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# Clinical Pharmacology Research Internships at the Interface between Academia and Industry: Students' Perceptions and Scientific Output

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**Abstract:** The Centre for Human Drug Research (CHDR) is a non-profit clinical research institute at the interface between academia and the pharmaceutical industry. CHDR hosts a research internship programme for undergraduate (bio)medical students. The aim of this study was (i) to investigate the student perceptions of the undergraduate research internship and (ii) to quantify the scientific output related to these internships. We surveyed former interns at the CHDR from the year 2007 to 2014 and quantified their scientific output with a PubMed search. There was a response rate to the survey of 61%, with a good overall rating of the internships. Many students considered their internship at CHDR to be (much) more broad (55%) and with a (much) stricter planning (48%), compared to previous internships at academic research groups. In turn, there were many aspects reported to be similar to academic research internships such as focus on research methodology and 'outcome-drivenness'. Twenty-four per cent of the internships resulted in a co-authorship on papers published in peer-reviewed journals with an average impact factor of 3.3. In conclusion, with appropriate management and supervision, effective research electives are possible in the more commercial environment of a clinical research organization.

Academic healthcare education has always struggled to find a balance between clinical and scientific education. It is the science component that is often short-changed in academic curricula: although most ( $\pm 75\%$ ) European medical schools offer research courses during the undergraduate curricula, there is still room for improvement of the science component in many schools [1]. This contrasts with the importance of skills developed during science and research education [2]. Science and research education teaches students how to critically assess scientific literature and familiarizes them with emerging areas of biomedical science and pharmaceutical science [3]. These skills are crucial to practicing evidence-based medicine later in their career [4].

But even for students with a more research-focused curriculum (e.g. biomedical sciences, biopharmaceutical sciences), there is no substitute for the experience gained during a research internship. The execution of an independent research project has been described as 'probably the most authentic way to develop research skills' [4,5]. Studies report that undergraduate research projects increase science career decisions, active learning and the ability to 'think like a scientist' [6,7].

The Centre for Human Drug Research (CHDR) is a non-profit clinical research organization with legal status of a foundation which focuses on biomarker development and data-intensive, early-phase pharmacokinetics and pharmacodynamics clinical trials in most therapeutic areas. At CHDR, an undergraduate research internship programme has been

running since CHDR's inception in 1987. CHDR has strong ties with the nearby Leiden University, with many of its senior staff holding faculty positions. However, the context in which the research internship is performed differs in several ways between a CHDR internship and an internship at an academic research group. One difference is the nature of research, which is more applied clinical research, as opposed to basic research at academia. Furthermore, the studies are often funded by the pharmaceutical industry which is also reflected in the more commercial organizational structure of CHDR. Revenue from these sponsored studies are used to fund investigator-initiated clinical studies, biomarker and method development, education of staff and students at Leiden University and Leiden University Medical Center, and CHDR's undergraduate internship programme.

The CHDR undergraduate internship programme primarily aims to convey knowledge, skills and experience in human drug development while giving students the opportunity to experience the scientific methods first-hand. In a typical year, 60–70 applicants will compete for up to 20 student internship positions. Students may apply from any country or training background as long as they can demonstrate: (i) being a self-directed learner; (ii) having a strong command of the English language; and (iii) possessing a reasonable familiarity with the research process. Once accepted, students are paired with a supervisor who is responsible for assessing the student's performance and level of completion of both the student's individual scientific and CHDR's internal training plans. The scientific training plan and requirements for successful completion of the internship are generally dictated by the student's course programme, so that they obtain study credit points for

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the internship. The intern is also provided with a trainer responsible for day-to-day guidance during the internship. The focus of the internship is the student's involvement in a specific research project at the CHDR (e.g. a part of clinical study or PK-PD modelling analysis). Interns are expected to participate in weekly educational sessions which include clinical pharmacology lectures and journal clubs. They also attend monthly scientific discussions where planned and completed trials are critically discussed. This exposes the students to the CHDR research community and makes them familiar with practical issues surrounding research, two factors that have been suggested to promote student engagement in academic medicine [8]. The research internships are concluded with an oral presentation and a written report that ideally leads to presentation at (inter)national conferences and publication in a peer-reviewed journal. After graduation, former interns occasionally return to CHDR to continue their education as a PhD candidate and CHDR project leader. An example internship project and curriculum vitae is given for illustration purposes (Supporting information).

