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# EDITORIAL

Today we are publishing a manuscript which is unusual in many respects. The data was collected via free-form patient-reporting from an Internet website, thus avoiding the requirement for IRB review. Further, the author collated an anecdotal collection of reports which do not meet any current standards for scientific veracity. Nevertheless, the anecdotes collated herein do have value. Even though "*the plural of anecdote is not data*," at large sample sizes there is indeed a finite likelihood that at least some of these anecdotal observations may be accurate. Further, the results reported here do not seem incredible to this editor. During 2006 I made a presentation to the FDA which detailed the manner in which Statins appeared to impact nuclear receptors far removed from their documented targets.[1] A later discussion in The Lancet [2] exposed many of the public misconceptions surrounding this class of small, highly active molecules.

The data contained in the author's supplementary documents can be further data-mined and validated. It is clear that if further analysis confirms the paper's conclusions, then public-health policies, and FDA post-marketing data collection, will be significantly impacted. I therefore commend this manuscript to your attention.

Prof. Trevor G Marshall, Editor, JOIMR

1. Marshall TG: Molecular genomics offers new insight into the exact mechanism of action of common drugs - ARBs, Statins, and Corticosteroids. FDA CDER Visiting Professor presentation, FDA Biosciences Library, Accession QH447.M27 2006
Transcript available from http://mpkb.org/doku.php/home:publications:marshall_fda_cder_2006

2: Marshall TG: Are statins analogs of vitamin D?. Correspondence to Grimes, DS. *The Lancet* 2006; 368:1234 doi:10.1016/S0140-6736(06)69509-3
Copy available from URL
http://www.thelancet.com/journals/lancet/article/PIIS0140673606695093/fulltext

# Adverse Events of Statins - An Informal Internet-based Study

**Abstract:**
This report was the result of gathering and collating information from self-reported accounts of adverse reactions to HMG-CoA reductase inhibitors. The information was gathered from 351 patients who had signed an e-petition which will be sent to the World Health Organisation.

Every patient reported adverse reactions to statins and 61% of the patients had reported they stopped taking the statins because the side-effects were too severe to persist with the treatment. Sixty three patients reported they had sustained permanent damage and one hundred and twenty people were still experiencing unresolved adverse reactions. Sifting through each patient account revealed there were eighteen cases of amyotrophic lateral sclerosis/motor neurone disease, with one case of ALS being diagnosed within six weeks of starting statin therapy.

There were twenty nine instances of major neurodegenerative disorders including Parkinson's disease, Alzheimer's disease, multiple system atrophy, progressive supra-nuclear polyneuropathy, chronic inflammatory demyelinating polyneuropathy and amyotrophic lateral sclerosis/motor neurone disease.

Sixty nine patients experienced memory loss and eighteen patients complained of cognitive impairment, while six patients experienced transient global amnesia. The information was related to the latest instruction from the Medical & Health Products Regulatory Agency where adjustments to the patient information leaflet for statins and a change in the information given to patients by their treating clinicians is now mandatory following a comprehensive Europe-wide review.

The report deals with the adverse reactions that were reported and the manner in which patients were dealt with by their treating clinicians. It was found that eighty two clinicians had failed to determine that statins were the cause of their patient's symptoms. The report opens a discussion of the reasons why clinicians should incorporate self-reported patient anecdotes into their clinical judgement decisions.

The cholesterol/heart disease hypothesis is briefly examined and the basis for cholesterol treatment regimes is related to Ancel Keys and his Seven Countries Study. Another area of the report provides some commentary on one aspect of the Framingham study and an excerpt from study director, Dr William Kannel's, findings.

Some discussion is devoted to the implications of very severe side effects causing the patients to abandon the statin therapy and to the information uncovered in the patient accounts.

The report ends with a brief look at potential areas for future research.

# Adverse Events of Statins - An Informal Internet-based Study

## Background:

The use of 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors (statins) to reduce LDL cholesterol and thereby lower the risk of coronary heart disease has spanned the last twenty years. One could be forgiven for assuming that two decades of prescribing statin therapies would have had a significant impact on the development and reduction of coronary heart disease in highly developed countries.

The issue of statin prescriptions became a matter for the Medical & Health Products Regulatory Agency in the recent MHRA Drug Safety Update[1]. Caution was advised following a recent European-wide review where it was agreed that new advice and information on the adverse effects of statin therapy were required. The MHRA has requested that the new advisory caution be reflected in the UK by compulsory adjustment of the patient information leaflet. The new information is to be discussed with patients before the initiation of a statin therapy regime.

Printed information leaflets provided to patients would now include references to sleep disturbances, sexual disturbances, depression, loss of memory and interstitial pneumopathy. Additional items for inclusion were non-productive cough, deterioration in general health, fatigue, weight loss, fever and dyspnoea. The update concluded by stating that there was *"sufficient evidence to support a causal relationship"* between statins and the newly acknowledged adverse reactions.

Many patients have been taking statins and they do appear to have been damaged by them. It was decided to give all such patients a voice by inviting them to sign an e-petition where they could choose to append up to 500 words in support of their signature. The intended endpoint was to send the e-petition information to the World Health Organisation to encourage that august body to examine the numerous cases where patients and care givers were witnessing what they genuinely believed was statin-mediated damage.

It is precisely this background which has been the impetus behind the author's determination to create a report reflecting the patients' self-reported adverse effects of statin therapy. The creation of hard numbers from qualitative information is a pursuit that is beset with pitfalls. It was the intention of the author to produce a set of softer-edged numbers (no less sobering for them having been derived from qualitative information) and an insight into how statin therapies are being viewed by the patients who are or were taking them.

## Limitations:

1. Self-reporting may be viewed (by the participants) as an invitation to dramatise or to needlessly embellish an account, possibly to gain more sympathy or credence for the unhappy tale. The author has recorded the facts which are clinically relevant and ignored any language that may be considered to be emotive. Each adverse reaction was recorded with no attempt to determine its impact in medical or social terms nor were such determinants used as indicators of adverse reaction severity.

2. People without benefit of medical training may tend to wrongly ascribe a reaction to one specific cause and they may be unaware that they have done this despite the fact that it colours their opinion as to what has taken place. The author has only recorded adverse reactions as they were described and does not speculate as to the accuracy of the patients' descriptions. The author does not make assumptions about the aetiology of the reported adverse reactions nor whether their genesis is properly ascribed to statin toxicity.

3. The information noted may be especially unreliable where the patients had not understood the use of the 500 word space which was provided to support their signature. The author has assumed that all accounts are true for the purposes of creating this report.

4. There is a suggestion that people who use the internet in order to write in any depth about themselves (for a survey) are a group of coherent, self-selecting and proactive people who tend to think in a broadly similar manner, thereby adding a palpable bias that must affect any findings; the author accepts this possibility. This document is a report of some of the observed phenomena which have been associated with statin therapy by the patients who used statins and by their care givers. As far as possible, the author has taken steps to exclude his own biases from the report. This has been accomplished by reporting solely upon the subject material recorded by the patients.

5. The difficult issue of trying to create hard data out of anecdotal information may seem to be unavoidable. In order to overcome this difficulty, the author has reported on the numerical information gathered only insofar as it is necessary for providing the reader with a broad feel for the numbers which are offered here for illustrative purposes. The feel for the numerical information may help researchers to understand the potential for the type of data which is derived from questioning all patients who take statins; in a well-designed and tightly controlled global multi-centre study.

The information provided in this report should serve to stimulate further fruitful discussion concerning the possibility that statins are harming more people than may have been readily apparent from the clinical studies previously conducted. The numerical information could serve as a gross evaluation tool, where its primary use would be to illuminate the areas which could be profitable in any putative future study.

**Method:**
An e-petition form was devised and posted onto the internet to a specialist petition site on April 3rd 2007. The information for this report was gathered from a total of 888 signatories, with the final signature included in this report being appended to the petition on June 23rd 2009. The text of the e-petition follows in italicised text.

*We, the undersigned, call on the World Health Organisation to initiate a full and impartial, global investigation into the damage caused by therapeutic doses of all available statins, for the treatment of all forms of hypercholesterolaemia. There are far too many casualties of statin therapy for them all to be statistically insignificant. We further call for the investigation to be free from pharmaceutical company sponsorship, to avoid the risk of taint.*

The e-petition permitted each signatory to append 500 words in support of their signature. When the first 100 signatures with a useful written patient account had been analysed, the wording of the instructional rubric was changed. The change was to encourage people to write additional specific details that could assist with the analysis of information provided. The change was encapsulated by the following paragraph:

*If you choose to write a comment of up to 500 words, please consider giving information about the statin name and dose and the length of time you had taken it. It would be helpful to know if you are male of female and your age. Please list the symptoms that have caused you to suffer and also try to make an assessment of your quality of life (QOL) on a scale of 1 to 100. It would be helpful to know if you are still taking a statin.*

It was established that 888 signatories would be selected for analysis and no further signatories were included. A spreadsheet was created and every symptom mentioned in the self-reported supporting texts was recorded. This was the first time that numerical information was derived and collated from the reports. The frequency of each symptom occurrence was recorded and the totals for each symptom were calculated. All calculated numerical information was grouped for ease of creating a written descriptive illustration and it was assembled in the format of this informal information report.

**Information Obtained:**
The reports were gathered from respondents in thirty seven different countries. The graph displays the spread of respondents by region. (Fig.1)

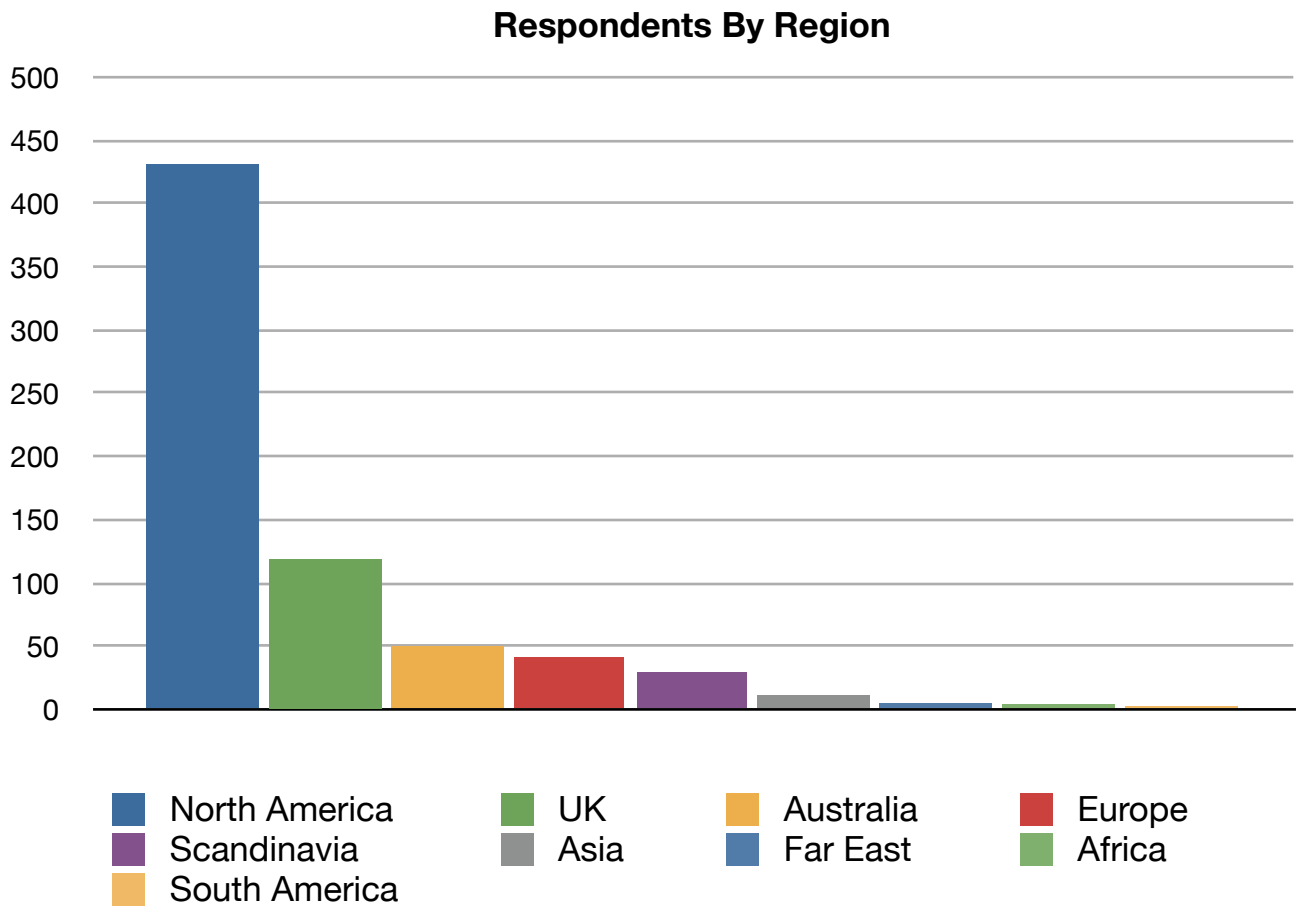


Fig.1

**Respondents by region:**
The UK produced a higher number of respondents (including three from the Republic of Ireland) than the rest of Europe and Scandinavia combined and it been listed separately.

