Aus der
Schön Klinik Roseneck
Direktor: Professor Dr. Ulrich Voderholzer

und der

Klinik und Poliklinik für Psychiatrie und
Psychotherapie Klinik der Universität München
Direktor: Professor Dr. Peter Falkai

Einflussfaktoren auf die Wirksamkeit einer stationären Behandlung der Anorexia nervosa

Dissertation
zum Erwerb des Doktorgrades der Medizin
an der Medizinischen Fakultät
der Ludwig-Maximilians-Universität zu München

vorgelegt von
Tabea Helga Bauman

aus
Melk an der Donau, Österreich

Jahr
2026

Mit Genehmigung der Medizinischen Fakultät
der Universität München

Berichterstatter:	Prof. Dr. Rebecca Schennach
Mitberichterstatter:	PD Dr. Katharina Bühren
	PD Dr. Tobias Schwerd
Mitbetreuung durch den promovierten Mitarbeiter:	Prof. Dr. Ulrich Voderholzer
Dekan:	Prof. Dr. med. Thomas Gudermann
Tag der mündlichen Prüfung:	29.01.2026

Inhaltsverzeichnis

1. Beitrag zu den Publikationen

1.1 Beitrag zu Publikation I

Die Publikation mit dem Titel „Inpatient Treatment Outcome in a Large Sample of Adolescents with Anorexia Nervosa“ der Autoren Norbert Quadflieg, Silke Naab, Sandra Schlegl, Tabea Bauman und Ulrich Voderholzer wurde 2023 in der Fachzeitschrift Nutrients veröffentlicht (Quadflieg et al., 2023). Die Autoren gehören einer gemeinsamen Arbeitsgruppe der Schön Klinik Roseneck - einer psychosomatischen Fachklinik und einem Spezialzentrum zur Behandlung von Essstörungen - und der Ludwig-Maximilians-Universität München an.

Die wissenschaftliche Fragestellung dieser Publikation wurde gemeinsam in der Arbeitsgruppe unter der Leitung von Herrn Prof. Dr. med. Ulrich Voderholzer formuliert. Die Entwicklung der Konzeption erfolgte durch Herrn Dr. rer. biol. hum. Dipl.-Psych. Norbert Quadflieg und wurde durch mich in klinischen Aspekten beratend unterstützt. Die Literaturrecherche erfolgte durch Herrn Dr. rer. biol. hum. Dipl.-Psych. Norbert Quadflieg und wurde durch mich ergänzt. Die Datenerhebung und Datenauswertung erfolgte durch Herrn Dr. rer. biol. hum. Dipl.-Psych. Norbert Quadflieg. Die Bewertung und Interpretation der Ergebnisse erfolgte gemeinsam in der Arbeitsgruppe. Die Manuskripterstellung erfolgte durch Herrn Dr. rer. biol. hum. Dipl.-Psych. Norbert Quadflieg unter meiner Beteiligung in den Abschnitten „Introduction“, „Materials and Methods“, „Discussion“ sowie „Conclusions“. Auch die Überarbeitung des Manuskripts im Rahmen des Review Verfahrens erfolgte durch Herrn Dr. rer. biol. hum. Dipl.-Psych. Norbert Quadflieg unter meiner Beteiligung in den Abschnitten „Introduction“, „Materials and Methods“, „Discussion“ sowie „Conclusions“. Der gesamte Prozess wurde durch Herrn Prof. Dr. med. Ulrich Voderholzer supervidiert.

Zusammenfassend erstreckte sich mein Beitrag zu dieser Publikation in Teilen auf die Entwicklung der wissenschaftlichen Fragestellung, die Entwicklung der Konzeption, die Literaturrecherche, die Bewertung und Interpretation der Ergebnisse sowie die Erstellung und Überarbeitung des zur Veröffentlichung eingereichten Manuskripts.

1.2 Beitrag zu Publikation II

Die Publikation mit dem Titel „Impact of Antipsychotic Medications on Weight Gain and Eating Disorder-Related Psychopathology in Adult Inpatients with Anorexia Nervosa“ der Autoren Tabea Bauman, David R. Kolar, Christoph U. Correll, Verena Haas und Ulrich Voderholzer wurde 2024 in der Fachzeitschrift Pharmacopsychiatry veröffentlicht (Bauman et al., 2024). Die Autoren gehören einer wissenschaftlichen Kooperation der Schön Klinik Roseneck - einer psychosomatischen Fachklinik und einem Spezialzentrum zur Behandlung von Essstörungen - und der Klinik für Psychiatrie, Psychosomatik und Psychotherapie des Kindes- und Jugendalters der Charité-Universitätsmedizin Berlin an.

Die wissenschaftliche Fragestellung dieser Publikation wurde durch mich initiiert und formuliert. Die Entwicklung der Konzeption erfolgte durch mich unter der Beratung von Herrn Prof. Dr. med. Christoph U. Correll und Herrn Prof. Dr. med. Ulrich Voderholzer. Die Literaturrecherche sowie die Datenerhebung erfolgten vollständig durch mich. Die Datenauswertung erfolgte durch Herrn Prof. Dr. rer. nat. David R. Kolar. Die Bewertung und Interpretation der Ergebnisse erfolgte gemeinsam mit allen Ko-Autoren. Die Erstellung des Manuskripts erfolgte mehrheitlich durch mich, unter der Beteiligung von Herrn Prof. Dr. rer. nat. David R. Kolar in den Abschnitten „Methods“ und „Results“. Die Prüfung des Manuskripts erfolgte durch alle Ko-Autoren. Die Überarbeitung des Manuskripts im Rahmen des Review Verfahrens erfolgte vollständig durch mich. Besonders hervorzuheben ist, dass die Koordination des gesamten Prozesses in meiner Verantwortung lag. Die Supervision des Prozesses erfolgte durch Herrn Prof. Dr. med. Christoph U. Correll, Frau Dr. oec. troph. Verena Haas und Herrn Prof. Dr. med. Ulrich Voderholzer.

Zusammenfassend erstreckte sich mein Beitrag zu dieser Publikation nahezu vollständig auf die Entwicklung der wissenschaftlichen Fragestellung, die Entwicklung der Konzeption, die Literaturrecherche, die Datenerhebung, die Begleitung der Datenauswertung, die Bewertung und Interpretation der Ergebnisse sowie die Erstellung und Überarbeitung des zur Veröffentlichung eingereichten Manuskripts.

2. Einleitung

2.1 Anorexia nervosa

2.1.1 Epidemiologie und Verlauf

Die Anorexia nervosa tritt zumeist in der Adoleszenz oder im jungen Erwachsenenalter auf (Smink et al., 2012; Silén et al., 2020; Solmi et al., 2022). Deutlich häufiger sind Mädchen und junge Frauen betroffen (Raevuori et al., 2014; Silén et al., 2020). Steigende Inzidenzen werden besonders bei jungen Mädchen beobachtet (Reas & Rø, 2018). Prognostisch zeigt sich in Langzeitstudien, dass etwa die Hälfte der Betroffenen die Erkrankung vollständig bewältigen können (Steinhausen, 2009; Zipfel et al., 2000; Solmi et al., 2024). Die übrigen Betroffenen nehmen allerdings einen chronischen Verlauf oder versterben an der Erkrankung. Die standardisierte Mortalitätsrate betrug in früheren Untersuchungen 5,9 und in einer aktuellen Metaanalyse 5,8, was einem fast sechsfach höheren Sterblichkeitsrisiko als in der altersentsprechenden Allgemeinbevölkerung entspricht (Arcelus et al., 2011; Solmi et al., 2024). Ein Erkrankungsbeginn in der Kindheit (Herpertz-Dahlmann et al., 2018), eine lange Erkrankungsdauer (Zipfel et al., 2000) und ein ausgeprägter Gewichtsverlust (Hebebrand et al., 1997) sowie der bulimische Typ der Anorexia nervosa (Fichter & Quadflieg, 1999) und Kinderlosigkeit (Fichter et al., 2017) sind prognostisch ungünstige Faktoren.

2.1.2 Pathogenese

Ätiologisch ist eine multifaktorielle Genese mit biologischen und psychosozialen Faktoren sowie eine wechselseitige Beeinflussung anzunehmen (Schmidt, 2003). Aus Zwillingsstudien wird eine starke genetische Komponente von ca. 50 % vermutet (Trace et al., 2013). Am ehesten starvationsbedingte neurobiologische Veränderungen betreffen unter anderem das serotonerge und dopaminerge Neurotransmittersystem im Bereich des präfrontalen Kortex sowie dem ventralen Striatum (Kaye et al., 2013). Die funktionelle Bildgebung weist auf Veränderungen im Belohnungssystem hin (Steinglass et al., 2019). Schon vor Jahrzehnten wurde eine Dopamin-Rezeptor-Überempfindlichkeit spekuliert (Barry & Klawans, 1976), von welcher ausgehend auch ein möglicher Benefit durch den Einsatz von Antipsychotika (Dopamin-Rezeptor-Antagonisten) in der Behandlung der Anorexia nervosa diskutiert wurde. Ebenfalls diskutiert wurden Assoziationen mit Autoimmunerkrankungen (Hedman et al., 2019). Auch Veränderungen des Darmmikrobioms könnten mit der Anorexia nervosa assoziiert sein (Hetterich et al., 2019). Angenommen wird, dass eine Veränderung der Bakterienbesiedelung des Darms zu einer Veränderung der Darmschleimhaut mit erhöhter Permeabilität und nachfolgender Immunantwort führen könnte (Seitz et al., 2019). Für Essstörungen sind außerdem eine hohe

Zahl an allgemeinen Risikofaktoren, wie das weibliche Geschlecht, Adoleszenz, psychische Erkrankungen in der Familie und westliche Gesellschaftsformen, bekannt (Keski-Rahkonen & Mustelin, 2016; Stice et al., 2017). Soziale Schichten mit höherer Bildung sind häufiger von Essstörungen betroffen (Goodman et al., 2014). Des Weiteren besteht ein Zusammenhang zwischen Essstörungen und sexuellen, physischen oder psychischen Gewalterfahrungen (Caslini et al., 2016).

2.1.3 Symptomatik

Untergewicht ist das zentrale Merkmal der Anorexia nervosa (World Health Organization, 1992; World Health Organization, 2022). Zur Beurteilung des Untergewichts wird der Body-Mass-Index (BMI) verwendet (World Health Organization, 2000). Dieser wird nach einer Formel errechnet und durch eine Einteilung der Weltgesundheitsorganisation (engl. World Health Organization) interpretiert (World Health Organization, 2000). Bei Erwachsenen liegt der Normalbereich des Körpergewichts bei einem BMI von 18,5 kg/m² bis 24,9 kg/m² (World Health Organization, 2000). Bei einem BMI < 18,5 kg/m² spricht man demnach von Untergewicht (World Health Organization, 2000). Bei Kindern und Jugendlichen werden aufgrund der altersabhängigen Veränderungen der Körperproportionen altersbezogene BMI-Perzentiltabellen verwendet (Kromeyer-Hauschild et al., 2001).

