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Modelling and Analysing Time-Dependent Health Outcomes

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1. Introduction

The widespread use of computers has lead to important health concerns. Musculoskeletal disorders (MSDs) have become an epidemic and their association with computer use has been well documented (Gerr et al, 2002, Punnett & Bergqvist, 1997, Juul-Kristensen & Jensen, 2005). It is believed that in addition to the magnitude of biomechanical load the duration and frequency of the exposures are of importance in the development of MSDs (Winkel & Mathiassen, 1999, Kryger et al., 2003). In other words, there is a dynamic interaction between the exposures and the pathophysiological responses leading to the symptoms and disorders (Armstrong et al, 1993, Sauter & Swanson, 1995). A number of approaches have been taken in attempting to understand the risk and the course during computer work. However, there remain significant gaps in our knowledge about the dynamic changes of health outcomes in response to computer-related workload. It is challenging to tackle this problem from mathematical modelling due to both measurement techniques and analysis methodologies.

From a measurement point of view, solo use of questionnaires may suffer from low accuracy of the estimated magnitude of the problem. On the other hand, measuring the exposures by observation or direct measures is expensive and therefore not feasible in large epidemiological studies (Winkel & Mathiassen, 1994). In this study, a combination of direct measure and survey techniques was adopted for data collection process. We have not seen this kind of data collection performed in the literature. Methodologically, no high muscular forces are needed in computer work and the postures are fairly constant. Traditional biomechanical models may not be applicable to such problems. Therefore, nearly all literature deals with risk factor issues through data collection and analysis. The data are often nonlinear. The application of linear models as primary tools, possibly, can not capture the complexity presented in the data in a static process, let alone a dynamic process. The interpretability of the model may be low.

In mathematical modelling, one of the main objectives is to select a suitable model for analysis purposes. When coping with large size data with nonlinear features, as the ones resulting from many subjects in poorly understood process, we do not know in advance suitable models. Therefore, the first aim should be to discover dominant patterns so that the possible nonlinear

models can be easily identified. This chapter aims to fulfill such objectives. The following sections present a mathematical model to illustrate the kind of complicated data that have been successfully simulated, and to perform a systematic analysis of computer-related health outcomes statically and dynamically.

2. Data

Data were gathered by measurement device and self-administered questionnaire-diaries consisting of items presenting health outcomes for 15 body parts. The study population consisted of 103 office workers in Finland. They did office work for at least four hours a day and had reported a moderate amount of musculoskeletal symptoms. About 58% of the study population were woman. The data collection procedure was carried out in two-week periods before an intervention, and at the 2-month and 10-month follow-up. The software (Work-Pace™, Niche Software Limited, New Zealand) was adopted to continuously monitor the workers' keyboard and mouse entries. The recorded files contain the exact history of keyboard and mouse events for each subject with an accuracy of ten milliseconds. Data were then summed up for indicating computer-related workload as a daily base. Simultaneously with the recordings of computer use the workers were asked to fill in a questionnaire-diary from current musculoskeletal-specific health outcome measures three times a day: in the morning, at noon and in the evening. The diary contained a body map diagram and questions about the existence of musculoskeletal discomfort in different body regions. Each item was assessed using 5-point rating scale from "5-feel good" to "1-feel very uncomfortable". A detailed description of the data collection procedures can be found in Ketola et al. 's paper (Ketola et al., 2002).

Due to some technical and human factors in the measurement and survey, there were holes in the collected data set. For some subjects, a large portion of data (up to 80%) was missing. Under this circumstance we couldn't include such subjects and the final number of the subjects was 69. Even for these 69 subjects, there were missing values in the dataset. Little and Rubin (Little & Rubin, 1987), among others, have demonstrated the dangers of simply deleting missing data cases. Imputation will most likely introduce bias into the model (e.g. Engels & Diehr, 2003). Another problem associated with the data was that the observation time periods varied with subjects and were short in general. Some subjects' data were collected for a single day and the maximum time duration was three weeks. Due to these shortcomings we decided to average the data to use a weekly model. Above all, we believe that long-term temporal variations may be superimposed to changes in weekly patterns.