The number of respondents from the region detailed as Australia, includes six respondents from New Zealand and one patient from New Caledonia. The North American region includes forty five respondents from Canada.

**Respondents:**
There were 442 male and 387 female respondents and fifty nine patient cases where the gender was not specified. Some of the respondents were reporting on behalf of a relative or a friend and there were seventy eight proxy reports. The age of the patient was provided by sixty seven people. The age range of the patients varied between 23 and 88 years of age. Among the people reporting statin-mediated side effects the most common age was 57 with five of the respondents sharing this age.

The responses were sorted into useful and non-useful categories. Useful responses comprised commentaries that contained information pertinent to the healthcare and treatment of a specific patient. Non-useful responses were commentaries detailing support for the e-petition or which had addressed statin therapies in general terms but did not refer to any specific patient. Non-useful responses were discarded.

The total number of 888 signatory responses was reduced to 885. Two signatories had signed twice and one textual account was an exact duplicate of a separate response. There were 392 signatories who had not provided any supporting text with their signature. There were 142 non-clinical written responses.

There were a total of 351 clinically useful responses and these were used for gathering the clinical information presented in this report. Sixty two clinicians and four pharmacists had added a commentary in support of their signatures.

**Treatment Days:**
The duration of statin treatment provided was recorded as days. The total number of years of statin therapy for all of the selected patients who had recorded a duration was 567.35 years. The duration of treatment ranged from 4 doses to 17 years. Adverse reactions were experienced by 100% of the qualified respondents. A total of 215 patients had stopped taking their statins. There was no obvious relationship between dosage, duration of treatment and the onset of the adverse reactions. The severity of the adverse reactions seemed unrelated to dosage or treatment duration.

**Statin Therapy:**
Information about each statin treatment was sifted for evidence of patients who were prescribed more than one statin drug during the treatment period. Four patients had been prescribed six different statin preparations. Twelve patients had been prescribed three different statin preparations and thirty four patients had been prescribed two different statin preparations. A total of 239 patients had named a specific statin.

Of the 215 patients who had stopped taking the statins prescribed for them, 132 people continued to experience adverse reactions after the cessation of treatment. The duration from the cessation of statin therapy to the resolution of adverse reactions was variable. Some adverse reactions appeared to result in permanent damage or they were noted as unresolved issues. The most common reason for treatment cessation (very occasionally with the consent of the treating medical practitioner) was cited as having adverse reactions to the statin therapy; frequently so severe that it was impossible for the patient to continue treatment.

The following two frequency graphs illustrate the frequency with which specific cholesterol reducing preparations were prescribed. (Fig.2 & Fig.3)

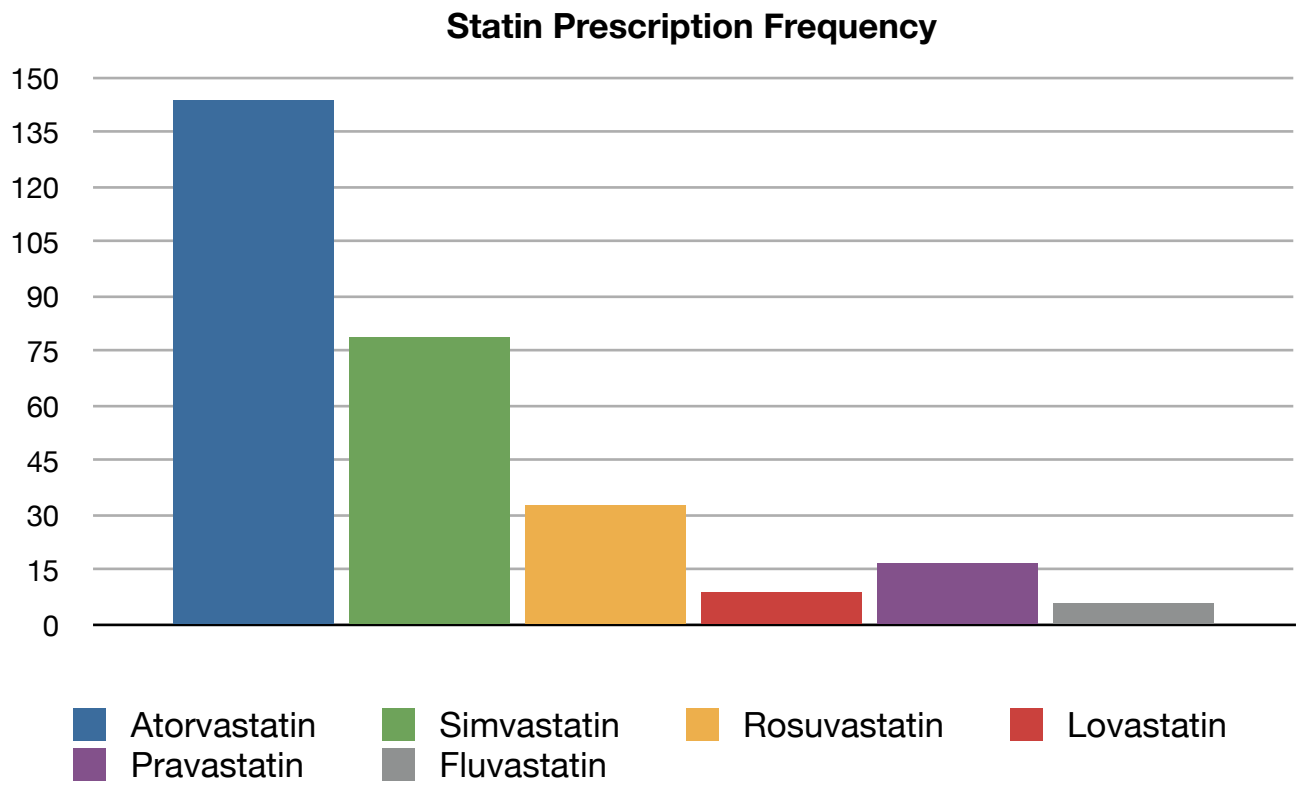
Statin Prescription Frequency
150
135
120
105
90
75
60
45
30
15
0
Atorvastatin
Simvastatin
Rosuvastatin
Lovastatin
Pravastatin
Fluvastatin

Fig.2

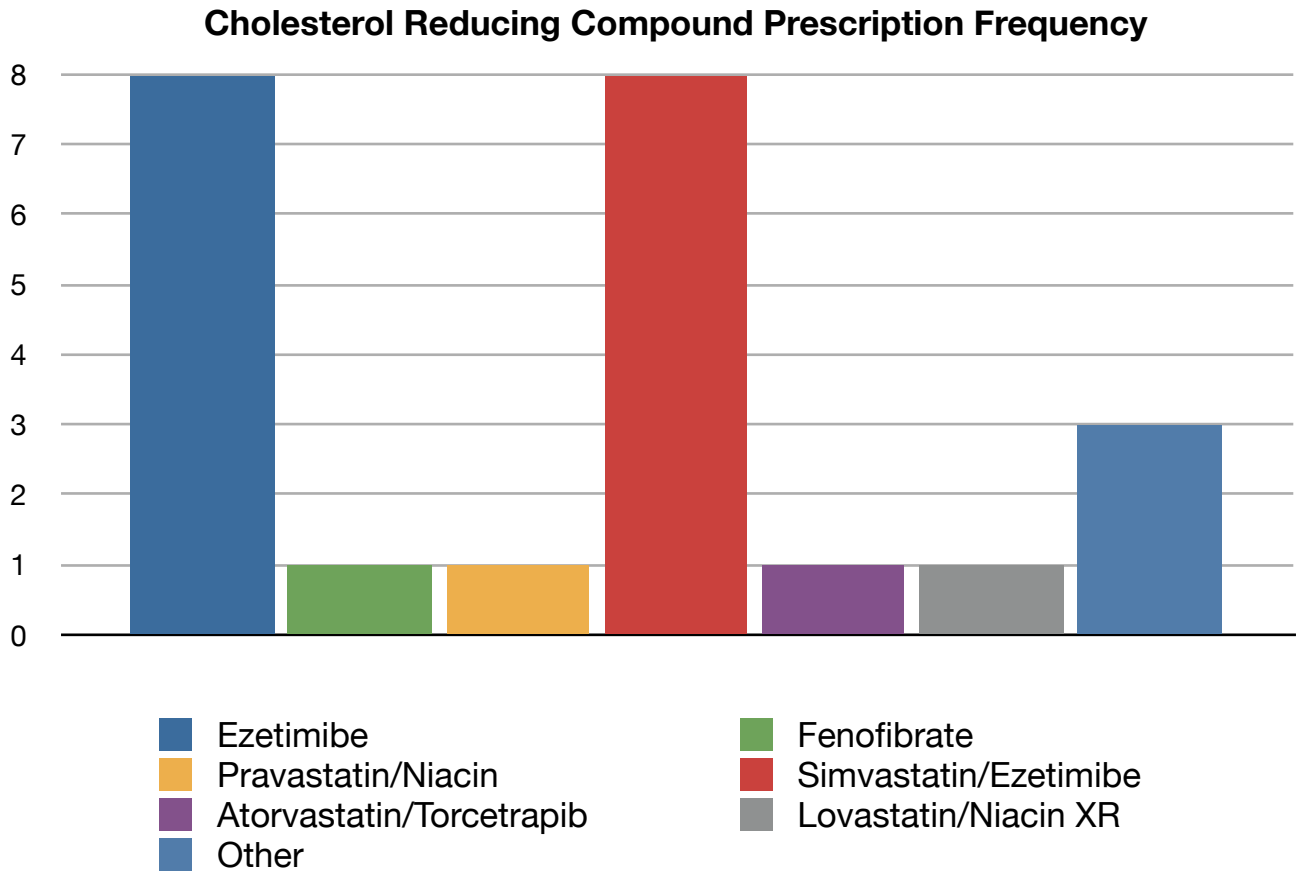
Cholesterol Reducing Compound Prescription Frequency
8
7
6
5
4
3
2
1
0
Ezetimibe
Fenofibrate
Pravastatin/Niacin
Simvastatin/Ezetimibe
Atorvastatin/Torcetrapib
Lovastatin/Niacin XR
Other