Trotz Untergewicht haben Betroffene typischerweise Angst davor zu dick zu sein und/oder zu dick zu werden (World Health Organization, 1992; World Health Organization, 2022). Die Art der veränderten Körperwahrnehmung wird als Körperschemastörung bezeichnet (World Health Organization, 1992; World Health Organization, 2022). Um ein niedriges Körpergewicht zu erreichen, schränken die Betroffenen in der Regel die Nahrungsmengen ein und/oder selektionieren die Nahrung durch Vermeidung bestimmter Lebensmittel, wie z.B. fett- und kohlenhydratreiche Speisen (World Health Organization, 1992; World Health Organization, 2022). Auch selbstinduziertes Erbrechen, exzessive körperliche Betätigung und Medikamentenmissbrauch können zur Gewichtsreduktion hinzukommen (World Health Organization, 1992; World Health Organization, 2022). Neben dem restriktiven und selektiven Essverhalten entwickeln die Betroffenen auch häufig in der klinischen Praxis zu beobachtende auffällige Essensrituale, wie das Kleinschneiden und das Überwürzen der Speisen sowie ein sehr langsames Esstempo.

Auf psychischer Ebene fallen häufig Rigidität, ein starkes Bedürfnis nach Kontrolle, Konfliktvermeidung und Schwierigkeiten im Umgang mit Gefühlen auf (Deutsche Gesellschaft für Essstörungen e.V. & Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften e.V., 2018). Auf körperlicher Ebene zeigen sich die Folgen der Mangelernährung

(Deutsche Gesellschaft für Essstörungen e.V. & Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften e.V., 2018). Je nach Alter zu Erkrankungsbeginn kann es zu einer Stagnation der körperlichen Entwicklung und Minderwuchs kommen (World Health Organization, 1992). Es kann zu einer Verzögerung der Pubertät mit einem Ausbleiben der Menarche oder zum Sistieren der Menstruation kommen (World Health Organization, 1992). Mit der Störung des endokrinen Systems kann sich auch eine Knochendichteminderung entwickeln (Deutsche Gesellschaft für Essstörungen e.V. & Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften e.V., 2018). Die Betroffenen können unter Haut- und Gefäßveränderungen leiden und es können sich Zahnschäden ausbilden (Deutsche Gesellschaft für Essstörungen e.V. & Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften e.V., 2018). An den inneren Organen können besonders das Herz und der Gastrointestinaltrakt betroffen sein (Deutsche Gesellschaft für Essstörungen e.V. & Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften e.V., 2018). Neurologisch können sich Nervenschäden und eine Gehirnatrophie entwickeln (Deutsche Gesellschaft für Essstörungen e.V. & Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften e.V., 2018).

Neben den psychischen und körperlichen Symptomen leiden Betroffene auch unter den weitreichenden sozialen Folgen der Erkrankung mit Einschränkungen wichtiger Entwicklungsschritte in allen Lebensphasen (Deutsche Gesellschaft für Essstörungen e.V. & Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften e.V., 2018). Anstelle einer normalen Identitätsentwicklung ist in der klinischen Praxis häufig zu beobachten, dass die Anorexia nervosa einen großen Anteil der Identität einnimmt und die Lebensqualität der Betroffenen dadurch drastisch beeinträchtigt wird.

2.1.4 Diagnostische Kriterien nach ICD-10 und ICD-11

Die Kriterien der Anorexia nervosa nach der Internationalen statistischen Klassifikation der Krankheiten und verwandter Gesundheitsprobleme in 10. Revision (ICD-10, engl. International Statistical Classification of Diseases and Related Health Problems, 10th Revision) umfassen ein selbst herbeigeführtes Untergewicht (BMI ≤ 17,5 kg/m² bei Erwachsenen oder ein Unterschreiten der 10. Perzentile bei Kindern und Jugendlichen), eine Körperschemastörung und eine endokrine Störung (World Health Organization, 1992). Das ICD-10 unterscheidet eine Anorexia nervosa ohne aktive Maßnahmen zur Gewichtsreduktion und mit aktiven Maßnahmen zur Gewichtsreduktion (World Health Organization, 1992). Gemeint sind dabei Erbrechen, exzessive Bewegung und Medikamentenmissbrauch (World Health Organization, 1992).

Diagnostische Kriterien der Anorexia nervosa nach ICD-10 (World Health Organization, 1992):

- Gewichtsverlust oder bei Kindern fehlende Gewichtszunahme. Dies führt zu einem Körpergewicht von mindestens 15 % unter dem normalen oder dem für das Alter und die Körpergröße erwarteten Gewicht.
- Der Gewichtsverlust ist selbst herbeigeführt durch Vermeidung von „fettmachenden" Speisen.
- Selbstwahrnehmung als „zu fett" verbunden mit einer sich aufdrängenden Furcht zu dick zu werden. Die Betroffenen legen für sich selbst eine sehr niedrige Gewichtsschwelle fest.
- Umfassende endokrine Störung der Hypothalamus-Hypophysen-Gonaden-Achse; sie manifestiert sich bei Frauen als Amenorrhoe, bei Männern als Interessenverlust an Sexualität und Potenzverlust. Eine Ausnahme stellt das Persistieren vaginaler Blutungen bei Frauen mit Anorexia nervosa dar die eine Hormonsubstitution erhalten (meist als kontrazeptive Medikation).
- Kommentar: Folgende Symptome bestätigen die Diagnose, sind aber nicht obligat: selbstinduziertes Erbrechen, übertriebene körperliche Aktivität, selbstinduziertes Abführen und Gebrauch von Appetitzüglern und/oder Diuretika.
- Dazugehörige Begriffe: Anorexie ohne aktive Maßnahmen zur Gewichtsabnahme / restriktive Form der Anorexie (F50.00); Anorexie mit aktiven Maßnahmen zur Gewichtsreduktion (Erbrechen, exzessive Bewegung, Medikamentenmissbrauch etc., u. U. in Verbindung mit Heißhungerattacken) / bulimische Form der Anorexie (F50.01)

Anders als im ICD-10 wird in der Internationalen statistischen Klassifikation der Krankheiten und verwandter Gesundheitsprobleme in 11. Revision (ICD-11, engl. International Statistical Classification of Diseases and Related Health Problems, 11th Revision) das Kriterium des Untergewichts mit einem BMI < 18,5 kg/m² bei Erwachsenen oder ein Unterschreiten der 5. Perzentile bei Kindern und Jugendlichen definiert (World Health Organization, 2022). Außerdem entfällt wie bereits im Diagnostischen und Statistischen Leitfaden psychischer Störungen in der 5. Auflage (DSM-5, engl. Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition) das Kriterium der endokrinen Störung (American Psychiatric Association, 2013; World Health Organization, 2022). Zudem soll in signifikant niedriges Körpergewicht (BMI zwischen 18,5 kg/m² und 14,0 kg/m² bei Erwachsenen oder zwischen 5. und 3. Perzentile bei Kindern und Jugendlichen) und gefährlich niedriges Körpergewicht (BMI < 14,0 kg/m² bei Erwachsenen oder ein Unterschreiten der 3. Perzentile bei Kindern und Jugendlichen) unterschieden werden (World Health Organization, 2022). Die Unterscheidung zwischen einem restriktiven Typ, d. h.

ohne aktive Maßnahmen zur Gewichtsreduktion, und einem bulimischen Typ, d. h. mit aktiven Maßnahmen zur Gewichtsreduktion, bleibt bestehen (World Health Organization, 2022).

2.1.5 Differentialdiagnostik und Komorbiditäten

Um die Anorexia nervosa zunächst von konstitutionellen Formen von Untergewicht abzugrenzen, sind die weiteren psychischen Merkmale und körperlichen Folgen zu beachten. Bei konstitutionellem, zumeist leichtem Untergewicht, sind diese nicht vorhanden (Deutsche Gesellschaft für Essstörungen e.V. & Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften e.V., 2018).

Differentialdiagnostisch ebenfalls zu erwägen sind Tumorerkrankungen, endokrine Erkrankungen, gastrointestinale Erkrankungen, infektiöse Erkrankungen und andere psychische Erkrankungen (Deutsche Gesellschaft für Essstörungen e.V. & Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften e.V., 2018).

Sehr häufig besteht eine Komorbidität mit einer anderen psychischen Erkrankung, wie vor allem Depressionen, Angststörungen, Zwangsstörungen und Suchterkrankungen (Salbach-Andrae et al., 2008). Zwanghaft und ängstlich-vermeidend sind die häufigsten komorbiden Persönlichkeitszüge oder -störungen bei einer Anorexia nervosa (Martinussen et al., 2017). Außerdem zeigen sich bei Betroffenen vermehrt Autismus-Spektrum-Störungen (Koch et al., 2015) sowie eine Aufmerksamkeitsdefizit-/Hyperaktivitätsstörung (Nazar et al., 2016).

2.1.6 Behandlung der Anorexia nervosa nach der S3-Leitlinie Diagnostik und Therapie der Essstörungen

Ziele in der Behandlung der Anorexia nervosa sind insbesondere die Wiederherstellung und das Halten eines für das Alter und die Größe angemessenen Körpergewichts, die Normalisierung des Ess- und Bewegungsverhaltens, die Behandlung der körperlichen Folgen, die Beeinflussung der dem Erkrankungsbild zugrundeliegenden Faktoren sowie die Förderung der sozialen Integration (Deutsche Gesellschaft für Essstörungen e.V. & Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften e.V., 2018; Resmark et al., 2019). Die Gewichtszunahme stellt dabei einen wichtigen prognostischen Faktor für den Behandlungsverlauf dar (Nazar et al., 2017).

Grundsätzlich ist Psychotherapie die Behandlungsmethode der Wahl (Deutsche Gesellschaft für Essstörungen e.V. & Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften e.V., 2018; Resmark et al., 2019). Wirksame Psychotherapieverfahren sind die erweiterte kognitive-behaviorale Therapie (CBT-E, engl. Enhanced Cognitive Behaviour Therapy), die fokale psychodynamische Therapie (FPT, engl. Focal Psychodynamic Therapy),

das Maudsley Model of Anorexia nervosa Treatment (MANTRA) sowie ein Specialist Supportive Clinical Management (SSCM) (Deutsche Gesellschaft für Essstörungen e.V. & Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften e.V., 2018; Resmark et al., 2019). MANTRA und SSCM sind in Deutschland allerdings keine anerkannten Psychotherapieverfahren. Anzumerken ist, dass alle Verfahren mit einem Monitoring des Gewichts zu kombinieren sind und diese sich insofern in der Durchführung weniger als bei anderen psychischen Erkrankungen voneinander unterscheiden. Darauf lässt sich zurückführen, dass bislang keines dieser spezifischen Verfahren einem anderen nachweislich überlegen ist (Zipfel et al., 2014; Zeeck et al., 2018).

