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February 15, 2004

VIA E-MAIL & FIRST CLASS MAIL

Andrew A. Chirls, Esq.
Wolf, Block, Schorr and Solis-Cohen LLP
1650 Arch Street, 22nd Floor
Philadelphia, PA 19103

Re: In Re: *Diet Drugs Products Liability Litigation*
MDL No. 1203

Dear Mr. Chirls:

Over the past several months we have conducted an exhaustive analysis of the alleged epidemiological basis of Wyeth and Class Counsel's projections regarding the number of anticipated Matrix claims. In conducting our analysis we provided our experts with the material submitted by Wyeth and Class Counsel at the fairness hearing and asked that they reconstruct Wyeth and Class Counsel's projections. To our surprise our expert concluded that there was a sound basis for the projections made by Class Counsel's epidemiologist, Dr. Steven Goodman. However, we have come to discover that not only were Dr. Goodman's calculations apparently ignored, but also that there is evidence that there may have been an intentional effort to reduce the number of projected claimants.

I have attached for your review the declaration of Paul N. Hopkins, M.D., MSPH. I do not believe that Dr. Hopkins' conclusions can be rebutted. Among other things Dr. Hopkins has stated:

> Having reviewed all of the material submitted by Class Counsel to support their claims regarding the number of potential class members who could possibly qualify for Fund B benefits, I find major discrepancies between the projections made on behalf of Class Counsel and what may easily be derived from published sources. These discrepancies are of a magnitude that is difficult to believe they were made without a preconceived effort to minimize the extent of the potential damage caused by fenfluramine and dexfenfluramine.

As you are aware, the disparity between Wyeth and Class Counsel's projections and the number of claims that have been actually filed, has served as the basis for virtually every effort undertaken by the Trust, Wyeth and Class Counsel to limit the processing and payment of claims. As the fiduciary, the Trust cannot ignore evidence that these projections may not only have been wrong, but may have been part of an intentional effort on the part of the parties to underestimate the number of potential claims.

It is deeply distressing that a 3.55 billion dollar settlement, which ultimately resulted in the waiver of the constitutional rights of millions of Americans, was based upon what may have been an intentional misrepresentation.

Both Class Counsel and Wyeth faced monumental challenges at the time of the settlement. Confronted with at least six million people who had been exposed to these deadly drugs and a rate of disease that ranged from approximately 10% to 30% of the exposed population, the prospects of any meaningful settlement must have seemed bleak.

Class Counsel relied upon three expert opinions to support their projections. epidemiologist, Dr. Steven Goodman; cardiologist, Dr. Dean Karalis; and economist, Dr. Samuel Kursh. Dr. Goodman based his projections of potential FDA qualifying class members upon a meta-analysis of the available epidemiological studies at the time. To be quite frank, his projections are almost identical to those of Dr. Paul N. Hopkins as stated in his declaration, to the extent that they predicted the number of potential FDA positives in the exposed population. Dr. Goodman however provided no breakdown between the various grades of regurgitation, while Dr. Hopkins does. Based upon Dr. Goodman's projections the following table can be compiled.

PONDIMIN AND REDUX: 6,000,000 TOTAL USERS:

DAYS OF THERAPY	USERS	FDA+AI	FDA+MR
1-30	2,670,000	109,470	93,450
31-60	1.216.000	62,016	42,560
61-90	672.000	40,992	23,520
91-120	442.000	31,381	15,470
121-150	310.000	25,110	10,850
151-180	218.000	19,838	7,630
181-210	164.000	16,564	5,740
211-240	106,000	11,766	3,710
241-270	80,000	9,680	2,800
271+	122,000	17,690	4,270
TOTAL		344,507	210,000

Total FDA+ AI	=	344,507
Total FDA+ MR	=	210,000
Total FDA+		554,507

This results in a minimum potential FDA positive population of 544,507 of which 237,012 would have used the drugs for greater than 60 days, while 307,496 would have used the drugs for 60 days or less. The numbers are staggering.

The Matrix was set up to assure that compensation would be based on severity of injury. However the Matrix places severe regurgitation at Level I and moderate mitral regurgitation at Level II. Common sense alone seems to indicate that this doesn't make sense. But as we are all aware, Level II claims also require the presence of a complicating condition one of which is left atrial enlargement. Left atrial enlargement is a common finding in obese populations (such as fen-phen users), and is very likely to be found in those with moderate or greater levels of mitral regurgitation.

Surprisingly, when one goes back to look at how Class Counsel projected the number of claims that would fall into Level I as opposed to Level II there is absolutely no detailed analysis available for review. The estimate of the number of potential Matrix qualifiers is based solely on the opinion of Dr. Dean Karalis, who stated that he expected anywhere from 5%-10% of FDA positives to eventually progress to Matrix Level. As Dr. Hopkins has shown in his declaration and analysis, there is no support for this critical assumption.

Applying Dr. Karalis' analysis, Class Counsel should have concluded that there would have been anywhere from 11,850 to 23,701 claims for Matrix A benefits and from 15,375-30,750 claims for Matrix B benefits. However we know that there projections were even lower.

Even using Dr. Karalis' flawed conclusions, the numbers were still far too high. A third reduction occurred, that is the final projection by Dr. Samuel Kursh. As Dr. Hopkins states in his declaration, Dr. Kursh actually ***eliminated those class members with greater than 60 days of use who had FDA positive mitral regurgitation*** from his calculations. Thus, right from the beginning, 210,000 FDA+ class members were removed from the projections with no explanation. It should come us no surprise then that the parties have claimed that there are an inordinate number of claims based upon moderate mitral regurgitation, since they deliberately did not include them in their calculations.

Even these efforts did not result in enough of a reduction.

Next, when calculating those who would be FDA positive with less than 60 days of use, Dr. Kursh applied the background rate of 2.1% as opposed to the exposed rate of 3.5% for FDA+ mitral regurgitation, resulting in an additional undercounting.

Finally a reduction in the number of FDA+ aortic claims for those who took the drugs for greater than 60 days occurred when Dr. Kursh did not include the background rate in his calculations and failed to follow Dr. Goodman's conclusions that the rate of disease increases 1% for each month of use. Dr. Kursh does not apply this multiple until month three.

Were these errors isolated it would be easy to claim that they were inadvertent, but they were clearly calculated and premeditated.

We have presented ***the most conservative estimate*** of the number of potential claims that should have been expected by way of Dr. Hopkins' declaration. A side by side comparison of Dr. Hopkins' projections to those offered to the Court at the time of the fairness hearings is as follows:

	Estimate for settlement	Hopkins, 2004
Number exposed	6,000,000	6,000,000
Duration of use distribution	provided by Wyeth	Same
FDA+ AR, number expected		
Used =60 days	237,020	217,610
Used >60 days	85,520	256,084
FDA+ MR, number expected		
Used =60 days	126,000	119,817
Used >60 days	0	79,546
Matrix A, number expected - total	8345	
Level I (severe AR+MR)	7511	21,545
Level II	834	24,350 – 49,161 (moderate MR+LAE only)
Matrix B (use =60 days), number - total	27,227	
Level I (severe AR+MR)	24,504	27,325
Level II	2,723	36,678 – 74,049 (moderate MR+LAE only)

We invite you to put Dr. Hopkins' findings to the test. This may well be a case of "mutual mistake." Given the striking discrepancies between the numbers projected for the Court at the time of the fairness hearings, and the supported numbers offered by Dr. Hopkins (and, indeed, by Class Counsel's epidemiologist Dr. Goodman), it is difficult to ignore the possibility that something more intentional could have been the cause.

The metamorphosis of the Trust from fiduciary to adversary has been unfortunate. Nonetheless, as counsel for the fiduciary your duty, and that of the AHP Settlement Trust, is clear.

Respectfully,

Mario D'Angelo

Enclosure: Declaration of Paul N. Hopkins, M.D.

IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF PENNSYLVANIA

IN RE: DIET DRUGS (Phentermine/ Fenfluramine/Dexfenfluramine) PRODUCTS LIABILITY LITIGATION	:	MDL Docket No. 1203
THIS DOCUMENT RELATES TO: SHEILA BROWN, SHARON GADDIE, VIVIAN NAUGLE, QUINTIN LAYER, and JOBY JACKSON-REID, individually and all others similarly situated, Plaintiffs, v. AMERICAN HOME PRODUCTS CORPORATION, Defendant.	:	CIVIL ACTION NO. 99-20593

DECLARATION OF PAUL N. HOPKINS, M.D., MSPH

I, Paul N. Hopkins, M.D., MSPH, hereby declare that the following statements are true to the best of my knowledge, information and belief:

1. I am a physician duly licensed to practice in the State of Utah. I am board certified in Public Health and General Preventive Medicine. My areas of expertise include cardiovascular epidemiology, particularly coronary artery disease risk factors, hypertension, and cardiovascular genetics. My clinical emphasis has been lipid intervention and reduction of coronary risk. I am a Professor of Internal Medicine at the University of Utah School of Medicine, Co-Director of Cardiovascular Genetics (a sub-division of the Cardiology Division), and Director of the Family Lipid Clinic in Preventive Cardiology. Annexed is a copy of most recent Curriculum Vitae.
2. I have been asked to evaluate and analyze the methodology used by Class Counsel and their experts to predict the total number of potential claims for

Fund B benefits (Matrix Benefits) that could be anticipated at the time the settlement with American Home Products Corporation was approved.

3. I have also been asked to evaluate those projections and to comment on whether they had or have today any scientific basis or rationale.
4. Drawing from my past research relating to diet drug exposure, I have also completed a meta-analysis of all of the scientifically reliable epidemiological studies relating to fenfluramine and/or dexfenfluramine and valvular regurgitation. My analysis allowed me to construct a model intended to predict the prevalence of valvular regurgitation in the exposed population and includes a projection of those who would qualify for Fund B benefits based upon the presence of FDA positive mitral regurgitation accompanied by one or more of the complicating factors required by the settlement.

SUMMARY OF MY OPINION

5. Having reviewed all of the material submitted by Class Counsel to support their claims regarding the number of potential class members who could possibly qualify for Fund B benefits, I find major discrepancies between the projections made on behalf of Class Counsel and what may easily be derived from published sources. These discrepancies are of a magnitude that is difficult to believe they were made without a preconceived effort to minimize the extent of the potential damage caused by fenfluramine and dexfenfluramine.
6. I performed a meta-analysis of the prevalence and severity of valvular regurgitation including studies by Wadden,[1] Burger,[2] Dahl,[3] Kancherla,[4] Lepor,[5] Teramae,[6] Khan,[7] Weissman,[8] Shively,[9] Hensrud,[10] Ryan,[11] Gardin,[12] Jollis,[13] and Davidoff.[14] A summary of my findings are given in the table immediately below.

	Estimate for settlement	Hopkins, 2004
Number exposed	6,000,000	6,000,000
Duration of use distribution	provided by Wyeth	same
FDA+ AR, number expected		
Used =60 days	237,020	217,610
Used >60 days	85,520***	256,084
FDA+ MR, number expected		
Used =60 days	126,000	119,817
Used >60 days	0*	79,546
Matrix A, number expected - total	8345	
Level I (severe AR+MR)	7511	21,545
Level II (moderate MR+LAE only)	834	24,350 – 49,161**
Matrix B (use =60 days), number - total	27,227	
Level I (severe AR+MR)	24,504	27,325
Level II (moderate MR+LAE only)	2,723	36,678 – 74,049**

* Note that in the settlement, all MR was included only in those exposed 60 days or less and only baseline rate (2.1%) was used, rather than exposed rate.

** Percent of patients with MR having left atrial enlargement were derived from two sources. The upper estimate (74.7% of those with moderate MR) was reported in the LIFE study, a analysis of persons with hypertension and left ventricular dysfunction.[15] The lower estimate comes from a Canadian study of healthy, normotensive obese

subjects (37%).[16] In the HyperGEN study, factors which correlate with MR and AR have been published.[17] In further, unpublished analyses of that data set, Dr. Hopkins estimated that among the entire population studied, 41% of those with moderate MR and BMI 27+ also had left atrial enlargement (diameter >4.0 cm) – an estimate the is within the range of the published studies.

*** The reason for the large discrepancy of FDA+ AR in those using drug >60 days is that no baseline rate was included in the percent estimates for the settlement projections.

7. The estimate that out of an exposed population of 6 million individuals only 8,345 individuals would qualify for Matrix A benefits while only 27,227 would qualify for Matrix B, under the settlement criteria is at least 3-fold too low and as much as 8-fold under-estimated.
8. During my review of just how these numbers were calculated I found a series of errors made at each step and assumptions that resulted in gross underestimates of the number affected.
9. These errors included the use of the background unexposed rate of mitral regurgitation, in lieu of the exposed rate, by Dr. Samuel Kursch to calculate the number class members who would have FDA positive mitral regurgitation. Further, this background rate was only applied to those who used the drugs 60 days or less. The net result of this failure is an under counting of those who have FDA positive regurgitation, most obviously in those using drugs 61 days or longer.
10. Particularly troubling is the total lack of any calculations by any of the experts employed by Class Counsel regarding the number of potential claims for

Matrix Level II benefits. This oversight results in a larger discrepancy when one considers that according to the epidemiology relied upon by Class Counsel there would be expected to be 210,000 class members who would be suffering from FDA positive mitral regurgitation (3.5% applied to 6,000,000 users). In my review of the documents and reports which make up the fairness hearing record, I was unable to find any analysis whatsoever as to how many of these class members would also have any of the other factors which would allow them to qualify for level II benefits. As one of the qualifying complications is left atrial enlargement and considering that left atrial enlargement is very common in overweight persons, surely some calculation should have been made regarding how many of them would also have left atrial enlargement.