Fig.3

**Adverse Reactions:**
Each of the selected patients described adverse reactions with the following outcomes: Not Stated - 69 Permanent Damage - 63 Unresolved - 120 Partial Resolution - 35 Substantial Resolution - 18 Full Resolution - 46. (Fig.4)

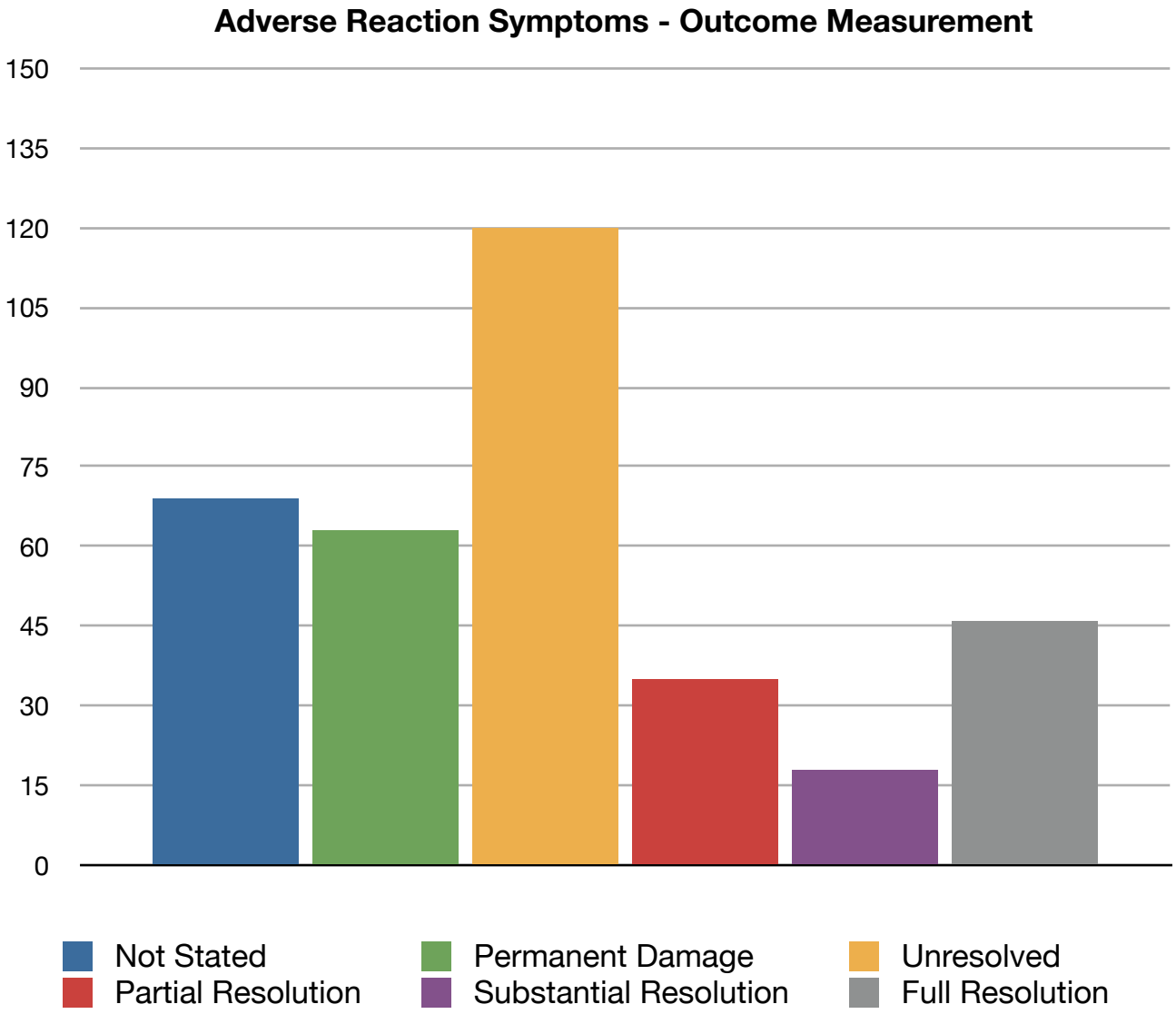


Fig.4

Permanent damage was identified as any damage recorded for any adverse event which the respondent had ascribed to statin therapy. Where was no discernible improvement in symptoms after years of cessation this was also considered to be permanent damage. There were also cases where the informant had stated that the adverse effects were clinically diagnosed as irrevocable. Unresolved reactions were those for which the patient had experienced the symptoms while taking a statin and for which the symptoms still remained to be resolved.

Partial resolution was used where the adverse reaction symptoms were improving but the cessation of therapy was recent and it was too soon to comment on the extent of symptom resolution. Some symptoms were assigned to this category because all improvement appeared to have taken place and there were remaining statin-induced adverse reactions symptoms which had become refractory to treatment.

Substantial resolution was used when patients described major improvements in their health with a concomitant reduction of adverse event symptoms after the cessation of statin treatment. Full resolution was used to indicate a patient's freedom from adverse reaction symptoms where patients had claimed to be fully recovered after they had stopped statin therapy.

Every adverse reaction was noted and assigned a category based upon the descriptions offered by the informant. No attempt was made to interpret the words used by the respondents. Each adverse reaction was listed precisely as it was described. The adverse reactions were grouped according to the body area and the body system involvement as well as the type of reaction experienced.

**Neurological Adverse Effects:**
Amyotrophic lateral sclerosis, motor neurone disease, Parkinson's disease, Alzheimer's disease, multiple system atrophy and chronic inflammatory demyelinating polyneuropathy were all grouped under the general heading of Major Neurodegenerative Disorders. Less serious cases of neuropathic events were recorded under the heading of Neurological Perturbation.

There were seventeen cases of amyotrophic lateral sclerosis along with one case of motor neurone disease and one case of multiple system atrophy. There was one case of Alzheimer's disease and eight cases of Parkinson's disease. One case of progressive supra-nuclear palsy was recorded.There was one unconfirmed but suspected case of chronic inflammatory demyelinating polyneuropathy. In all, there were twenty nine reports of major neurodegenerative disorders which were associated with the use of statins by their respective reporting informants. One female informant had reported a diagnosis of amyotrophic lateral sclerosis which was made within six weeks of her starting statin therapy. (Fig.5)

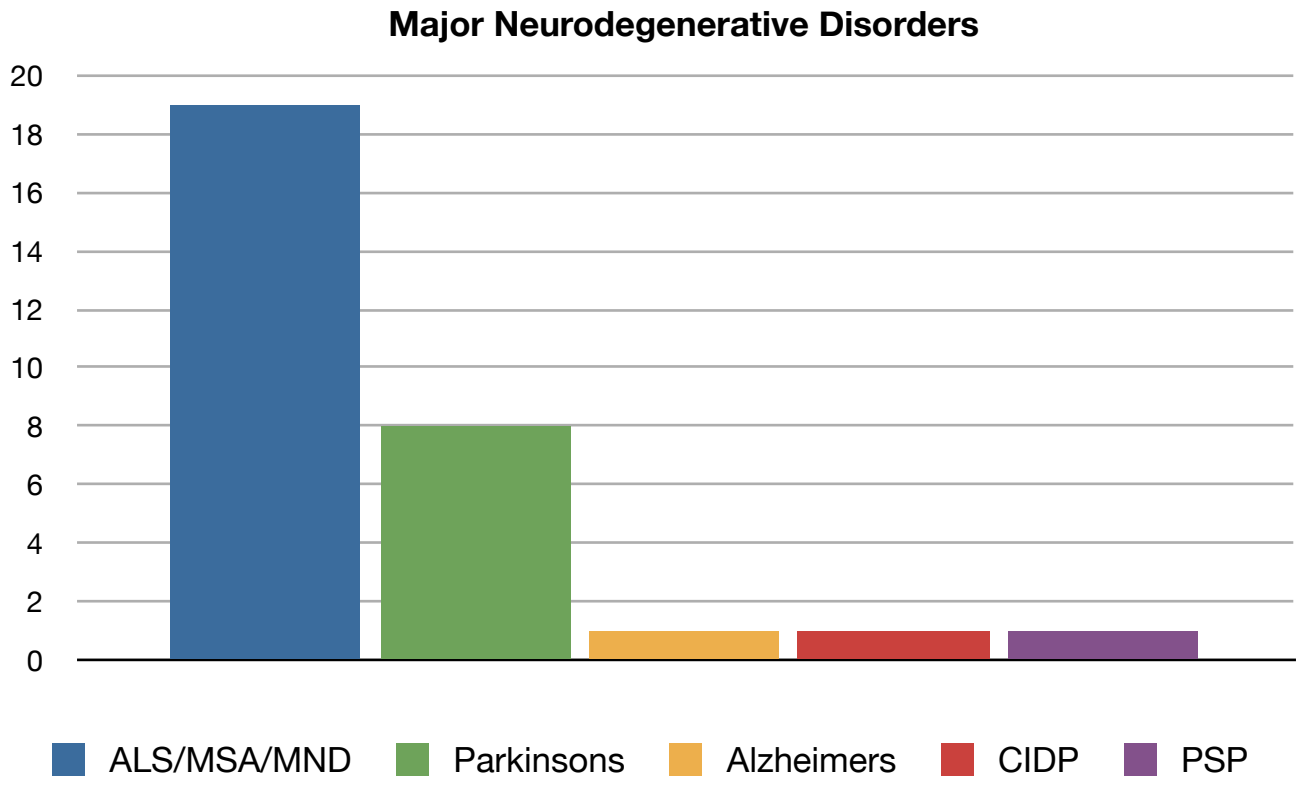


Fig.5

One category of adverse effects concerned several types of neurological disturbance. The events which were assigned to this category included neuropathy, parasthesia, neuralgia, slurred speech and dysphagia. The respondents' complaints about symptoms were often localised to one or two limbs or several digits. There were twenty four reports of neuropathy while parasthesia was reported by sixteen of the respondents.

