Diagnostic accuracy of the care dependency scale

Dijkstra, Ate; Tiesinga, LJ; Plantinga, L; Dassen, TWN; Veltman, G.

Published in:
Journal of Advanced Nursing

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2005

Link to publication in University of Groningen/UMCG research database

Citation for published version (APA):

Copyright
Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

Take-down policy
If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): http://www.rug.nl/research/portal. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.
Diagnostic accuracy of the Care Dependency Scale

Ate Dijkstra MEd PhD RN
Senior Researcher, Northern Centre for Healthcare Research, University of Groningen, Groningen, The Netherlands

Lucas J. Tiesinga PhD RN
Assistant Professor, Faculty of Medical Sciences, University of Groningen, Groningen, The Netherlands

Liesbeth Plantinga MSN RN
Researcher, Centre for Rehabilitation, Academic Hospital Groningen, Beatrixoord, Haren

Getine Veltman MSN RN
Researcher, Medical Centre Leeuwarden, Leeuwarden, The Netherlands

Theo W.N. Dassen PhD FEANS RN
Professor, Department of Nursing Science, Humboldt University, Berlin, Germany

Accepted for publication 5 July 2004

Correspondence:
Ate Dijkstra,
Zorggroep Noorderbreedte – Stafbureau Ouderenzorg,
Postbus 888,
8901 BR Leeuwarden,
The Netherlands.
E-mail: ate.dijkstra@znb.nl

Diagnostic accuracy of the Care Dependency Scale

Aim. This paper reports an investigation of the diagnostic accuracy of the Care Dependency Scale (CDS).

Background. Assessment tools can be described in terms of diagnostic accuracy, or the ability to correctly classify subjects into clinically relevant subgroups. Diagnostic accuracy can be determined by several techniques as sensitivity, specificity, receiver operating curve analysis and likelihood ratios.

Method. A cross-sectional design was used with data from 237 patients from two studies. Data were collected using a questionnaire consisting of the CDS and the Barthel Index (BI). The CDS is a relatively new instrument and should be validated by comparison against an established gold standard, in this case the BI. Measures to quantify the validity of diagnostic tests, such as sensitivity, specificity, positive and negative predictive values, prevalence and likelihood ratios were calculated. In addition, the receiver operating characteristics (ROC) curve analysis was used to report the test accuracy of the CDS and to determine an appropriate cut-off point for care dependency detection.

Findings. The prevalence in the sample study was very high (84%). The area under the ROC curve for the CDS was 0.81, which indicates moderate diagnostic accuracy. Patients with a CDS sumscore ≤68 (rule-out cut-off point) were classified as care dependent, all others as independent. The determination of the appropriate cut-off point was based on sensitivity (0.85) and positive predictive valued (0.90).

Conclusion. The CDS may be used for to estimate care dependency among hospital patients with various conditions.

Keywords: hospital patients, nursing, dependency, diagnostic accuracy, gold standard, receiver operating characteristics curve analysis
Introduction

Assessment of patients’ function is an essential part of nursing practice and much nursing research is carried out to try to improve methods of assessment, e.g. measurement instruments. Especially validated and reliable measuring instruments are relevant in research and in clinical practice because they are able to assess useful nursing phenomena.

This study centres on the phenomenon of care dependency, and more precisely the assessment of this using the Care Dependency Scale (CDS). The CDS was originally developed in the Netherlands in 1994 as an instrument for care planning (Dijkstra 1998). The reason for its development was the fact that nurses were confronted with older patients with increasing needs for care as a result of their health problems. In order to support individual needs and avoid routine provision of care, nurses were interested in a short, practicable instrument to assess patients’ dependency on nursing care. Nursing care dependency can be defined as the support which the nurse offer a patient whose self-care abilities have decreased and whose needs make them to a certain degree dependent, with the aim of restoring this patient’s independence in performing self-care (Dijkstra 1998, Lohrmann 2003). Existing tools were unsuited to providing the specific information needed by nurses, because they were designed to indicate where help was needed without regard to the care dependency status that arises from these needs. In practice, the CDS is intended to be used in the first stage of the nursing process as a case-finding and need assessment tool.