11. According to published medical studies available at the time of the settlement, a large percent of overweight persons with moderate mitral regurgitation would be expected to have LAE (see footnotes for table above). This was apparently overlooked in Class Counsel's projections, either ignorantly or knowingly.

THE CLAIMS PROJECTIONS RELIED UPON BY CLASS COUNSEL AND WYETH

12. In preparation of my analysis I was provided with the following material:

    a) Declaration of Dean G. Karalis, M.D., dated February 29, 2000, (Diet Drug Class Exhibit P0095), with attachments;

    b) Declaration and Supplemental Declaration on Sanjiv Kaul, M.D., dated March 6, 2000, (Diet Drug Class Exhibit AHP609), with attachments;

c) Declaration of Steven N. Goodman, M.D., M.H.S., Ph.D., dated February 28, 2000 and Supplemental Declaration dated March 20, 2000, (Diet Drug Class Exhibit P0090), with attachments;

d) Expert report, Center For Forensic Economic Studies, dated March 24, 2000, (Diet Drug Class Exhibit P0094), with attachments;

e) Declaration (Feb. 28, 2000) and Supplemental Declaration (May 7, 2000) of Walter F. Stewart, Ph.D., M.P.H., (Diet Drug Class Exhibit AHP611), with attachments;

f) Declaration (Mar. 24, 2000) and Supplemental Declaration (May 8, 2000) of Dr. Mark McClellan, (Diet Drug Class Exhibit AHP614), with attachments;

15. The projections that formed the basis of the settlement we recalculated based upon the submissions of Goodman, Karalis and Kursh. Each building upon the other.

16. The foundation of the projections is based upon several assumptions. First, it is accepted by Class Counsel that the entire population of exposed class members consists of 6 million users. This number is derived from a marketing study supplied by Wyeth. While this estimate of ever-users may well be an under-estimate, I have made my projections based on this assumption of 6 million users. Of the six million class members exposed to fenfluramine and/or dexfenfluramine it is assumed that 4 million took Pondimin and 2 million took Redux. In my estimates I have combined these since associated risk is generally assumed to be identical.

increases 1% per month for the first nine months of use. For those who took the drugs for more than 9 months the risk of developing FDA positive aortic regurgitation is 14.5%.

22. With respect to severity, he concluded that 16.5% of the total exposed population who have FDA positive aortic regurgitation will have moderate to severe levels of aortic regurgitation

23. In determining the rate of FDA Positive mitral regurgitation Dr. Goodman found that the baseline rate of FDA positive mitral regurgitation was 2.1%. For those exposed to Pondimin and/or Redux he concluded that the overall risk of FDA positive mitral regurgitation was 3.5%, with no relationship to duration of exposure.

24. Based upon Dr. Goodman's conclusions the following projections can be made with respect to the number of potential FDA positive class members.

Pondimin and Redux: 6,000,000 total users:

Days of Therapy	Users	FDA+AI	FDA+MR
1-30	2,670,000	109,470	93,450
31-60	1,216,000	62,016	42,560
61-90	672,000	40,992	23,520
91-120	442,000	31,381	15,470
121-150	310,000	25,110	10,850
151-180	218,000	19,838	7,630
181-210	164,000	16,564	5,740
211-240	106,000	11,766	3,710
241-270	80,000	9,680	2,800
271+	122,000	17,690	4,270

Total FDA+ AI= 344,508
Total FDA+ MR= 210,000

Total FDA+ 544,508

CLASS COUNSEL'S MATRIX PROJECTION

25. As will shown below, there are few differences with respect to my calculations and analysis of the total number of FDA+ class members, and the calculations made by Dr. Goodman. However, I can find no support for the subsequent calculations made by Dr. Samuel Kursh regarding the projected

17. The rate of exposure in turn is determined by Wyeth's marketing data and is presented below.

Pondimin: 4,000,000 total users:

Days of Therapy	Percentage	Users
1-30	39.2%	1,568,000
31-60	20.9%	836,000
61-90	11.9%	476,000
91-120	8.3%	332,000
121-150	6.0%	240,000
151-180	4.3%	172,000
181-210	3.3%	132,000
211-240	2.1%	84,000
241-270	1.6%	64,000
271+	2.4%	96,000

Redux: 2,000,000 total users:

Days of Therapy	Percentage	Users
1-30	55.1%	1,102,000
31-60	19.0%	380,000
61-90	9.8%	196,000
91-120	5.5%	110,000
121-150	3.5%	70,000
151-180	2.3%	46,000
181-210	1.6%	32,000
211-240	1.1%	22,000
241-270	0.8%	16,000
271+	1.3%	26,000

COMPUTING THE RATE OF FDA POSITIVE REGURGITATION

19. In calculating the number of potential class members who would have FDA positive levels of valvular regurgitation Class Counsel relied upon the declaration of Dr. Goodman.

20. Dr. Goodman in his Supplemental Declaration dated March 20, 2000 provides an analysis of the available epidemiological studies and offers his opinions as to the prevalence of FDA positive levels of regurgitation.

21. With respect to the prevalence of FDA Positive aortic regurgitation Dr. Goodman states that the baseline risk of FDA positive aortic regurgitation is 3.1%. He further states that with exposure to Pondimin and/or Redux the rate

number of matrix qualifying class members. In fact Dr. Kursh made several errors which contradicted many of Dr. Goodman's conclusions.

26. The most glaring error made by Dr. Kursh was his use of Dr. Goodman's calculation of the background rate of FDA+ mitral regurgitation (2.1%) instead of the exposed rate of 3.5% and applying these number only to persons using drug 60 days or less.

27. The settlement sets forth five levels of injury which were to be compensated. The criteria for qualifying is set forth in detail in the agreement and was made a part of the material submitted to me for review. For the purposes of this analysis, only Level I and Level II are addressed, since the overwhelming number of class members will qualify at these two levels.

28. Matrix Level I is defined as severe aortic or mitral regurgitation without complicating factors, measured according to the Sigh criteria.[18]

29. Claims based upon a finding of moderate mitral regurgitation are required to meet the requirements for level II compensation as set forth in the settlement agreement. The settlement requires that in addition to a finding of moderate mitral regurgitation, one or more of the following must also be present:

> (b) Moderate MR (20% 40%RJA/LAA) or Severe MR (>40%RJA/LAA) with one or more of the following:
> i) Pulmonary hypertension secondary to valvular heart disease with peak systolic pulmonary artery pressure >40 mm Hg measured by cardiac cauterizations or with a peak systolic pulmonary artery pressure >45 mm Hg measured by Doppler electrocardiography,at rest, utilizing the procedures described in Section F.2.(a)(i);
>
> ii) Abnormal left atrial supero-inferior systolic dimension >5.3 cm (apical four chamber view) or abnormal left atrial antero-posterior systolic dimension >4.0 cm (parasternal long axis view)measured by 2-D directed M-mode or 2-D echocardiography with normal sinus rhythm using sites of measurement recommended by the American Society of Echocardiography;
>
> iii) Abnormal left ventricular end-systolic dimension e45 mm 20 by M-mode or 2-D Echocardiogram;

iv) Ejection fraction of ≤60%;

v) Arrhythmias,defined as chronic atrial fibrillation/flutter that cannot be converted to normal sinus rhythm,or atrial fibrillation/flutter requiring ongoing medical therapy,either of which are associated with left atrial enlargement;as defined in Section F.2.(b)(ii).

30. From my analysis of the material submitted to support the settlement, there was no effort made to estimate the number of class members who would qualify initially for level II benefits based upon the presence of moderate or greater mitral regurgitation and any of the other factors listed above.

31. Instead Dr. Kursh relies upon a series of assumptions provided to him. These assumptions include the declaration of Dean G. Karalis, M.D., that out of the entire population of exposed FDA+ class members only 5-10% could be expected to enter and progress through the severity (payment) matrix.

32. None of the studies cited by Dr. Karalis in paragraph 43 of his declaration provide any data which would allow him to estimate how many people would qualify for level II benefits based upon one or more of the complicating factors cited in the settlement.

33. Thus relying solely upon Dr. Karalis' statements, Dr. Kursh concludes that out of the entire population of six million users only 8,345 class members could qualify for Matrix A benefits while 27,727 would qualify for Matrix B benefits. Of these, it was assumed that 90% would fall in level I and 10% in level II.

34. These assumptions result in entirely spurious estimates of those who would qualify for level II benefits.

35. Data existed at the time to permit a more detailed projection as to the number of class members who would initially qualify for benefits at Level I and Level II. The lack of any such effort to estimate the number of potential Matrix Level I is surprising when one considers that Dr. Goodman found that 16.5% of the total exposed population who have FDA positive aortic regurgitation will

have moderate to severe levels of aortic regurgitation. Based upon his findings approximately 57,000 class members would be afflicted with moderate or severe aortic regurgitation, a substantial number of who would qualify for Matrix benefits, even assuming Dr. Karalis' assumptions.

IT WAS AND IS POSSIBLE TO ACCURATELY CALCULATE THE NUMBER OF CLASS MEMBERS WHO WOULD QUALIFY FOR MATRIX LEVEL BENEFITS

36. Since 1997 there have been a number of well known published epidemiological studies which have examined the effects of fenfluramine and dexfenfluramine (cited in paragraph 6). All these studies except for Dahl[3] were included in my published analysis of relative risk.[19] In order to determine the prevalence of valvular regurgitation in the exposed population a meta-analysis was performed. Data regarding prevalence of all mild or greater aortic or mitral regurgitation reported in each of the cited studies was extracted along with reported levels of severity and exposure duration. Controls in these studies served as a means to estimate baseline (unexposed) levels of aortic and mitral regurgitation. To estimate overall prevalence of FDA+ valvular disease each study was weighted by number of subjects. An overall estimate of the distribution of severity was made. Aortic regurgitation was significantly related to duration of exposure. Prevalence was modeled as a non-linear logarithmic function of duration as implemented in SAS Proc NLIM (Statistical Analysis Package, Cary, North Carolina). Similar to Dr. Goodman's findings, mitral regurgitation was found not to be clearly related to duration of exposure. Therefore, an overall prevalence was calculated for all users. These estimates of prevalence were used in the attached spreadsheet to model projected number having regurgitation (exhibit A).

37. To determine of prevalence of left atrial enlargement in the exposed population I based my estimates upon several published studies.

38. The prevalence of left atrial enlargement increases dramatically with BMI. This is especially significant when one considers that the vast majority fen-phen users were overweight.

39. In one study it was found that in normotensive individuals with BMI >28, 37% of them were found to have left atrial size greater than 4.0 as measured in the posteroanterior dimension. This finding is notable because patients were excluded if they had no other potential factors that may have influenced left atrial size.[16]

40. In Gottdiener, et al,[20] BMI was the strongest predictor of LA size. Further, "mean left atrial size differed significantly ($p \leq 0.0001$ by ANOVA) across obesity categories. Based on the Tukey procedure, obese patients had a greater LA size (44.2 ± 5.7 mm) than overweight (41.6 ± 5.9 mm) or normal weight (38.9 ± 6.2 mm) patients." The obesity categories were >30, 27-30, and <27 BMI for obese, overweight, and normal weight respectively. The simple correlation between BMI or weight and LA size was between 0.36 and 0.40 (r, correlation coefficients). In this study, systolic and diastolic blood pressures were not determinants of LA size. This would suggest that over 50% of overweight persons would have LA size greater than 40 mm.

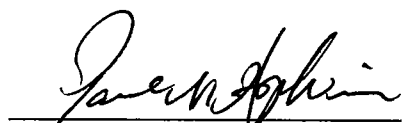
41. As Dr. Karalis alluded to in his declaration, there is also a relationship between mitral regurgitation and left atrial enlargement. In a study published in 1992, 92 patients had echocardiographic and angiographic examinations demonstrating MR. Severe regurgitation was found in 45 patients while 47 were found to have mild to moderate regurgitation. For those patients with mild-moderate mitral regurgitation the mean left atrial size was 46 ± 9, while the mean left atrial size was 51 ± 9 for those with severe mitral regurgitation.[21]

42. Based on the above, I performed estimates of the projected number affected at various levels of severity and compared them with estimates performed previously as part of the settlement. The table in paragraph 6 shows my findings.

CONCLUSION

43. The projections and estimates made by Class Counsel with respect to the number and types of potential claims for Matrix Benefits cannot be considered accurate or reliable. These estimates contain serious errors and severely underestimated, either intentionally or ignorantly, the number of injured people who could potentially qualify for benefits.

Dated: February 11, 2004



Paul N. Hopkins, M.D., MSPH

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14. Davidoff R, McTiernan A, Constantine G, Davis KD, Balady GJ, Mendes LA, Rudolph RE, Bowen DJ. Echocardiographic examination of women previously treated with fenfluramine: long-term follow-up of a randomized, double-blind, placebo-controlled trial. Arch Intern Med 2001; 161:1429-1436.
15. Gerdts E, Oikarinen L, Palmieri V, Otterstad JE, Wachtell K, Boman K, Dahlof B, Devereux RB. Correlates of left atrial size in hypertensive patients with left ventricular hypertrophy: the Losartan Intervention For Endpoint Reduction in Hypertension (LIFE) Study. Hypertension 2002; 39:739-743.
16. Sasson Z, Rasooly Y, Gupta R, Rasooly I. Left atrial enlargement in healthy obese: prevalence and relation to left ventricular mass and diastolic function. Can J Cardiol 1996; 12:257-263.
17. Palmieri V, Bella JN, Arnett DK, Oberman A, Kitzman DW, Hopkins PN, Rao DC, Roman MJ, Devereux RB. Associations of aortic and mitral regurgitation with body composition and myocardial energy expenditure in adults with hypertension: the Hypertension Genetic Epidemiology Network study. Am Heart J 2003; 145:1071-1077.
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19. Hopkins PN, Polukoff GI. Risk of valvular heart disease associated with use of fenfluramine. BMC Cardiovasc Disord 2003; 3:5.
20. Gottdiener JS, Reda DJ, Williams DW, Materson BJ. Left atrial size in hypertensive men: influence of obesity, race and age. Department of Veterans Affairs Cooperative Study Group on Antihypertensive Agents. J Am Coll Cardiol 1997; 29:651-658.
21. Burwash IG, Blackmore GL, Koilpillai CJ. Usefulness of left atrial and left ventricular chamber sizes as predictors of the severity of mitral regurgitation. Am J Cardiol 1992; 70:774-779.