Neuralgia was mentioned by eleven respondents. Slurred speech was a complaint made by eight respondents and dysphagia was reported by one person. Neurological damage was reported by nine informants. Thirty patients had reported muscle spasm/cramp/ fasciculation. Auditory disturbance was reported by seven people and visual disturbance was reported by twelve respondents. Tremor was reported in three cases. (Fig. 6)

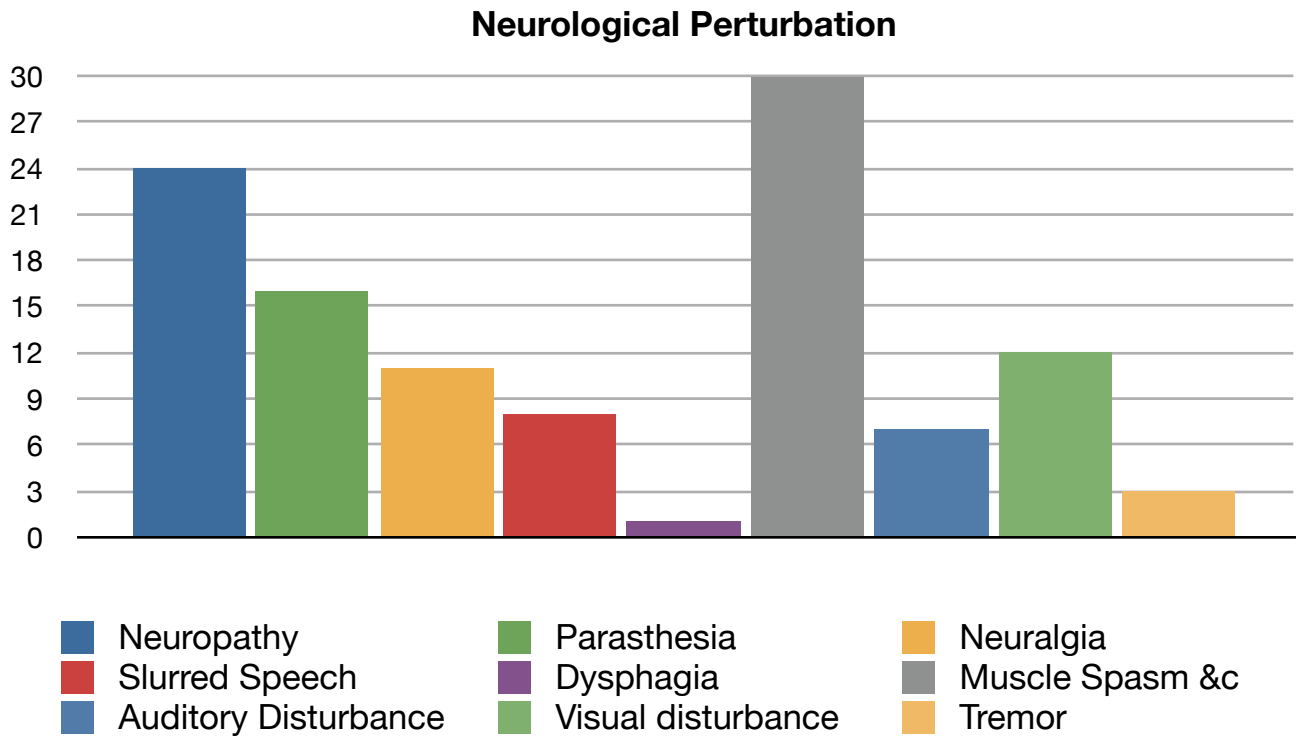


Fig.6

**Thought Processing:**
This group of adverse events refers to the phenomena from which the informants perceived some interference with their normal thinking processes. A list of major adverse effects included a report by eighteen informants of cognitive impairment. Transient global amnesia was reported by six respondents. Memory loss or memory impairment was reported by sixty nine respondents. Mental confusion was reported by twenty eight of the respondents and this confusion was occasionally referred to as 'brain fog'.

Thirty people had reported depression and four patients had reported suicidal ideation. One person had reported the death of her son who was taking a statin. He had stopped taking the statin because he was having 'bad thoughts'.

He subsequently was re-challenged with a statin by his clinician and sadly, he killed himself within a few days of recommencing his statin therapy. His mother's distress was then compounded by the attempted suicide of her husband, no less than 3 times (he was also taking statins) and he was admitted for four years to a hospital for psychiatric illnesses. (Fig.7)

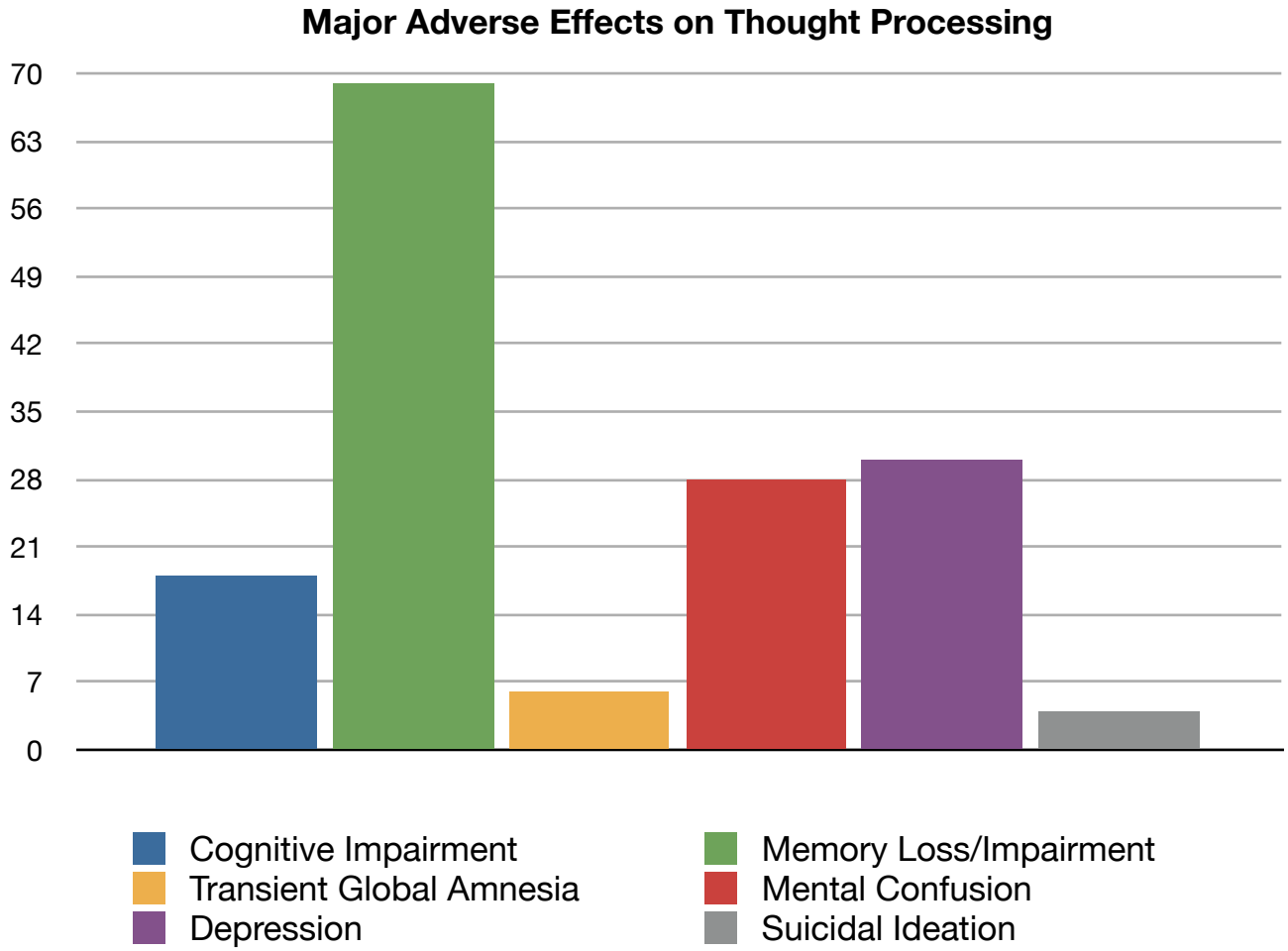


Fig.7

Other significant unwanted effects that also involved thought processing were described by the respondents. While these events may appear to be less severe than those already listed, it does not automatically follow that the impact on the lives of the patients was any less disruptive. The division of these side-effects from those already described was arbitrary. The device was used to assist in the provision of a report that would be easy to read and follow for a lay audience.

In this group of unwanted effects there were eight descriptions of loss of concentration. Reports of sleep disturbances numbered twenty and three people had complained of having nightmares. The loss of dreams was reported by one person. Irritability had been described by six patients and anxiety was noted by four people.

Dementia was described by five informants and nine people complained about mood swings and aggression. One person had written an account of her previously mild-mannered father, who was aged 70 and taking a statin. He was jailed for the first time in his life after attacking a neighbour whom he believed was harassing him. The attack was described as being completely out of character. (Fig.8)

All of these adverse events would have a deleterious impact on the lives of the patients and their families. People do not function well within society when they cannot reason or they have “holes in their memory”. (from one respondent’s descriptive statement)

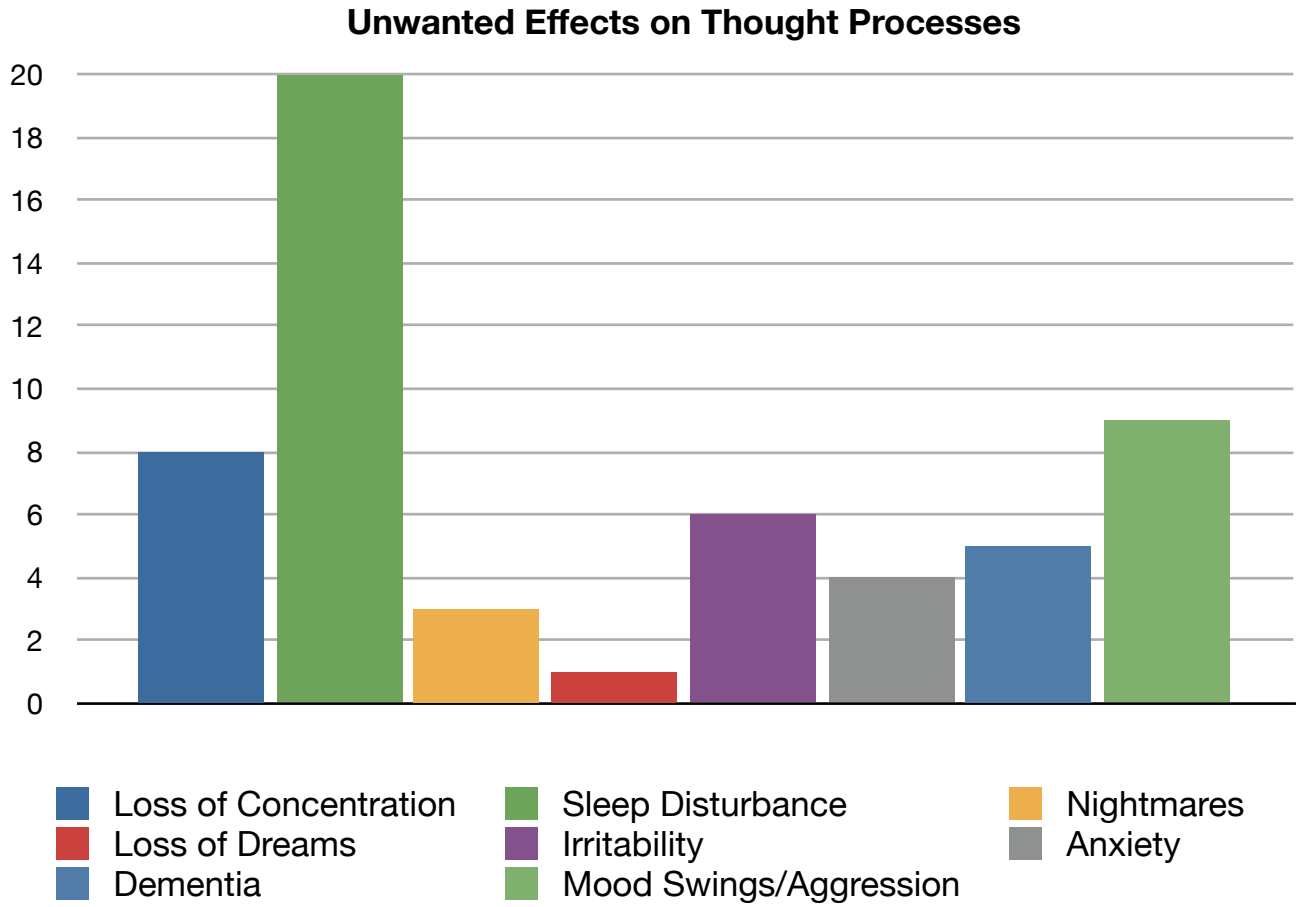


Fig.8

**Adverse Reactions Affecting Muscles:**
One group of adverse reactions involving significant numbers of patient reports, were those which affected the muscles. These adverse reactions spanned a spectrum that ran from minor muscle aches through to rhabdomyolysis. Fifty eight people reported their mobility was affected. Restriction of movement was reported in fourteen cases. Four respondents had described an alteration in their gait. Falling and balance issues were reported by fourteen respondents. Rhabdomyolysis was experienced by eight people. Muscle damage affected eleven respondents. Muscle atrophy was recorded by nineteen of the participating respondents. (Fig.9)

Muscle pain was cited in eighty seven cases. Muscle weakness was reported by forty two people. Muscle aches were noted by seventeen people and twenty people recorded an adverse reaction under the general heading of muscle problem. Lassitude was noted by seventeen patients and thirty seven respondents recorded fatigue. Myopathy was cited by one patient. Non-specific pain affected seventy one people and general weakness was recorded by twenty respondents. (Fig.10)

The severity of the pain-inducing symptoms was recorded by one hundred and nine respondents. This pain assessment was allocated to one of three categories based upon the words used to describe the pain. Three records were allocated to the category labelled mild. One record was allocated to the category labelled moderate. One hundred and five records were allocated to the category labelled severe. Inclusion in the *severe* category was triggered by the respondents' use of the words such as 'extreme', 'excruciating' and 'unbelievable' when referring to their pain.