This study aimed to evaluate the views of former interns regarding the CHDR internship programme with a questionnaire. The questionnaire included some general questions on the intern's satisfaction with certain elements of the internship programme. Other questions focused on the context of a research internship at CHDR, and asked students to compare their experiences at CHDR with previous internships at academic research groups. In addition to the questionnaire, we assessed the scientific output of the programme by identifying co-authorships by former interns on publications or manuscripts directly related to their internship at CHDR.

### Material and Methods

**Survey.** An anonymous 32-item questionnaire was created using Google Forms<sup>®</sup> (Google Inc., Mountain View, CA, USA) and validated by two CHDR employees. Eighty-seven students that started their internship at CHDR in the years 2007–2014 were identified and invited by email to participate in the survey. One week after the initial invitation, a reminder was sent by email to all non-responders. The first part of the questionnaire consisted of questions regarding demographic data including starting year, internship duration and education phase during the internship. Six questions evaluated the students' attitudes towards the quality of the supervision, scientific value and commercial influence by means of Likert statements while an additional three questions assessed perception of their own performance, their own knowledge of clinical research methodologies and overall satisfaction with the internship. Students were asked to compare their internship at CHDR internships with internships at academic research groups. Lastly, open-ended questions were offered to query strengths and weaknesses and inviting any additional comments or suggestions. The questionnaire was composed of multiple-choice questions, multiple-answer questions and 4- or 5-point Likert-type scales. All survey participants answered voluntarily and none of the questions was marked mandatory to enable students to answer freely.

Under the Netherlands Law for Research on Human Subjects (WMO), this study was considered as an observational study in which the subjects are not submitted to risks or special requirements other than a short questionnaire. Additionally, the objectives of the study

were not medical research but rather educational research. Because of this, ethical clearance in the Netherlands is unnecessary and the study was therefore only reviewed by the scientific advisory board of our institution. The consent to participate was obtained from each individual prior to answering the survey.

**Analysis.** Survey responses were automatically collected in a Google Docs spreadsheet<sup>®</sup>. Data analysis and visualization was performed with R version 3.1.2 with R packages 'vcdExtra' 0.6-5 and 'likert' 1.2.1 [9–11]. Answers to the open-ended questions were screened to identify common themes. The Wilcoxon rank-sum test was used for statistical comparison of internships performed during Master phase or pre-master phase of the intern's study. The Goodman–Kruskal gamma was calculated to test for significant correlation between answers to different questions, where appropriate.

The questions regarding the comparison of the context of academic and CHDR internships focus on (bio)medical research internships. We therefore excluded answers to these questions if: (i) the CHDR internship focused exclusively on business/management (ii) the respondents were not believed to have participated in a research internship at an academic group previously. Examples of 'b' include students who performed a CHDR internship during the pre-master phase or students with a business/management background. After these exclusions, answers from 32 respondents were left for the analysis of the 'comparison of context' questions.

**Scientific output.** A PubMed<sup>®</sup> search was performed on 6 January 2015 to identify publications with contributions from (former) CHDR interns (in the period of 2007–2014) with CHDR affiliation. Hits were confirmed by abstract reading and verification of correctness with senior staff. All manuscripts currently in preparation or in the submission process were derived from senior staff of CHDR in January 2015. Journal impact factors were obtained from the Journal Citation Reports<sup>®</sup> 2013 [12].

### Results

#### Demographics.

A total of 87 students started an internship at CHDR in the period of 2007–2014, and 53 (61%) of them consented and responded to the survey. Three students could not be contacted due to expired contact details, and the remainder did not respond to the survey invitations. Demographics of the survey respondents are shown in table 1. Student interns have various backgrounds including biopharmaceutical sciences (45.3%), biomedical sciences (17.0%), medicine (17.0%) and pharmacy (9%). Most of the students performed their internship during the Master phase of their study (73.6%). The most common nationality of the respondents was Dutch (73.6%) with the remainder coming from other countries across the world, such as Mexico, USA and Japan. The most common internship durations were 21–27 weeks (26.4%) and  $\geq 36$  weeks (28.3%). The area of research of the respondents' internships is summarized in fig. 1. Students were allowed to choose multiple keywords to describe the scope of their internship research. The most commonly selected keywords were Central Nervous System (CNS) (45.3%), Clinical Pharmacology (43.4%) and PK-PD modelling (37.7%), which match important areas of research at CHDR. Only five students (9.4%) indicated that their internship entailed (any) business/management components.