Curriculum Vitae

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January 2004

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PERSONAL DATA

Birthdate:	September 13, 1952	Social Security #:	545-96-3972
Birthplace:	Fort Belvoir, Virginia	Medical License #:	Utah 173718-1205
Citizenship:	USA	DEA #:	AH 3263794
Ethnicity:	White		

EDUCATION

		Location	Major
Undergraduate:			
1976	B.S.	University of California at Los Angeles	Biochemistry
Advanced Degrees:			
1978	M.S.P.H.	UCLA School of Public Health	Nutrition
1984	M.D.	University of Utah School of Medicine	Medicine
Residency Training:			
1984 - 1985		Mayo Graduate School of Medicine	Internal Medicine
1985 - 1986		University of Utah	Preventive Medicine
Board Certification:			
1990		American Board of Preventive Medicine	

SCHOLASTIC HONORS

1976	Magna cum laude - Biochemistry, UCLA
1976	Phi Beta Kappa

PROFESSIONAL EXPERIENCE

2002 – present	Professor of Internal Medicine - University of Utah School of Medicine.
1993 - 2002	Associate Professor of Internal Medicine - University of Utah School of Medicine. Changed from Research to Tenure track February 2000.
1993 - 2002	Adjunct Associate Professor - Department of Foods and Nutrition, University of Utah.
1986 - 1993	Assistant Professor of Internal Medicine - University of Utah School of Medicine
1987 - 1993	Adjunct Assistant Professor - Department of Food and Nutrition, University of Utah.
1985 - 1986	Staff physician with Humana MedFirst - general and family primary care (30 hours/week).
1978 - 1986	Medical research with Roger R. Williams, M.D. at the University of Utah Department of Cardiovascular Genetics. Full and part time.
1978 - 1979	Laboratory technician for J. Walter Woodbury, Ph.D. in the Department of Physiology, University of Utah.

RESEARCH EXPERIENCE/AWARDS

1. "Genetic and Environmental Determinants of Hypertension". NIH R0-1 grant, 1981 - August 1992. Roger R. Williams, M.D., PI. Participating physician from 1986-1992.
2. "Characterization of Coronary Prone Pedigrees". NIH R0-1 grant 1981 - 1991. Roger R. Williams, M.D., PI. Participating physician 1986-1991
3. "Genetic Determinants of Response to Diet in Utah Pedigrees with Familial Hypercholesterolemia". CRC protocol #88-07. Pilot completed May 1991. Principal Investigator.
4. "A Double-Blind, Multicenter Study to Evaluate the Safety, Tolerability and Efficacy of Simvastatin and Placebo in Patients with Hyercholesterolemia". Sponsored by Merck, Sharpe and Dohme Research Labs. January 1, 1990 - March 31, 1991. Principal Investigator for Utah branch.
5. "Effect of Pravastatin on Controlling Hypercholesterolemia: A Special Patient Population Study". Bristol-Myers Squibb, December 1991 - June 1993. Principal Investigator for Utah branch.
6. "A Randomized, Double-Blind, Placebo-Controlled, Multicenter Study of Lovastatin as an Adjunct to Diet in the Treatment of Adolescent Males With Hypercholesterolemia of Familial Basis". Merck, Sharpe and Dohme Research Labs. December 1991 - December 1993. Principal Investigator for Utah branch.
7. "Non-modulation in Essential Hypertension". NIH grant. Collaboration with Gordon Williams, M.D., Richard Lifton, M.D., Ph.D., Robert Dluhy, M.D., and Norman Hollenberg, M.D. at the Brigham and Women's Hospital, Boston, Mass. Co-Investigator responsible for Utah branch of the study. 1986 - 1991.
8. "Genetics of Human Hypertension". NIH grant, July 1991 - May 1996. Continued as component of a SCOR May 1996 – present (renewed February 2001

as "SCOR Molecular Genetics of Hypertension. Project 1 Genetic Determinants of the Renin-Angiotensin-Aldosterone System Involved in the Pathogenesis of Hypertension" NIH 2 P50 HL55000-06), Gordon H. Williams, M.D., PI for SCOR. Principal Investigator for Utah clinical subcontract.

9. "Evaluation of Sibling Pairs: a Risk Intervention Trial (ESPRIT)". Zeneca Pharmaceutical Group, April 1992 - December 1996. Co-Principal Investigator of Utah site.
10. "A 54-WEEK Open Label Assessment of the Safety and Efficacy Profile of Atorvastatin as Compared to Fluvastatin, Lovastatin, Simvastatin, and Pravastatin When Used to Optimally Control Primary Hypercholesterolemia (Type IIa) and Mixed Dyslipidemia (Type IIb)". Parke-Davis and Pfizer, April 1997 - present. Principal Investigator for Utah site.
11. "A Study to Compare Remnant Like Particle-Cholesterol (RLP-C) immunoseparation Reagent Kit with Other Lipoprotein Remnant Methods in Measurement of Remnants in Patients with Type IIb, III, and IV Hyperlipoproteinemia". Otsuka America Pharmaceutical, Inc., June 1997 – November 1998. Principal Investigator for Utah site (of 2 clinical sites).
12. "Genetic Interactions and Atherosclerosis Risk in Familial Hypercholesterolemia". NIH Grant (R0-1). Principal Investigator. Funding August 8, 1992 - July 31, 1997. Total 5-year budget $1,485,488 direct costs.
13. "A Randomized, Double Blind, Parallel Group Evaluation of Cerivastatin 0.8 mg Compared to Cerivastatin 0.4 mg and Placebo / Pravastatin 40 mg Once Daily in Patients with Hypercholesterolemia". Bayer Corporation (ID 97-008), Feb 1998 – July 1999. Principal Investigator for Utah site.
14. "A Multi-Center, Randomized, Double Blind, Placebo Controlled, Parallel 8 Week Ambulatory Blood Pressure Monitoring Study of Three Dose Regimens of Omapatrilat Administered Once-Daily or Twice Daily in the Treatment of Mild to Moderate Hypertension". Bristol-Myers Squibb (CV 137-036), June 1998 – August 1999. Principal Investigator for Utah site.
15. "A 28-Week, Double Blind and Observer Blind to Lipid Values, Active Controlled, Randomized, Parallel-Group, Multicenter Study to Assess the Safety and Efficacy of Fluvastatin Slow Release Form (80 mg) Administered Once Daily at Bedtime in Patients with Primary Hypercholesterolemia Compared to Lescol 40 mg". Novartis Pharmaceuticals (XUO F351-00/001), May 1998 – November 1999. Principal Investigator for Utah site.
16. "A Double-Blind, Randomized, Placebo-Controlled, Crossover Trial of the Effects of Simvastatin on Plasma Lipids in Patients with Abnormal Lipoprotein Remnant Accumulation". Merck Medical School Grant. Approximately $60,000 direct costs. June 1999 – present. Principal Investigator
17. "A Double-Blind, Randomized, Placebo-Controlled Trial to Evaluate the Efficacy and Safety of Lovastatin in Adolescent Girls (protocol 083-01)". Merck & Co., Inc. September 1999 – December 2000. Principal Investigator for Utah site.
18. "A 24-Week Randomized Double-Blind Multicenter Multinational Trial to Evaluate the Efficacy and Safety of ZD4522 and Atorvastatin in the Treatment of Subjects with Heterozygous Familial Hypercholesterolemia (ZD4522IL/0030)". AstraZeneca Pharmaceuticals, October 1999 – June 2000. Principal Investigator for Utah site.
19. "A 24-Week Randomized Multicenter Trial to Evaluate the Efficacy and Safety of ZD4522 and NIASPAN, Alone and in Combination, in the Treatment of Subjects

with Type IIb and IV Hyperlipidemia (ZD4522IL/0029)". AstraZeneca Pharmaceuticals, November 1999 – December 2000. Principal Investigator for Utah site.

20. "A 12-Week Multicenter Randomized Double-Blind Placebo-Controlled Trial to Evaluate the Efficacy and Safety of ZD4522 (5, 10, 20, 40, and 80 mg) in the Treatment of Subjects with Hypertriglyceridemia (ZD4522IL/0035)". AstraZeneca Pharmaceuticals, November 1999 – January 2001. Principal Investigator for Utah site.
21. "A 12-Week Randomized Open-Label Multicenter Trial to Evaluate the Efficacy and Safety and Tolerability of ZD4522 and the Combination of ZD4522 and QUESTRAN Light in the Treatment of Subjects with Severe Hypercholesterolemia (ZD4522IL/0031)". AstraZeneca Pharmaceuticals, November 1999 – December 2000. Principal Investigator for Utah site.
22. "An Open-label, Multinational, Multicenter, Extension Trial to Assess the Long-Term Safety and Efficacy of ZD4522 in Subjects in the ZD4522 Clinical Trial Program (ZD4522IL/0034)". AstraZeneca Pharmaceuticals, April 2000 – present. Principal Investigator for Utah site.
23. "Genetics of Coronary Heart Disease". An ongoing collaboration between Cardiovascular Genetics and Myriad Genetics. Principal Investigator for Cardiovascular Genetics.
24. "A Randomized, Double-Blind, Placebo Controlled Trial of Once Per Day vs. Split Dosing of GT102-279 in Patients with Primary Hypercholesterolemia". Geltex Pharmaceuticals (GTC102-55-202), May 2000 – December 2000. Principal Investigator for Utah site.
25. "A Multicenter, Double-Blind, Randomized, Parallel, 28-Week Study to Evaluate the Efficacy and Safety of Simvastatin 80 mg/day Versus Atorvastatin 80 mg/day in Patients with Hypercholesterolemia (CHESS: Comparative HDL Efficacy and Safety Study)". Protocol number 188-00/ZOC488. Merck, December 2000 – present. Principal Investigator for Utah site.
26. "A Multicenter, Randomized, Double-Blind, Parallel Group, Multiple Dose Study of the Safety and Effectiveness of Cerivastatin vs. Placebo in Pediatric or Adolescent Patients with Heterozygous Familial Hypercholesterolemia (BAY-PEDS Trial)". Bayer, January 2001 – present. Principal Investigator for Utah site.
27. "A Dose-Ranging Study of NK-104 in Patients with Primary Hypercholesterolemia: NK-104-209". Sankyo Pharma Development, June 2001 – present.
28. "A Six-Week, Dose-Comparison Study to Evaluate the Safety and Efficacy of Rosuvastatin Versus Atorvastatin, Cerivastatin, Pravastatin, and Simvastatin in Subjects with Hypercholesterolemia (4522IL/0065) (STELLAR)". AstraZenica Pharmaceuticals, June 2001 – present.
29. "HyperGEN: Genetics of Left Ventricular Hypertrophy". NIH Grant - Donna K. Arnett, Ph.D. is PI for entire project. Principal Investigator for Utah site.
30. "Oxidation Risk Factors and IMT Progression in FH (Familial Hypercholesterolemia)". NIH Grant (R01 HL63349), 5-year award, September 2000 - present. Principal Investigator for grant.
31. "Genetic Epidemiology & Aging in Utah Pedigrees". NIH Aging Institute, 5-year award, March 2001 – present. Steven C. Hunt, Ph.D., PI. Co-investigator.

32. "Hostility, Marital Interaction and Health in Aging". NIH Grant, 4-year award, April 2001 – present. Timothy Smith, Ph.D. PI. Co-Investigator.
33. "Treatment of Hypercholesterolemia with Rosuvastatin (protocol 091)". AstraZeneca, June 2002-present. PI of Utah center.
34. Participating physician in ongoing collaboration between Cardiovascular Genetics and Jean Marc Lalouel, M.D., D.Sc. of the Howard Hughes Medical Institute at the University of Utah. Projects include molecular genetic studies of lipoprotein metabolism in high-risk CHD families and, more recently, studies of molecular mechanisms of hypertension.

ADMINISTRATIVE EXPERIENCE

1. Chairman, Steering Committee, International and U.S. MEDPED (Make Early Diagnoses to Prevent Early Deaths in Medical Pedigrees), an international humanitarian organization to find and help persons with familial hypercholesterolemia. MEDPED was founded by the late Roger R. Williams, M.D. who died in the crash of Swissair flight 111 to Geneva, September 2, 1998 on his way to chair an international MEDPED meeting at the World Health Organization.
2. Director Family Lipid Clinic, Preventive Cardiology, Cardiology Division, University of Utah School of Medicine.
3. Co-Director of Cardiovascular Genetics Research Clinic.
4. Principal investigator for grants listed above (see research experience).
5. Participate in organizational planning and scientific meetings for research projects in Cardiovascular Genetics.

CLINICAL ACTIVIES

Clinical Innovation and Referral Attraction

1. Developed and direct the Family Lipid Clinic in the Madsen Preventive Cardiology Clinic, a model lipid clinic for treatment of familial lipid disorders, especially familial hypercholesterolemia, familial combined hyperlipidemia, and other severe lipid disorders.
2. Participate in a variety of clinical and research studies with various outreach methods to recruit participants who are then screened and evaluated for cardiovascular risk factors. Some of these patients are referred for further medical care as indicated.

Routine Clinical Activities

1. See patients in Family Lipid Clinic (weekly clinic).
2. Occasional consults for lipid abnormalities at University Hospital.
3. Advisor for interpretation of ambulatory blood pressure monitor results for Cardiology division.