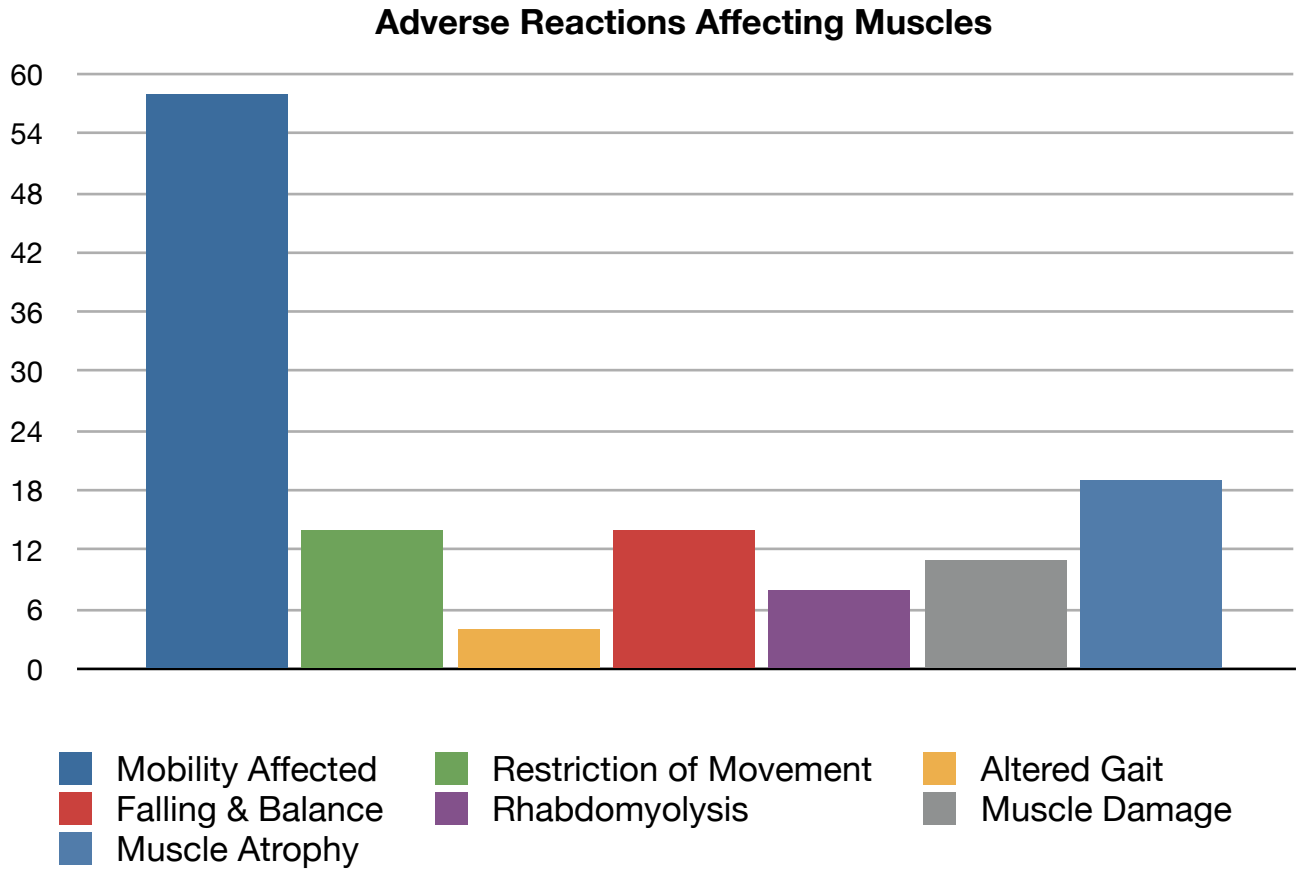
Adverse Reactions Affecting Muscles
60
54
48
42
36
30
24
18
12
6
0
Mobility Affected
Restriction of Movement
Altered Gait
Falling & Balance
Rhabdomyolysis
Muscle Damage
Muscle Atrophy

Fig.9

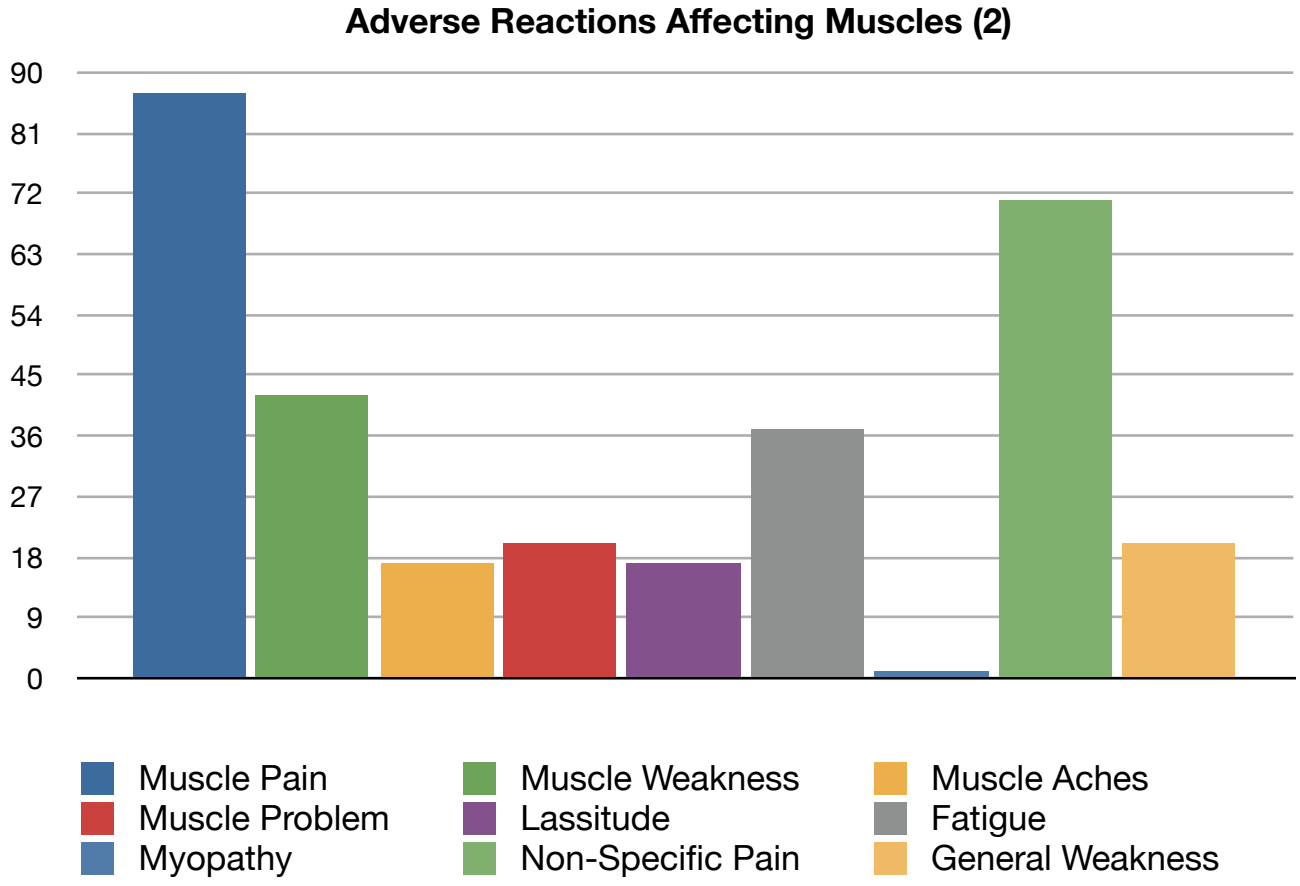
Adverse Reactions Affecting Muscles (2)
90
81
72
63
54
45
36
27
18
9
0
Muscle Pain
Muscle Weakness
Muscle Aches
Muscle Problem
Lassitude
Fatigue
Myopathy
Non-Specific Pain
General Weakness

Fig.10

Muscle adverse reactions were noted by eleven patients as an issue affecting all of their muscles. Five people noted their whole body was affected. Another potential culprit for reducing patient mobility was joint pain. It was noted by twenty two of the informants. Two respondents recorded painful side-effects in all of their joints. Oedema was recorded by 6 patients. (Fig.11)

Some respondents recorded a reaction that affected a specific part of their body. Back pain was noted by twenty informants. Headaches featured in eleven cases with neck pain mentioned by twelve people and two reactions affected the face. The shoulder was painful in twenty three reports. Arm pain was noted in twenty five records and elbow pain was cited by two patients. Painful hands and fingers were recorded in fifteen cases. (Fig.12)

The chest was mentioned in three reports of pain and the abdomen was noted in six responses. Respondents complained about painful hips eleven times. The legs were featured in seventy reports made by patients and painful knees were reported by eleven different respondents. There were twenty nine respondents who noted their toes were affected by their statin treatment. The tendons were recorded by four people as having been affected by statins. (Fig.13)

Several respondents complained about the statins exerting an effect on their immune systems. Fibromyalgia was cited by three people and four of the respondents mentioned a reduction in their immunity while six patients had succumbed to an autoimmune condition.