Table 1.

Demographics of respondents of the survey (N = 53).

Variables	Respondents n (%)
<b>Origin</b>	
The Netherlands	39 (73.6)
Other European countries	3 (5.7)
The Americas	5 (9.4)
Other countries	4 (7.5)
No response	2 (3.8)
<b>Background</b>	
Bio-Pharmaceutical Sciences	24 (45.3)
Medicine	9 (17.0)
Bio medical Sciences	9 (17.0)
Pharmacy	5 (9.4)
Other	7 (13.2)
<b>Education phase during internship</b>	
Pre-master	10 (18.9)
Master	39 (73.6)
Other	4 (7.5)
<b>Internship duration</b>	
≤6 weeks	2 (3.8)
7–14 weeks	7 (13.2)
15–20 weeks	5 (9.4)
21–27 weeks	14 (26.4)
28–35 weeks	10 (18.9)
≥36 weeks	15 (28.3)

#### Open-ended questions.

We identified several common (>10% occurrence) themes in the open-ended questions on the strengths and weaknesses of the CHDR internship programme. Respondents appreciated that they were able to experience clinical drug development (44%) in a commercial setting (19%) and also mentioned interdisciplinary collaboration as one of the strengths of the CHDR internship programme (26%). While some students (19%) reported that they would have benefited from additional guidance from their supervisor, others (19%) appreciated the level of responsibility and independence that they were given as an intern. Sometimes, the clinical trial that was the subject of the intern's research was postponed or cancelled. Although these situations were often outside of CHDR's control, they would sometimes require that intern to focus on a different research topic. This uncertainty was mentioned by several students (17%) as a weakness of the internship programme.

#### Likert statements on general internship quality.

Students were asked to evaluate five positive and one negative statements regarding their internship using a 4-point Likert-type scale ranging from *Strongly Disagree* – 1 to *Strongly Agree* – 4 (fig. 2). 80.5% of the respondents strongly agreed that the internship was helpful to their career. Most of the students (strongly) agreed with other positive statements regarding the scientific value of the research project, and the quality of supervision: 97.8% and 91.8%, respectively. Most students (78.5%) reported having been able to complete their research project during their internship and generally (84.8%) agreed that their project's research question was clearly stated. In contrast, all but one student (strongly) disagreed with the

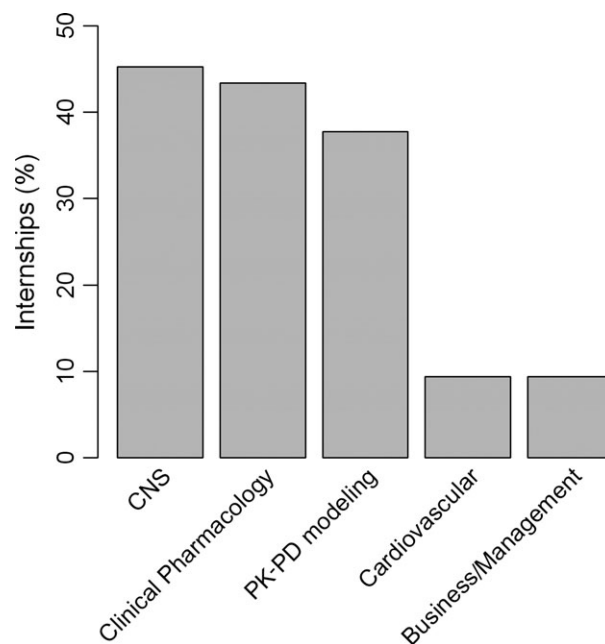


Fig. 1. Scope of internships 2007–2014 as reported by elective students. Respondents were allowed to select multiple keywords for the description. Only keywords selected by at least five respondents are shown.

negative statement regarding the distraction caused by the commercial setting of CHDR.

