib food)	Fast	variable	90	days	y	19.5%	66.0%	0.001	mean	Experiment	2008	63	
64	<i>Drosophila melanogaster</i>	Fruit fly	Multiple diets varying in sugar:yeast ratios	Fast	variable	70	days	y	NA	NA	NA	mean	Experiment	2008	64	
65	<i>Mus musculus</i>	Mouse	Normal/ad libitum diet and 40% CR diet	Fast	positive	131	days	n	NA	13.2%	0.024	median	Experiment	2008	65 <sup>a</sup>	
66	<i>Saccharomyces cerevisiae</i>	Yeast	Glucose, galactose, raffinose and glycerol/ethanol diets varying in concentration from 0.2-3.0%	Fast	variable	36	hours	n	40.0%	100.0%	0.04	mean	Experiment	2008	66	
67	<i>Kluyveromyces lactis</i>	Yeast	Glucose, galactose, raffinose and glycerol/ethanol diets varying in concentration from 0.2-3.0%	Fast	negative	36	hours	n	40.0%	95.0%	0.04	mean	Experiment	2008	66	
68	<i>Saccharomyces cerevisiae</i>	Yeast	Normal diet (2% glucose) and CR	Fast	positive	150	hours	n	10 <sup>2</sup>	10 <sup>3</sup>	NA	mean	Experiment	2008	67	



			diet (0.5% glucose)													
69	<i>Caenorhabditis elegans</i>	Nematode	Normal/ad libitum diet and CR diet (bacterial deprivation), individuals moved from normal diet to CR diet (and vice versa) at different ages; treatments initiated at two temperatures (20°C and 38°C)	Fast	positive	54	days	y	14.0%	70.0%	0.0001	mean	Experiment	2008	68	
70	<i>Caenorhabditis elegans</i>	Nematode	Normal/ad libitum diet and CR diet (bacterial deprivation after 4th day of adulthood)	Fast	positive	44	days	n	23.0%	51.0%	0.0001	mean	Experiment	2008	69 <sup>a</sup>	
<b>Study</b>	<b>Scientific name</b>	<b>Common name</b>	<b>Treatment</b>	<b>Life history speed</b>	<b>CR response</b>	<b>Study length</b>	<b>Study length units</b>	<b>Interaction</b>	<b>Effect size (min)</b>	<b>Effect size (max)</b>	<b>p-value</b>	<b>Longevity measure</b>	<b>Manuscript type</b>	<b>Date</b>	<b>Ref.</b>	
71	<i>Caenorhabditis elegans</i>	Nematode	Normal/ad libitum diet and CR diet (bacterial deprivation after	Fast	variable	71	days	n	4.0%	41.0%	0.73-0.0001	mean	Experiment	2008	69 <sup>a</sup>	

			4th day of adulthood)													
72	<i>Caenorhabditis elegans</i>	Nematode	Multiple diets varying in glucose concentration (0.05%, 0.5%, 1%, 2%, 10% and 20%)	Fast	positive	36	days	n	15.0%	80.0%	NA	mean	Experiment	2008	70	
73	<i>Rattus norvegicus</i>	Rat	Normal/ad libitum diet and 30% CR diet	Fast	positive	215	weeks	n	0.0%	22.7%	<0.05	mean	Experiment	2008	71 <sup>a</sup>	
74	<i>Saccharomyces cerevisiae</i>	Yeast	Normal diet (2%) and CR diet (0.5%) using glucose and 9 alternative monosaccharide carbon sources	Fast	positive	25	days	n	NA	10 <sup>5</sup>	NA	mean	Experiment	2007	72	
75	<i>Caenorhabditis elegans</i>	Nematode	Normal/ad libitum diet of live bacteria and CR diet of growth-arrested bacteria	Fast	positive	40	days	n	NA	31.0%	0.0001	mean	Experiment	2007	73	
76	<i>Mus musculus</i>	Mouse	Normal/ad libitum diet and 40% CR diet	Fast	positive	48	months	n	NA	24.0%	0.0001	median	Experiment	2007	74 <sup>a</sup>	
77	<i>Drosophila melanogaster</i>	Fruit fly	Several diets increasing in concentration (concentrations differed for each	Fast	variable	75	days	n	10.0%	40.0%	0.0001	median	Experiment	2007	75	

diet, all were increasing from an initial low, CR, concentration); diets were sugar, agar and several yeast options with various quality