Eine Psychopharmakotherapie kann nach bisheriger Evidenzlage in der Behandlung der Anorexia nervosa nicht routinemäßig empfohlen werden (Deutsche Gesellschaft für Essstörungen e.V. & Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften e.V., 2018; Resmark et al., 2019). Die S3-Leitlinie in ihrer gegenwärtigen Version empfiehlt eine psychopharmakologische Behandlung daher auch nur in Einzelfällen bei spezifischer Symptomatik im Rahmen eines Gesamtbehandlungsplans und nicht zum dauerhaften Gebrauch (Deutsche Gesellschaft für Essstörungen e.V. & Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften e.V., 2018; Resmark et al., 2019).

2.1.7 Stationäre Behandlung der Anorexia nervosa in der klinischen Praxis

Nach der S3-Leitlinie sind Kriterien für eine stationäre Behandlung der Anorexia nervosa ein rapider oder anhaltender Gewichtsverlust (> 20 % über sechs Monate), gravierendes Untergewicht (BMI < 15 kg/m^2 bzw. bei Kindern und Jugendlichen unterhalb der 3. Perzentile), anhaltender Gewichtsverlust oder unzureichende Gewichtszunahme über 3 Monate (bei Kindern und Jugendlichen früher) trotz ambulanter oder tagesklinischer Behandlung, soziale oder familiäre Einflussfaktoren, eine ausgeprägte psychische Komorbidität und/oder Suizidalität, eine schwere bulimische Symptomatik und/oder ein exzessiver Bewegungsdrang, körperliche Gefährdung oder Komplikationen, eine geringe Krankheitseinsicht, Überforderung im ambulanten oder tagesklinischen Setting sowie die Notwendigkeit der Behandlung durch ein multiprofessionelles Team (Deutsche Gesellschaft für Essstörungen e.V. & Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften e.V., 2018). Das zentrale Ziel der Behandlung ist die Gewichtsnormalisierung (Deutsche Gesellschaft für Essstörungen e.V. & Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften e.V., 2018). Im ambulanten Setting sollte eine Gewichtszunahme von 200 - 500 g pro Woche erreicht werden (Deutsche Gesellschaft für Essstörungen e.V. & Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften e.V., 2018). Im stationären Setting wird eine Gewichtszunahme von 500 - 1000 g pro Woche angestrebt (Deutsche Gesellschaft für Essstörungen e.V.

& Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften e.V., 2018). Insgesamt ist anzumerken, dass die Langzeitprognose besser ist, je näher das Entlassungsgewicht einem normalen Gewicht entspricht und je besser die Gewichtszunahme stabilisiert werden konnte (Kaplan et al., 2009).

In der Behandlung der Anorexia nervosa ist es zum einen besonders wichtig Motivationsstrategien einzusetzen, da Betroffene oft eine starke Ambivalenz gegenüber der Aufgabe ihrer Erkrankung haben (Legenbauer & Vocks, 2014). Zum anderen unterscheidet man in der klinischen Praxis der Essstörungsbehandlung dann typischerweise zwei Behandlungswege. Ein Weg dient dem Ziel der Gewichtszunahme durch Normalisierung von Essverhalten und der Aufgabe von eventuellen gegenregulatorischen Maßnahmen (Legenbauer & Vocks, 2014). Unter Normalisierung des Essverhaltens ist eine Normalisierung von Essensmenge und Essensauswahl zu verstehen sowie die Aufgabe von erkrankungstypischen, essensbezogenen Ritualen und die zunehmende Verselbstständigung im Umgang mit Essen (Legenbauer & Vocks, 2014). Der andere und zum Teil parallele Weg in der Essstörungsbehandlung greift die auslösenden und aufrechterhaltenden Bedingungen der Erkrankung im Rahmen eines individuellen Erkrankungsmodells auf (Legenbauer & Vocks, 2014). Zudem ist es essentiell an einer Verbesserung der Körperakzeptanz zu arbeiten (Legenbauer & Vocks, 2014).

Am Beispiel der Schön Klinik Roseneck, einer psychosomatischen Fachklinik, erfolgt die essstörungsspezifische Behandlung in Einzel- sowie Gruppentherapie und wird durch Fachtherapien (d. h. insbesondere Ökotrophologie mit Lehrküche und Einkaufstraining, Gestaltungstherapie, gewichtsadaptierte Sport- und Bewegungstherapie) ergänzt. Neben einer festen Mahlzeitenstruktur und therapeutisch begleitetem Essen sind wesentliche therapeutische Themen die Psychoedukation zum Erkrankungsbild, die Bearbeitung der Funktionalität der Erkrankung, die Wahrnehmung und Regulation von Gefühlen, die Auseinandersetzung mit dem Körperbild, ggf. der Aufbau eines gesunden Bewegungsverhaltens, ggf. die Reduktion bzw. Aufgabe bulimischer Verhaltensweisen, Expositionen in den Bereichen Ernährung, Bewegung und Körperbild, der Einbezug von Angehörigen sowie der Transfer in das häusliche Umfeld und die Rückfallprophylaxe.

2.1.8 Überblick zur Forschungslage zu Antipsychotika in der Behandlung der Anorexia nervosa

Gewichtszunahme ist eine Nebenwirkung der meisten Antipsychotika (Bak et al., 2014; Barton et al., 2020). Dieser Effekt ließ sich jedoch überraschenderweise in der Mehrzahl bisheriger Metaanalysen bei Anorexia nervosa nicht nachweisen (Kishi et al., 2012; Lebow et al., 2013; de Vos et al., 2014; Dold et al., 2015). Es ist unklar, ob dies auf physiologische Veränderungen

oder psychologische Faktoren zurückzuführen ist. Denkbar ist jedoch, dass die krankheitsimmanente Angst vor einer Gewichtszunahme zu einem Widerstand auf Verhaltensebene führt und damit eine mögliche medikamentös bedingte Gewichtszunahme verhindert werden könnte.

Antipsychotika der 1. Generation werden wegen des Nebenwirkungsprofils in der Behandlung der Anorexia nervosa nicht eingesetzt. Dementsprechend wurden auch kaum Studien zu Antipsychotika der 1. Generation bei Anorexia nervosa durchgeführt. Es wurden in einer offenen Studie Haloperidol (Cassano et al., 2003; N = 11) sowie in je einer randomisiert-kontrollierten Studie Pimozid (Vandereycken & Pierloot, 1982; N = 10) und Sulpirid (Vandereycken, 1984; N = 18) untersucht. Insgesamt waren keine Therapieeffekte zu identifizieren.

Aus der Gruppe der Antipsychotika der 2. Generation liegen Studien zu Risperidon, Quetiapin, Aripiprazol und insbesondere zu Olanzapin bei Anorexia nervosa vor. Randomisiert-kontrollierte Studien zu Risperidon (Hagman et al., 2011; N = 40) und Quetiapin (Powers et al., 2012; N = 21) erbrachten jeweils keinen positiven Wirksamkeitsnachweis. Zu Aripiprazol liegen positive Fallberichte und Fall-Kontroll-Studien vor (Trunko et al., 2011; Marzola et al., 2015; Frank, 2016; Frank et al., 2017; Tahıllıoğlu et al., 2020). Im Gegensatz dazu ist die Datenlage zu Olanzapin umfassender. Vier kleine randomisiert-kontrollierte Studien ergaben ursprünglich ein gemischtes Bild über mögliche positive Effekte von Olanzapin auf die Gewichtszunahme bei Anorexia nervosa. Brambilla et al., 2007 (N = 30; Dosis 2,5 – 5 mg/Tag) und Kafantaris et al., 2011 (N = 20; Dosis 2,5 – 10 mg/Tag) beschrieben keinen Unterschied zwischen Olanzapin und Placebo. Bissada et al., 2008 (N = 34; Dosis 2,5 – 10 mg/Tag) und Attia et al., 2011 (N = 23; Dosis 2,5 – 10 mg/Tag) konnten hingegen positive Effekte nachweisen. Bissada et al., 2008 beschrieben eine signifikante Erhöhung des Gewichts in beiden Gruppen mit schnellerer Gewichtszunahme in der Olanzapin Gruppe sowie eine Reduktion von Zwangssymptomatik. Attia et al., 2011 fanden eine signifikante Erhöhung des Gewichts durch Olanzapin aber im Gegensatz zu Bissada et al., 2008 keine Auswirkungen auf psychologische Symptome der Anorexia nervosa. 2019 wurde von Attia und Kollegen eine weitere randomisiert-kontrollierte Studie publiziert (Attia et al., 2019). In dieser bislang größten Studie (N = 152) zeigte sich ein moderater Effekt von Olanzapin mit einer täglichen Dosis von bis zu 10 mg auf die Gewichtszunahme bei ambulant behandelten Patientinnen und Patienten mit Anorexia nervosa (Mehrzunahme von etwa 450 g pro Monat in der Olanzapin Gruppe vs. Placebo). Signifikante Unterschiede in der Veränderung psychologischer Symptome, wie besonders die Reduktion von Zwangssymptomen, waren allerdings erneut nicht nachweisbar. Des Weiteren beschrieben Attia et al., 2019 eine gute Verträglichkeit von Olanzapin. Überdies wurde in der jüngsten Metaanalyse von Han et al., 2022 im Gegensatz zu früheren Metaanalysen ein signifikant höherer

Anstieg des BMI unter Olanzapin im Vergleich zu Placebo bei erwachsenen Anorexie Patientinnen und Patienten gezeigt (N = 239).

Zusammenfassend ist nach gegenwärtiger Forschungslage unklar, ob der Einsatz von Antipsychotika einen zusätzlichen Nutzen in der Behandlung der Anorexia nervosa erbringen kann. Die Tatsache, dass die einzige Studie mit ausreichend hoher Fallzahl einen signifikanten gewichtssteigernden Effekt von Olanzapin zeigte (Attia et al., 2019), kann jedoch als Hinweis gewertet werden, dass frühere negative Studien an zu kleinen Fallzahlen durchgeführt wurden sowie möglicherweise auch zu niedrige Dosierungen verwendet wurden. Da die Rolle der Antipsychotika, insbesondere von Olanzapin, in der Behandlung der Anorexia nervosa damit noch nicht abschließend geklärt ist, sind für die weitere Forschung in diesem Gebiet die Höhe der Fallzahlen, die Dosierung und das Behandlungssetting von besonderer Relevanz.