#### Likert-type scale self-assessment and internship perception.

As part of this survey, students rated their own knowledge and performance, and several aspects of the internship using a 5-point Likert-type scale ranging from *Poor* – 1 to *Excellent* – 5 (fig. 3). Respondents were confident about their own performance and knowledge of (clinical) research, with over 90% of them scoring *Average* – 3 or higher. Both the educational programme of CHDR and the overall rating of the internship scored high; the percentages of students rating these aspects as either *Good* – 4 or *Excellent* – 5 were 86.8% and 84.9%, respectively. In addition, none of the respondents scored the overall rating of the internship below *Average* – 3. This resulted in an average score of 4.26 out of 5. Some students (18.9%) reported either a *Poor* – 1 or *Moderate* – 2 link between their internship project and their prior knowledge. Interestingly, respondents who performed their internship during the pre-master phase of their study scored significantly lower on this aspect than those who did during the Master phase ( $p < 0.01$ ). We observed the same trend in the students' score on 'Own knowledge of (clinical) research' ( $p < 0.01$ ). This parameter was also positively correlated to the duration of the internship (Goodman–Kruskal gamma = 0.37,  $p < 0.05$ ).

#### Comparison of context with previous (academic) internships.

One part of the survey was explicitly dedicated to the comparison between the CHDR research internship and previous internships – typically performed at an academic research

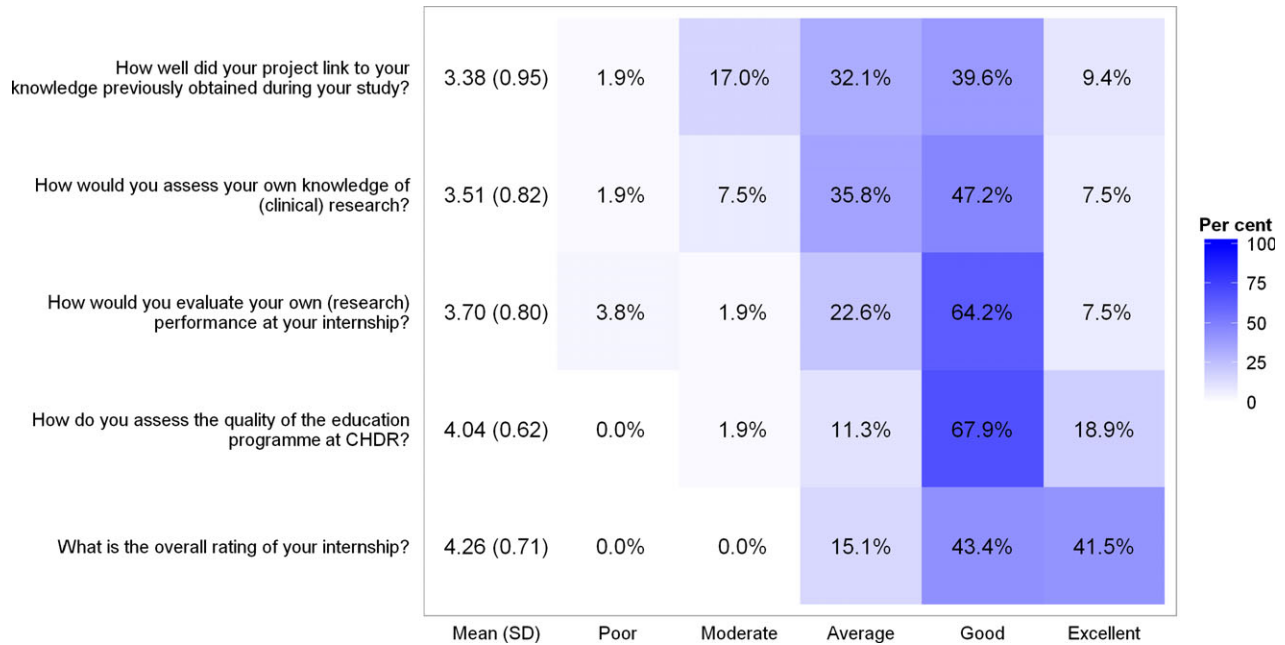


Fig. 2. Heat map of Likert statements evaluating the internship in general and self-assessment. The colour corresponds to the percentage of respondents who selected that option for a particular statement. Mean and standard deviation (S.D.) are given to aid interpretation: strongly disagree – 1; disagree – 2; agree – 3; strongly agree – 4.