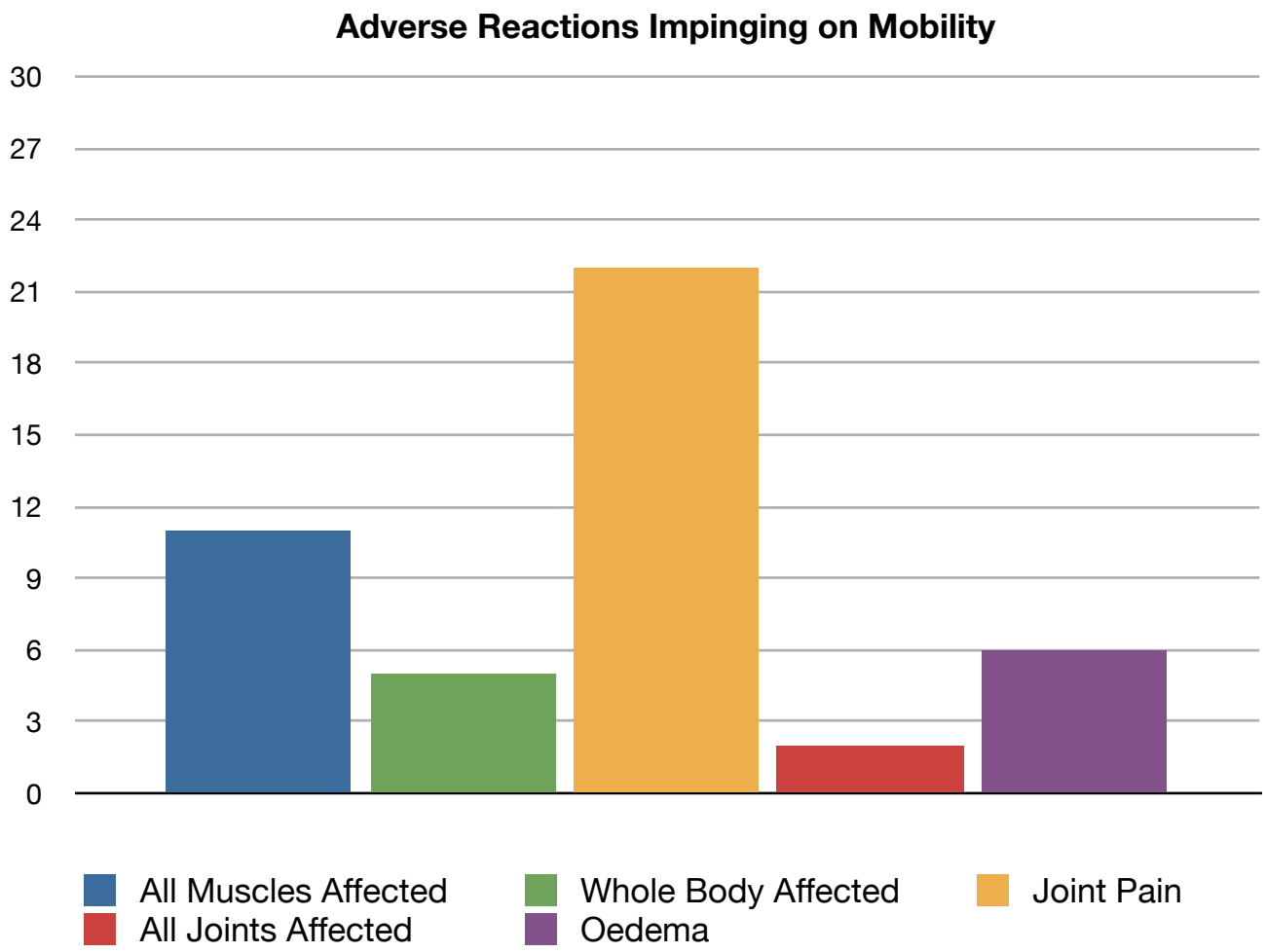


Fig.11

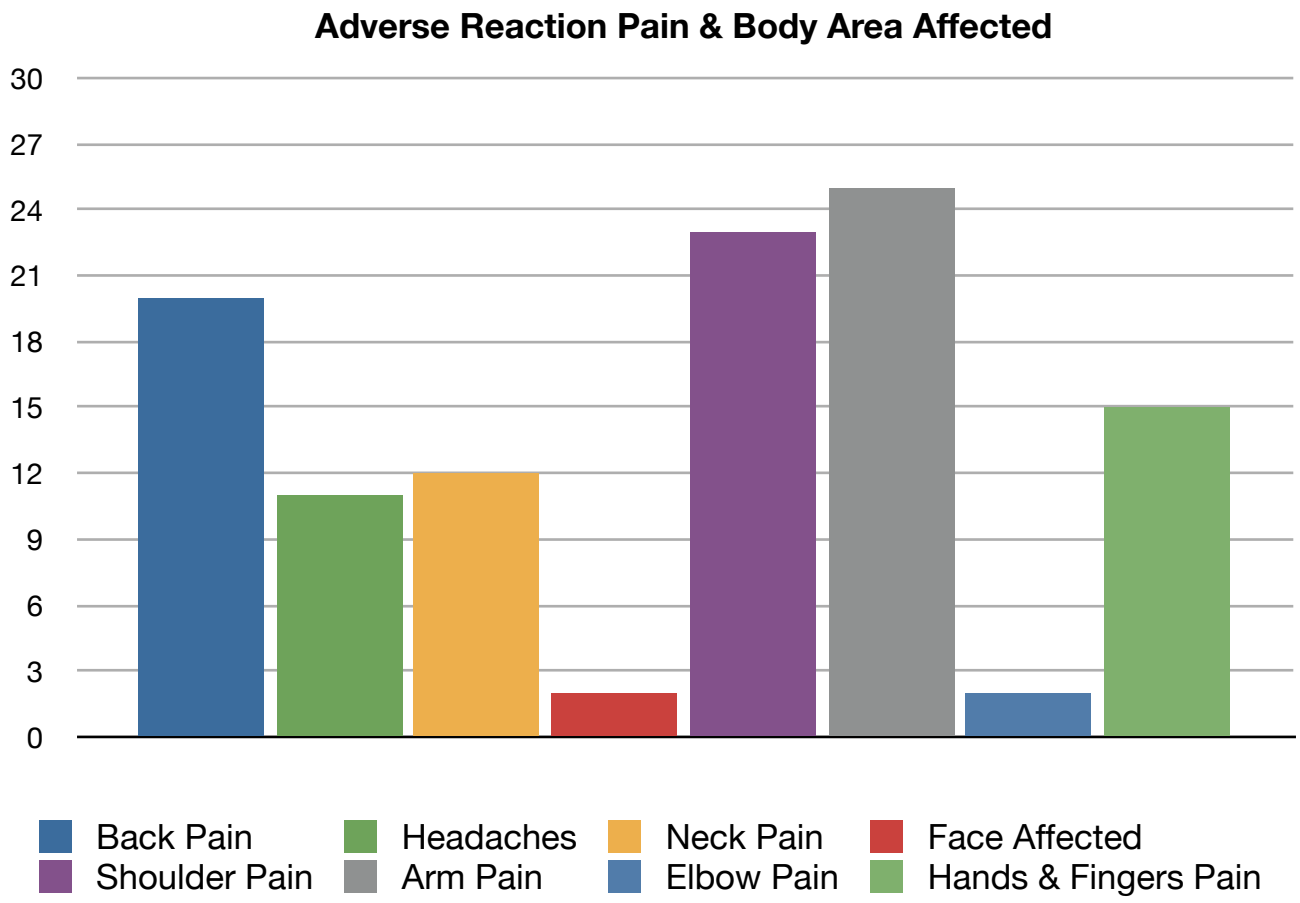
Adverse Reaction Pain & Body Area Affected
30
27
24
21
18
15
12
9
6
3
0
Back Pain
Headaches
Neck Pain
Face Affected
Shoulder Pain
Arm Pain
Elbow Pain
Hands & Fingers Pain

Fig.12

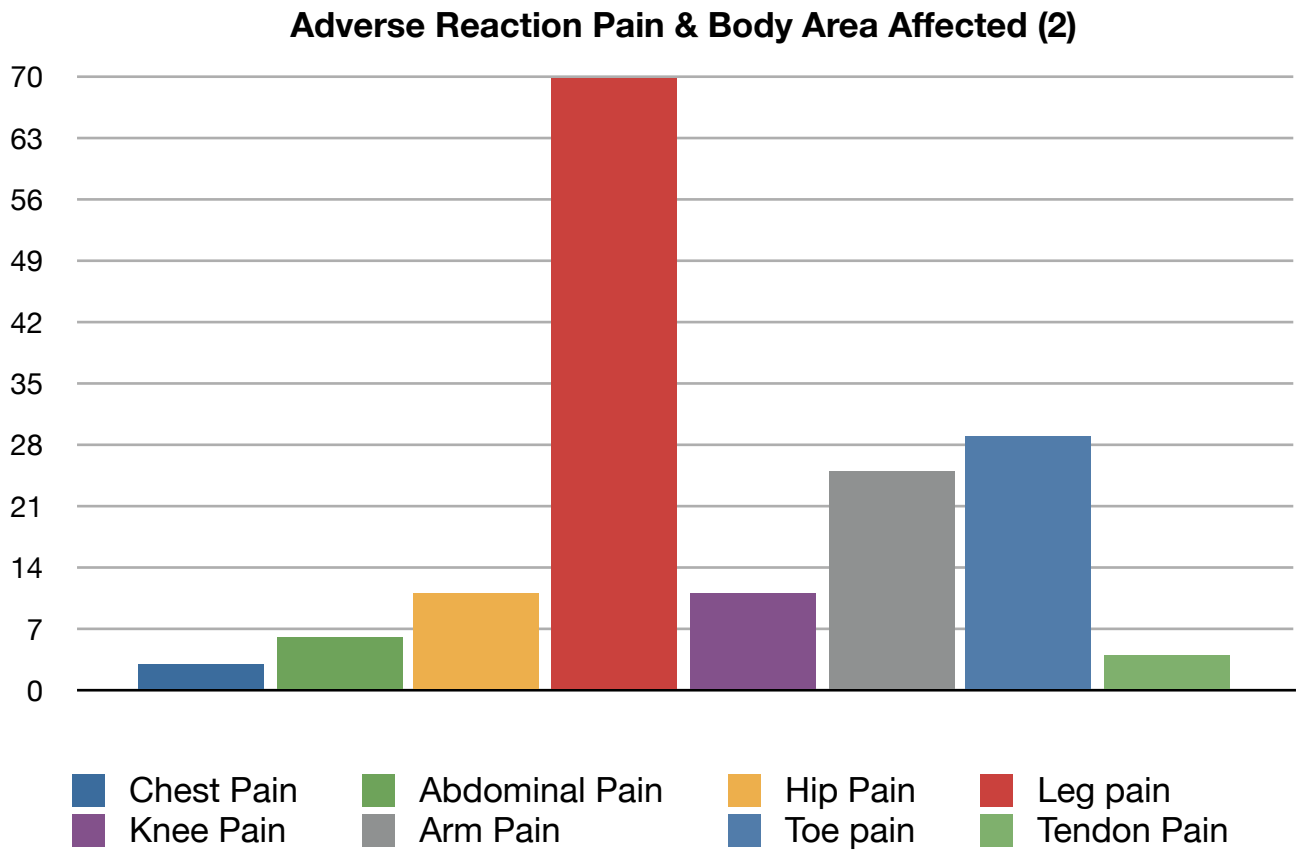
Adverse Reaction Pain & Body Area Affected (2)
70
63
56
49
42
35
28
21
14
7
0
Chest Pain
Abdominal Pain
Hip Pain
Leg pain
Knee Pain
Arm Pain
Toe pain
Tendon Pain

Fig.13

Several unconnected symptoms were recorded with some frequency. Nine people reported that they suffered with a sexual dysfunction. The dysfunction was recorded as a reduction in libido, impotency or it remained unspecified. Twelve people recorded some sort of skin problem that was frequently a very persistent skin rash or dry skin.