2.2 Darstellung des Forschungsvorhabens

Das übergeordnete Ziel dieser Arbeit war, an einem naturalistischen Patientenkollektiv Einflussfaktoren auf die Therapieergebnisse einer stationären Behandlung der Anorexia nervosa zu identifizieren. Hierfür wurden die Behandlungsdaten jugendlicher sowie erwachsener Patientinnen und Patienten eines Spezialzentrums zur Behandlung von Essstörungen retrospektiv ausgewertet. Die Forschungsarbeit in Publikation I evaluierte eine multimodale, kognitiv-verhaltenstherapeutisch orientierte stationäre Behandlung der Anorexia nervosa in ihrer Wirksamkeit und untersuchte allgemeine Prädiktoren des Behandlungsverlaufs (Quadflieg et al., 2023). Die daran anschließende Forschungsfrage in Publikation II war, ob eine Antipsychotika Gabe einen zusätzlichen Nutzen zur multimodalen, kognitiv-verhaltenstherapeutisch orientierten Behandlung der Anorexia nervosa im stationären Setting erbringen kann (Bauman et al., 2024).

Hintergrund ist, dass wie in der allgemeinen Einleitung zum Erkrankungsbild beschrieben wurde, die Anorexia nervosa ein schwerwiegendes psychisches Erkrankungsbild ist und Limitationen in der Behandlung bestehen, was die Forschungsfrage nach der Wirksamkeit einer multimodalen, kognitiv-verhaltenstherapeutisch orientierten stationären Behandlung und Prädiktoren im Allgemeinen sowie möglicher Einflussfaktoren im Speziellen aufwirft. Ausgewertet wurden zunächst die Daten jugendlicher, stationär behandelter Patientinnen und Patienten mit Anorexia nervosa unter der Annahme, dass ein Wissen um erkrankungsgeschichtlich frühe Prädiktoren auch spätere Behandlungsverläufe beeinflussen könnte. Das zweite Forschungsvorhaben generierte sich ausgehend von der auf einen klinischen Eindruck gestützten Hypothese, dass eine Antipsychotika Gabe während einer stationären Behandlung der Anorexia nervosa einen zusätzlichen Nutzen erbringen könnte. Zumal, wie in der allgemeinen Einleitung zum Erkrankungsbild ebenfalls dargestellt wurde, die bisherige Forschungslage hierzu unzureichend ist. In Ergänzung zu dem ersten Forschungsvorgaben sowie der bisherigen Studienlage zu den Effekten einer Psychopharmakotherapie bei Anorexia nervosa wurden für das zweite Forschungsvorhaben die Daten erwachsener, stationär behandelter, ausschließlich weiblicher Patientinnen mit Anorexia nervosa ausgewertet. Zusammengenommen wurde damit auch das gesamte Altersspektrum der Erkrankung berücksichtigt.

Begünstigend für die Entwicklung und Realisierung beider Forschungsvorhaben war die Tätigkeit an der Schön Klinik Roseneck, einer psychosomatischen Fachklinik und einem Spezialzentrum zur Behandlung von Essstörungen. Zum einen durch die Kenntnisse um das Erkrankungsbild aus der täglichen klinischen Praxis und die daraus gewonnene Motivation zur zusätzlichen wissenschaftlichen Auseinandersetzung mit der Erkrankung. Zum anderen durch

den erleichterten Zugang zu umfangreichen Routinedaten. Andererseits stellten Behandlungssetting und Datengrundlage auch eine Einschränkung dar, da sich in diesem kein randomisiert-kontrolliertes Studiendesign realisieren lassen würde und Datenqualität sowie Datenumfang in der retrospektiven Auswertung auch begrenzt waren. Zusammengenommen handelte es sich jedoch um ein hoch relevantes und praxisnahes Forschungsvorhaben, das in zwei Forschungsarbeiten und den darauffolgenden Publikationen bearbeitet wurde.

3. Zusammenfassung

Hintergrund: Beiden Publikationen gemeinsam ist die Auseinandersetzung mit den stationären Behandlungsergebnissen eines Spezialzentrums zur Behandlung der Anorexia nervosa. Anhand von Routinedaten wurden Faktoren analysiert, welche die Behandlungsergebnisse beeinflussen können. Bei Jugendlichen wurden eine multimodale, kognitiv-verhaltenstherapeutisch orientierte stationäre Behandlung in ihrer Wirksamkeit evaluiert und allgemeine Prädiktoren des Behandlungsverlaufs erfasst. Bei Erwachsenen wurde ausgewertet, ob eine Psychopharmakotherapie in Form einer Antipsychotika Gabe einen zusätzlichen Nutzen in der stationären Behandlung der Anorexia nervosa erbringen kann.

Material und Methoden: In Publikation I wurden an einer Stichprobe von 962 jugendlichen Patientinnen und Patienten der Body-Mass-Index (BMI) (World Health Organization, 2000) sowie das Eating Disorder Inventory-2 (EDI-2) als Messgröße essstörungstypischer Symptomatik (Garner, 1991; Paul & Thiel, 2004), das Brief Symptom Inventory (BSI) als Messgröße allgemeiner psychischer Belastung (Derogatis & Melisaratos, 1983; Franke, 2000) und das Beck-Depressions-Inventar (BDI-II) als Messgröße depressiver Symptomatik (Beck et al., 1996) erfasst und von Aufnahme zu Entlassung ausgewertet. Zudem wurden Prädiktoren für eine gute Gewichtsentwicklung identifiziert. In Publikation II wurden an einer Stichprobe von 775 erwachsenen, ausschließlich weiblichen Patientinnen der BMI (World Health Organization, 2000) sowie die EDI-2 Subskalen für Schlankheitsstreben und Körperunzufriedenheit (Garner, 1991; Paul & Thiel, 2004) erfasst und ebenfalls von Aufnahme zu Entlassung analysiert. Zudem wurden wöchentliche Gewichtszunahmen sowie die Gewichtszunahme vor und nach dem Beginn einer Antipsychotika Therapie verglichen.

Ergebnisse: Die Ergebnisse der Studie in Publikation I zeigten einen signifikanten BMI Anstieg von 14,93 kg/m^2 bei Aufnahme auf 17,53 kg/m^2 bei Entlassung ($p < 0{,}001$). Ebenfalls nahmen die essstörungstypische Symptomatik, die allgemeine Psychopathologie und die depressive Symptomatik signifikant ab ($p < 0{,}001$). Eine gute Gewichtsentwicklung wurde durch einen höheren BMI bei Aufnahme, ein Alter von 15 Jahren oder mehr bei Beginn der Erkrankung und höhere Werte für Somatisierung, Angst und Bulimie prognostiziert. Die Ergebnisse der Studie in Publikation II zeigten, dass fast 22 % der erwachsenen, stationär behandelten Anorexie Patientinnen auch mit Antipsychotika in Form von Olanzapin oder Quetiapin behandelt wurden, wobei dabei aber die Gewichtszunahme bei Patientinnen mit Antipsychotika Therapie nicht signifikant höher war als bei Patientinnen ohne Antipsychotika Therapie. Dennoch wurde nach Beginn der Behandlung mit einem Antipsychotikum im Verlauf der stationären Behandlung eine etwas höhere Gewichtszunahme festgestellt ($p = 0{,}011$; $p \leq 0{,}001$). Ebenfalls keine signifikanten Unterschiede ergaben sich bei den EDI-2 Subskalenwerten.

Diskussion: In der Zusammenschau der beiden Studien zeigte sich eine hohe Wirksamkeit eines multimodalen, spezialisierten stationären Konzeptes zur Behandlung der Anorexia nervosa sowie das niedrig dosierte Antipsychotika keinen zusätzlichen Effekt auf die multimodale stationäre Behandlung unter Routinebedingungen haben. Prognostisch günstige Faktoren zu kennen ist wiederrum für den Behandlungsverlauf von hoher Relevanz. Zusammenfassend ist somit festzustellen, dass die beiden Studien anhand großer Stichproben relevante Aspekte aus der klinischen Praxis aufgreifen und zusammen betrachtet wichtige Hinweise für die Behandlung von Patientinnen und Patienten mit Anorexia nervosa geben.

4. Abstract

Introduction: Both publications examined treatment results of inpatients with anorexia nervosa and analyzed factors which can influence treatment outcomes. The study in publication I evaluated multimodal, cognitive-behavioral inpatient treatment of adolescents with anorexia nervosa. The study in publication II examined the impact of antipsychotics on weight gain and eating disorder-related psychopathology in adult inpatients with anorexia nervosa.

Material and Methods: In the study of publication I routine data of 962 adolescent female and male inpatients were analyzed regarding change of Body Mass Index (BMI) (World Health Organization, 2000), Eating Disorder Inventory (EDI-2) (Garner, 1991; Paul & Thiel, 2004), Brief Symptom Inventory (BSI) (Derogatis & Melisaratos, 1983; Franke, 2000) and Beck Depression Inventory (BDI-II) (Beck et al., 1996) from admission to discharge. Furthermore, predictors of good body weight outcome were identified. In the study of publication II routine data of 775 adult female inpatients were analyzed regarding change of BMI (World Health Organization, 2000) as well as change of EDI-2 subscale scores drive for thinness and body dissatisfaction (Garner, 1991; Paul & Thiel, 2004) from admission to discharge. In addition, BMI trajectories and weight gain before versus after antipsychotic onset were compared.

Results: Study results of publication I showed a significant increase in BMI from 14.93 kg/m^2 at admission to 17.53 kg/m^2 at discharge ($p < 0.001$) as well as all scores of EDI-2, BSI and BDI-II decreased significantly ($p < 0.001$). A good body weight outcome was predicted by higher BMI at admission, age at onset at 15 years or higher, and higher somatization, anxiety and bulimia scores. Study results of publication II reveal that almost 22 % of adult inpatients with anorexia nervosa were treated with olanzapine or quetiapine with overall no higher increase in weight or better improvement in core psychological symptoms than psychopharmacologically untreated inpatients. Nevertheless, a slightly higher weight gain was seen after the onset of antipsychotics during the course of inpatient treatment ($p = 0.011$; $p \leq 0.001$).