78	<i>Saccharomyces cerevisiae</i>	Yeast	Normal diet (2% glucose) and CR diet (0.5% glucose)	Fast	positive	55	generations	n	NA	23.0%	NA	mean	Experiment	2007	76
Study	Scientific name	Common name	Treatment	Life history speed	CR response	Study length	Study length units	Interaction	Effect size (min)	Effect size (max)	p-value	Longevity measure	Manuscript type	Date	Ref.
79	<i>Elosa worallii</i>	Rotifer	Normal/ad lib diet (1.5mg C/l) and CR diet (0.15mg C/l); CR diets applied for different lengths of time (days) with one permanent CR diet	Fast	positive	26	days	y	0.0%	47.0%	0.01	median	Experiment	2007	77 <sup>a</sup>
80	<i>Cephalodella acidophila</i>	Rotifer	Normal/ad lib diet (1.5mg C/) and CR diet (1.5mg C/)	Fast	negative	8	days	n	NA	56.0%	0.001	median	Experiment	2007	77 <sup>a</sup>

81	<i>Podospora anserina</i>	Filamentous fungus	Normal/ad libitum diet and CR diet (100-fold reduction in glucose); fungus with plasmid strain and fungus without plasmid strain given diets	Fast	variable	700	hours	y	10.0%	45.0%	NA	mean	Experiment	2007	78
82	<i>Saccharomyces cerevisiae</i>	Yeast	Diets varying in glucose concentration (0.05%, 0.5% and 2%)	Fast	positive	50	generations	n	10.0%	30.0%	NA	mean	Experiment	2007	79 <sup>a</sup>
83	<i>Drosophila melanogaster</i>	Fruit fly	Normal diet (15% glucose) and CR diet (5% glucose)	Fast	no effect	91	days	n	NA	0.0%	>0.05	mean	Experiment	2007	80 <sup>a</sup>
84	<i>Saccharomyces cerevisiae</i>	Yeast	Normal diet (2% glucose) and CR diet (0.5% glucose)	Fast	positive	4	days	n	NA	40.0%	<0.05	mean	Experiment	2007	81
85	<i>Saccharomyces cerevisiae</i>	Yeast	Normal diet (2% glucose) and CR diet (0.5% glucose)	Fast	positive	15	days	n	80.0%	90.0%	NA	mean	Experiment	2007	82
86	<i>Caenorhabditis elegans</i>	Nematode	Normal/ad libitum diet, 90% CR diet and absence of food diet; absence of	Fast	positive	50	days	y	20.0%	50.0%	NA	median	Experiment	2006	83 <sup>a</sup>

Study	Scientific name	Common name	Treatment	Life history speed	CR response	Study length	Study length units	Interaction	Effect size (min)	Effect size (max)	p-value	Longevity measure	Manuscript type	Date	Ref.
87	<i>Saccharomyces cerevisiae</i>	Yeast	Diets varying in glucose concentration (0.005%, 0.05%, 0.5% and 2%)	Fast	positive	70	generations	n	10.0%	19.5%	0.0001	mean	Experiment	2006	84
88	<i>Romalea microptera</i>	Lubber grasshopper	Normal/ad libitum diet, 40% CR diet and 30% CR diet; additional time diet (late onset CR diet), ad lib food for first 49 days then 40% CR until death	Fast	positive	150	days	y	60.0%	98.0%	0.0001	median	Experiment	2006	85 <sup>a</sup>
89	<i>Mus musculus</i>	Mouse	Normal/ad libitum diet and 30% CR diet; gradual 30% CR by receiving 90% of ad lib diet in initial week, 80% in second week and 70% throughout the rest of the study.	Fast	positive	1382	days	n	19.0%	25.0%	<0.05	median	Experiment	2006	86 <sup>a</sup>