Weight Gain was listed as an effect of the statin therapy by eight people and one of those reports was supplied by a veterinary surgeon. Feeling aged beyond one's years was a complaint made by seven people. Reactions affecting renal function were described by seven respondents. Three respondents reported that they had become intolerant to exercise. (Fig.14)

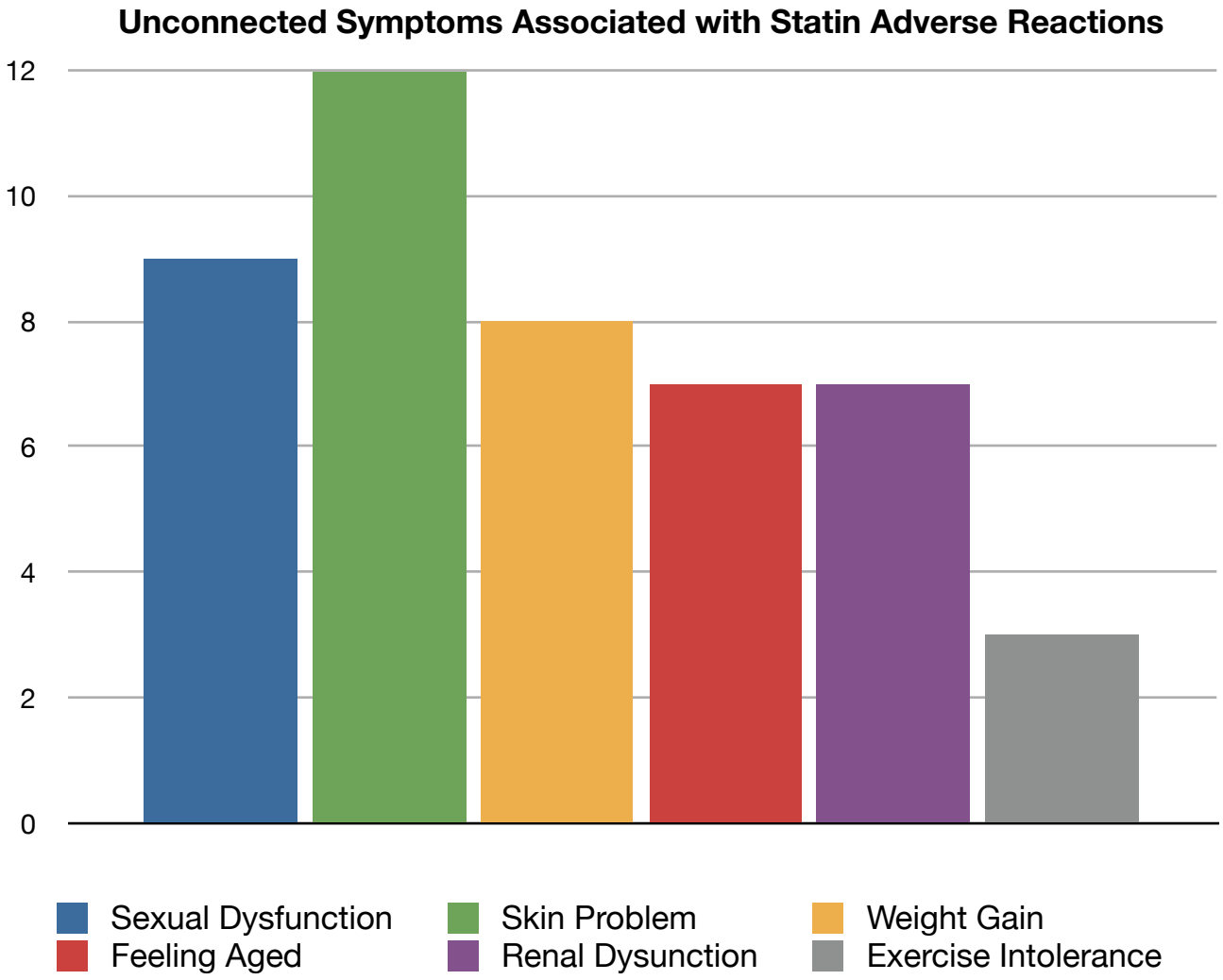


Fig.14

General malaise was noted by four patients. Mitochondrial Myopathy was recorded by one person. Four people noted abnormal blood screen results which they ascribed to their statin therapy. Reflux was mentioned by three people. Psoriatic arthritis was recorded by one respondent. Nonalcoholic steato-hepatitis was noted by one person.

The written reports were scanned for the use of L. Carnitine and Coenzyme Q10 in a measure to determine whether any of the patients were using these supplements to assist their recovery from their statin induced adverse reactions. The use of L. Carnitine was noted by two respondents and Coenzyme Q10 was used by eleven of the informants.

One issue became apparent during the gathering and collating of this information: there were a number of respondents claiming their treating clinician was unwilling to listen to any criticism of the statin therapy regime. This appears to be wrong considering a complaint had been made by the patient about an adverse reaction. Eighty two clinicians were implicated in an apparent failure to recognise statin-mediated adverse reactions.

Among the 351 cases which were selected for analysis there were six deaths recorded. It should be remembered that twenty nine serious cases of neurodegenerative disorder have already been noted in the selected group. People stated that there were seventeen cases of patients who were dying or whose condition was rapidly deteriorating at the time their accounts were written. These were patients who were quite likely to die prematurely because of the prognosis which was implicit in their medical conditions.

Sixty four cases of statin-mediated adverse effects were noted without any specific reactions being recorded. Statin dosages ranged from 5 to 80mg. Where multiple statins had been prescribed to the same patient then the dosage was usually seen to increase upon the introduction of a new statin medication.

**Discussion:**
Because the reduction of cholesterol is seen as a desirable endpoint, the administration of therapeutic products from the group of drugs known as HMG-CoA reductase inhibitors (statins) is uncontested by clinicians. This report is concerned primarily with the issue of how the ideas of patients, concerning clinical decisions which are made on their behalf by their treating clinician, are being viewed by clinicians. It also questions the routine prescription of statins given the deeply toxic nature of statin therapies. There is some questioning of the bedrock knowledge that is the basis for prescribing statin therapy.

Information about statin therapy has become available by way of the medical literature. It has been derived from the various clinical trials which have tested the statin group of pharmaceutical products and judged them to be sound in both concept and efficacy. Only a cursory look at the literature is required to reveal that there are many questions which are not yet answered satisfactorily by the would-be protagonists for the administration of statins to ever-increasing numbers of patients.

There are huge numbers of people who have been newly discovered to be ‘ill’ with ‘cholesterol levels’ disease and they are said to be at a higher risk for developing heart disease because of their high cholesterol levels. The threshold for the declaration of ‘cholesterol levels’ disease appears to be falling with each passing year. It is not clear whether two decades of statin therapy and low fat diets have reduced the incidence of coronary heart disease and obesity or whether medicine is now much improved when treating acute myocardial infarction during the pre-hospital phase of treatment.

In the face of the currently accepted wisdom regarding cholesterol levels, patients who are experiencing difficulties while taking their prescribed statin medication are evidently finding it difficult to persuade their treating clinicians that it is the statins which are responsible for causing their adverse reaction symptoms. One surprising discovery while sifting through the patient accounts and writing this information report was the discovery of eighty two clinicians who did not associate their patient’s symptoms with an adverse reaction to statin therapy.

The written accounts revealed clinicians who had refused to accept that statins could be causing their patients to experience adverse reactions. Several of the respondents had detailed cases of being prescribed statins without having any sort of clinical consultation. Blood results from a routine blood analysis had caused their treating clinicians to prescribe the statin and then instruct the practice receptionist to make a request to the patient to stop by and collect the prescription. It would appear that no advice, regarding the potential for statin induced adverse reactions could have been offered at the point of collection. More seriously, it would have to be true that no consent to treatment could have been obtained. This cavalier attitude towards the patient has no place in the practice of medicine. When were the clinicians hoping to obtain an informed consent?

When the patient experiences any adverse reaction to a treatment that their clinician has prescribed it is an especially worrying time for the patient. It is reasonable to suppose that any thoughtful patient will have fears about their mortality and go on to consider the extent of the clinician's knowledge and skill. When the patient is met with ridicule because they had dared to pose a question about their treatment and its progress, to the clinician, they are far more likely to question the clinician's ability in all other matters and that has implications for compliance with treatment. Where a patient has given a coherent, albeit anecdotal account of their experiences while they are taking a particular treatment, it should cause the clinician to listen with attentiveness and care.

Many patients received prescriptions for multiple statin agents, having complained and explained to their clinician about their adverse reactions to the initial statin prescription preparation. The prescribing of two or three different agents, on the back of complaints about unwanted effects that were caused by the initial prescription, betrays a lack of knowledge about the action of statins. The prescribing of six different agents under precisely the same circumstances displays an unexpected indifference to the healthcare needs of patients.

One fragment of information that was gained from the patient accounts is the apparent incidence of major neurodegenerative diseases which may well have been precipitated by statin therapy. While it is difficult to be certain about the incidence of Alzheimer's and Parkinson's diseases, there is an estimated prevalence rate of 67 and 9.5 respectively[2]. Chronic Inflammatory Demyelinating Neuropathy is uncommon and the incidence is put at 1.6:100,000[3]. Progressive Supra-Nuclear Palsy has an incidence rate that has been put at 5.3:100,000[4]. Multiple System Atrophy is attributed an incidence rate of 4.4:100,000[5]. Amyotrophic Lateral Sclerosis (ALS/MND) has an incidence rate of 1:200,000[6].

The rarest of these conditions is ALS and yet in just 351 reports there were enough cases to have made the prediction (based upon incidence statistics) that an expected three million six hundred thousand accounts would have to be written before eighteen ALS/MND cases would have been revealed. This is such an astonishingly high number of cases to report within such a small participant group that it would be right to ask whether a fundamental error has been made. Absent any error it is also right to ask: What is really happening? What is the real risk posed by statin therapy? By what mechanism can statins be linked to the development of ALS/MND? Is it ethical to continue to prescribe statins if any hypothetical association is suspected and has not yet been falsified, let alone if the association is demonstrated?

The use of 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors is grounded in the notion that an inhibition of the synthesis of cholesterol within the mevalonate metabolic pathway is the appropriate measure to reduce the incidence of heart disease. This appropriate measure does nothing to address the unwanted inhibition of other vital processes within the mevalonate metabolic pathway (MMP).

Ubiquinone (Coenzyme Q10) is also produced within the MMP. The original Merck Patent[7] had recognised that myopathy could result when statins were administered and Coenzyme Q10 was depleted. A compelling quotation from the original patent application states the following: *"the present invention relates to a method of counter-acting HMG-CoA reductase inhibitor-associated myopathy in a patient receiving HMG-CoA reductase therapy which comprises the adjunct administration of an effective amount of an HMG-CoA reductase inhibitor and an effective amount of Q10."*

If this information is known, then it begs the question: Why is Coenzyme Q10 not routinely given to patients who are prescribed statin therapy? If the manufacturers of a statin have acknowledged the causal relationship between taking a statin and the subsequent development of myopathy more than 19 years ago, is it not wrong-headed to prescribe such a drug without taking steps to reduce the potential for patient harm where they are certain to have a debilitating adverse reaction to that drug?

Heme A is another product which is synthesised within the MMP. It is essential for the production of energy and it is found only within the mitochondria of cells. Any reduction in Heme A may lead to the accelerated decay of mitochondria. Reductions in Heme A may also cause neural damage and damage to the DNA. Cells may age prematurely where Heme A is reduced. Mitochondrial oxidative decay is accelerated by common micronutrient deficiencies[8]. The potential damage arising from the certain inhibition of the biosynthesis of Heme A appears to be an unjustified risk taken for a small and dubious patient benefit.

Dolichol synthesis is inevitably inhibited within the MMP by statins which produce an inhibitory blockade of cholesterol synthesis. The role of Dolichols in the endoplasmic reticulum assembly of peptides is well understood. Dolichols are essential to mediating the process that contributes to neuropeptide formation as well as cell identification, cell communication and immune system functionality. The question that appears never to have been asked is this: Why are these vital body functions permitted to be inhibited, despite the resulting harm to the organism, while pursuing the goal of cholesterol level perfection? The human body could be encapsulated by the word, 'equilibrium' and to change the value of cholesterol at the expense of all other chemicals present is a foolhardy act.