Discussion: Altogether, the two studies revealed a high effectiveness of a multimodal, specialized inpatient treatment approach of anorexia nervosa, as well as the finding that low-dose antipsychotics had no additional effect in routine inpatient treatment of anorexia nervosa. On the other hand, knowing prognostically favorable factors is highly relevant for the course of treatment. In conclusion, it can be stated that the two studies, based on large sample sizes, address relevant aspects from clinical practice and, when considered together, provide important insights for the treatment of patients with anorexia nervosa.

5. Abkürzungsverzeichnis

BDI-II	Beck-Depressions-Inventar / Beck Depression Inventory
BMI	Body-Mass-Index / Body Mass Index
BSI	Brief Symptom Inventory
CBT-E	Enhanced Cognitive Behaviour Therapy
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition
EDI-2	Eating Disorder Inventory
FPT	Focal Psychodynamic Therapy
ICD-10	International Statistical Classification of Diseases and Related Health Problems, 10th Revision
ICD-11	International Statistical Classification of Diseases and Related Health Problems, 11th Revision
MANTRA	Maudsley Model of Anorexia Nervosa Treatment
SSCM	Specialist Supportive Clinical Management

6. Literaturverzeichnis

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). American Psychiatric Association.

Arcelus, J., Mitchell, A. J., Wales, J. & Nielsen, S. (2011). Mortality rates in patients with anorexia nervosa and other eating disorders. A meta-analysis of 36 studies. *Archives of General Psychiatry, 68(7),* 724-731. https://doi.org/10.1001/archgenpsychiatry.2011.74

Attia, E., Kaplan, A. S., Walsh, B. T., Gershkovich, M., Yilmaz, Z., Musante, D. & Wang, Y. (2011). Olanzapine versus placebo for out-patients with anorexia nervosa. *Psychological Medicine, 41(10),* 2177-2182. https://doi.org/10.1017/S0033291711000390

Attia, E., Steinglass, J. E., Walsh, T. B., Wang, Y., Wu, P., Schreyer, C., Wildes, J., Yilmaz, Z., Guarda, A. S., Kaplan, A. S. & Marcus, M. D. (2019). Olanzapine versus placebo in adult outpatients with anorexia nervosa: A randomized clinical trial. *American Journal of Psychiatry, 176(6),* 449-456. https://doi.org/10.1176/appi.ajp.2018.18101125

Bak, M., Fransen, A., Janssen, J., van Os, J. & Drukker, M. (2014). Almost all antipsychotics result in weight gain: A meta-analysis. *PLoS One, 9(4),* e94112. https://doi.org/10.1371/journal.pone.0094112

Barry, V. C. & Klawans, H. L. (1976). On the role of dopamine in the pathophysiology of anorexia nervosa. *Journal of Neural Transmission, 38(2),* 107-122. https://doi.org/10.1007/BF01262969

Barton, B. B., Segger, F., Fischer, K., Obermeier, M. & Musil, R. (2020). Update on weight-gain caused by antipsychotics: A systematic review and meta-analysis. *Expert Opinion on Drug Safety, 19(3),* 295-314. https://doi.org/10.1080/14740338.2020.1713091

Bauman, T., Kolar, D. R., Correll C. U., Haas, V. & Voderholzer, U. (2024). Impact of antipsychotic medications on weight gain and eating disorder-related psychopathology in adult inpatients with anorexia nervosa. *Pharmacopsychiatry*. Online-Vorabpublikation. https://doi.org/10.1055/a-2436-9552

Beck, A. T., Steer, R. A., Brown, G. K. (1996). *Beck Depression Inventory* (2nd ed.). The Psychological Corporation.

Bissada, H., Tasca, G. A., Barber, A. M. & Bradwejn, J. (2008). Olanzapine in the treatment of low body weight and obsessive thinking in women with anorexia nervosa: A randomized, double-blind, placebo-controlled trial. *American Journal of Psychiatry, 165(10),* 1281-1288. https://doi.org/10.1176/appi.ajp.2008.07121900

Brambilla, F., Garcia, C. S., Fassino, S., Daga, G. A., Favaro, A., Santonastaso, P., Ramaciotti, C., Bondi, E., Mellado, C., Borriello, R. & Monteleone, P. (2007). Olanzapine therapy in anorexia nervosa: Psychobiological effects. *International Clinical Psychopharmacology, 22(4),* 197-204. https://doi.org/10.1097/YIC.0b013e328080ca31

Caslini, M., Bartoli, F., Crocamo, C., Dakanalis, A., Clerici, M. & Carrà, G. (2016). Disentangling the association between child abuse and eating disorders: A systematic review and meta-analysis. *Psychosomatic Medicine, 78(1),* 79-90. https://doi.org/10.1097/PSY.0000000000000233

Cassano, G. B., Miniati, M., Pini, S., Rotondo, A., Banti, S., Borri, C., Camilleri, V. & Mauri, M. (2003). Six-month open trial of haloperidol as an adjunctive treatment of anorexia nervosa: A preliminary report. *International Journal of Eating Disorders, 33(2),* 172-177. https://doi.org/10.1002/eat.10130

Derogatis, L. R. & Melisaratos, N. (1983). The Brief Symptom Inventory: An introductory report. *Psychological Medicine, 13(3),* 595-605. https://doi.org/10.1017/S0033291700048017

Deutsche Gesellschaft für Essstörungen e.V. & Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften e.V. (2018). *S3-Leitlinie: Diagnostik und Therapie der Essstörungen.*

de Vos, J., Houtzager, L., Katsaragaki, G., van de Berg, E., Cuijpers, P. & Dekker, J. (2014). Meta analysis on the efficacy of pharmacotherapy versus placebo on anorexia nervosa. *Journal of Eating Disorders, 2(1),* 27. https://doi.org/10.1186/s40337-014-0027-x

Dold, M., Aigner, M., Klabunde, M., Treasure, J. & Kasper, S. (2015). Second-generation antipsychotic drugs in anorexia nervosa: A meta-analysis of randomized controlled trials. *Psychotherapy and Psychosomatics, 84(2),* 110-116. https://doi.org/10.1159/000369978

Fichter, M. M., Quadflieg, N., Crosby, R. D. & Koch, S. (2017). Long-term outcome of anorexia nervosa: Results from a large clinical longitudinal study. *International Journal of Eating Disorders, 50(9),* 1018-1030. https://doi.org/10.1002/eat.22736

Fichter, M. M. & Quadflieg, N. (1999). Six-year course and outcome of anorexia nervosa. *International Journal of Eating Disorders, 26(4),* 359-385. https://doi.org/10.1002/(sici)1098-108x(199912)26:4<359::aid-eat2>3.0.co;2-7

Frank, G. K. W. (2016). Aripiprazole, a partial dopamine agonist to improve adolescent anorexia nervosa – A case series. *International Journal of Eating Disorders, 49(5),* 529-533. https://doi.org/10.1002/eat.22485

Frank, G. K. W., Shott, M. E., Hagman, J. O., Schiel, M. A., DeGuzman, M. C. & Rossi, B. (2017). The partial dopamine D2 receptor agonist aripiprazole is associated with weight gain in adolescent anorexia nervosa. *International Journal of Eating Disorders, 50(4),* 447-450. https://doi.org/10.1002/eat.22704

Franke, G. H. (2000). *BSI – Brief Symptom Inventory von Derogatis (Kurzform der SCL-90-R) – Deutsche Version.* Hogrefe.

Garner, D. M. (1991). *Eating disorder inventory-2: Professional manual.* Psychological Assessment Resources.

Goodman, A., Heshmati, A. & Koupil, I. (2014). Family history of education predicts eating disorders across multiple generations among 2 million Swedish males and females. *PLoS One, 9(8),* e106475. https://doi.org/10.1371/journal.pone.0106475

Hagman, J., Gralla, J., Sigel, E., Ellert, S., Dodge, M., Gardner, R., O`Lonergan, T., Frank, G. & Wamboldt, M. Z. (2011). A double-blind, placebo-controlled study of risperidone for the treatment of adolescents and young adults with anorexia nervosa: A pilot study. *Journal of the American Academy of Child & Adolescent Psychiatry, 50(9),* 915-924. https://doi.org/10.1016/j.jaac.2011.06.009

Han, R., Bian, Q. & Chen, H. (2022). Effectiveness of olanzapine in the treatment of anorexia nervosa: A systematic review and meta-analysis. *Brain and Behaviour, 12(2),* e2498. https://doi.org/10.1002/brb3.2498

Hebebrand, J., Himmelmann, G. W., Herzog, W., Herpertz-Dahlmann, B. M., Steinhausen, H. C., Amstein, M., Seidel, R., Deter, H. C., Remschmidt, H. & Schäfer, H. (1997). Prediction of low body weight at long-term follow-up in acute anorexia nervosa by low body weight at referral. *American Journal of Psychiatry, 154(4),* 566-569. https://doi.org/10.1176/ajp.154.4.566

Hedman, A., Breithaupt, L., Hübel, C., Thornton, L. M., Tillander, A., Norring, C., Birgegård, A., Larsson, H., Ludvigsson, J. F., Sävendahl, L., Almqvist, C. & Bulik, C. M. (2019). Bidirectional relationship between eating disorders and autoimmune diseases. *Journal of Child Psychology and Psychiatry, 60(7),* 803-812. https://doi.org/10.1111/jcpp.12958

Herpertz-Dahlmann, B., Dempfle, A., Egberts, K. M., Kappel, V., Konrad, K., Vloet, J. A. & Bühren, K. (2018). Outcome of childhood anorexia nervosa – The results of a five- to ten-year follow-up study. *International Journal of Eating Disorders, 51(4),* 295-304. https://doi.org/10.1002/eat.22840

Hetterich, L., Mack, I., Giel, K. E., Zipfel, S. & Stengel, A. (2019). An update on gastrointestinal disturbances in eating disorders. *Molecular and Cellular Endocrinology, 497,* 110318. https://doi.org/10.1016/j.mce.2018.10.016

Kafantaris, V., Leigh, E., Hertz, S., Berest, A., Schebendach, J., Meyer Sterling, W., Saito, E., Sunday, S., Higdon, C., Golden, N. H. & Malhotra, A. K. (2011). A placebo-controlled pilot study of adjunctive olanzapine for adolescents with anorexia nervosa. *Journal of Child and Adolescent Psychopharmacology, 21(3),* 207-212. https://doi.org/10.1089/cap.2010.0139

Kaplan, A. S., Walsh, B. T., Olmsted, M., Attia, E., Carter, J. C., Devlin, M. J., Pike, K. M., Woodside, B., Rockert, W., Roberto, C. A. & Parides, M. (2009). The slippery slope: prediction of successful weight maintenance in anorexia nervosa. *Psychological Medicine, 39(6),* 1037-1045. https://doi.org/10.1017/S003329170800442X