In addition, the responses of health outcomes or discomfort ratings were treated as continuous variables since they have continuous properties and distribution and there is no computation restriction against fitting continuous models to ordinal data. In clinical trials for example, investigators often need to deal with underlying continuous responses that are recorded as ordinal variables such as in our dataset. In some cases, it is possible that a continuous model may not be appropriate to ordinal outcomes even though it can fit the ordinal data. In our data, variables are continuous in nature and it is appropriate to treat them as continuous variable even though outcomes are ordinal due to the insufficient performance of measurement. Therefore, the following data process was made:

• The health outcomes, denoted as discomfort ratings, for the morning, noon and afternoon were averaged as daily ratings;

• The discomfort ratings were treated as interval values;
• The discomfort ratings for the left and right parts of the body were combined by selecting the smaller rating value (more serious discomfort outcome);
• The computer workload indicating the daily keyboard and mouse entries of the study subjects were accumulated from the starting date Monday. Missing data didn't contribute to the average.

3. Mathematical Model

A mathematical model was developed which describes the temporal associations between discomfort and computer-related workload in multiple body regions. The associations are formulated in an explicit dose-response relationship which is parametrized by body region parameters (Lu & Takala, 2008). The validation of the model gave a good accuracy. The model was further evaluated and confirmed by using commercialized statistical software package SAS. Therefore, we can use the model to assess the impact of computer-related work exposure on discomfort in different body regions in order to better understand the dynamic effects of computer workload. The stages of the proposed methodology, including basic concepts of Singular Value Decomposition (SVD), are briefly given as follows:
• Generating a sample matrix from the dataset;
• Applying SVD to the matrix to capture the dominant temporal patterns;
• Regressing towards the dominant temporal patterns;
• Summarising the model equations;
• Applying standard statistical software to estimate both the standard errors of the parameters and the accuracy of the model.

3.1 Generation of Sample Matrix
Consider a sample $m \times n$ matrix a_t generated from the data as

$$a_t = \begin{pmatrix} a_1(t_1) & a_1(t_2) & ... & a_1(t_{n-1}) & a_1(t_n) \\ a_2(t_1) & a_2(t_2) & ... & a_2(t_{n-1}) & a_2(t_n) \\ ... & ... & ... & ... & ... \\ a_{m-1}(t_1) & a_{m-1}(t_2) & ... & a_{m-1}(t_{n-1}) & a_{m-1}(t_n) \\ a_m(t_1) & a_m(t_2) & ... & a_m(t_{n-1}) & a_m(t_n) \end{pmatrix} \tag{1}$$

where $a_j(t_i)$, $j = 1...m$ & $i = 1...n$ presents regional discomfort rating for sample j at time t_i. The matrix may also present a single sample's measures with periodic patterns depending on the data structure and the study purpose.

3.2 Application of Singular Value Decomposition
Applying SVD (Golub & van Loan, 1996) to Equation 1 gives

$$a_t = UDV_t^T = \sum_{i=1}^{n} u_i d_i v_{it}^T \tag{2}$$

where columns u_i and v_i of U and V are called the left and right singular vectors, respectively. The diagonal elements d_i of D, sorted in the descending order with upper left value the largest, are called the singular values. The singular values are the square roots of the eigenvalues of the matrix $a_t a_t^T$ or $a_t^T a_t$ whilst the singular vectors are the correspondent eigenvectors

One key in applying SVD is that the truncated matrix $\sum_{i=1}^{r} u_i d_i v_{it}^{T}$ is the closest rank-r matrix to a_t (Golub &Van Loan 1996). Note that r is always smaller than both m and n. This property is extremely useful when r is much smaller than n. In practical applications, d_i, $n \geq i \geq r+1$, may not be zero due to the presence of noise such as individual disturbances in the measurement data, but they are very close to zero. Then by dropping the last n-r singular values, a good approximation of a_t is obtained with an r dimensional matrix. The corresponding singular values can be used as a measure of relative significance of the approximation for explaining a_t. Very often, a good matrix approximation can be obtained with only a small fraction of the singular values.