PROFESSIONAL AND UNIVERSITY COMMUNITY ACTIVITIES

1. Member of the Diet Evaluation Committee of the Salt Lake County Medical Society (1982 - 1984).
2. Member of Promotions, Retention and Tenure Committee, University of Utah School of Medicine (1984).
3. Member of the Nutrition Committee, Utah Heart Association (1986 - 1992).
4. Member of the Cholesterol Committee, Utah Medical Association (1989 - 1993).
5. Member of the Utah Academy of Preventive Medicine (1989 – 1999)
6. Consultant for AMA Drug Evaluations "Treatment of Disorders of Cholesterol and Lipoprotein Metabolism" 1993 Summer supplement.
7. Member Institutional Review Board, University of Utah (1994-1996)
8. Review manuscripts for: *Annals of Internal Medicine, Arteriosclerosis Thrombosis and Vascular Biology, Circulation, Clinical Chemistry, Diabetes, European Journal of Public Health, Hypertension, Kidney International, JAMA, Journal of Investigative Medicine, Lancet*
9. Reviewer for National Heart, Lung, and Blood Institute study section (EDC1), February 1995.
10. Participant in the Special Emphasis Panel on Homocysteinemia and Cardiovascular Disease. September 1995.
11. Consultant for Roche for studies on mibefradil, May 1997.
12. Consultant for Pharmacia-Upjohn, July 1997.
13. Consultant for Eli Lily, 1999 – present.
14. Consultant for Merck, 1998 – present.
15. Consultant for AstraZeneca 2000 – present.

TEACHING AND PRESENTATIONS

Preceptor

1. Clinical diagnosis preceptor for sophomore medical students (1993 - 2000).
2. Internal Medicine residents and Cardiology fellows rotating through Family Lipid Clinic.
3. Dietetics trainees rotating through Family Lipid Clinic.

Graduate Student Committees for Theses:

1. Walter Hemelstrand, for Ph.D., Department of Health Education, 1989.
2. Rosana Roberson, R.D., for M.S., College of Health, Division of Foods and Nutrition, 1989-1991.
3. Joseph J. Cimmarusti, for M.S., College of Health, Division of Foods and Nutrition, 1990-1992. Master's thesis defence - August 1992.
4. Mike Manfull, for M.S., College of Health, Division of Foods and Nutrition, 1993-1994
5. Geraldine Wade, M.D. for M.S., Medical Informatics, 1998 - 1999.

Lectures for Graduate/Medical Students

1. "Prostaglandins and Fish Oil". Yearly lecture to nutrition graduate students (8-12 students). Started winter quarter 1991.
2. Management of lipids. Yearly lecture to Cardiology Fellows.
3. Hyperlipidemia. Cardiology organ systems lecture for 2nd year medical students.
4. Hypertension. Cardiology organ systems lecture for 2nd year medical students.
5. Introduction to Atherosclerosis. Nutrition graduate students.

Invited Lectures (selected from a longer list)

1. "Cholesterol screening. Vital new developments in cholesterol screening and counseling for the young student." Brigham Young University. March 31, 1987. Approved for 1 1/2 hours of category 1 CMD credit.
2. "Treatment programs for families with hyperlipidemia." 8th Annual Nutrition in Contemporary Medicine Symposium. Sponsored by University of Utah Division of Foods and Nutrition and School of Medicine Division of Gastroenterology. February 17, 1989.
3. "Using medical family history data in risk assessment." Southwest Regional meeting of the American College of Sports Medicine, Las Vegas, Nevada, December 3, 1988.
4. "Stearic acid, oleic acid and omega-3's - what do they mean for your patient?" Utah Heart Association Scientific Session, April 7, 1989.
5. "Stratifying patients at risk from elevated serum cholesterol." Ogden Clinic. Sponsored by Merck, Sharp & Dohme, June 23, 1989.
6. "Diagnosis of Hyperlipidemias." Cottonwood Hospital. Sponsored by Merck, Sharp & Dohme, August 8, 1989.
7. "Stratifying patients at risk from elevated serum cholesterol." Billings Clinic. Sponsored by Merck, Sharp & Dohme, October 28, 1989.
8. "High Risk Families for Cardiovascular Disease" Red Lion Hotel, Salt Lake City. At 14th Annual Conference on Cardiovascular Health, "Parnerships in Prevention". Sponsored by the Utah Department of Health and Merck Sharp & Dohme, April 6, 1990.
9. "Pathogenesis of Atherosclerosis and Metabolism and Regulation of Lipoproteins." Holiday Inn, St. George, Utah. In a continuing medical education program sponsored by the University of Utah School of Medicine, Department of Internal Medicine and Merck, Sharp & Dohme, May 12, 1990.
10. "Hypertension, Hyperlipidemia, and Insulin Resistance." Park City, Utah. Sponsored by Rorer Pharmaceuticals, May 16, 1990.
11. "A Practical Approach to High Risk Coronary Families: Risks and Benefits of Exercise and Other Interventions." A tutorial lecture at the Annual Meeting of the American College of Sports Medicine, Salt Lake City, UT, May 25, 1990.
12. "Women and Coronary Heart Disease." Lakeview Hospital. Sponsored by Parke-Davis, June 14, 1990. Also at Logan Regional Hospital, October 17, 1990 and at Salt Lake Clinic May 23, 1991.
13. "Hypercholesterolemia - What Lipid Fractions Are Important." Humana Hospital, West Anaheim, CA. 1 hour CME credit. Sponsored by Merck, Sharp & Dohme, June 15, 1990.

14. "Hypertension: Who to Treat and How to Treat". Part of a Symposium: Management of hypertension and other cardiovascular risk factors. June 12, 1991, Salt Lake City, UT. Jointly sponsored by Temple University School of Medicine and Pfizer-Roerig.
15. "Cholesterol Lowering Agents". Part of the 15th annual Castle Country Medical Symposium. June 13, 1991 in Price, UT. Sponsored by Bristol-Myers Squibb.
16. "Nutritional Considerations in Genetic Syndromes Leading to Early Familial Coronary Disease". International Life Sciences Institute, North America 1992 Annual Meeting, January 19-22, 1992. Miami Beach, FL.
17. "Advances in Therapy for Hyperlipidemia". May 1994, Prescott, Arizona. Sponsored by Sandoz.
18. "Secondary Prevention of Coronary Artery Disease". October 4, 1994. Internal Medicine Grand Rounds, Cottonwood Hospital, Salt Lake City, UT. Sponsored by Marion-Merrell-Dow.
19. "Cholesterol Lowering to Prevent a Second MI". March 8, 1995. At FHP, Salt Lake City. Sponsored by Bristol-Myers Squibb.
20. "Secondary Prevention of Coronary Artery Disease". May, 1995. At FHP, Salt Lake City. Sponsored by Sandoz.
21. "Advances in Preventing Coronary Disease". CME credit program. January 26, 1996. McKay-Dee Hospital, Department of Medicine meeting. Sponsored by Bristol-Myers Squibb.
22. "What's New with Coronary Artery Disease". CME credit program. April 23, 1996. St. Mary's Hospital, Grand Junction, CO.
23. "Protective Aspects of Diet on Coronary Disease". In Foods as Nutrition symposium May 17, 1996. University of Utah Continuing Education Center, Park City, UT. Sponsored by University of Utah College of Health, Division of Foods and Nutrition.
24. Sponsored preceptorship for drug representatives on atherosclerotic disease and intervention. Presented 3 of the 6 lectures including "Management of Coronary Disease: Hopes and Promises", "Proof of the Lipid Hypothesis - Clinical Trials", and "Management of Dyslipidemia". January 21, 1997. Preventive Cardiology, University of Utah, Salt Lake City. Sponsored by Parke-Davis and Pfizer.
25. "New Developments in Treating Hyperlipidemia". CME credit program. March 28, 1997. Dixie Regional Medical Center, St. George, Utah. Sponsored by Parke-Davis.
26. "How Low Should You Go – New Advances in Lipid Intervention to Prevent Coronary Artery Disease". September 16, 1998 (and multiple other dates). Pfizer and Parke-Davis sponsored events.
27. "Triglycerides and Coronary Artery Disease – The Rest of the Lipid Story". September 17, 1998. Internal Medicine Grand Rounds. University of Utah School of Medicine, Salt Lake City.
28. "Pharmacologic Management of Lipid Disorders: The Clinical Rationale for Aggressive Lipid Lowering" a 40 minute presentation in a program entitled "The Cardiovascular Dysmetabolic Profile – Key to Outpatient management of Cardiovascular Disease". September 26, 1998. Hyatt Regency, Sacramento. CME credit program sponsored by The Mercy Heart Institute and The Division of Cardiovascular Medicine, University of California, Davis
29. "Database Issues in Cardiovascular Genetics". November 2, 1999. University of Miami Division of Cardiology and Miami Heart Research Institute, Miami.

30. "Evidence-Based Management of CAD Risk Factors. Lipids and CAD Outcome." November 5, 1999. Winter Sports Park, Park City, Utah. Sponsored by Merck & Co.
31. "Results of the Treatment Support Program in MEDPED". November 6, 1999. Atlanta. Annual MEDPED USA meeting.
32. "Prevention of Atherosclerosis". February10, 2000. Park City, UT. Advances in Internal Medicine. Sponsored by the University of Utah School of Medicine.
33. "New Approaches in Lipid Intervention to Prevent Coronary Artery Disease: Focus on Cerivastatin". July 20, 2000. St. George Utah. Sponsored by Bayer.
34. "Novel Coronary Risk Factors: Beyond LDL, Triglycerides, and HDL". September 29, 2000. VA Medical Center, Salt Lake City.
35. "Family History: A Major Modifiable Risk Factor for Premature Coronary Artery Disease". September 30, 2000, National Clinical Symposium, American College of Nurse Practitioners, at The Salt Palace, Salt Lake City, Utah.
36. "Aggressive LDL Reduction: Focus on Primary Prevention". October 3, 2000, Tacoma, Washington. CME program sponsored by the Postgraduate Institute for Medicine and the Veritas Institute for Medical Education, Inc. Supported through an unrestricted education grant from Parke-Davis and Pfizer, facilitated by APEX communications. Also presented in Boise, Westlake, CA, other locations during September – November 2000.
37. "Triglycerides and Coronary Artery Disease. Does Genetic Epidemiology Provide New Insights?" October 7, 2000. Masters Conference on Lipid Management at the LaFonda Hotel, Santa Fe, New Mexico. Sponsored by KU Medical Center, Lipid, Atherosclerosis & Metabolic Clinic, Patrick M. Moriarty, M.D., Director. Supported by a grant from Bayer.
38. "The Big Four Drugs of Secondary Prevention (Aspirin, Beta-Blockers, ACE Inhibitors, and Statins). What is Their Role in Primary Prevention?" October 14, 2000 at Homestead Resort in Midway, Utah. Presentation in CME program "Cardiovascular Update. What Works and What's New for Primary Care Providers and Specialists". Sponsored by Intermountain Health Care.
39. "The Genetics of Human Hypercholesterolemic Syndromes. An Update for the Clinician." University of Utah Internal Medicine retreat. November 2, 2000, University of Utah, Eccles Human Genetics Auditorium.
40. "Genetics of Coronary Artery Disease. Family History as a Major *Modifiable* Risk Factor for Premature Coronary Artery Disease". CME lecture for Dixie Symposium, sponsored by Intermountain Health Care, St. George Holiday Inn, February 23, 2001.
41. "Lipid Lowering: for Whom, With What, and Why?" CME lecture for Cardiology Spring Meeting, sponsored by University of Utah Cardiology Division, Stein Eriksen Lodge, Deer Valley, May 10, 2001.
42. "Diet, Antioxidants, and Hormone Replacement: What Should We Now Be Recommending?" CME lecture for Cardiology Spring Meeting, sponsored by University of Utah Cardiology Division, Stein Eriksen Lodge, Deer Valley, May 10, 2001.
43. "Implications of the New Guidelines (NCEP III) for Lifestyle Modification and Lipid-lowering Therapy" CME lecture for Cardiology Update 2001, sponsored by the University of Utah Cardiology Division, Thanksgiving Point, October 27, 2001.

44. "Managing Multiple Risk Factors in Primary Care: An Interactive Workshop" CME program sponsored by The Impact Group, supported by Pfizer, Staples Center, Los Angeles, December 15, 2001.
45. "Advances in Prevention through Optimizing Lipid Lowering: Utilizing the Most Recent Therapies in Getting Patients to Goal" CME sponsored by The France Foundation, supported by Astra-Zeneca, Log Haven, Salt Lake City, January 15, 2002.
46. "The New NCEP ATP III Guidelines for Lipid Management: How to use them, and do they really make a difference?" CME sponsored by University of Utah School of Medicine, Department of Internal Medicine, Advances in Internal Medicine, The Lodges at Deer Valley Park City, Utah, March 21, 2002.

Abstract Presentations

1. American Heart Association Meetings, November 14, 1989. "Familial Combined Hyperlipidemia (FCHL) and Familial Dyslipidemic Hypertension (FDH): The Most Common Syndromes in Utah Coronary Pedigrees". Abstract #826. Circulation 1989; 80 (Suppl II): II-207.
2. American Heart Association Meetings, November 11, 1998. "Type III Hyperlipidemia and Lipoprotein Remnants in Early Onset Familial Coronary Artery Disease". Abstract #4146. Circulation 1998; 98 (suppl I): I-791.
3. American Heart Association Epidemiology Council Meetings, March 1, 2001, San Antonio. "Is the Heat Labile Variant of Methylene Tetrahydrofolate Reductase (MTHFR-HL) Associated with Elevated Plasma Total Homocysteine (tHcy) and Premature Coronary Artery Disease (CAD)?" Poster presentation.
4. American Heart Association Epidemiology Council Meetings, March 2, 2001, San Antonio. "Benefits of the MEDPED Treatment Support Program" Poster presentation.
5. American Heart Association Meetings, November 12, 2001. "Gender bias in treatment of lipids among patients with familial hypercholesterolemia". Abstract #3712. Circulation 2001; 104:II-790.