With case-finding, it is self-evident that nurses should only use measurement instruments with proven diagnostic accuracy: the ability to discriminate between two subclasses of subjects (Zweig & Campbell 1993). Such a requirement ensures the effective, efficient and economic use of nursing knowledge and resources. But the question remains of how sure nurses can be that their assessment is correct.

According to Altman (1991), the main difficulty is to decide how good the instrument (in this case the CDS) is to establish the presence or absence of care dependency) should be to be valuable in nursing practice. Greenhalgh (1997) states that a diagnostic instrument is valid if it detects most people with the target disorder (the presence of care dependency) and excludes most people without the disorder (the absence of care dependency).

The psychometric testing of the CDS is described in several studies (Dijkstra et al. 1996a, 1996b, 1998a, 1998b, 1999a, 2000b). Although reliability in terms of internal consistency, equivalence and stability, and validity in terms of construct validity and criterion-related validity, have been investigated, until now no study lacked has evaluated its diagnostic accuracy.

The study

Aim

The aim of the study was to investigate the diagnostic accuracy of the CDS. Therefore the following research questions were posed:

1 What are the values for the CDS of measures commonly used to assess the validity of diagnostic tests?
2 What is the appropriate cut-off score of the CDS to determine the presence or absence of care dependency?
3 What are the mean CDS sumscores among care dependent and independent patients, based on the rule-out cut-off point from the data used in this study?

Participants and setting

The study was based on data gathered in two earlier studies. The aim of the first study was to investigate quality of life among patients 4 months after stroke. A group of 55 patients participated. These patients had been admitted to the neurological department of two general hospitals in The Netherlands between September 1998 and December 1999 (Veltman 1999).

The second study took place in 2001 at the rehabilitation department of a university hospital in The Netherlands. The aim was to determine whether care dependency, in combination with care complexity, identifies nursing intensity. In this study 182 patients were included (Plantinga 2002). All were chronically ill or receiving rehabilitation because of temporary or permanent impairment and had a variety of conditions, e.g. stroke, diabetes, rheumatism, tuberculosis, spinal cord lesion, amputation, cardiac or lung diseases. The final convenience sample from both studies consisted of 237 patients.

Data collection

In both initial studies data were collected using a questionnaire which included the CDS and Barthel Index (BI). In the Veltman (1999) study, two researchers filled in the questionnaire in consultation with patients and nurses. For the Plantinga (2002) study, nurses most involved in the daily care of the patients completed the questionnaire. All raters were trained in using the CDS and BI. The training consisted of information on the research procedure and the principles of assessment, and instruction in the practical use of the CDS and BI.
Instruments

The CDS provides a framework for assessing the care dependency status of institutionalized patients. Based on Virginia Henderson’s (1966) framework of human needs, it measures 15 basic needs, as shown in Table 1.

Besides the item description, each item has five care dependency criteria. Nurses rate all items by selecting one criterion out of the five. Low scores indicate that patients are completely dependent on care, while high scores mean that patients are almost independent of care. The CDS is easy to administer, normally taking <5 minutes. Psychometric analyses showed that the Dutch version of the CDS was reliable in terms of internal consistency, equivalence and stability and valid in terms of construct validity and criterion-related validity. In addition to these studies, the international psychometric properties of the CDS have been determined using data sets from Canada, Italy, Norway and The Netherlands (Dijkstra et al. 2000a), from Germany (Lohrmann 2003) and from Finland, Spain and the United Kingdom (Dijkstra et al. 2003). The results for reliability and validity from these studies were in accordance with those obtained in the Dutch studies.

The 10-item BI contains the following questions concerning dependency in activities of daily living (ADL): feeding, moving from wheelchair to bed and returning, personal hygiene, getting on and off toilet, bathing self, walking, ascending and descending stairs, dressing, and controlling bowels and bladder (Mahoney & Barthel 1965). The BI is useful in evaluating a patient’s state of independence before treatment, their progress as they undergo treatment and when they reach maximum benefit. It can be scored quickly using the item definitions. The items have two to four response categories and a total score between 0 (complete dependent) and 20 (complete independent) is obtained. The BI has proved to be a valid and reliable measure of ADL dependency and has been recommended as the ‘gold standard’ for other ADL rating scales and as the benchmark for evaluating newer scales (McDowell & Newell 1987, Collin et al. 1988, Wade & Collin 1988, Wade 1992, Post et al. 2002). The psychometric properties of the Dutch BI were comparable with those of the English version (de Haan et al. 1993).