Applying Equation 1 and Equation 2 to our measurement data and checking the rank of a_t, we found that $r = 1$ and the approximation $u_1 d_1 v_{1t}^T$ can explain 90% of the variation of a_t. So we get the following approximation

$$a_t = \begin{pmatrix} a_1(t_1) & a_1(t_2) & ... & a_1(t_{n-1}) & a_1(t_n) \\ a_2(t_1) & a_2(t_2) & ... & a_2(t_{n-1}) & a_2(t_n) \\ ... & ... & ... & ... & ... \\ a_{m-1}(t_1) & a_{m-1}(t_2) & ... & a_{m-1}(t_{n-1}) & a_{m-1}(t_n) \\ a_m(t_1) & a_m(t_2) & ... & a_m(t_{n-1}) & a_m(t_n) \end{pmatrix} \approx u_1 d_1 v_{1t}^T = \boldsymbol{u}\, \boldsymbol{v_t}^T \tag{3}$$

where $\boldsymbol{u} = u_1 = \begin{pmatrix} u_1 & u_2 & ... & u_{(m-1)} & u_m \end{pmatrix}^T$ and $\boldsymbol{v_t} = d_1 v_{1t} = (v(t_1), v(t_2) ... v(t_{n-1}), v(t_n))^T$.

It is easy to see that a time-dependent model problem a_t is simplified through Equation 3. The time series outcomes for all subjects are expressed in terms of the time series $\boldsymbol{v_t}$ with linear combination coefficients of the elements of $\boldsymbol{u}$ which describe the differences among all subjects. Therefore, $\boldsymbol{v_t}$ presents the captured dominant time pattern and $\boldsymbol{u}$ the individual sample differences. The next step deals with the regression of $\boldsymbol{v_t}$ and a_t.

3.3 Regression of the Dominant Patterns

To test whether the captured dominant time pattern $\boldsymbol{v_t}$ is linear or nonlinear or just random noise, we plotted $\boldsymbol{v_t}$ and made a visual inspection in data variability and goodness of fit through regression analysis. We found that $\boldsymbol{v_t}$ obeys a certain nonlinear properties. A dose-response relation was identified and proved to be significant. It is worth mentioning that this way, by incorporating visual inspection of the plotted curve and nonlinear regression analysis, can reduce the potential errors introduced especially by large unseen data.

The regression function $a(t)$ of a_t can then be obtained based on the regression function $v(t)$ of $\boldsymbol{v_t}$ through Equation 3 as

$$a(t) \approx \boldsymbol{u}\, v(t) \tag{4}$$

To make Equation 4 more clear, remember the following point: $a(t)$ denotes the regional discomfort ratings in continuous time, $v(t)$ the dominant dynamic patterns and $\boldsymbol{u}$ the correspondent linear coefficient vector which presents kind of 'individual differences' of the outcomes in response to the dominant pattern. The final model equation can be derived by averaging $\boldsymbol{u}$ over the studied time period as

$$\bar{a}(t) \approx \bar{\boldsymbol{u}}\, v(t) \tag{5}$$

3.4 Summary of the Model Equations

To summarise, here are the key features of the model equations:

•Computer-related workload: The computer-related workload varied linearly with time. This simple linear dependence suggests that it is adequate to study time-dependent health outcomes as the result can be easily applied to workload-induced behaviour;

•Health outcomes: The developed explicit model equations can be expressed with the following general functional form from Equation 5 as

$$\bar{a}(t) \approx \left(\alpha_1 + \frac{\alpha_2 - \alpha_1}{1 + 10^{t-\alpha_3}} \right) \tag{6}$$

where $\bar{a}(t)$ presents the musculoskeletal discomfort rating ranged from 1 to 5 and α_1, α_2, α_3 are body region dependent parameters. Equation 6 is parametrized by body region parameters;