PUBLICATIONS

Books and Textbook Chapters[1-11]

Abstracts and Letters[12-27]

Journal Articles, Monograph Chapters
Before 2000[28-102]
2000 and later[103-153]

1. Williams RR, Hunt SC, Hopkins PN, Wu LL, Hasstedt SJ, Stults BM, Kuida H. Genes, hypertension, and early familial coronary heart disease. In: Laragh JH, Brenner BM, eds. Hypertension: pathophysiology, diagnosis and management. New York: Raven Press; 1990:127-136.

2. Hopkins PN. Hyperlipidemia: detection and treatment. In: Yanowitz FG, ed. Coronary heart disease prevention A view towards the 21st century. New York: Marcel Dekker, Inc; 1992:189-249.
3. Hopkins PN, Wu LL, Williams RR. Dyslipidemias. In: Noe DA, Rock RC, eds. Laboratory medicine The selection and interpretation of clinical laboratory studies. Baltimore: Williams & Wilkins; 1994:476-511.
4. Williams RR, Hopkins PN, Hunt SG, Schumacher MC, Stults BM, Wu LL, Hasstedt SJ. Inherited susceptibility to metabolic complications of obesity. In: Bouchard C, ed. The genetics of obesity. Boca Raton, Florida: CRC Press; 1994:147-159.
5. Wu LH, Wu JT, Hopkins PN. Apolipoprotein E: laboratory determinations and clinical significance. In: Rifai N, Warnick GR, Dominiczak MH, eds. Handbook of lipoprotein testing. Washington, D. C.: AACC Press; 1997:329-356.
6. Williams RR, Hopkins PN, Wu LL, Schumacher MC, Hunt SC. Evaluating family history to prevent early CHD. In: Pearson TA, Criqui MH, Luepker RV, Oberman A, Winston M, eds. Primer in preventive cardiology. Dallas: American Heart Association; 1994:93-106.
7. Hunt SC, Hopkins PN, Williams RR. Hypertension: genetics and mechanisms. In: Fuster V, Ross R, Topol EJ, eds. Atherosclerosis and coronary artery disease. Philadelphia: Lippincott-Raven Publishers; 1996:209-235.
8. Williams RR, Hunt SC, Hopkins PN, Wu L, Stephenson S. Practical benefits from understanding the genetics of chronic diseases. In: Day I, Humphries S, eds. Genetics of common diseases: future therapeutic and diagnostic possibilities. Oxford: BIOS Scientific Publishers Limited; 1997:185-202.
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EXHIBIT A

Source	meanage	pwomen	fendose	dexfendose	duration	timeoff	nar
Wadden	46.3	100	39	0	24.3	0.0	20
Burger	46.9	0.50%	27.37522124	0	12.5	3.2	226
Dahl	46	91	.	.	7.9	.	753
Kancherla	45	87.5	.	.	6.5	0.0	169
Lepor	48	84.7	72	.	10.7	0.0	85
Teramae	47	86	45	26	9.0	0.0	191
Khan	46.0	87.1	90	0	26.5	3.9	233
Weissman	45.1	79.9	0	30	2.4	1.3	671
Shively	50.0	81.6	0	30	6.9	8.5	223
Hensrud	42.0	68.4	40	0	9.6	1.5	19
Ryan	49.1	19.8	60	30	16.7	12.2	79
Gardin	46.9	74.6	46	0	11.9	6.8	452
Gardin	46.9	74.6	46	0	6.0	6.8	470
Jollis	46.1	85.0	60	0	2.0	15.0	25
Jollis	46.1	85.0	60	0	4.5	15.0	313
Jollis	46.1	85.0	60	0	9.0	15.0	415
Jollis	46.1	85.0	60	0	18.0	15.0	315
Jollis	46.1	85.0	60	0	30.0	15.0	86
Davidoff	48.8	100.0	60	0	2.5	53.0	276
Khan	46.0	87.1	0	0	0.0	.	233
Weissman	45.1	79.9	0	0	0.0	.	330
Shively	50.0	81.6	0	0	0.0	.	189
Hensrud	42.0	68.4	0	0	0.0	.	11
Gardin	46.9	74.6	0	0	0.0	.	536
Jollis	46.1	85.0	0	0	0.0	.	669
Davidoff	48.8	100.0	0	0	0.0	.	254
All controls							2222
All exposed							4268
				For percent mild, moderate, and severe AR			3515
Dahl 2004	47.1	85.0			8.6		3390

fdaposar	mildar	modar	sevar	pfdaposar	pmildar	pmodar	psevar	pmodsevar	paffmildar
5	4	1	0	25.00%	20.00%	5.00%	0.00%	5.00%	80.00%
15	12	3	0	6.64%	5.31%	1.33%	0.00%	1.33%	80.00%
125				16.60%					
18	9	8	1	10.65%	5.33%	4.73%	0.59%	5.33%	50.00%
24	12	10	2	28.24%	14.12%	11.76%	2.35%	14.12%	50.00%
55	36	17	2	28.80%	18.85%	8.90%	1.05%	9.95%	65.45%
51	35	16	0	21.89%	15.02%	6.87%	0.00%	6.87%	68.63%
36	33	3	0	5.37%	4.92%	0.45%	0.00%	0.45%	91.67%
14	14	0	0	6.28%	6.28%	0.00%	0.00%	0.00%	100.00%
5	5	0	0	26.32%	26.32%	0.00%	0.00%	0.00%	100.00%
13	12	1	0	16.46%	15.19%	1.27%	0.00%	1.27%	92.31%
62	56	5	1	13.72%	12.39%	1.11%	0.22%	1.33%	90.32%
42	39	3	0	8.94%	8.30%	0.64%	0.00%	0.64%	92.86%
1	1	0	0	4.00%	4.00%	0.00%	0.00%	0.00%	100.00%
14	10	2	2	4.47%	3.19%	0.64%	0.64%	1.28%	71.43%
29	24	3	2	6.99%	5.78%	0.72%	0.48%	1.20%	82.76%
43	32	9	2	13.65%	10.16%	2.86%	0.63%	3.49%	74.42%
15	12	3	0	17.44%	13.95%	3.49%	0.00%	3.49%	80.00%
17	11	4	2	6.16%	3.99%	1.45%	0.72%	2.17%	64.71%
3	3	0	0	1.29%	1.29%	0.00%	0.00%	0.00%	100.00%
12	10	2	0	3.64%	3.03%	0.61%	0.00%	0.61%	83.33%
3	3	0	0	1.59%	1.59%	0.00%	0.00%	0.00%	100.00%
1	1	0	0	9.09%	9.09%	0.00%	0.00%	0.00%	100.00%
22	19	2	1	4.10%	3.54%	0.37%	0.19%	0.56%	86.36%
24	20	3	1	3.59%	2.99%	0.45%	0.15%	0.60%	83.33%
11	9	2	0	4.33%	3.54%	0.79%	0.00%	0.79%	81.82%
76	65	9	2	3.42%	2.93%	0.41%	0.09%	0.50%	85.53%
584	357	88	14	13.68%					
459	357	88	14		10.16%	2.50%	0.40%	2.90%	77.78%
616	430	169	17	18.17%	12.68%	4.99%	0.50%	5.49%	69.81%

paffmodar	paffsevar	paffmodsevar		nmr	fdaposmr	mildmr	modmr	sevmr
20.00%	0.00%	20.00%		20	2	2	2	0
20.00%	0.00%	20.00%		226	3	23	3	0
				753	28			
44.44%	5.56%	50.00%		169	6	21	6	0
41.67%	8.33%	50.00%		85	9	34	8	1
30.91%	3.64%	34.55%		191	12		6	6
31.37%	0.00%	31.37%		233	2		2	0
8.33%	0.00%	8.33%		677	12	59	11	1
0.00%	0.00%	0.00%		223	3	122	3	0
0.00%	0.00%	0.00%		19	0		0	0
7.69%	0.00%	7.69%		79	1		1	0
8.06%	1.61%	9.68%		452	23	131	17	6
7.14%	0.00%	7.14%		472	23	124	20	3
0.00%	0.00%	0.00%		25	0	3	0	0
14.29%	14.29%	28.57%		313	7	36	7	0
10.34%	6.90%	17.24%		412	12	57	12	0
20.93%	4.65%	25.58%		315	8	39	4	4
20.00%	0.00%	20.00%		86	2	9	0	2
23.53%	11.76%	35.29%		276	14	73	13	1
0.00%	0.00%	0.00%		233	0		0	0
16.67%	0.00%	16.67%		333	4	17	4	0
0.00%	0.00%	0.00%		189	1	94	1	0
0.00%	0.00%	0.00%		11	0		0	0
9.09%	4.55%	13.64%		537	17	111	14	3
12.50%	4.17%	16.67%		668	10	77	9	1
18.18%	0.00%	18.18%		254	12	58	12	0
11.84%	2.63%	14.47%		2225	44	357	40	4
				5026	167	733	115	24
19.17%	3.05%	22.22%	% moderate and severe MR	4273	139	733	115	24
			% all MR controls	1981	44	357	40	4
			% all MR exposed	3751	124	733	106	18
27.44%	2.76%	30.19%		3385	160	1444	132	28

pfdaposmr	pallmr	pmildmr	pmodmr	psevmr	pallmildmr	pallmodmr	pallsevmr	paffmodmr	paffsevmr
10.00%	20.00%	10.00%	10.00%	0.00%	50.00%	50.00%	0.00%	100.00%	0.00%
1.33%	11.50%	10.18%	1.33%	0.00%	88.46%	11.54%	0.00%	100.00%	0.00%
3.72%									
3.55%	15.98%	12.43%	3.55%	0.00%	77.78%	22.22%	0.00%	100.00%	0.00%
10.59%	50.59%	40.00%	9.41%	1.18%	79.07%	18.60%	2.33%	88.89%	11.11%
6.28%			3.14%	3.14%	0.00%				50.00%
0.86%			0.86%	0.00%	0.00%				0.00%
1.77%	10.49%	8.71%	1.62%	0.15%	83.10%	15.49%	1.41%	91.67%	8.33%
1.35%	56.05%	54.71%	1.35%	0.00%	97.60%	2.40%	0.00%	100.00%	0.00%
0.00%			0.00%	0.00%					
1.27%			1.27%	0.00%				100.00%	0.00%
5.09%	34.07%	28.98%	3.76%	1.33%	85.06%	11.04%	3.90%	73.91%	26.09%
4.87%	31.14%	26.27%	4.24%	0.64%	84.35%	13.61%	2.04%	86.96%	13.04%
0.00%	12.00%	12.00%	0.00%	0.00%	100.00%	0.00%	0.00%		
2.24%	13.74%	11.50%	2.24%	0.00%	83.72%	16.28%	0.00%	100.00%	0.00%
2.91%	16.75%	13.83%	2.91%	0.00%	82.61%	17.39%	0.00%	100.00%	0.00%
2.54%	14.92%	12.38%	1.27%	1.27%	82.98%	8.51%	8.51%	50.00%	50.00%
2.33%	12.79%	10.47%	0.00%	2.33%	81.82%	0.00%	18.18%	0.00%	100.00%
5.07%	31.52%	26.45%	4.71%	0.36%	83.91%	14.94%	1.15%	92.86%	7.14%
0.00%			0.00%	0.00%					
1.20%	6.31%	5.11%	1.20%	0.00%	80.95%	19.05%	0.00%	100.00%	0.00%
0.53%	50.26%	49.74%	0.53%	0.00%	98.95%	1.05%	0.00%	100.00%	0.00%
0.00%			0.00%	0.00%					
3.17%	23.84%	20.67%	2.61%	0.56%	86.72%	10.94%	2.34%	82.35%	17.65%
1.50%	13.02%	11.53%	1.35%	0.15%	88.51%	10.34%	1.15%	90.00%	10.00%
4.72%	27.56%	22.83%	4.72%	0.00%	82.86%	17.14%	0.00%	100.00%	0.00%
1.98%			1.80%	0.18%			1.00%	90.91%	9.09%
3.32%									
3.25%			2.69%	0.56%	84.06%	13.19%	2.75%	82.73%	17.27%
	20.24%	18.02%	2.02%	0.20%					
	22.85%	19.54%	2.83%	0.48%					
4.73%	47.39%	42.66%	3.90%	0.83%	90.02%	8.23%	1.75%	82.50%	17.50%

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Will apply percent affected for averaged exposed groups to overall FDA positive

duration	estimated AR	% mod/sev AR	% mild AR	% mod AR
0	3.42	0.50%	2.93%	0.41%
1	5.462219924	1.21382665	4.248393274	1.047222992
2	7.108305864	1.579623525	5.528682338	1.362812453
3	8.487249827	1.886055517	6.60119431	1.627185152
4	9.673773765	2.149727503	7.524046261	1.854666866
5	10.71506156	2.381124791	8.333936769	2.054303741
6	11.64282219	2.58729382	9.055528368	2.23217506
7	12.47939476	2.773198836	9.706195924	2.392563701
8	13.2411114	2.942469201	10.2986422	2.538600879
9	13.9402749	3.097838867	10.84243604	2.672645297
10	14.58638402	3.241418671	11.34496535	2.796518069
11	15.18692577	3.374872393	11.81205338	2.911654614
12	15.74790624	3.49953472	12.24837152	3.019206425
13	16.27421712	3.616492694	12.65772443	3.120111344
14	16.76989541	3.726643425	13.04325199	3.215143347
15	17.23831162	3.830735916	13.40757571	3.304948634
16	17.68230887	3.92940197	13.7529069	3.390072288
17	18.10430746	4.023179435	14.08112802	3.470978336
18	18.5063848	4.112529955	14.39385484	3.548065059
19	18.89033725	4.197852722	14.69248453	3.621676858
20	19.25772864	4.279495253	14.97823338	3.692113551
21	19.60992875	4.357761944	15.2521668	3.759637755
22	19.94814414	4.43292092	15.51522322	3.824480794
23	20.27344311	4.50520958	15.76823353	3.886847481
24	20.58677602	4.574839117	16.01193691	3.946920022
25	20.88899208	4.64199824	16.24699384	4.004861227
26	21.18085316	4.706856258	16.4739969	4.060817164
27	21.46304541	4.769565648	16.69347977	4.114919382
28	21.73618898	4.830264217	16.90592476	4.167286775
29	22.00084616	4.889076925	17.11176924	4.218027151
30	22.25752846	4.946117435	17.31141102	4.267238572