Procedure and statistical analysis

Step 1 in accuracy assessment of the CDS.

In relation to research question 1, common measures to quantify the validity of diagnostic tests, namely sensitivity, specificity, positive and negative predictive values (NPV), were calculated. Sensitivity and specificity may be defined, respectively, as the proportion of positives that are correctly identified by the test and the proportion of negatives that are correctly identified by the test (Altman 1991). As sensitivity and specificity do not take into account disease prevalence in the particular population, it is helpful to calculate indices which do (Henderson 1993). These are the positive predictive value (PPV), defined as the proportion of patients with positive test results who are correctly diagnosed, and the NPV, which is the proportion of patients with negative test results who are correctly diagnosed (Altman 1991). Apart from its sensitivity and specificity, the diagnostic value of a test depends also upon the prevalence of the phenomenon in the sample being investigated (Bouter & van Dongen 1991).

| Table 1 Care Dependency Scale (CDS) items and item descriptions |
|---------------------------------|---------------------------------|
| CDS items | CDS item description |
| Eating and drinking | The extent to which the patient is able to satisfy his/her need for food and drink unaided |
| Incontinence | The extent to which the patient is able to control the discharge of urine and/or faeces voluntarily |
| Body posture | The extent to which the patient is able to adopt a position appropriate to a certain activity |
| Mobility | The extent to which the patient is able to move about unaided |
| Day/night pattern | The extent to which the patient can maintain an appropriate day/night cycle unaided |
| Getting dressed and undressed | The extent to which the patient is able to get dressed and undressed unaided |
| Body temperature | The extent to which the patient is able to protect his/her body temperature against external influences unaided |
| Hygiene | The extent to which the patient is able to take care of his/her personal hygiene unaided |
| Avoidance of danger | The extent to which the patient is able to assure his/her own safety unaided |
| Communication | The extent to which the patient is able to communicate |
| Contact with others | The extent to which the patient is able to appropriately make, maintain and end social contacts |
| Sense of rules and values | The extent to which the patient is able to observe rules/social norms by him/herself |
| Daily activities | The extent to which the patient is able to structure daily activities unaided |
| Recreational activities | The extent to which the patient is able to participate in activities outside the hospital unaided |
| Learning activity | The extent to which the patient is able to acquire knowledge and/or skills and/or to retain that which was previously learnt unaided |
Methodological issues in nursing research

Prevalence has been defined as the proportion of participants with the abnormality (Altman 1991).

With regard to research question 2, receiver operating characteristics (ROC) curve analysis was used to report the test accuracy of the CDS in care dependency detection. The ROC curve shows how the true positive proportion (vertical axis) varies with the false positive proportion (horizontal axis), as the decision criterion is varied. The area under the ROC curve, standard error and 95% confidence interval (CI) were also calculated. The area under the ROC curve is described as a better measure of predictive accuracy than sensitivity and specificity (see below), as it yields an index independent of the cut-off point and prevalence (Swets 1996). Swets (1988) suggests that areas of 0.5 to 0.7 indicate low test accuracy, 0.7 to 0.9 moderate accuracy and >0.9 high accuracy.

Step 2 in accuracy assessment of the CDS

This second step is required to assess the value of the test in clinical practice (Henderson 1993). According to Greenhalgh (1997), the best measure of the usefulness of a test is probably the likelihood ratio, which indicates how likely a given test result is for someone with the disorder, compared with someone without the disorder. For a positive test result, LR+ is given by (sensitivity/1 − specificity); for a negative result, LR− is given by (1 − sensitivity/specificity). To determine the value of the likelihood ratio, Henderson (1993) states that, as a general rule, a good LR+ value exceeds two whereas a good LR− is near to zero.