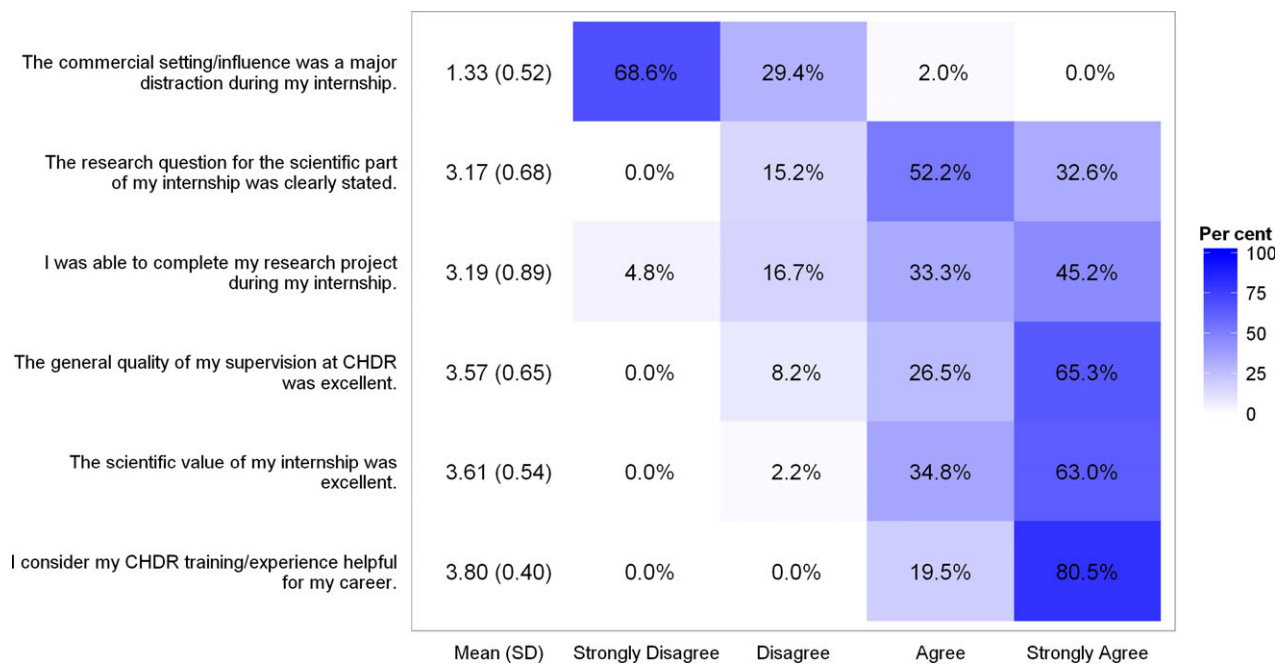


Fig. 3. Heat map of Likert-type scale outcome of context based questions and comparison to academic internships. The colour corresponds to the percentage of respondents who selected that option for a particular question. Mean and standard deviation (S.D.) are given to aid interpretation: poor – 1; moderate – 2; average – 3; good – 4; excellent – 5.

group at a university or academic hospital. Students were asked to rate several aspects on a 5-point Likert-type scale ranging from *Much less* – 1 to *Much more* – 5. The strongest trends in respondent answers were that CHDR internships were characterized as having a (much) broader scope (55%) and (much) stricter planning (48%) (fig. 4). Although the

majority of the students scored *Same* – 3 on focus on research methodology (63%) and outcome-drivenness (55%), there was a trend towards *More/Much more* on these aspects. The strictness of supervision and education, and the level of hands-on research experience are comparable to that experienced by students in previous internships, with no clear trends.