• Model validation: The validation is performed by direct comparison of observations and forecast as illustrated in Figure 1. The accuracy is good.
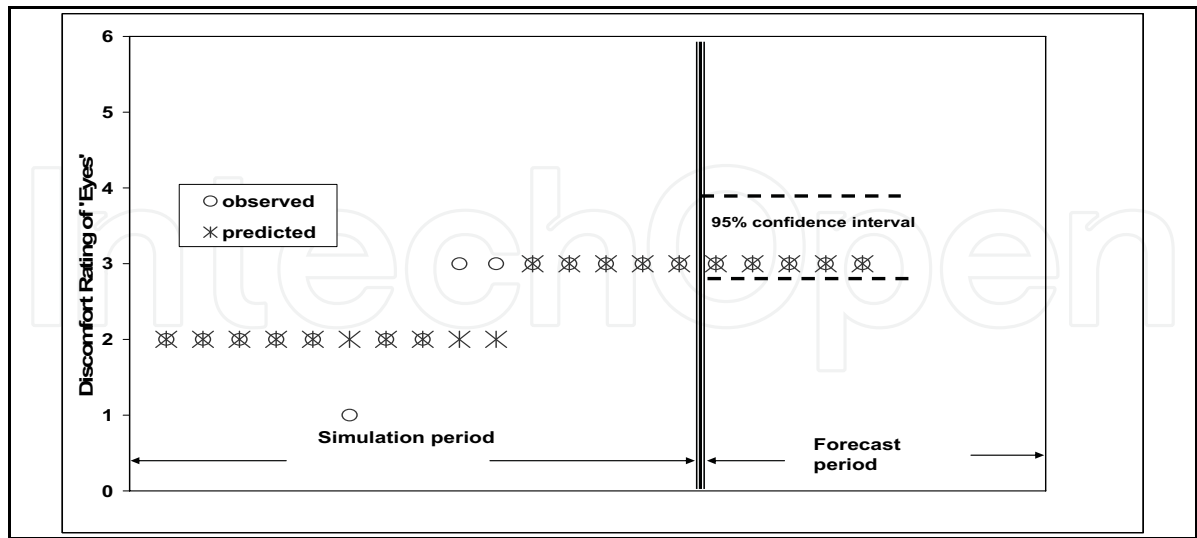

Fig. 1. Simulation and forecast of discomfort ratings (5 = 'feel good', 1 = 'feel very uncomfortable') in body region 'eyes' for an individual subject. Based on the measured ratings during the first period ('Simulation period') a forecast was fitted (stars) and compared to observations (circles). The horizontal dotted lines show the 95% confidence limits for the predicted period

3.5 Application of Standard Statistical Software

Next we evaluate the standard errors of the model parameters and the accuracy of the model through commercial statistics based software packages SAS. SAS's procedure PROC NLMIXED was employed which addresses the sequential correlation issue directly by modelling the covariance structure. Table 1 gives these parameter values (Lu & Takala, 2008). As a single dose-response model could not be fitted to all the curves, the data for the outcome 'mood' were modelled separately with an extra exponential function represented through the parameters α_4 and α_5. The parameters α_4 and α_5 were not statistically discernible at the 5 percent probability level and therefore were eliminated from the model. The goodness-of-fit tests (result not shown here) for the model also demonstrated that the proposed model (Equation 6) performed better than the linear model, the most common model in handling such data. Figure 2 displays the model $\overline{a}(t)$ for 15 body parts ranged from 1 to 5. The x-axis represents time in days or scaled computer-related workload due to their linear relationship.

Body regions	a_1 (SE)	a_2(SE)	a_3(SE)	a_4(SE)	a_5(SE)
head	3.87***(0.08)	4.00*** (0.08)	2.63***(0.38)	-	-
eyes	3.72***(0.09)	3.89***(0.10)	2.29***(0.49)	-	-
neck	3.58***(0.10)	3.74***(0.10)	2.19***(0.38)	-	-
shoulder	3.64***(0.10)	3.77***(0.10)	2.25***(0.39)	-	-
shoulder joint/ upper arm	3.75***(0.10)	3.87***(0.10)	2.63***(0.48)	-	-
forearm	4.02***(0.10)	4.07***(0.10)	3.15**(1.33)	-	-
wrist	4.02***(0.10)	4.09***(0.10)	3.73***(0.65)	-	-
fingers	3.99***(0.11)	4.07***(0.11)	3.83***(0.41)	-	-
upper back	3.75***(0.11)	3.87***(0.11)	2.78***(0.38)	-	-
low back	3.84***(0.11)	3.89***(0.11)	3.43***(1.06)	-	-
hips	4.29***(0.09)	4.30***(0.09)	3.51***(1.24)	-	-
thighs	4.30***(0.09)	4.32***(0.10)	3.44***(1.37)	-	-
knees/shin	4.21***(0.11)	4.26***(0.11)	3.72***(0.63)	-	-
feet	4.18***(0.10)	4.23***(0.10)	4.14***(0.93)	-	-
mood	4.04***(0.79)	3.57***(0.49)	2.88***(0.39)	0.41(0.77)	0.41(0.61)