One of the important functions of the ROC curve was to establish the CDS cut-off point to be used in case finding. Because the CDS is a discovery test of care dependency, the rule-out cut-off point (a test with high sensitivity) was used to establish when care dependency was present and should not be missed, and false positive results would not have serious consequences for the patient. Research question 3 was answered based on the established rule-out cut-off point.

The values mentioned above, namely for sensitivity, specificity, PPV, NPV, prevalence and likelihood ratio, could only be computed when participants who were really care dependent were known. This meant that an accepted ‘gold standard’ must be available and that the dependency status of every patient was categorized by the use of this gold standard test into those who were or were not care dependent (Bouter & van Dongen 1991). In this study, the BI was used as ‘gold standard’ (Mahoney & Barthel 1965). Based on the findings of de Haan et al. (1993), the optimal cut-off point of the BI used to determine the group of dependent and independent patients was 20.

Data were analysed using the Statistical Package for the Social Sciences, version 9.0 (SPSS Inc., Chicago, IL, USA).

Outcomes were calculated using descriptive statistics, cross-tabulations, t-tests and ROC graphs. A level of $P < 0.05$ was considered statistically significant.

Ethical considerations

Permission for the study protocol of Veltman (1999) was granted from the Local Research Ethics Committee. For the Plantinga (2002) study, permission was obtained from the health care authorities of the participating hospital. The researchers explained both studies to the nurses in the participating hospitals and their managers. All staff agreed to participate after written and verbal information about the study including its aim, methods and questionnaires. To ensure the confidentiality and anonymity, the names of the participants were encoded.

Findings

Sample characteristics

The mean age of the group ($n = 237$) whose data were used in this study was 59.8 (sd 17.1) years, and 43.5% were male. CDS sumscores were calculated by adding the outcome on the 15 CDS item scores. The mean CDS sumscores (sd, range) were respectively: males 55.5 (12.2, 17−75), females 55.5 (15.4, 15−75) and for the total sample 55.5 (14.0, 15−75).

Sensitivity, specificity, predictive values and ROC curve

For each CDS sumscore, the sensitivity, specificity, positive and NPVs was determined. In Table 2 (step 1 figures) the results of the calculations are partly given for the CDS sumscores between 55 and 75. The reason for this limited range is the finding from an earlier study that all patients with a CDS sumscore $<70$ can be described as dependent on nursing care (Dijkstra et al. 1999b). Table 2 reveals that as CDS sumscore decreases, sensitivity decreases, specificity increases, PPV increases but to a lesser extent than specificity, and NPV stays fairly constant. The observed prevalence of care dependency in the study sample measured by the CDS was 84%, which means a very high prevalence.

Figure 1 shows the ROC curve that is conventionally prepared by plotting the true positive rate (sensitivity) against the false positive rate (1-specificity), varying the cut-off point over the entire range of CDS sumscores. CDS sumscores (48, 53, 58, 63, 68 and 73) are indicated on the curve in Figure 1 and show that, as the cut-off point increases, sensitivity increases and specificity decreases. The area under the ROC curve for the CDS was 0.81. Based on Swets (1988), this
Table 2 Calculations of Care Dependency Scale (CDS) sensitivity (Se), specificity (Sp), positive predictive value (PPV), negative predictive value (NPV) and likelihood ratio (LR+ and LR−) of the diagnostic test care dependency, with Barthel Index <20 as the criterion.