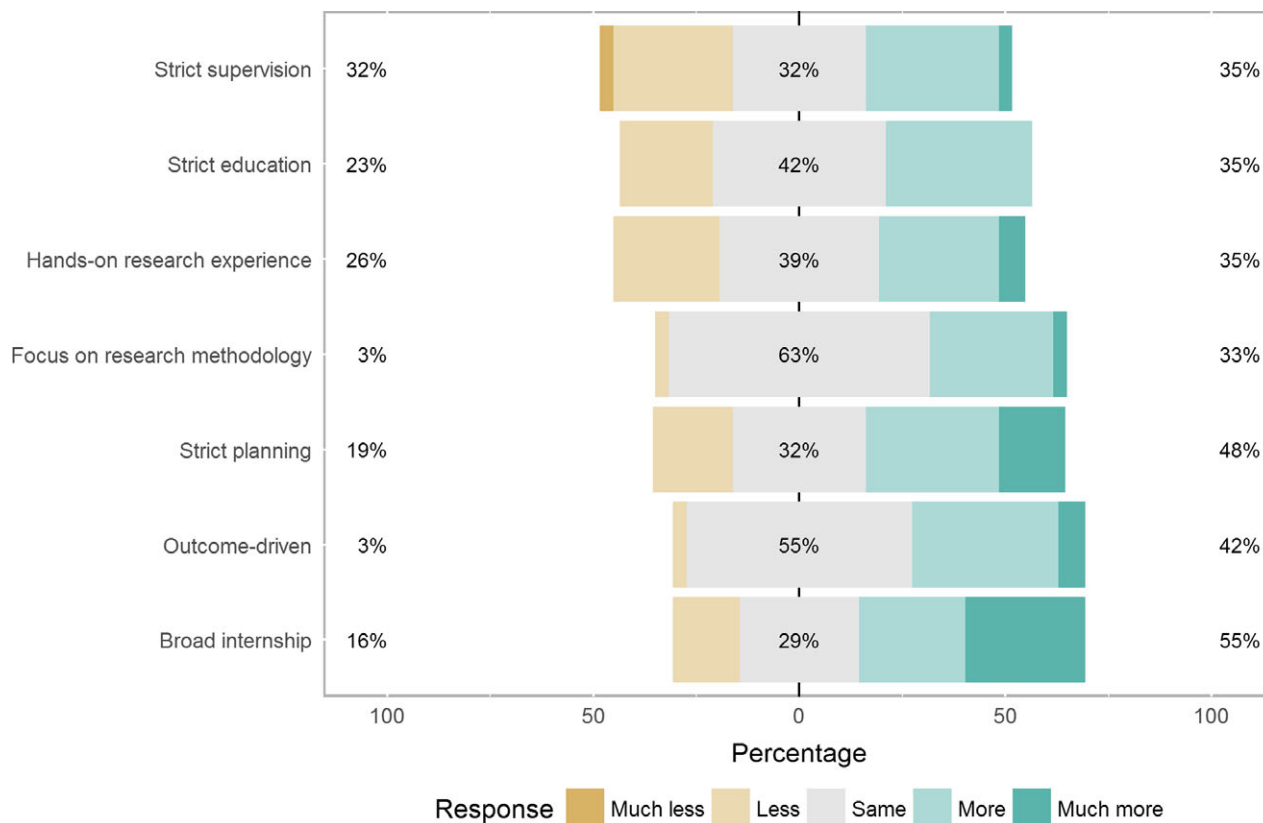


Fig. 4. Comparison of academic and CHDR research internships. Students were asked: 'Compare the following aspects of a CHDR internship to an academic research internship. At CHDR that aspect is: much less/less/same/more/much more'. Results from internships with only a business/management scope were excluded from this figure, as were respondents who were not believed to have participated in an academic research internship previously.

#### Scientific output.

A total of 21 CHDR interns of 2007–2014 (24%) are listed co-authors on 23 papers that are related to their internships. These papers were published in peer-reviewed journals with an average impact factor of 3.3 ( $\pm 1.9$ ). Furthermore, interns contributed to three recently submitted manuscripts and seven manuscripts with students in the author list are currently in preparation, adding up to a total of 33 manuscripts. In total, 28 interns (32%) were at some point involved in the writing of a manuscript related to their internship.

#### Discussion

Scientific training is an important pillar of education of (bio) medical students [1]. CHDR provides a unique environment for this: a non-profit clinical research organization at the interface between academia and the pharmaceutical industry. We are not aware of any scientific literature regarding undergraduate research internships in a comparable environment. This study therefore likely represents the first attempt to evaluate student perceptions and scientific output of such research internships.

Being able to experience clinical research in an interdisciplinary environment is one of the strengths that former interns often reported in open-ended questions. Students tended to (strongly) agree with all positive Likert statements (ranging

from 78.5% to 100% of all responses). In comparison with academic internships, the internships at CHDR were rated to be broader in scope. This reflects CHDR's interdisciplinary research in many therapeutic areas.