Table 1. Fitted parameters a_1 a_2 a_3 a_4 a_5 in model equations (Equation 6) for dose – response relationship (SE-standard error; ***p<0.001; **p<0.05)
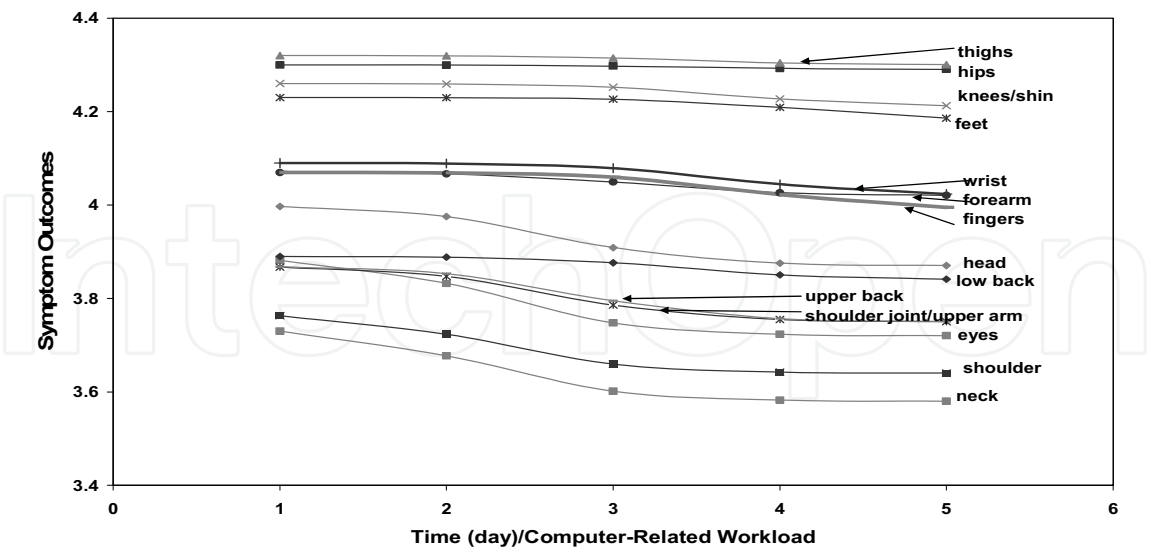
Fig. 2. Discomfort ratings in different body regions (Y-axis: 5 = 'feel good, 1 = 'feel very uncomfortable'; X-axis: 1 = 'Monday', 5 = 'Friday')

4. Analysis Results

Using the developed model, we performed extensive investigations of the health outcomes. We compared the risk body regions and provided various severity rankings of the discomfort rate changes with respect to computer-related workload statically and dynamically.

4.1 Average Ranking of Discomfort Severities

Firstly we performed two Waller-Duncan k-ratio t tests for $\bar{a}(t)$ (Equation 6 and Figure 2) in order to investigate detailed contrast of the health outcomes in different body regions. Table 2 shows the results.

Waller Grouping	Mean	Locations
6	4.58	mood
5	4.31	thighs
5	4.30	hips
5	4.24	knees/shin
5	4.22	feet
4	4.07	wrist
4	4.05	forearm
4	4.04	fingers
3	3.93	head
3	3.87	low back

2	3.80	upper back
2	3.80	shoulder joint/upper arm
2	3.78	eyes
1	3.67	shoulders
1	3.63	neck

Table 2. Average ranking of discomfort severities in different body regions

The results show that the severity levels of musculoskeletal discomfort can be grouped into the following categories roughly from severe to moderate as
• level 1: neck and shoulder;
• level 2: eyes, shoulder joint/upper arm and upper back;
• level 3: low back and head;
• level 4: fingers, forearm and wrist;
• level 5: feet, knees/shin, hips and thighs;
• level 6: mood.
Note that this testing is for multiple means comparison which probably has too rough classification results for nonlinear data. In the following we give a much more detailed classification scheme for the severity levels of musculoskeletal discomfort.