<table>
<thead>
<tr>
<th>CDS sumscore (n = 237)</th>
<th>Step 1 in accuracy assessment of the CDS</th>
<th>Step 2 in accuracy assessment of the CDS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Se</td>
<td>Sp</td>
</tr>
<tr>
<td>75</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>74</td>
<td>0.96</td>
<td>0.10</td>
</tr>
<tr>
<td>73</td>
<td>0.95</td>
<td>0.26</td>
</tr>
<tr>
<td>72</td>
<td>0.91</td>
<td>0.26</td>
</tr>
<tr>
<td>71</td>
<td>0.88</td>
<td>0.31</td>
</tr>
<tr>
<td>70</td>
<td>0.87</td>
<td>0.41</td>
</tr>
<tr>
<td>69</td>
<td>0.87</td>
<td>0.46</td>
</tr>
<tr>
<td>68</td>
<td>0.85</td>
<td>0.52</td>
</tr>
<tr>
<td>67</td>
<td>0.83</td>
<td>0.56</td>
</tr>
<tr>
<td>66</td>
<td>0.81</td>
<td>0.62</td>
</tr>
<tr>
<td>65</td>
<td>0.80</td>
<td>0.62</td>
</tr>
<tr>
<td>64</td>
<td>0.77</td>
<td>0.67</td>
</tr>
<tr>
<td>63</td>
<td>0.75</td>
<td>0.72</td>
</tr>
<tr>
<td>62</td>
<td>0.73</td>
<td>0.74</td>
</tr>
<tr>
<td>61</td>
<td>0.68</td>
<td>0.79</td>
</tr>
<tr>
<td>60</td>
<td>0.66</td>
<td>0.85</td>
</tr>
<tr>
<td>59</td>
<td>0.65</td>
<td>0.87</td>
</tr>
<tr>
<td>58</td>
<td>0.61</td>
<td>0.92</td>
</tr>
<tr>
<td>57</td>
<td>0.58</td>
<td>0.95</td>
</tr>
<tr>
<td>56</td>
<td>0.56</td>
<td>0.95</td>
</tr>
<tr>
<td>55</td>
<td>0.53</td>
<td>0.95</td>
</tr>
</tbody>
</table>

Figure 1 Receiver operating characteristics curve for establishing care dependency status.

This means that the CDS has moderate diagnostic accuracy. The standard error was 0.03 and the 95% CI is 0.76–0.87. The 95% CI does not incorporate 0.5, showing that the CDS predicts care dependency better than chance.

Appropriate cut-off point

Table 2 (step 2 figures) shows the results for the likelihood ratios. Findings of LR+ and LR− values ranged respectively from 10.6 and 0.49, associated with CDS sumscore 55, to 1.07 and 0.40, which are associated with respectively CDS sumscores 74 and 75. For a positive test result, LR+ should be greater, ideally much greater, than one (Henderson 1993). This was the case at a CDS sumscore <67. For a negative test result, LR− should be much less than one, and this was found at all CDS sumscores given in Table 2.

To determine the appropriate cut-off point, it is very important to have high sensitivity and PPV, because a positive result will probably lead to a nursing diagnosis of care dependency and nursing interventions. For this reason we chose as cut-off point the CDS sumscore ≤68, based on a sensitivity of 0.85 and PPV of 0.90. Patients with a score ≤68 were classified as care dependent, and all others as independent.

CDS sumscore of dependent and independent patients

Based on the rule-out cut-off point of the CDS sumscore ≤68, Table 3 shows the comparison between males and females separately for dependent and independent patients. Comparisons for the total group and gender show that they differ significantly. Controlling for gender, the mean CDS sumscores of dependent and independent male and female patients were tested and showed no statistically significant results: respectively, 52.3 vs. 49.8 (t = 1.42; P = 0.156; n = 188) and 72.3 vs. 72.8 (t = −0.73; P = 0.473; n = 49).

Discussion

In this study we sought to evaluate whether the CDS is valuable in nursing practice for diagnosing patient care dependency.

Table 3 Comparisons of mean Care Dependency Scale sumscores for dependent and independent patients, based on a cut-off point ≤68

<table>
<thead>
<tr>
<th></th>
<th>Dependent</th>
<th>Independent</th>
<th>t-Test</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>n Mean sd</td>
<td>n Mean sd</td>
<td>t value</td>
<td>P value</td>
</tr>
<tr>
<td>Total</td>
<td>237 188</td>
<td>51.0 12.3</td>
<td>49.72</td>
<td>6.1</td>
</tr>
<tr>
<td>Men</td>
<td>103 87</td>
<td>52.3 10.6</td>
<td>72.7</td>
<td>2.02</td>
</tr>
<tr>
<td>Woman</td>
<td>134 101</td>
<td>49.8 13.5</td>
<td>72.7</td>
<td>1.98</td>
</tr>
</tbody>
</table>
What is already known about this topic

- The development of the Dutch Care Dependency Scale has been described in several studies.
- The reliability and validity of the Care Dependency Scale have been determined using data sets from a number of countries.