Kaye, W. H., Wierenga, C. E., Bailer, U. F., Simmons, A. N. & Bischoff-Grethe, A. (2013). Nothing tastes as good as skinny feels: the neurobiology of anorexia nervosa. *Trends in Neurosciences, 36(2),* 110-120. https://doi.org/10.1016/j.tins.2013.01.003

Keski-Rahkonen, A. & Mustelin, L. (2016). Epidemiology of eating disorders in Europe: prevalence, incidence, comorbidity, course, consequences, and risk factors. *Current Opinion in Psychiatry, 29(6),* 340-345. https://doi.org/10.1097/YCO.0000000000000278

Kishi, T., Kafantaris, V., Sunday, S., Sheridan, E. M. & Correll, C. U. (2012). Are antipsychotics effective for the treatment of anorexia nervosa? Results from a systematic review and meta-analysis. *Journal of Clinical Psychiatry, 73(6),* 757-766. https://doi.org/10.4088/JCP.12r07691

Koch, S. V., Larsen, J. T., Mouridsen, S. E., Bentz, M., Petersen, L., Bulik, C., Mortensen, P. B. & Plessen, K. J. (2015). Autism spectrum disorder in individuals with anorexia nervosa

and in their first- and second-degree relatives: Danish nationwide register-based cohort-study. *British Journal of Psychiatry, 206(5),* 401-407. https://doi.org/10.1192/bjp.bp.114.153221

Kromeyer-Hauschild, K., Wabitsch, M., Kunze, D., Geller, F., Geiß, H. C., Hesse, V., von Hippel, A., Jaeger, U., Johnsen, D., Korte, W., Menner, K., Müller, G., Müller, J. M., Niemann-Pilatus, A., Remer, T., Schaefer, F., Wittchen, H.-U., Zabransky, S., Zellner, K., Ziegler, A. & Hebebrand, J. (2001). Perzentile für den Body-mass-Index für das Kindes- und Jugendalter unter Heranziehung verschiedener deutscher Stichproben. *Monatsschrift Kinderheilkunde, 149(8),* 807-818. https://doi.org/10.1007/s001120170107

Lebow, J., Sim, L. A., Erwin, P. J. & Murad, M. H. (2013). The effect of atypical antipsychotic medications in individuals with anorexia nervosa: A systematic review and meta-analysis. *International Journal of Eating Disorders, 46(4),* 332-339. https://doi.org/10.1002/eat.22059

Legenbauer, T. & Vocks, S. (2014). *Manual der kognitiven Verhaltenstherapie bei Anorexie und Bulimie* (2. Aufl.). Springer.

Martinussen, M., Friborg, O., Schmierer, P., Kaiser, S., Øvergård, K. T., Neunhoeffer, A.-L., Martinsen, E. W. & Rosenvinge, J. H. (2017). The comorbidity of personality disorders in eating disorders: A meta-analysis. *Eating and Weight Disorders, 22(2),* 201-209. https://doi.org/10.1007/s40519-016-0345-x

Marzola, E., Desedime, N., Giovannone, C., Amianto, F., Fassino, S. & Abbate-Daga, G. (2015). Atypical antipsychotics as augmentation therapy in anorexia nervosa. *PLoS One, 10(4),* e0125569. https://doi.org/10.1371/journal.pone.0125569

Nazar, B. P., Bernardes, C., Peachey, G., Sergeant, J., Mattos, P. & Treasure, J. (2016). The risk of eating disorders comorbid with attention-deficit/hyperactivity disorder: A systematic review and meta-analysis. *International Journal of Eating Disorders, 49(12),* 1045-1057. https://doi.org/10.1002/eat.22643

Nazar, B. P., Gregor, L. K., Albano, G., Marchica, A., Coco, G. L., Cardi, V. & Treasure, J. (2017). Early response to treatment in eating disorders: A systematic review and a diagnostic test accuracy meta-analysis. *European Eating Disorders Review, 25(2),* 67-79. https://doi.org/10.1002/erv.2495

Paul, T. & Thiel, A. (2004). *Eating Disorder Inventory 2, German Version.* Hogrefe.

Powers, P. S., Klabunde, M. & Kaye, W. (2012). Double-blind placebo-controlled trial of quetiapine in anorexia nervosa. *European Eating Disorders Review, 20(4),* 331-334. https://doi.org/10.1002/erv.2169

Quadflieg, N., Naab, S., Schlegl, S., Bauman, T. & Voderholzer, U. (2023). Inpatient treatment outcome in a large sample of adolescents with anorexia nervosa. *Nutrients, 15(19),* 4247. https://doi.org/doi: 10.3390/nu15194247

Raevuori, A., Keski-Rahkonen, A. & Hoek, H. W. (2014). A review of eating disorders in males. *Current Opinion in Psychiatry, 27(6),* 426-430. https://doi.org/10.1097/YCO.0000000000000113

Reas, D. L. & Rø, Ø. (2018). Time trends in healthcare-detected incidence of anorexia nervosa and bulimia nervosa in the Norwegian National Patient Register (2010 - 2016*). International Journal of Eating Disorders, 51(10),* 1144-1152. https://doi.org/10.1002/eat.22949

Resmark, G., Herpertz, S., Herpertz-Dahlmann, B. & Zeeck, A. (2019). Treatment of anorexia nervosa – new evidence-based guidelines. *Journal of Clinical Medicine, 8(2),* 153. https://doi.org/10.3390/jcm8020153

Salbach-Andrae, H., Lenz, K., Simmendinger, N., Klinkowski, N., Lehmkuhl, U. & Pfeiffer, E. (2008). Psychiatric comorbidities among female adolescents with anorexia nervosa. *Child Psychiatry and Human Development, 39(3),* 261-272. https://doi.org/10.1007/s10578-007-0086-1

Schmidt, U. (2003). Aetiology of eating disorders in the 21(st) century: New answers to old questions. *European Child & Adolescent Psychiatry, 12(1),* 30-37. https://doi.org/10.1007/s00787-003-1105-9

Seitz, J., Trinh, S. & Herpertz-Dahlmann, B. (2019). The microbiome and eating disorders. *Psychiatric Clinics of North America, 42(1),* 93-103. https://doi.org/10.1016/j.psc.2018.10.004

Silén, Y., Sipilä, P. N., Raevuori, A., Mustelin, L., Marttunen, M., Kaprio, J. & Keski-Rahkonen, A. (2020). DSM-5 eating disorders among adolescents and young adults in Finland: A public health concern*. International Journal of Eating Disorders, 53(5),* 520-531. https://doi.org/10.1002/eat.23236

Smink, F. R., van Hoeken, D. & Hoek, H. W. (2012). Epidemiology of eating disorders: Incidence, prevalence and mortality rates. *Current Psychiatry Reports, 14(4),* 406-414. https://doi.org/10.1007/s11920-012-0282-y

Solmi, M., Monaco, F., Højlund, M., Monteleone, A. M., Trott, M., Firth, J., Carfagno, M., Eaton, M., De Toffol, M., Vergine, M., Meneguzzo, P., Collantoni, E., Gallicchio, D., Stubbs, B., Girardi, A., Busetto, P., Favaro, A., Carvalho, A. F., Steinhausen, H.-C. & Correll, C. U. (2024). Outcomes in people with eating disorders: A transdiagnostic and disorder-specific systematic review, meta-analysis and multivariable meta-regression analysis. *World Psychiatry, 23(1),* 124-138. https://doi.org/10.1002/wps.21182

Solmi, M., Radua, J., Olivola, M., Croce, E., Soardo, L., Salazar de Pablo, G., Il Shin, J., Kirkbride, J. B., Jones, P., Kim, J. H., Kim, J. Y., Carvalho, A. F., Seeman, M. V., Correll, C. U. & Fusar-Poli, P. (2022). Age at onset of mental disorders worldwide: Large-scale meta-analysis of 192 epidemiological studies. *Molecular Psychiatry, 27(1),* 281-295. https://doi.org/10.1038/s41380-021-01161-7

Steinglass, J. E., Dalack, M. & Foerde, K. (2019). The promise of neurobiological research in anorexia nervosa. *Current Opinion in Psychiatry, 32(6),* 491-497. https://doi.org/10.1097/YCO.0000000000000540

Steinhausen, H.-C. (2009). Outcome of eating disorders. *Child and Adolescent Psychiatric Clinics of North America, 18(1),* 225-242. https://doi.org/10.1016/j.chc.2008.07.013

Stice, E., Gau, J. M., Rohde, P. & Shaw, H. (2017). Risk factors that predict future onset of each DSM-5 eating disorder: Predictive specificity in high-risk adolescent females. *Journal of Abnormal Psychology, 126(1),* 38-51. https://doi.org/10.1037/abn0000219

Tahıllıoğlu, A., Özcan, T., Yüksel, G., Majroh, N., Köse, S. & Özbaran, B. (2020). Is aripiprazole a key to unlock anorexia nervosa?: A case series. *Clinical Case Reports, 8(12),* 2827-2834. https://doi.org/10.1002/ccr3.3271

Trace, S. E., Baker, J. H., Peñas-Lledó, E. & Bulik, C. M. (2013). The genetics of eating disorders. *Annual Review of Clinical Psychology, 9,* 589-620. https://doi.org/10.1146/annurev-clinpsy-050212-185546

Trunko, M. E., Schwartz, T. A., Duvvuri, V. & Kaye, W. H. (2011). Aripiprazole in anorexia nervosa and low-weight bulimia nervosa: Case reports*. International Journal of Eating Disorders, 44(3),* 269-275. https://doi.org/10.1002/eat.20807

Vandereycken, W. (1984). Neuroleptics in the short-term treatment of anorexia nervosa. A double-blind placebo-controlled study with sulpiride. *British Journal of Psychiatry, 144,* 288-292. https://doi.org/10.1192/bjp.144.3.288

Vandereycken, W. & Pierloot, R. (1982). Pimozide combined with behavior therapy in the short-term treatment of anorexia nervosa. A double-blind placebo-controlled cross-over study. *Acta Psychiatrica Scandinavica, 66(6),* 445-450. https://doi.org/10.1111/j.1600-0447.1982.tb04501.x

World Health Organization. (1992). *ICD-10: International statistical classification of diseases and related health problems* (10th revision). World Health Organization.

World Health Organization. (2022). *ICD-11: International statistical classification of diseases and related health problems* (11th revision). World Health Organization.

World Health Organization. (2000). *Obesity: Preventing and managing the global epidemic* (Technical Report Series 894). World Health Organization.