The commercial nature of CHDR is reflected in the survey results by being more outcome-driven and having a stricter planning, compared to academic internships. Several students (>10%) thought that the commercial nature was a benefit, as it allowed them to experience research in this setting during their CHDR internship. The open-ended questions also revealed some possible downsides of the commercial nature. In a commercial organization, employees might be less able to spend time supervising interns; several respondents reported that they required additional supervision during their internship. Other students seemed to appreciate the amount of supervision and they reported that having responsibilities taught them to work independently. This reflects differences between students in the level of support they need, which has been mentioned in the literature [13].

Because most of the clinical trials performed at CHDR are industry-sponsored, trials can sometimes be cancelled or delayed due to circumstances outside of CHDR's control. This could cause uncertainty about an intern's research project and was listed as one of the weaknesses of the CHDR internship programme. Overall, however, the commercial nature was not

considered a distraction during the internship by most (98%) of the respondents, suggesting that the interaction of CHDR with the pharmaceutical industry did not hinder the training of its interns.

Pre-master students scored significantly lower on both 'link between internship and prior knowledge' and 'Own knowledge of (clinical) research' than Master students. This might be explained by their difference in level of education at the time of the internship. Students that participated in longer internships scored significantly higher on 'own knowledge of (clinical) research'. This suggests increased learning during longer internships at the CHDR, although it could also be explained by the fact that pre-master students generally participated in shorter internships than Master students (who have had more prior education). In future studies, obtaining a self-assessment both before and after the internship would help to discriminate between these two explanations. Together, these data suggest that pre-master students and students participating in short internships might benefit from additional guidance during their internship. This will ensure that interns have a sufficient knowledge level for an effective internship.

For many of the students, their internship at CHDR was their first hands-on encounter with clinical research. This led to involvement in the writing of manuscripts for 32% of the interns. This is higher than the percentage of Dutch medical students that published during the final three years of their study (14.5%), although it should be mentioned that our literature search also included work published after graduation [14]. Publication rates of medical students reported in other literature range from 8 to 85%. While the publication rate of CHDR interns is reasonable, we aim to investigate whether there is room for improvement, as publication of results enhances the acquisition of research skills by the students [8,15]. This is especially true for medical students, as research has a less prominent role in their curriculum compared to biopharmaceutical and biomedical students; medical students are more likely to pursue an academic career if they have experienced research during their education [16,17]. Furthermore, several students submitted abstracts of their research projects to poster sessions at (inter)national meetings, but we did not quantify this scientific output. This can be a relevant experience for students, as it trains their ability to communicate their findings to a broader audience [15].

The response rate to the survey was 61%. Therefore, response bias cannot be excluded, as it is possible that response rates depend on a student's attitude towards (their internship at) CHDR. The results on the comparison between a CHDR and a previous academic internship might be affected by some level of selection bias, as both the students' decision to apply to the programme and their chance of acceptance can be considered non-random. The results of this study cannot therefore be directly extrapolated to the general (bio)medical student population.

Another limitation is that we did not gather detailed information about the previous internships performed by the students. This makes the interpretation of the questions regarding the context comparison more difficult, as the point of

reference is unclear. In future research, it would be better to compare student perceptions of a cohort of CHDR interns with those of a comparable cohort of interns at an academic research group. Such a study might also assess outcome that does not rely on student self-report, such as the grade rewarded for the internship or for the final report.

The use of the Likert statements in this study might have introduced bias due to acquiescence, the tendency to provide confirmatory answers regardless of the statement [18]. While this could have contributed to higher level of agreements to the statements in fig. 3, it is important to note that 98% of the respondents disagreed with the statement regarding the distraction caused by the commercial setting. Finally, the unidimensional Likert items used in this questionnaire provide little information on the factors that underlie these answers. Therefore, we obtained such information with the open questions regarding the strengths and weaknesses of the CHDR internship programme. Future research should consider a more in-depth exploration of factors that contribute to the student's perception.

### Conclusion

In general, student satisfaction was high, and many aspects were reported similar to academic research electives such as focus on research methodology and strictness. However, we identified some differences, that is a broader scope and stricter planning at CHDR electives. Importantly, by engaging in a clinical research project, important research skills and attributes are acquired, such as: critical appraisal, an enquiring mind, ability to work in a team and understanding of ethics involved in human subject research [19]. Therefore, we would advocate for combining undergraduate training with interdisciplinary clinical research in the (bio)medical curriculum, as we believe it can have a major contribution to the training of the (bio)medical professionals of tomorrow. Furthermore, we stipulate involvement of young academics in clinical drug development as this is crucial for the increasingly complex process of question-based drug development [20]. With proper supervision and management of expectations, effective research internships are possible within the commercial environment of a clinical research organization.