% sev AR	estimated FDA+ MR	% mild MR	% mod MR	% sev MR
0.09%	1.98%	18.02%	1.80%	0.18%
0.166603658	3.32%	19.54%	2.75%	0.57%
0.216811072	3.32%	19.54%	2.75%	0.57%
0.258870365	3.32%	19.54%	2.75%	0.57%
0.295060638	3.32%	19.54%	2.75%	0.57%
0.32682105	3.32%	19.54%	2.75%	0.57%
0.35511876	3.32%	19.54%	2.75%	0.57%
0.380635134	3.32%	19.54%	2.75%	0.57%
0.403868322	3.32%	19.54%	2.75%	0.57%
0.42519357	3.32%	19.54%	2.75%	0.57%
0.444900602	3.32%	19.54%	2.75%	0.57%
0.463217779	3.32%	19.54%	2.75%	0.57%
0.480328295	3.32%	19.54%	2.75%	0.57%
0.49638135	3.32%	19.54%	2.75%	0.57%
0.511500078	3.32%	19.54%	2.75%	0.57%
0.525787283	3.32%	19.54%	2.75%	0.57%
0.539329682	3.32%	19.54%	2.75%	0.57%
0.552201099	3.32%	19.54%	2.75%	0.57%
0.564464896	3.32%	19.54%	2.75%	0.57%
0.576175864	3.32%	19.54%	2.75%	0.57%
0.587381701	3.32%	19.54%	2.75%	0.57%
0.598124188	3.32%	19.54%	2.75%	0.57%
0.608440126	3.32%	19.54%	2.75%	0.57%
0.618362099	3.32%	19.54%	2.75%	0.57%
0.627919094	3.32%	19.54%	2.75%	0.57%
0.637137013	3.32%	19.54%	2.75%	0.57%
0.646039094	3.32%	19.54%	2.75%	0.57%
0.654646265	3.32%	19.54%	2.75%	0.57%
0.662977442	3.32%	19.54%	2.75%	0.57%
0.671049774	3.32%	19.54%	2.75%	0.57%
0.678878864	3.32%	19.54%	2.75%	0.57%

Estimates of number affected

	duration (mo)	% of users	# users	# FDA pos AR	# FDA pos MR
	0				
	1	39.20%	2,352,000	128,471	78,150
	2	20.90%	1,254,000	89,138	41,667
(61-90 days)	3	11.90%	714,000	60,599	23,724
	4	8.30%	498,000	48,175	16,547
	5	6.00%	360,000	38,574	11,962
	6	4.30%	258,000	30,038	8,573
	7	3.30%	198,000	24,709	6,579
	8	2.10%	126,000	16,684	4,187
	9	1.60%	96,000	13,383	3,190
	10	1.00%	60,000	8,752	1,994
	11	0.40%	24,000	3,645	797
	12	0.10%	6,000	945	199
	13	0.05%	3,000	488	100
	14	0.05%	3,000	503	100
	15	0.05%	3,000	517	100
	16	0.05%	3,000	530	100
	17	0.05%	3,000	543	100
	18	0.05%	3,000	555	100
	19	0.05%	3,000	567	100
	20	0.05%	3,000	578	100
	21	0.05%	3,000	588	100
	22	0.05%	3,000	598	100
	23	0.05%	3,000	608	100
	24	0.05%	3,000	618	100
	25	0.05%	3,000	627	100
	26	0.05%	3,000	635	100
	27	0.05%	3,000	644	100
	28	0.05%	3,000	652	100
	29	0.05%	3,000	660	100
	30	0.05%	3,000	668	100
	total	100.00%	6,000,000	473,694	199,363
			Totals 60 days or less =	217,610	119,817
			Totals in excess of 60 days =	256,084	79,546

% of FDA+ in those 60 days or less=

% of FDA+ in those in excess of 60 days=

% FDA+ AR moderate or severe - 60 days or less= 22.2%

% FDA+ AR moderate or severe - 61 days or more= 22.2%

note - percent affected with mild, moderate and severe was estimated for all studies in exposed groups and these percentages were applied to total FDA+ regardless of duration.

	Total users =	6,000,000			
mild AR	moderate AR	severe AR	mild MR	moderate MR	severe MR
99,922	24,631	3,919	459,615	64,657	13,494
69,330	17,090	2,719	245,050	34,473	7,194
47,133	11,618	1,848	139,526	19,628	4,096
37,470	9,236	1,469	97,316	13,690	2,857
30,002	7,395	1,177	70,349	9,896	2,065
23,363	5,759	916	50,417	7,092	1,480
19,218	4,737	754	38,692	5,443	1,136
12,976	3,199	509	24,622	3,464	723
10,409	2,566	408	18,760	2,639	551
6,807	1,678	267	11,725	1,649	344
2,835	699	111	4,690	660	138
735	181	29	1,172	165	34
380	94	15	586	82	17
391	96	15	586	82	17
402	99	16	586	82	17
413	102	16	586	82	17
422	104	17	586	82	17
432	106	17	586	82	17
441	109	17	586	82	17
449	111	18	586	82	17
458	113	18	586	82	17
465	115	18	586	82	17
473	117	19	586	82	17
480	118	19	586	82	17
487	120	19	586	82	17
494	122	19	586	82	17
501	123	20	586	82	17
507	125	20	586	82	17
513	127	20	586	82	17
519	128	20	586	82	17
368,429	90,817	14,448	1,172,487	164,941	34,422
169,252	41,720	6,637	704,665	99,129	20,688
199,177	49,097	7,811	467,822	65,811	13,735
77.8%	19.2%	3.1%	588.1%	82.7%	17.3%
77.8%	19.2%	3.1%	588.1%	82.7%	17.3%

Goodman estimates

severe AR+MR	% FDA+ AR	% FDA+ MR	Pondimin %	Redux %	# exposed	# FDA+ AR
17,412	4.1	3.5	39.20%	55.10%	2,670,000	109,470
9,913	5.1	3.5	20.90%	19.00%	1,216,000	62,016
5,945	6.1	3.5	11.90%	9.80%	672,000	40,992
4,326	7.1	3.5	8.30%	5.50%	442,000	31,382
3,242	8.1	3.5	6.00%	3.50%	310,000	25,110
2,396	9.1	3.5	4.30%	2.30%	218,000	19,838
1,890	10.1	3.5	3.30%	1.60%	164,000	16,564
1,232	11.1	3.5	2.10%	1.10%	106,000	11,766
959	12.1	3.5	1.60%	0.80%	80,000	9,680
611	14.5	3.5	2.40%	1.30%	122,000	17,690
249						
63						
32						
33						
33						
33						
34						
34						
34						
35						
35						
35						
36						
36						
36						
37						
37						
37						
37						
38						
48,871			100.00%	100.00%		344,508
27,325		>60 day users				173,022
21,545						

# FDA+ - baseline Pondimin	# FDA+ - baseline - Redux	# FDA+ - baseline	my estimate - Goodman
15,680	11,020	26,700	19,001
16,720	7,600	24,320	27,122
14,280	5,880	20,160	19,607
13,280	4,400	17,680	16,793
12,000	3,500	15,500	13,464
10,320	2,760	13,080	10,200
9,240	2,240	11,480	8,145
6,720	1,760	8,480	4,918
5,760	1,440	7,200	3,703
13,920	3,770	17,690	6,232

13,920

162,290 129,186

111,270

This 111,270 represents the number of mild+ AR only v
3.1% - and not considering the number from users of ju
include the number of MR cases at all.

The 210,000 MR cases is defined using Goodman's est
a figure of 2.1% - for unexposed - was used in the estin

mod/sev AR	# FDA+ MR
18,063	93,450
10,233	42,560
6,764	23,520
5,178	15,470
4,143	10,850
3,273	7,630
2,733	5,740
1,941	3,710
1,597	2,800
2,919	4,270
56,844	210,000

AR only without including baseline rate of
sers of just 1 and 2 months. It also does not

man's estimate for exposed (3.5%). However,
the estimate presented.

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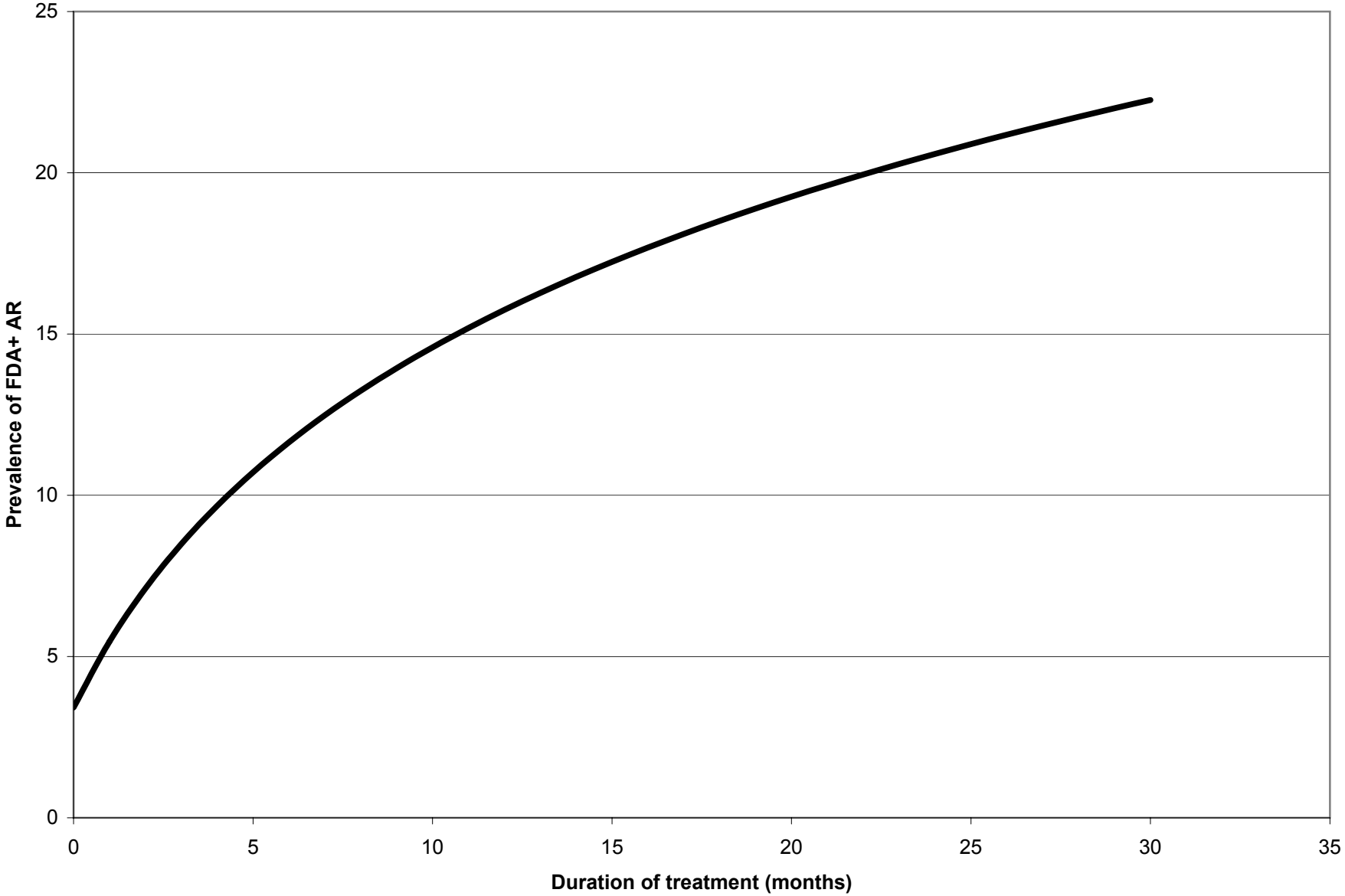
25
20
15
10
5
0
Prevalence of FDA+ AR
0
5
10
15
20
25
30
35
Duration of treatment (months)