Zeeck, A., Herpertz-Dahlmann, B., Friederich, H.-C., Brockmeyer, T., Resmark, G., Hagenah, U., Ehrlich, S., Cuntz, U., Zipfel, S. & Hartmann, A. (2018). Psychotherapeutic treatment for anorexia nervosa: A systematic review and network meta-analysis. *Frontiers in Psychiatry, 9,* 158. https://doi.org/10.3389/fpsyt.2018.00158

Zipfel, S., Löwe, B., Reas, D. L., Deter, H. C. & Herzog, W. (2000). Long-term prognosis in anorexia nervosa: Lessons from a 21-year follow-up study. *Lancet, 355(9205),* 721-722. https://doi.org/10.1016/S0140-6736(99)05363-5

Zipfel, S., Wild, B., Groß, G., Friederich, H.-C., Teufel, M., Schellberg, D., Giel, K. E., de Zwaan, M., Dinkel, A., Herpertz, S., Burgmer, M., Löwe, B., Tagay, S., von Wietersheim, J., Zeeck, A., Schade-Brittinger, C., Schauenburg, H., Herzog, W., ANTOP study group. (2014). Focal psychodynamic therapy, cognitive behaviour therapy, and optimised treatment as usual in outpatients with anorexia nervosa (ANTOP study): Randomised controlled trial. *Lancet, 383(9912),* 127-137. https://doi.org/10.1016/S0140-6736(13)61746-8

7. Publikation I

nutrients

MDPI

Article

Inpatient Treatment Outcome in a Large Sample of Adolescents with Anorexia Nervosa

Norbert Quadflieg [1,*], Silke Naab [2], Sandra Schlegl [1], Tabea Bauman [2] and Ulrich Voderholzer [1,2,3]

[1] Department of Psychiatry and Psychotherapy, LMU University Hospital, Ludwig-Maximilians-University Munich (LMU), 80336 Munich, Germany; sandra.schlegl@med.uni-muenchen.de (S.S.); uvoderholzer@schoen-klinik.de (U.V.)
[2] Schoen Clinic Roseneck Affiliated with the Medical Faculty of the University of Munich (LMU), 83209 Prien, Germany; snaab@schoen-klinik.de (S.N.); tbauman@schoen-klinik.de (T.B.)
[3] Department of Psychiatry and Psychotherapy, University Hospital, 79106 Freiburg, Germany
* Correspondence: norbert.quadflieg@med.uni-muenchen.de; Tel.: +49-89-4400-5-34-38; Fax: +49-89-4400-5-45-72

Abstract: Anorexia nervosa is an illness affecting primarily adolescent girls and young women. Clinical guidelines recommend early intervention, with inpatient treatment for more severe cases. We present an evaluation of a multi-modal cognitive–behavioral inpatient treatment (CBT-E) involving carers in specialized units for adolescents. Routine data of 962 adolescent inpatients (26 boys) (mean age 15.48 [1.26]; range 12–17 years) were analyzed. Predictors of good body weight outcome (achieving a discharge BMI of at least 18.5 kg/m^2) were identified by logistic regression analysis. Mean inpatient treatment lasted 96.69 (45.96) days. The BMI increased significantly from 14.93 (1.38) kg/m^2 at admission to 17.53 (1.58) kg/m^2 at discharge (z = 26.41; $p < 0.001$; d = 1.708). Drive for thinness decreased from 29.08 (9.87) to 22.63 (9.77; z = 18.41; $p < 0.001$; d = 0.787). All other subscores of the Eating Disorder Inventory also decreased significantly, with small to medium effect sizes. General psychopathology also showed significant decreases. The Beck Depression Inventory-II score decreased from 26.06 (11.74) to 16.35 (12.51; z = 18.41; $p < 0.001$; d = 0.883). A good body weight outcome was predicted by a higher BMI at admission (OR = 1.828), age at onset at 15 years or higher (OR = 1.722), and higher Somatization (OR = 1.436), Anxiety (OR = 1.320), and Bulimia (OR = 1.029) scores. CBT-E involving carers is an efficient intervention for adolescents with anorexia nervosa.

Keywords: adolescents; anorexia nervosa; eating disorder; treatment; CBT-E; outcome

Citation: Quadflieg, N.; Naab, S.; Schlegl, S.; Bauman, T.; Voderholzer, U. Inpatient Treatment Outcome in a Large Sample of Adolescents with Anorexia Nervosa. *Nutrients* **2023**, *15*, 4247. https://doi.org/10.3390/nu15194247

Academic Editor: Antonios Dakanalis

Received: 28 August 2023
Revised: 25 September 2023
Accepted: 26 September 2023
Published: 2 October 2023

1. Introduction

Anorexia nervosa (AN) is a life-threatening eating disorder (ED). The main clinical symptom is a self-induced loss of body weight resulting in a low body mass index (BMI) of less than 18.5 kg/m^2 associated with an intense fear of gaining weight and a preoccupation with body weight and shape. This condition not only negatively affects health-related quality of life [1], but also affects later young adulthood [2], causing concerns in near relatives and family members [3]. Diagnostic manuals describe two basic types of AN. Patients with a restrictive type of AN try to achieve low weight exclusively through restrictive eating, fasting, or an increase in expenditure of energy (burning of calories) by excessive exercise and movement. Patients with a binge-eating/purging type of AN have eating binges and experience a loss of control overeating, even when consuming only small amounts of food. This type of AN also includes purging behaviors like self-induced vomiting or the use of laxatives, diuretics, and other substances to prevent weight gain or to achieve weight loss [4].

The most frequent onset of AN is in childhood and adolescence [5]. This is a period involving a high risk for developing an ED. Physical changes during puberty have effects on self-esteem and body dissatisfaction, and they are a potential cause for developing AN.

However, other significant psychosocial and biological changes occur in the same time period, and the role of pubertal changes is not clear [6].

To avoid a poor course and chronification of AN, current clinical guidelines recommend early intervention [7]. Treatment options include outpatient, inpatient, or day-clinic treatment, as well as—more recently—home treatment [8]. The choice of the treatment setting is usually determined by symptom severity, comorbidity, and the national health system and its associated costs. All treatment options have to address the restoration of normal weight, medical problems, the psychological symptoms of AN (fear of gaining weight, fixation on body weight and shape, and food), as well as comorbid psychiatric and personality disorders [9]. Inpatient treatment for adolescents with AN is recommended for health conditions including very low body weight, low energy intake by solid and fluid food, severe comorbidity and medical conditions, and severe psychosocial impairment [7].

A number of previous studies supported the effectiveness of inpatient treatment for AN in adolescents. However, sample size was usually low, varying between 11 and 74 participants [10–18]. More recently, two studies reported larger sample sizes of 126 [19] and 289 [20] adolescents with AN. An additional study included 218 adolescents with AN in a mixed adolescent and adult sample, but it did not report results for adolescents separately [21]. The results of these studies will be described in more detail in the discussion of the present study.

Treatment outcome in a sample of 238 female adolescent inpatients of the Schoen Clinic Roseneck with AN was reported by Schlegl et al. [22]. This study found a significant increase in body weight and improvement of ED-specific and non-ED specific psychopathology during treatment. Multivariate linear regression analysis identified longer inpatient treatment, lower age, and no previous inpatient treatment as correlates or predictors of and increase in BMI. The present study reports the treatment outcome in adolescent inpatients with AN with the aim to expand the sample of Schlegl et al. [22] to a very large number of adolescent inpatients, with a sample size larger than the combined sample size from other inpatient studies, in order to provide reliable data on the effectiveness of cognitive–behavioral inpatient psychotherapy (CBT-E). A second aim was to identify predictors of good body weight outcome, applying a BMI threshold indicative of weight recovery to the normal range.

2. Materials and Methods

2.1. Participants

Between August 2013 and December 2020, 1123 adolescents aged between 12 and 17 years were admitted to treatment for AN at the Schoen Clinic Roseneck in Prien, Germany. For 161 patients, the BMI at discharge could not be extracted from the database. Thus, 962 adolescents (26 boys [2.7%]; age 15.48 [1.26]) provided information on body weight at admission and discharge and were included in this study. ICD-10 diagnoses included F50.00 (restrictive AN; N = 864, 89.8%), F50.01 (AN binge-eating/purging type; N = 52, 5.4%), and F50.1 (atypical AN; N = 46, 4.8%). The number of patients was 66 in age group 12/13 years, 393 in age group 14/15 years, and 503 in age group 16/17 years at the time of treatment. Mean inpatient treatment for the included patients lasted 96.69 (45.96) days.

2.2. Treatment

Patients were treated in specialized ED units for adolescents by a multidisciplinary team of psychologists, physicians, co-therapists, and professionals from other disciplines (e.g., nutritionists). All treatment was voluntary in open units. Patients in need of compulsory treatment were not admitted to the clinic. Psychotherapy included a manualized ED coping training consisting of multimodal disorder-specific and age-adapted CBT-E with individual and group sessions. The nine group therapy sessions included behavior and functional analysis, ED-symptom-maintaining cognitions, dealing with emotions and needs, relapse prevention, acceptance of one's body, and psychoeducation. All ED behaviors were considered in therapy, including binge-eating and purging behaviors. The frequency of

therapy sessions was one to three times a week for group sessions (90 min), and individual therapy (50 min) once or twice a week. In addition, treatment included social skills training, art therapy, therapeutically supervised cooking training, and gradually expanded elements of sports and movement therapy depending on the physical condition and weight gain of the patients. At the beginning of therapy, three therapeutically supervised meals per day were obligatory, and patients with AN were required to gain 500–1000 g per week following the recommendations of the German S3-guidelines [7]. Patients were weighed twice a week on average by the clinical staff and weight gain was visualized on charts. If patients did not gain weight, food intake requirements were increased, and food intake was monitored during mealtimes. In case of problems with excessive exercise, the activity levels were gradually reduced. In rare, extreme cases, high caloric fluids and nasal tube feeding were administered. Patients were discharged from inpatient treatment after having improved in body weight, medical factors, and comorbid conditions. Discharge could also be initiated by the patient, often against the advice of the therapists. Discharges by the clinic for disciplinary breaches were also possible. Another reason for discharge could be that the patient's health insurance would no longer cover the costs of inpatient treatment.

Parents or other carers were involved through telephone consultations and at least three family therapy sessions [23]. They also provided information on the development of actual ED symptoms and other behaviors of the patient, which was included in the clinical documentation and used in the psychotherapy of the patient.

2.3. Assessment Instruments

As part of the routine intake procedure, patients answered a questionnaire package, which included the following assessments.