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### Declaration of interests

The authors report no conflict of interests. The authors alone are responsible for the content and writing of the article.

### References

- 1 Van SC, Marz R, Garcia-Seoane J. Exploring the integration of the biomedical research component in undergraduate medical education. *Med Teach* 2013;**35**:e1243–51.
- 2 Association of American Medical Colleges-Howard Hughes Medical Institute (AAMC-HHMI). *Scientific Foundations for Future Physicians*. AAMC, Washington, DC, 2009;1–46.

- 3 Cooke M. Science for physicians. *Science* 2010;**329**:1573.
- 4 Zee M, de Boer M, Jaarsma AD. Acquiring evidence-based medicine and research skills in the undergraduate medical curriculum: three different didactical formats compared. *Perspect Med Educ* 2014;**3**:357–70.
- 5 Laidlaw A, Aiton J, Struthers J, Guild S. Developing research skills in medical students: AMEE Guide No. 69. *Med Teach* 2012;**34**:e754–71.
- 6 Auchincloss LC, Laursen SL, Branchaw JL, Eagan K, Graham N, Hanauer DI *et al.* Assessment of course-based undergraduate research experiences: a meeting report. *CBE Life Sci Educ* 2014;**13**:29–40.
- 7 Lopatto D. Undergraduate research experiences support science career decisions and active learning. *CBE Life Sci Educ* 2007;**6**: 297–306.
- 8 Lawson MA, Saunders C, Velu PP, Iredale J, Hor K, Russell CD. Twelve tips for teachers to encourage student engagement in academic medicine. *Med Teach* 2013;**35**:549–54.
- 9 R Core Team. R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing, 2014. <http://www.R-project.org/>.
- 10 Bryer J, Speerschneider K. Likert: Functions to analyze and visualize likert type items, 2014. <http://jason.bryer.org/likert> (last accessed on 23 March 2015).
- 11 Friendly M. vcdExtra: vcd Extensions and Additions. 2015. <http://CRAN.R-project.org/package=vcdExtra> (last accessed on 23 March 2015).
- 12 Thomson Reuters. 2013 Journal Citation Reports® Science Edition. Thomson Reuters, New York, 2015.
- 13 Siddiqui ZS, Jonas-Dwyer DR. Twelve tips for supervising research students. *Med Teach* 2012;**34**:530–3.
- 14 van Eyk HJ, Hooiveld MH, Van Leeuwen TN, Van der Wurff BL, De Craen AJ, Dekker FW. Scientific output of Dutch medical students. *Med Teach* 2012;**32**:231–5.
- 15 Griffin MF, Hindocha S. Publication practices of medical students at British medical schools: experience, attitudes and barriers to publish. *Med Teach* 2011;**33**:e1–8.
- 16 Greenberg RB, Ziegler CH, Borges NJ, Elam CL, Stratton TD, Woods S. Medical student interest in academic medical careers: a multi-institutional study. *Perspect Med Educ* 2013;**2**:298–316.
- 17 Borges NJ, Navarro AM, Grover A, Hoban JD. How, when, and why do physicians choose careers in academic medicine? A literature review. *Acad Med* 2010;**85**:680–6.
- 18 Hinz A, Michalski D, Schwarz R, Herzberg PY. The acquiescence effect in responding to a questionnaire. *GMS Psychosoc Med* 2007;**4**:Doc07.
- 19 Laidlaw A, Guild S, Struthers J. Graduate attributes in the disciplines of Medicine, Dentistry and Veterinary Medicine: a survey of expert opinions. *BMC Med Educ* 2009;**9**:28.
- 20 Cohen AF, Burggraag J, van Gerven JM, Moerland M, Groeneveld GJ. The use of biomarkers in human pharmacology (Phase I) studies. *Annu Rev Pharmacol Toxicol* 2015;**55**:55–74.

### Supporting Information

Additional Supporting Information may be found online in the supporting information tab for this article:

**Appendix S1.** Representative example elective.