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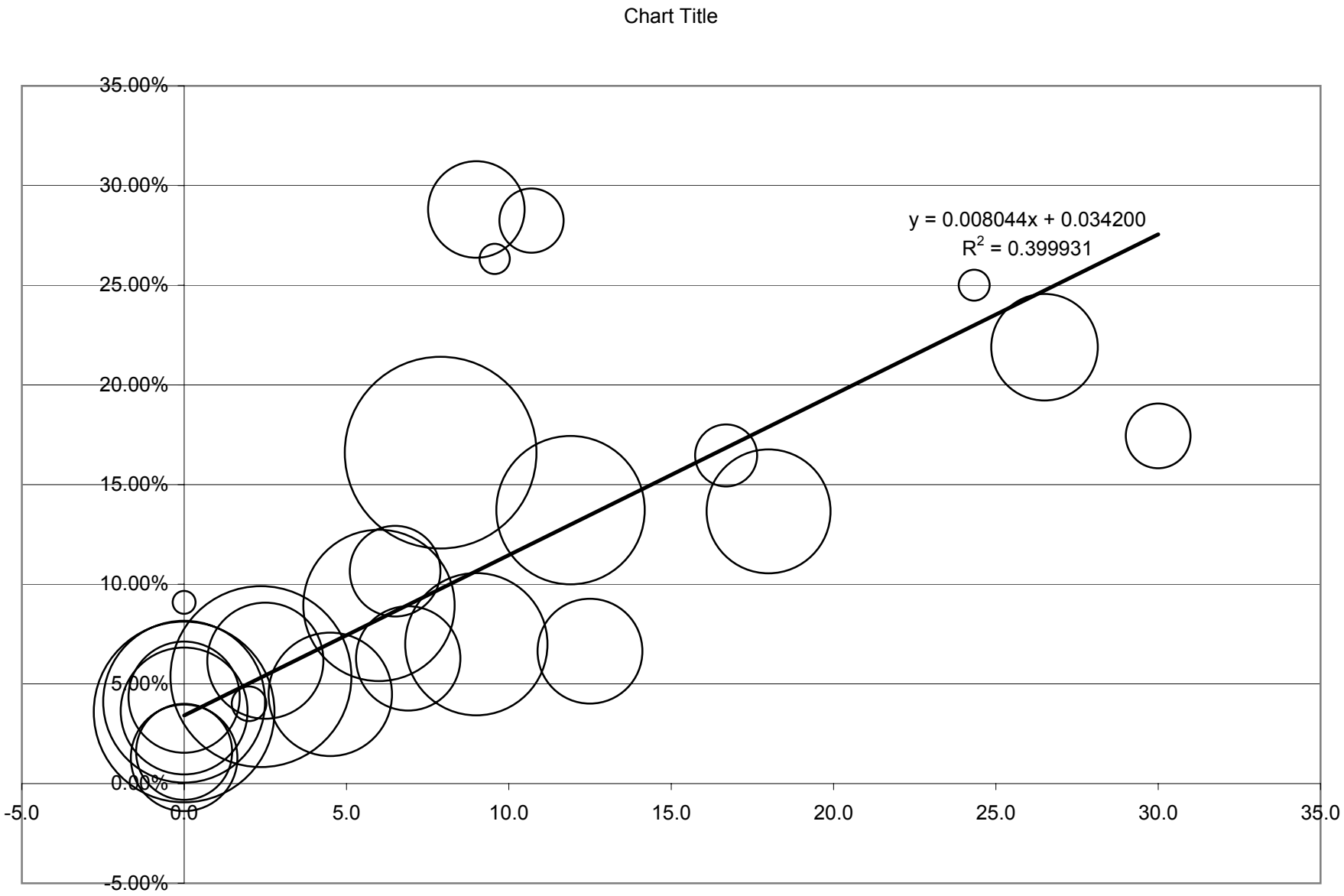
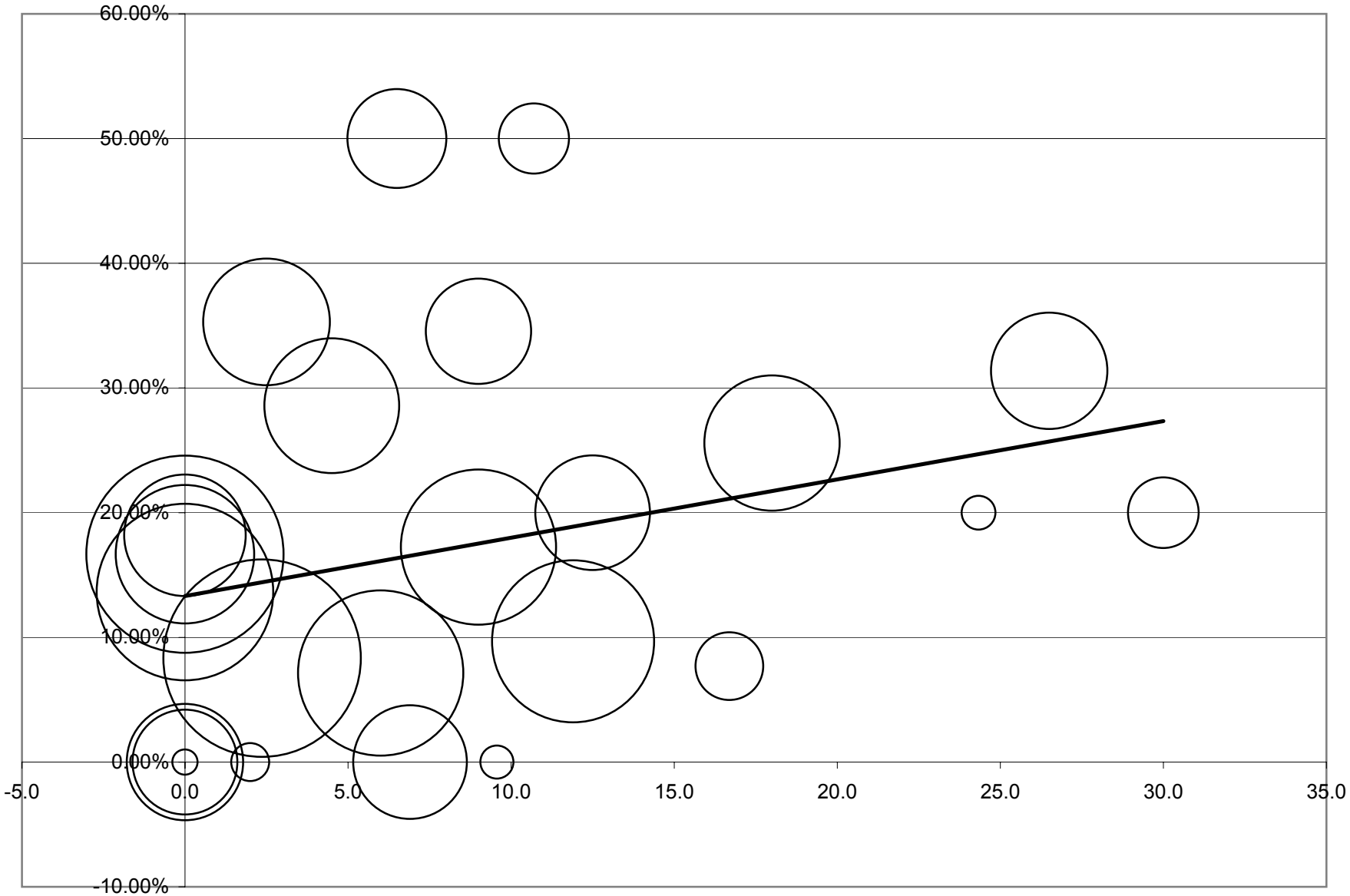
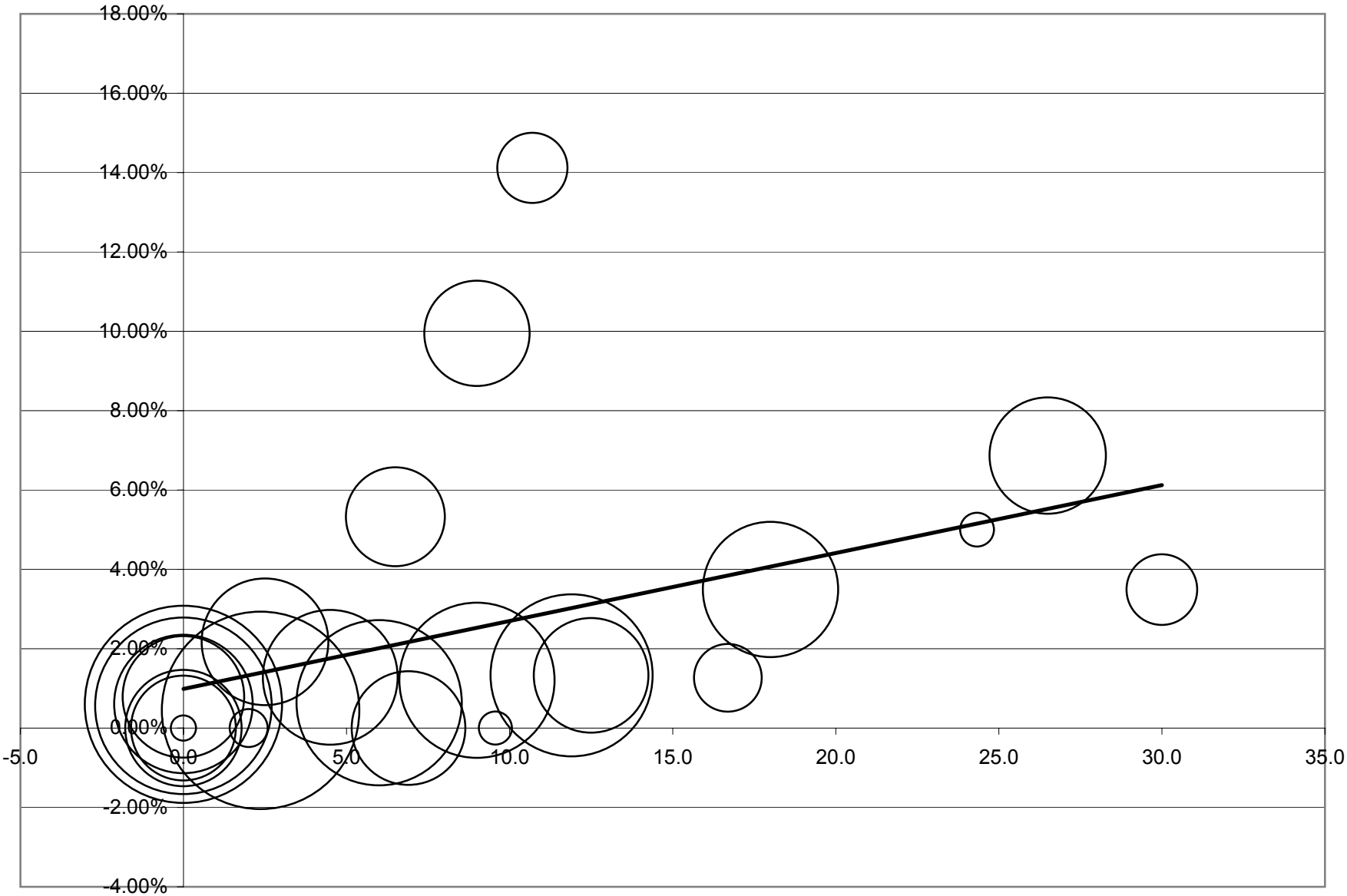


Chart Title
35.00%
30.00%
25.00%
20.00%
15.00%
10.00%
5.00%
0.00%
-5.00%
-5.0
0.0
5.0
10.0
15.0
20.0
25.0
30.0
35.0
y = 0.008044x + 0.034200
R2 = 0.399931


60.00%
50.00%
40.00%
30.00%
20.00%
10.00%
0.00%
-10.00%
-5.0
0.0
5.0
10.0
15.0
20.0
25.0
30.0
35.0


18.00%
16.00%
14.00%
12.00%
10.00%
8.00%
6.00%
4.00%
2.00%
0.00%
-2.00%
-4.00%
-5.0
0.0
5.0
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15.0
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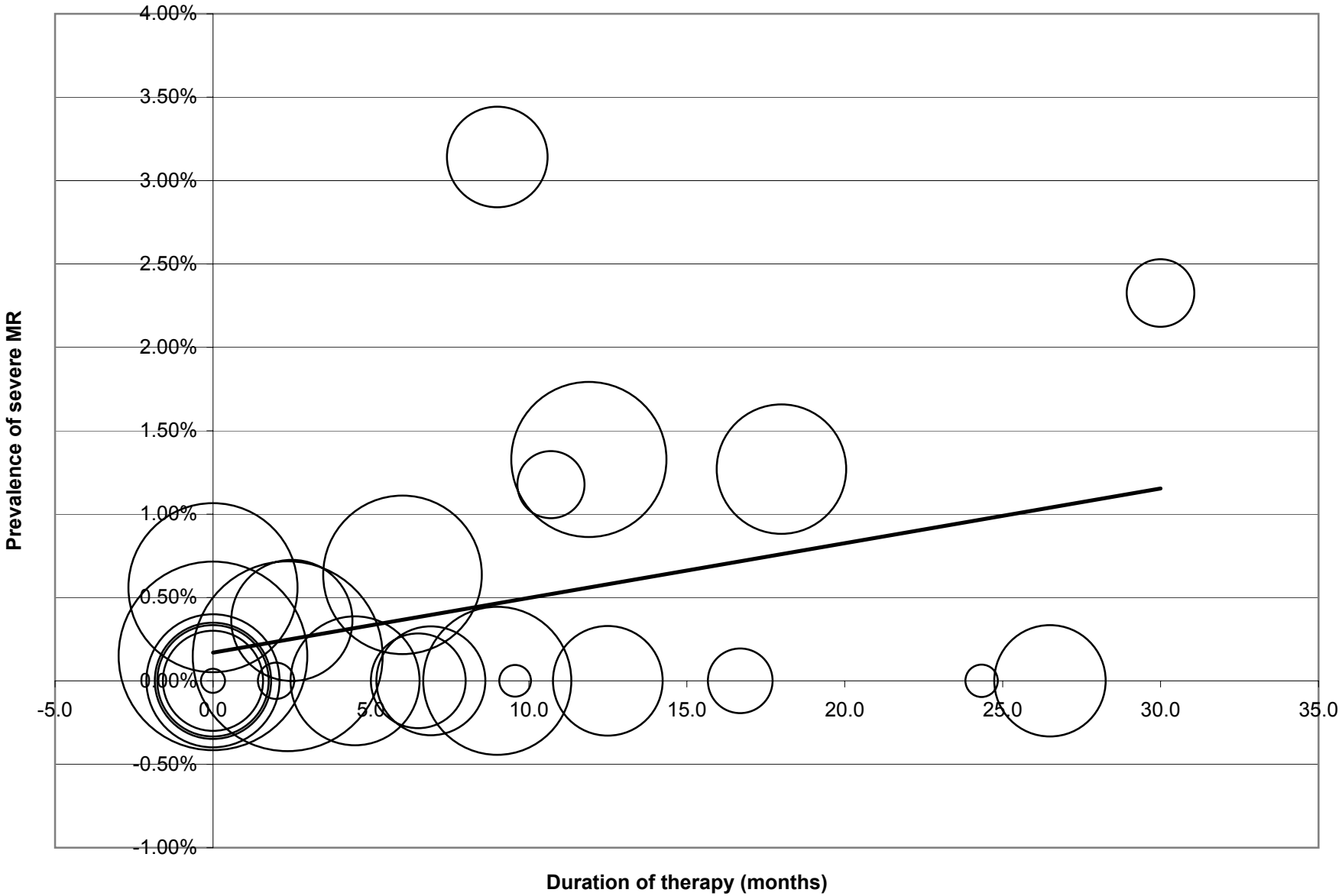
25.0
30.0
35.0