The inclusion of interstitial pneumopathy as a side effect of statins for which *"there is sufficient evidence to support a causal relationship"* as was published by the Medical & Health Products Regulatory Agency in the recent MHRA Drug Safety Update[1], is a warning that the twelve respondents who had complained of having dyspnoea, were all potential candidates for suffering with interstitial pneumopathy. Would these patients have been believed if they had consulted a clinician about their statin-mediated dyspnoea before this instruction was made public?

The same MHRA publication included memory loss within the new instructions. Sixty nine of the subjects had complained about memory loss or impairment. No mention of memory loss was made in the patient information leaflets for statins during the previous 20 years in the UK. Clearly, it is now regarded as a plausible reaction to statin therapy.

With almost 20% of the participants complaining about memory loss, it would appear to represent a significant adverse reaction given its effect on the lives of the patients. The first-hand accounts describe the relief of the patients on recovering their memory after stopping statin therapy. Transient global amnesia is another aspect of the same type of adverse effect and it would be prudent to have it included in the approved list of side effects that are potentially induced by statins.

One clear difficulty with the age group that usually receive statin therapies is that they are frequently middle-aged or elderly people. It is far too easy for the clinician to ascribe complaints that appear to mimic dementia as being a recognised part of the aging process. It is probably a major reason why patients with memory loss complaints are never quite taken seriously enough. The depressing concomitant is that reports to supervising agencies such as the MHRA and the FDA are made with less frequency than is desirable particularly when reporting upon the toxic unwanted effects of statins.

Twenty nine respondents indicated that they had suffered with depression. It is well-known that statin-induced depression was a potential adverse reaction where the patient had lower serum cholesterol. A clinical study of 29,133 men[9] between the ages of 50 and 69 years and where the men were followed up for between five to eight years, noted that low serum cholesterol was associated with depression and suicide. When the potential result of having a low serum cholesterol is that the patient is exposed to an increased and significant risk of depression and suicide, it should cause clinicians to consider which risk is more likely to damage the patient. Patients do not die because they do not have sufficient statins in their body.

Consigning patients to suffer with substantial cognitive issues is a strategy based upon an incomplete grasp of the strength and scope of the debilitating adverse effects that attend the use of statins. One may argue that if the patient is unaware of their newly found good health (lower cholesterol) because of their inability to reason, which was impoverished by their use of statins, then what is the purpose of forcing patient compliance? Why should we expect patients to undergo treatment for an ‘illness’ that has no effect on their well-being?  Being unable to reason is a major disability and inevitably, it has a significant impact on the lives of the patients and their families.

The outcome measurements used in this report were devised to gain an idea of what was necessary for determining when a patient had recovered from the statin-induced effects. It is distressing to note that 52% of the participating group had not found any resolution for their side-effects. That 18% of the sample had claimed to be permanently damaged is a salutary lesson and a clear warning for clinicians and pharmaceutical companies. With the number of statins being prescribed increasing exponentially, it is clear that many more people will be damaged and the harm will be unavoidable because of the manner in which statins work. It is long overdue; when a global moratorium on the wholesale prescribing of statins (pending a completely impartial investigation) should have been instituted.

It is clear from the soft-edged numbers which have been derived from this informal collection of information that patients do have a significant contribution to make to their own healthcare despite it being anecdotal. Whether clinicians agree is another matter. The bullying of patients into taking statins where there are no discernible benefits to the patient and the claimed benefits remain scientifically unproven borders on the immoral. The primary justification for the use of cholesterol reducing medication is predicated on the dubious science promulgated by Ancel Keys. He had only presented the research data that was in agreement with his hypothesis and thus favourable to his research.

Here is short history of some statements which were made by Ancel Keys:

**1953**
All fats raise serum cholesterol
Nearly half of total fat comes from vegetable fat and oils
No difference between animal and vegetable fats in effect on coronary heart disease

**1956**
Type of fat makes no difference
Need to reduce margarine and shortening

**1957 - 1959**
All fats are comparable
Saturated fats raise and polyunsaturated fats lower cholesterol
Hydrogenated vegetable fats are the problem
Animal fats are the problem

These quotations reveal that he was both inconsistent and contradictory. The famous Seven Countries Study was a 20 year study of 12,000 men who were aged from 40 to 59 years. They sample was drawn from 16 different communities in Finland, Holland, Italy, Japan, the Greek Islands, Yugoslavia and the USA. Keys chose to study those countries where saturated fats consumption and heart disease were high. The countries where a similar diet was eaten but the population were enjoying low rates of heart disease, were excluded from the researches of Keys.

The statistician, Russell H. Smith, was one of many people who were critical of The Seven Countries Study. He went on to say the following:

***"The dietary assessment methodology was highly inconsistent across cohorts and thoroughly suspect. In addition, careful examination of the death rates and associations between diet and death rates reveal a massive set of inconsistencies and contradictions. . .***

***It is almost inconceivable that the Seven Countries study was performed with such scientific abandon. It is also dumbfounding how the NHLBI/AHA alliance ignored such sloppiness in their many "rave reviews" of the study. . .***

***In summary, the diet-CHD relationship reported for the Seven Countries study cannot be taken seriously by the objective and critical scientist."***

*– Diet, Blood Cholesterol and Coronary Heart Disease:*
*A Critical Review of the Literature, Volume 2, November 1991*

The indictment is contained within the final sentence. If you are an objective and critical scientist, then the Seven Countries Study cannot be taken seriously. Nevertheless, it was the genesis of the cholesterol/heart disease hypothesis. The hypothesis has been falsified on numerous occasions and still it refuses to die. It is a perverse omission that belies the collective intelligence that resides within the medical profession.

Another frequently quoted study is Framingham. The study director, Dr William Kannel, gave an interview to a newspaper named The News, Framingham-Natick newspaper for the edition printed on Friday, October 30th 1970.

Dr Kannel's comments had appeared under the following heading.
"Findings of the Framingham Diet Study Clarified"

"Framingham - Although ***there is no discernible relationship between reported diet intake and serum cholesterol levels*** in the Framingham Diet Study Group, it is incorrect to interpret this finding to mean that diet has no connection with blood cholesterol."

The good Dr Kannel was correct in his statement written in the emboldened italics. He was completely wrong insofar as the remainder of his statement can be interpreted. It is certain that any thoughtful clinician will detect that the two clauses are mutually exclusive. Either the relationship existed and it could be discovered and determined, or it did not exist and therefore could not be found.

Framingham still forms the basis of UK government policy for treating high cholesterol. It is astounding to witness this form of myopia. Clinicians are supposed to be men of science and the current conduct of the medical profession is not redolent of the scientific mind with which one expects one's clinician to be imbued. The ersatz science of Ancel Keys and Dr William Kannel provide a poor foundation for a theory of good health.

It is imperative that the medical profession wrest the control of clinical trial results away from rapacious pharmaceutical companies who are not above manipulating study data. If the medical profession is to earn the automatic trust it currently enjoys, which is placed in its members without question by the patients, then it has no choice but to end mass poisoning of the public with a toxic treatment for a non-existent disease. Clinical judgement ought to be a continuous reflection of the needs of the patient rather than a mirror for the agendas of various departments of health, government agencies, governments, pharmaceutical companies and clinicians who are paid consultants to the pharmaceutical industry.

The e-petition pages stand as mute testimony to the considerable damage caused by statins and they also point to the comprehensive failure of the medical profession to listen closely to its patients. The MHRA reporting system is underused by clinicians for reporting issues which concern the safety of statins because of the tendency to ascribe these adverse reactions to an age-related category. The MHRA drug safety monitoring system requires a high level of literacy and a computer, from patients if they are to successfully navigate the convoluted web page system and use it to make coherent reports about the safety of any particular drug. Written reports also require good literacy and for lay people making reports is a relatively difficult process that must militate against good reporting.

Patients have no choice but to trust their treating clinician. It is incumbent upon the clinicians to listen to what their patients have been saying about statins. It is the clinician's responsibility to understand the proposed treatment so thoroughly that they can assist their patients with making wise and informed choices.

The mantra that would have us all acknowledge that cholesterol is bad and statins are good is a long way short of factual. The public have a right to be treated decently and it is only by reviewing the anecdotal evidence of their patients that clinicians will be able to adopt a position which precipitates appropriate and decent treatment.

It is wrong for clinicians to prescribe treatments for which they do not have complete understanding. MIMS or the annual data sheet compendium are not the proper places to learn about the use of statins. Clinicians owe their patients a duty of care. It is an integral part of that duty to understand the effects and the actions of the chemical agents which they are prescribing before any prescription is written.

Clinicians should be educated regarding the role of cholesterol in the body. It is a simple matter to discover that our dietary intake of cholesterol has absolutely no effect on our serum cholesterol level. Why is mortality higher in people with lower cholesterol values? How do statins exert their effect on the neurological system? Is cholesterol needed for the production of myelin? What is the outcome of inhibiting the biosynthesis of Dolichols, Prenylated Proteins, Ubiquinone, Heme A and Cholesterol? Can the body function without these substances or when they have been reduced? Why is a high fat, low carbohydrate diet healthy?

Of the 351 case accounts used in creating this informal report, 61% were unable to comply with the treatment as prescribed. This information should send a loud message to the manufacturers of statin pharmaceuticals and to the clinicians who are prescribing statins. This low compliance rate underpins the difficulties ordinary people are having when trying to comply with their statin therapy. It may be argued that the incidence of heart disease is not falling because of the non-compliance of patients. Blaming the patients for the failure of the cholesterol/heart disease hypothesis to deliver healthy populations is an unwarranted response.

One of the tenets of cardiac care is to keep the patient active. This small sample demonstrates that statins have produced muscle aches, weakness, severe pain and restriction of movement issues. The respondents' complained of problems affecting their mobility (16.5%) and giving them severe pain (30%) while the patients who cited muscle issues numbered 51%.

All of these problems would appear to militate against an improvement in cardiovascular health, if the patient is in severe pain and cannot move. It may also be one contributory factor in the weight gain described by eight respondents. People were also finding it difficult to be mobile because of peripheral neuropathy or muscle spasms in the lower limbs. With 20% of the patients complaining about leg problems, it would appear that statins are not ideal for assisting patients with mobility issues.

Add the impairment of cognition, confusional states, depression and memory loss and it is difficult to see how patients are deriving a benefit from taking statins. Lower cholesterol appears to have become a meme and thereby encouraged the medical profession to suspend its sense of critical discrimination while chasing the goal of lowering serum cholesterol levels.

The end justifies the means is undoubtedly a wrong-headed philosophy and there is no rationale that can justify harming patients to the depth and the extent that this modest information report has uncovered in this small number of cases. Were these numbers replicated in a formal research project, the medical profession would be culpable for a serious wrongdoing to the unquestioning patients that trust its members unreservedly.

**Suggestions for future research:**
Anecdotal accounts are not as amenable to the same sort of controls as the variables used in formally conducted studies. Many patients who are taking a statin are liable to experience adverse reactions to the drug. The inhibition of other processes within the MMP almost guarantees that the patient will complain of some unwanted side-effects that will be attributable to the statins.

It would be helpful to replicate this report by collecting the patient information using a formally designed and formally administered questionnaire. That would eliminate the wide variation between apparently similar accounts and it would collect consistent data across all of the participating study subjects.

It is suggested that a multi-centre study would be relatively easy and economical to set up and the study would probably be able to rapidly accumulate reliable information if it was run in a cardiac clinic. In the alternative, the study could be administered to the patients of any GP practice in numerous locations concurrently.

The actual numbers and severity of adverse reactions to statin therapy would readily and rapidly become known and the large patient numbers could serve as a national database and become a useful repository of knowledge and a tuition aid for the medical profession. The opportunity to gain a thorough understanding of adverse reactions that are mediated by statins is before the reader.

Jeff Cable - November 2009
The author retired from working as a clinical nurse specialist in 2001.
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