90	<i>Drosophila melanogaster</i>	Fruit fly	Multiple diets varying in yeast concentration (1%, 2%, 4%, 8 and 16%)	Fast	positive	68	days	n	50.0 %	67.0%	0.0001	median	Experiment	2006	87
91	<i>Drosophila melanogaster</i>	Fruit fly	Several diets increasing in concentration; brewer's yeast, sucrose, agar and tegosept, 0.5X, 1X, 1.5X and 3X concentrations	Fast	positive	100	days	n	42.0 %	121.0 %	0.0001	median	Experiment	2005	88 <sup>a</sup>
92	<i>Mus musculus</i>	Mouse	Normal/ad libitum diet and 40% CR diet; individual caged singly or multiply (4 individuals)	Fast	positive	1460	days	y	17.0 %	22.0%	0.001	median	Experiment	2005	89 <sup>a</sup>
93	<i>Saccharomyces cerevisiae</i>	Yeast	Normal diet (2% glucose) and CR diet (0.05% glucose)	Fast	positive	60	generations	n	16.0 %	21.0%	NA	mean	Experiment	2005	90
94	<i>Saccharomyces cerevisiae</i>	Yeast	Normal diet (2% glucose) and CR diet; for CR diet the first 3 days was 2% glucose medium followed by starvation	Fast	positive	40	generations	n	NA	170.0 %	NA	mean	Experiment	2005	91

95	<i>Saccharomyces cerevisiae</i>	Yeast	Normal diet (2% glucose) and CR diet (0.05% glucose)	Fast	positive	60	generations	n	29.0%	52.0%	NA	mean	Experiment	2005	92
Study	Scientific name	Common name	Treatment	Life history speed	CR response	Study length	Study length units	Interaction	Effect size (min)	Effect size (max)	p-value	Longevity measure	Manuscript type	Date	Ref.
96	<i>Ceratitis capitata</i>	Mediterranean fruit fly	Multiple diets varying in yeast concentration (0%, 1%, 1.96%, 4.76%, 5%, 7.7% and 25%). Diets given to virgin and mated males and females	Fast	variable	60	days	y	0.0%	33.0%	0.0001	median	Experiment	2005	93
97	<i>Saccharomyces cerevisiae</i>	Yeast	Normal diet (2% glucose) and CR diet (0.5% glucose)	Fast	positive	60	generations	n	16.0%	48.0%	NA	mean	Experiment	2005	94
98	<i>Drosophila melanogaster</i>	Fruit fly	Diets of yeast:sugar medium; diets varied in yeast and sugar concentration (low and high)	Fast	variable	65	days	y	8.7%	82.6%	0.0001	median	Experiment	2005	95 <sup>a</sup>
99	<i>Rattus norvegicus</i>	Rat	Ad lib diet and varying calorie diets (high and low) with two feeding regimes;	Fast	positive	138	weeks	y	6.67%	9.96%	0.001	mean	Experiment	2005	96 <sup>a</sup>

			constant regime was either high and low calorie diets, switched regimes were moving from ad lib to high and low diets													
100	<i>Ceratitis capitata</i>	Mediterranean fruit fly	High quality and low quality diets with animals switching between diets with various probabilities and spending time on each diet for various lengths of time during lifetime	Fast	variable	80	days	y	41.0%	57.0%	0.0001	mean	Experiment	2005	97	
101	<i>Saccharomyces cerevisiae</i>	Yeast	Normal diet (2% glucose) and CR diet (0.1% glucose); at a certain density, for both diets, transferred to water	Fast	negative	11	days	y	NA	60.0%	NA	mean	Experiment	2005	98	
102	<i>Saccharomyces cerevisiae</i>	Yeast	Normal diet (2% glucose) and CR diet (0.5% glucose)	Fast	positive	4	days	n	NA	NA	NA	mean	Experiment	2004	99	



Study	Scientific name	Common name	Treatment	Life history speed	CR response	Study length	Study length units	Interaction	Effect size (min)	Effect size (max)	p-value	Longevity measure	Manuscript type	Date	Ref.
103	<i>Podospora anserina</i>	Filamentous fungus	Normal/ad libitum diet and CR diet (100-fold reduction in glucose); fungus with plasmid strain and fungus without plasmid strain given diets	Fast	variable	1500	hours	y	2.0%	400.0%	0.0001	mean	Experiment	2004	100 <sup>a</sup>
104	<i>Saccharomyces cerevisiae</i>	Yeast	Diets varying in glucose concentration (0.05%, 0.1%, 0.5% and 2%)	Fast	positive	60	generations	n	15.0%	25.0%	<0.05	mean	Experiment	2004	101 <sup>a</sup>
105	<i>Saccharomyces cerevisiae</i>	Yeast	Normal diet (2% glucose) and CR diet (0.5% glucose)	Fast	positive	60	days	n	NA	85.0%	NA	mean	Experiment	2004	102
106	<i>Drosophila melanogaster</i>	Fruit fly	Normal/ad libitum diet and 50% CR diet. Constant diet regime given to fully mated and once-mated females; switched diet regime (starting	Fast	positive	80	days	y	36.0%	63.0%	0.0001	median	Experiment	2004	103 <sup>a</sup>