4.00%
3.50%
3.00%
2.50%
2.00%
1.50%
1.00%
0.50%
0.00%
-0.50%
-1.00%
-5.0
0.0
5.0
10.0
15.0
20.0
25.0
30.0
35.0
Prevalence of severe MR
Duration of therapy (months)

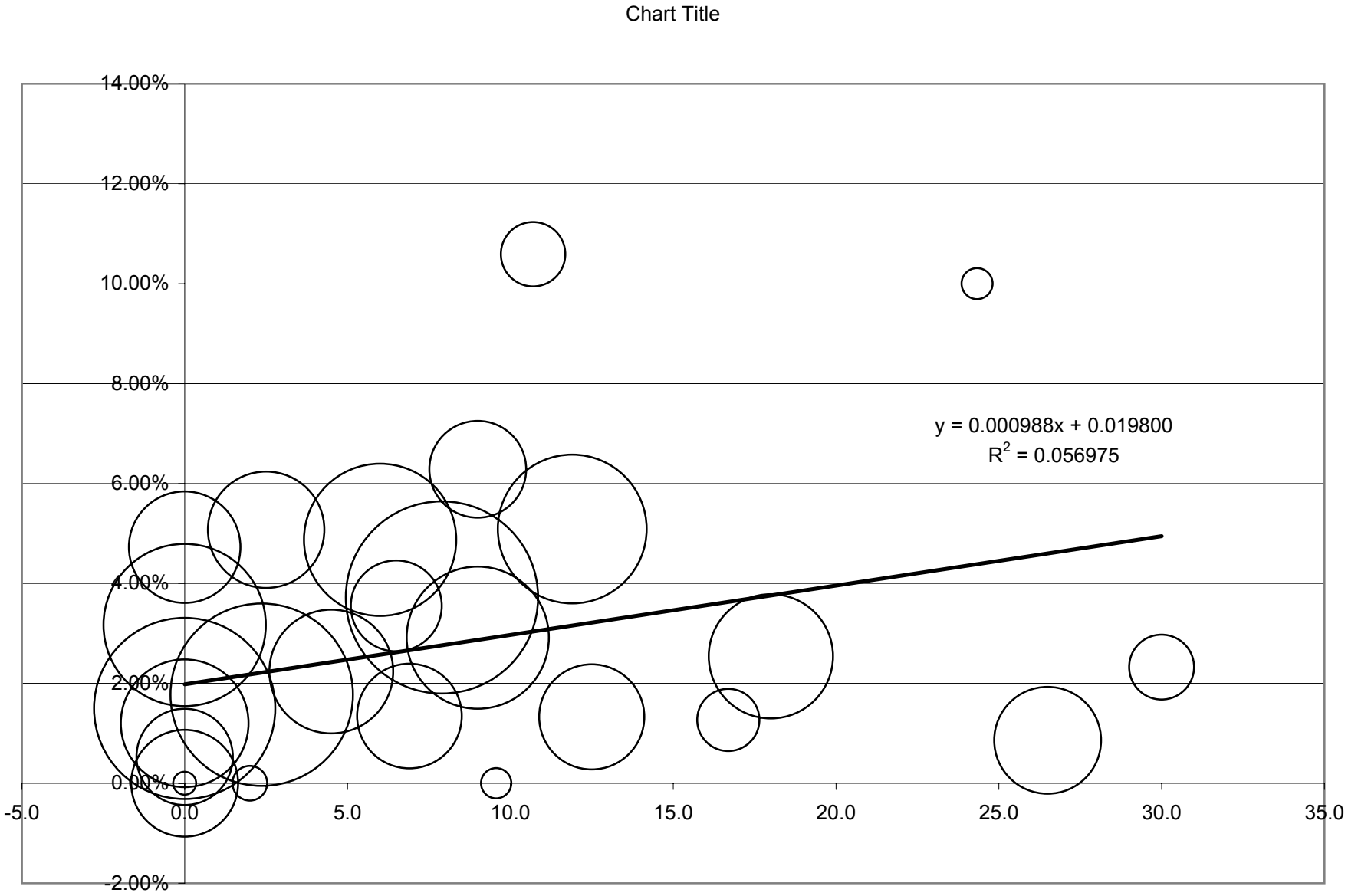
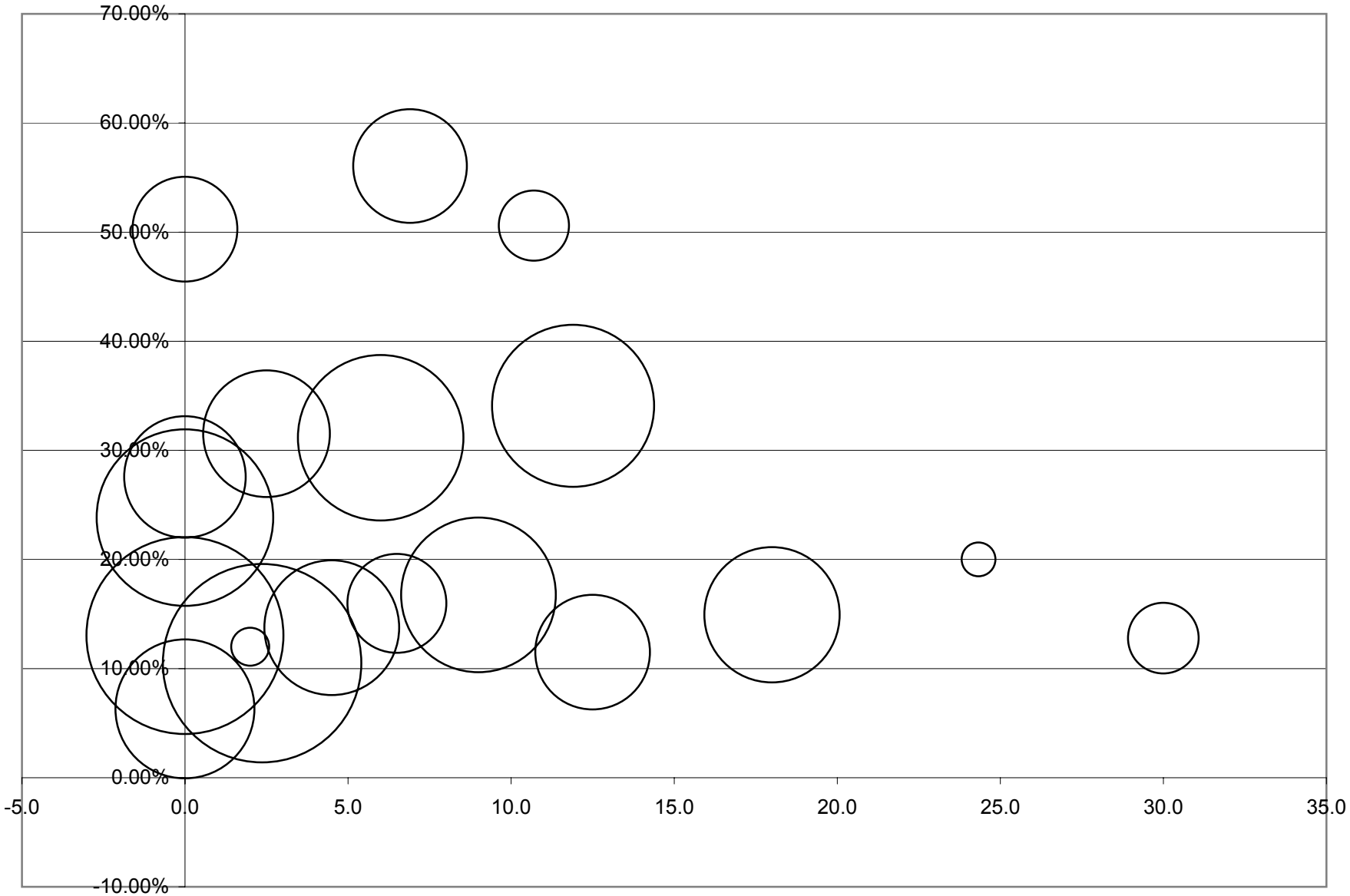
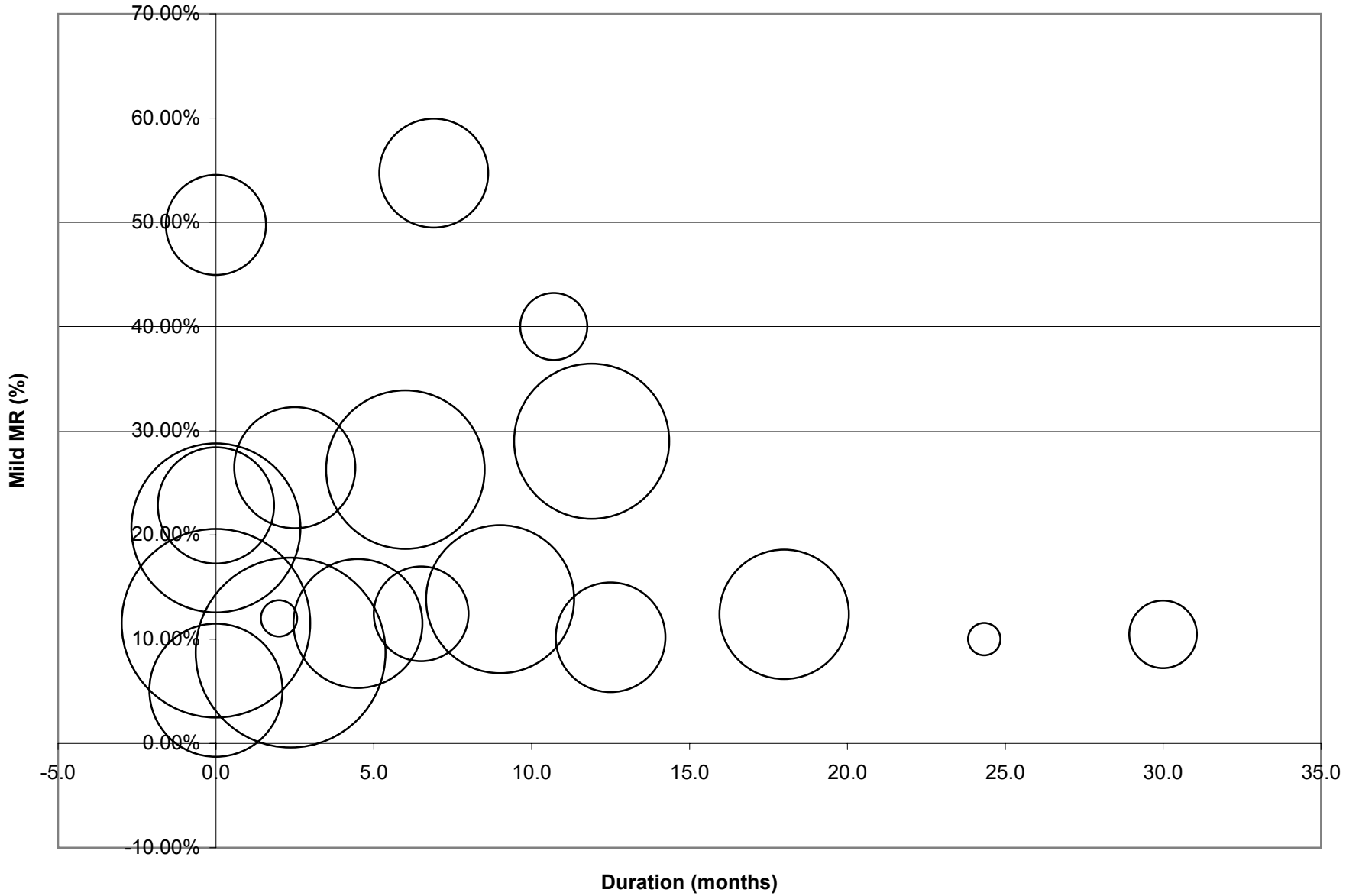


Chart Title
14.00%
12.00%
10.00%
8.00%
6.00%
4.00%
2.00%
0.00%
-2.00%
-5.0
0.0
5.0
10.0
15.0
20.0
25.0
30.0
35.0
y = 0.000988x + 0.019800
R2 = 0.056975


70.00%
60.00%
50.00%
40.00%
30.00%
20.00%
10.00%
0.00%
-10.00%
-5.0
0.0
5.0
10.0
15.0
20.0
25.0
30.0
35.0


70.00%
60.00%
50.00%
40.00%
30.00%
20.00%
10.00%
0.00%
-10.00%
Mild MR (%)
-5.0
0.0
5.0
10.0
15.0
20.0
25.0
30.0
35.0
Duration (months)