4.2 Average Weekly Changing of Discomfort Severities
Regarding to weekly severity changes over time, Table 3 demonstrates some of the elementary evaluations: weekly change rates and weekly changes with respect to initial discomfort rates. Using these two parameters, we perform another Waller-Duncan k-ratio t test and the results show that the dynamic changes of discomfort ratings can be grouped into two categories:
• bigger change group: mood, neck, eyes, head, shoulder, shoulder joint/upper arm and upper back;
• smaller change group: fingers, wrist, low back, forearm, knees/shin, feet, thighs and hips.
This result implies that computer-related workload is more likely to be associated with upper extremity symptoms. The discomfort ratings of hips and thighs keep nearly constants over the working week meaning that practically no association between the computer-related workload and fatigue symptoms in these body regions. A weak association exists between the computer-related workload and fatigue symptoms in fingers, wrist, low back, forearm, knees/shin and feet.

Body regions	Weekly change	Weekly change/initial discomfort rating
head	0.126	0.032
eyes	0.126	0.042
neck	0.150	0.040
shoulder	0.123	0.033
shoulder joint/upper arm	0.117	0.030
forearm	0.049	0.012

wrist	0.066	0.016
fingers	0.075	0.018
upper back	0.117	0.030
low back	0.049	0.012
hips	0.010	0.002
thighs	0.019	0.004
knees/shin	0.047	0.011
feet	0.044	0.010
mood	0.948	0.019

Table 3. Weekly changes of discomfort ratings in different body regions

4.3 Dynamic Weekly Changing of Discomfort Severities

Recall that the dose-response relation between the time and discomfort ratings has been described in Equation 6 with three parameters a_1, a_2, a_3, dependent on body regions as listed in Table 1. The model parameters have biological meanings, supposing accumulated fatigue due to the exposures leading to discomfort. We give biological interpretations in this section.

Firstly, a_3 in Equation 6 describes the halfway result of the discomfort ratings from Monday (t = 1) to Friday (t = 5). Take the body region 'neck' as an example, Table 1 shows that at 2.19 days the discomfort level is half of the levels at Monday and Friday which presents the minimum value. This means that neck gets tired much quicker than other body regions. The halfway results of the studied body regions in increasing order are: neck (2.19 days), shoulder (2.25 days), eyes (2.29 days), head (2.63 days), shoulder joint/upper arm (2.63 days), upper back (2.78 days), mood (2.88 days), forearm (3.15 days), low back (3.43 days), thighs (3.44 days), hips (3.51 days), knees/shin (3.72 days), wrist (3.73 days), fingers (3.83 days) and feet (4.14 days). The order is consistent with Table 2 and many published reports. Note that such halfway outcome for feet appears at the day 4.14 which means that no discomfort or a little discomfort was developed in feet among the study subjects.

Secondly, for the change rates of discomfort ratings during the working week presented as a_2 - a_1, the rate for eyes decreases maxima unit of 0.17. This means the resulting weekly discomfort appear to be maximum in eyes. More results of such evaluations are illustrated in Table 4. The decreased units of discomfort ratings in descending order are: eyes (0.17), neck (0.16), head (0.13), shoulder (0.13), shoulder joint/upper arm (0.12), upper back (0.12), fingers (0.08), wrist (0.07), low back (0.05), forearm (0.05), knees/shin (0.05), feet (0.05), thighs (0.02), hips (0.01) and mood (-0.47).

Body regions	a_2 - a_1
eyes	0.17
neck	0.16
head	0.13
shoulder	0.13
shoulder joint/upper arm	0.12
upper back	0.12
fingers	0.08
wrist	0.07

low back	0.05
forearm	0.05
knees/shin	0.05
feet	0.05
thighs	0.02
hips	0.01
mood	-0.47

Table 4. Dynamic weekly changes of discomfort ratings in different body regions

An interesting result is obtained for the discomfort rating 'mood' with negative sign which means that the discomfort severity of mood decreases during the week. The office staff tended to be in much better moods during the weekend Friday. The result seems to be rational based on our common knowledge.