			on one then switching to another for both diets) given to once-mated females													
107	<i>Mus musculus</i>	Mouse	Normal/ad libitum diet and CR diet; gradual CR by receiving 20% CR for first month then 41% CR thereafter, CR initiated at 14 months.	Fast	positive	50	months	n	NA	13.0%	0.0001	mean	Experiment	2004	104 <sup>a</sup>	
108	<i>Mus musculus</i>	Mouse	Normal/ad libitum diet and CR diet; gradual CR by receiving 17% CR for first month then 44% CR thereafter, CR initiated at 19 months.	Fast	positive	46	months	n	NA	15.0%	0.0001		Experiment	2004	105	
109	<i>Saccharomyces cerevisiae</i>	Yeast	Normal diet (2% glucose) and CR diet (0.5% glucose)	Fast	positive	50	generations	n	NA	30.0%	NA	mean	Experiment	2004	106 <sup>a</sup>	
Study	Scientific name	Common name	Treatment	Life history speed	CR response	Study length	Study length units	Interaction	Effect size (min)	Effect size (max)	p-value	Longevity measure	Manuscript type	Date	Ref.	

110	<i>Drosophila melanogaster</i>	Fruit fly	Diets of yeast:sugar medium; diets varied in yeast and sugar concentration (low and high)	Fast	variable	50	days	y	19.0%	67.0%	0.0001	mean	Experiment	2003	107
111	<i>Saccharomyces cerevisiae</i>	Yeast	Normal diet (2% glucose) and CR diet (0.5% glucose)	Fast	positive	55	generations	n	NA	51.0%	NA	mean	Experiment	2003	108
112	<i>Rattus norvegicus</i>	Rat	Normal/ad libitum diet and 40% CR diet; CR initiated at 6 weeks old.	Fast	positive	1200	days	n	NA	25.0%	NA	mean	Experiment	2003	109
113	<i>Saccharomyces cerevisiae</i>	Yeast	Normal diet (2% glucose) and CR diet (0.5% glucose)	Fast	positive	55	generations	n	NA	26.0%	NA	mean	Experiment	2002	110
114	<i>Mus musculus</i>	Mouse	Normal/ad lib diet, 40% CR diet and CR fasting diet; on CR fasting diet individuals were on ad lib diet and fasted one day a week; CR initiated at 10 months old.	Fast	positive	96	weeks	n	14.0%	24.0%	0.001	mean	Experiment	2002	111 <sup>a</sup>

115	<i>Drosophila melanogaster</i>	Fruit fly	Normal/ad libitum diet and 66% CR diet	Fast	positive	78	days	n	NA	82.0%	NA	mean	Experiment	2002	112
116	<i>Mus musculus</i>	Mouse	Normal/ad libitum diet and CR diet; CR initiated through gradual food reduction to achieve body weight of 60-70% of ad lib cohort, CR initiated at 12 weeks of age	Fast	positive	78	weeks	n	15.7%	63.5%	0.02	mean	Experiment	2002	113 <sup>a</sup>
117	<i>Saccharomyces cerevisiae</i>	Yeast	Normal diet (2% glucose) and CR diet (0.5% glucose)	Fast	positive	50	generations	n	NA	24.0%	NA	mean	Experiment	2000	114
118	<i>Mus musculus</i>	Mouse	Normal/ad lib diet and 40% CR diet; CR initiated at 4 months old.	Fast	positive	45	months	n	NA	43.0%	NA	mean	Experiment	1994	115 <sup>a</sup>
Study	Scientific name	Common name	Treatment	Life history speed	CR response	Study length	Study length units	Interaction	Effect size (min)	Effect size (max)	p-value	Longevity measure	Manuscript type	Date	Ref.
119	<i>Mus musculus</i>	Mouse	Normal/ad lib diet and CR diet; CR initiated gradually, first two months 20% CR after which 40% CR; CR	Fast	positive	32	months	n	NA	9.0%	NA	mean	Experiment	1993	116

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			initiated at 14 months old.													
120	<i>Mus musculus</i>	Mouse	Normal/ad lib diet and CR diet; CR diet had 50% lipids and 35% carbohydrates replaced by fibre, estimated CR of 12-22%	Fast	positive	32	months	n	NA	55.5%	NA	mean	Experiment	1991	117	

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