What this paper adds

- The Care Dependency Scale is valid in terms of sensitivity and specificity.
- The Care Dependency Scale can be used as a diagnostic test to determine whether a patient is dependent on nursing care or not.

The first research question concerned the sensitivity, specificity, predictive values and ROC curve of the CDS. To determine these figures, according to Greenhalgh (1997), it is important to assess if (in this case) the CDS has been compared with a true gold standard. Therefore, for two reasons the BI was used as ‘gold standard’. First, the items of the BI largely correspond with the CDS items. Secondly, the BI has been recommended as the ‘gold standard’ for other ADL rating scales and the benchmark for evaluating newer scales.

At first sight, this simple determination of the sensitivity and specificity of a measurement instrument appears to have answered the question posed about the validity of the CDS. But it is also important to know how good the test is at predicting care dependency. In other words, we looked at the probability of the test giving the correct assessment, whether it was positive or negative. This gives a direct assessment of the usefulness of the CDS in practice.

If the BI is the gold standard, then why is the CDS needed? The practical advantage of the CDS is that it measures a broader range of patient needs, based on Henderson’s (1966) human need theory. Another advantage is that the aim of CDS assessment is to determine the patient’s potential for future self-care, whereas the BI does not measure what patients should potentially be able to do (de Haan et al. 1993). Furthermore, new tests should be validated against an established gold standard when seeking an instrument which may subsequently be shown to define better (in this case) patient function (Henderson 1993).

The area under the ROC curve yields a measure of predictive accuracy independent of the decision criterion and uncontaminated by the processes that affect the response, such as the underlying disease prevalence. Our results showed that the CDS has an area under the ROC curve of 0.81, which means a moderate diagnostic accuracy.

For assessment instruments in this setting, it is very important to have high sensitivity and PPV, because a positive result will probably lead to a nursing diagnosis of care dependency and nursing interventions (Altman 1991). As mentioned earlier, the CDS will be used at the beginning of the nursing diagnostic process as a case-finding instrument to identify patients who are care dependent and to eliminate those who are not. To determine an appropriate cut-off point for the CDS, the following aspects play a role: the consequence of giving a false diagnosis and the prevalence of the phenomenon in the study population. In other words, the ‘best’ cut-off point is sought to establish when care dependency is present and should not be missed, and false positive results do not have serious consequences for the patient during the clinical interventions that will follow a positive test.

Furthermore, it must be emphasized that the simple dichotomous classification of dependent and independent patients does not always reflect reality, and everyday experience suggests that borderline results are commonplace. Diagnostic problems caused by results falling into this middle zone may often be resolved by applying the same test later. The consequence of the latter will be that, after the CDS case-finding procedure, further additional diagnostic testing is necessary to ensure that all cases will be detected and early nursing intervention may be started.

In addition it must be stressed that, although the ‘best’ cut-off point must be chosen for a test to be used in patient care, there is no need to choose any particular cut-off for assessing accuracy. Assessing performance at a single point may result in misleading impressions about test performance (Zweig & Campbell 1993). According to Bouter and van Dongen (1991), the decision about an optimal cut-off point is arbitrary. Therefore, the given cut-off point is only applicable to the specific population studied. Consequently, the cut-off point (≤68) cannot be generalized as the impact of differing field conditions and spectra of disease on the absolute and relative accuracy of the CDS is at present unknown.

Conclusion

The main conclusion of this study is that the CDS may be used for accurate estimation of patients’ care dependency among hospital patients with various conditions. An appropriate cut-off score (≤68) has been given for determining the presence or absence of care dependency. Calculations of the sensitivity and PPVs, in this study, justify this conclusion. Furthermore, the data support the usefulness of the CDS, which discriminates areas of statistical significance between
care dependent and independent patients admitted in a general hospital.

Although the results of the present study are convincing and useful for patients admitted to a general hospital, further (international) research needs to be conducted with patients receiving home care and those admitted to other care settings, e.g. nursing homes and residential homes.

**Author contributions**

Study conception and design/Data analysis/Drafting of manuscript – AD; Data collection – LP, GV; Critical revision of the manuscript – AD, LT, TD; Statistical expertise – AD, TD.

**References**