4.4 More Findings

Take the body regions 'neck' and 'eyes' as an example, we can find that the faster fatigue rate is discovered in neck, however eyes has the largest discomfort change over weekly time due to the nonlinearity of the week change for discomfort rates. This implies that the fatigue rate is faster in neck at the beginning of the week and gradually slows down over the week, or in another word the fatigue rate of eyes is faster at the end of week when comparing neck and eyes. This conclusion is also valid to the discomfort ratings of the following body site pairs with the same dynamic behavior: shoulder and eyes, see some examples displayed in Table 5.

Faster fatigue change in early week	Faster fatigue change in late week
neck	eyes
shoulders	eyes
shoulders	head
forearm	low back
low back, forearm	fingers, wrist
thighs	fingers, wrist, knees/shin, feet
hip	fingers, wrist, knees/shin, feet

Table 5. Comparison of weekly change rates of discomfort ratings in different body regions

5. Conclusion

We obtained a model that represents functional variations of discomfort levels of different body sites associated with computer-related workload. The advantages with such explicitly functional model over 'black box' of risk factor models are enormous. The explicit-formed model can provide an insight into dynamic interplay between time duration, workload and health outcomes. For example, an implication of the model is that the discomforts of eyes and neck, compared with other body regions, are maximal regarding to the changes of severity over time. It is, therefore, easy to see that the study of such interplay can lead to better understanding of biological responses to workload over time among office workers. This kind of modelling might help in the identification of potentials for the prevention of

MSDs. There is scarce information in literature that deals with the dynamic relationship between health outcomes and computer-related workload due to the involvement of many unknown social psychological and individual factors. This chapter makes a contribution to such research.

The application of the proposed model to the systematic analysis of dynamic changes of health outcomes, represented as discomfort ratings, in head, eyes, neck, shoulder, arms and almost all body regions, in response to computer-related workload among the office workers were illustrated. It was discovered that the highest average severity level of the discomfort existed in neck, shoulder, eyes, shoulder joint/upper arm, upper back, low back and head etc. The biggest weekly changes of discomfort rates were in eyes, neck, head, shoulder, shoulder joint/upper arm and upper back etc. The fastest discomfort rate was found in neck, followed by shoulder, eyes, head, shoulder joint/upper arm and upper back etc. It is obvious that analysis of cross-sectional data, which is the most common technique in such research, cannot provide such broad findings especially related to dynamic changes.

Several limitations need to be considered. Firstly, the size of the study population was not large. Missing data existed in the dataset especially for the survey data of the musculoskeletal outcomes. Moreover, collection of time series of these data was short and the sample sizes varied very much in the dataset. The longest duration was three weeks. The collected time duration varied a lot and it was impossible to select common time duration for all the subjects. Therefore our study was limited for weekly model only. However, in practice, people get recovery during the weekends. So the musculoskeletal discomfort often demonstrates periodic properties during the working weeks. Hence, a weekly model should be enough. Secondly, assessment of the computer-related workload on the basis of cumulative duration of keystrokes and mouse clicks was somewhat crude. In this study, the study population consisted of secretaries, technicians, architects and engineers etc. whose work composed of multiple tasks, each of them with its own specific exposure profile. The associations with work-related exposures occurring as use of keyboard or mouse in combination with other tasks should be considered in future studies. Our exposure measurement did not include environmental factors that can have effects on discomfort on different body regions. Thirdly, self-reported response for musculoskeletal outcomes was adopted. The self-reports might be prone to response error.

In spite of these limitations of the available data, a broad of findings were found and most of them are consistent with the literature (Lu et al., 2009). In a review of the literature, we did not find any single report that covered such broad spectrum of investigations. The findings provide important addition to the available literature.

Finally, the mathematical methodology described in this chapter can be easily extended to accommodate more complicated medical data such as (i) rank r of the sample matrix is bigger than 1. Then more terms have to be added in Equation 3. The calculation load is small. For example, the main calculation procedures, SVD for example, contain only a few lines of code in MATLAB. The proposed methodology is a flexible and broadly applicable one, which can be utilized by a variety of research.

6. Acknowledgements

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Recent Advances in Technologies

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