(1) The Eating Disorder Inventory-2 (EDI-2) [24,25] assessed ED symptoms and psychological features in 11 subscales with higher scores indicating more symptom severity (Cronbach's α at admission in our sample indicated in parentheses): Drive for Thinness (α = 0.92), Bulimia (α = 0.87), Body Dissatisfaction (α = 0.87), Ineffectiveness (α = 0.89), Perfectionism (α = 0.77), Interpersonal Distrust (α = 0.81), Interoceptive Awareness (α = 0.86), Maturity Fears (α = 0.76), Asceticism (α = 0.79), Impulse Regulation (α = 0.81), and Social Insecurity (α = 0.79).

(2) The Brief Symptom Inventory (BSI) [26,27] assessed general psychopathology in nine subscales: Somatization (α = 0.82), Obsessive–Compulsive Symptoms (α = 0.81), Interpersonal Sensitivity (α = 0.81), Depression (α = 0.86), Anxiety (α = 0.79), Anger–Hostility (α = 0.69), Phobic Anxiety (α = 0.76), Paranoid Ideation (α = 0.72), and Psychoticism (α = 0.75), with higher values indicating more psychopathology.

(3) The Beck Depression Inventory-II (BDI-II) [28] provides a single sum score of Depression (α = 0.92) with higher scores indicating more depression.

(4) Information on sociodemographic characteristics, pretreatment, height, weight, and psychiatric comorbidity were taken from the hospital documentation.

2.4. Statistical Analyses

Means and standard deviations at admission and discharge, or frequencies, are reported. In testing for statistically significant differences, non-parametric Wilcoxon and Mann–Whitney U-tests for repeated measures and comparison of independent groups (respectively) with a critical p-value of $p < 0.05$ were applied. All analyses included both boys and girls. Effect sizes are reported as Cohen's d with small effects indicated by d = 0.2–0.5, medium effects by d = 0.5–0.8, and large effects by d > 0.8 [29]. For comparing the change of the BMI over treatment between different age groups, repeated measures analysis of variance on the ranks with post-hoc pairwise comparison was used. Partial eta-square (η^2) of 0.01, 0.06, and 0.14 indicate small, medium, and large effect sizes in this analysis, respectively [29]. Not all patients filled out the questionnaires at discharge, reducing the number of cases for comparison of admission and discharge values. The exact number of cases included is reported for each analysis.

Reaching a BMI of at least 18.5 kg/m^2 at discharge defined a good body weight outcome. Predictors of a good body weight outcome were identified by logistic regression analysis (0 = poor, 1 = good body weight outcome) using stepwise forward selection. Potential predictors were available from the routine assessment at admission and included age, sex, age at onset, pretreatment, BMI, the subscales of the EDI-2, BDI-II score, the subscales of the BSI, and the presence of psychiatric comorbidity (yes/no).

3. Results

The 161 patients, mentioned above as not included in the study did not differ from the 962 participants in age (15.42 [1.26] versus 15.48 [1.26] years, z = 0.575, p = 0.565, d = 0.051) and BMI (15.08 [1.44] kg/m^2 versus 14.93 [1.38] kg/m^2, z = 1.230, p = 0.219, d = 0.105) at admission, but had a shorter duration of treatment (75.02 [49.83] versus 96.69 [45.96] days, z = 4.883, p < 0.001, d = 0.466).

3.1. Eating Disorder Symptom Outcome

The BMI increased significantly from 14.93 (1.38) kg/m^2 to 17.53 (1.58) kg/m^2 over treatment (z = 26.409, p < 0.001) with a high effect size (d = 1.708). Average weight gain per week was 570 (682) g. The increase in BMI was similar in age groups 12–13 years, 14–15 years, and 16–17 years. The two older groups showed a nearly identical course, differing significantly from the youngest age group (p < 0.05). The interaction of time and age group, however, was not statistically significant (Figure 1).

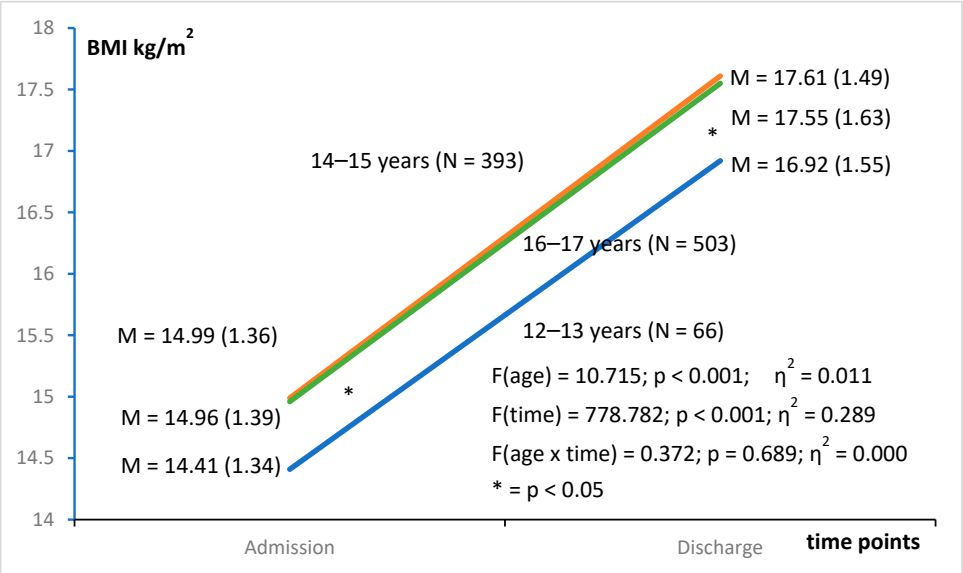


Figure 1. Increase in body mass index during inpatient treatment in three age groups of adolescents with anorexia nervosa.

Table 1 gives an overview of the EDI-2 subscale scores at admission and discharge. All scores decreased significantly (p < 0.001) over treatment with small to medium effect sizes. For the most important ED-specific subscales, this is also illustrated in Figure 2. Drive for Thinness showed a steeper decrease in symptom severity than Bulimia and Body Dissatisfaction.

3.2. General Psychopathology Outcome

Table 2 lists the scores of the BSI and BDI-II at admission and discharge. All scores decreased significantly (p < 0.001) over treatment, with the BSI scores showing small to medium effect sizes. A high effect size (d = 0.883) was observed for the BDI-II score.

Table 1. Change of body mass index and Eating Disorder Inventory-2 scores over treatment in adolescents with anorexia nervosa.

	Admission	**Discharge**	**Statistics**		
	Mean (SD)	**Mean (SD)**	***z*-Value**	***p*-Value**	**d**
Body Mass Index kg/m^2 N = 962	14.93 (1.38)	17.53 (1.58)	26.409	<0.001	1.708
Drive for Thinness N = 807	29.08 (9.87)	22.63 (9.77)	18.406	<0.001	0.787
Bulimia N = 806	12.36 (6.82)	9.44 (3.94)	14.430	<0.001	0.519
Body Dissatisfaction N = 794	38.67 (9.98)	35.59 (11.12)	8.816	<0.001	0.342
Ineffectiveness N = 763	35.33 (10.46)	31.48 (10.88)	11.522	<0.001	0.446
Perfectionism N = 803	20.24 (6.27)	19.35 (6.12)	5.465	<0.001	0.191
Interpersonal Distrust N = 802	22.71 (6.44)	21.76 (6.58)	5.125	<0.001	0.176
Interoceptive Awareness N = 800	33.74 (10.00)	28.80 (10.33)	14.110	<0.001	0.560
Maturity Fears N = 784	28.71 (7.16)	26.44 (7.34)	10.718	<0.001	0.406
Asceticism N = 775	24.38 (7.63)	21.14 (7.56)	12.982	<0.001	0.523
Impulse Regulation N = 805	26.44 (8.22)	24.16 (8.33)	9.735	<0.001	0.348
Social Insecurity N = 803	27.63 (6.89)	25.61 (7.39)	9.758	<0.001	0.351

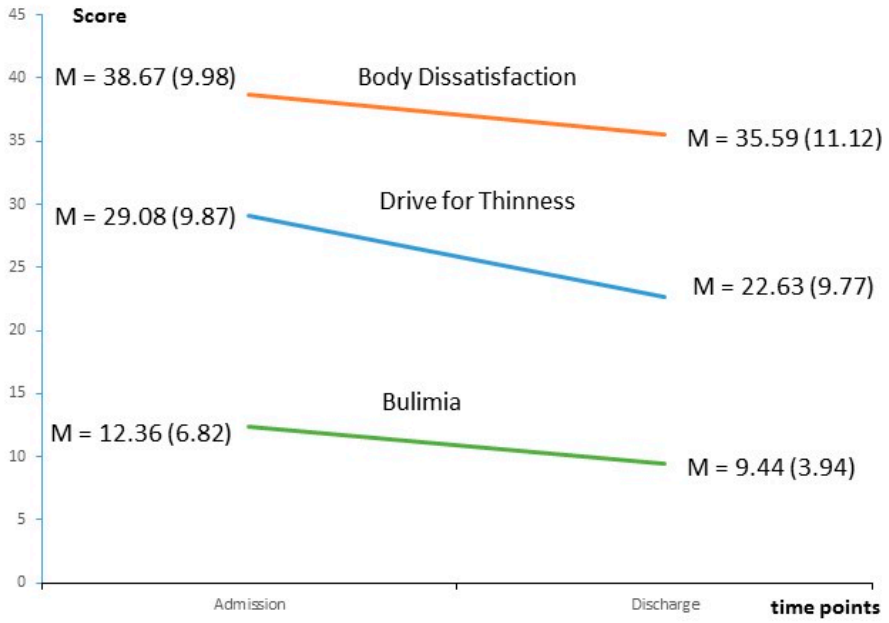


Figure 2. Change of ED-specific subscale scores of the Eating Disorder Inventory-2 from admission to discharge in adolescent inpatients with anorexia nervosa. All changes from admission to discharge were significant ($p < 0.05$).

Table 2. Change of Brief Symptom Inventory and Beck Depression Inventory-II (BDI-II) scores over treatment in adolescents with anorexia nervosa.

	Admission	Discharge	Statistics		
	Mean (SD)	**Mean (SD)**	***z*-Value**	***p*-Value**	**d**
Somatization N = 828	0.99 (0.80)	0.56 (0.58)	16.002	<0.001	0.599
Obsessive–Compulsive Symptoms N = 828	1.36 (0.91)	0.92 (0.79)	14.080	<0.001	0.533
Interpersonal Sensitivity N = 827	1.59 (1.05)	1.26 (1.00)	9.439	<0.001	0.353
Depression N = 828	1.50 (1.00)	1.04 (0.95)	13.472	<0.001	0.501
Anxiety N = 828	1.09 (0.81)	0.82 (0.72)	10.623	<0.001	0.369
Anger–Hostility N = 828	0.98 (0.71)	0.62 (0.63)	13.845	<0.001	0.509
Phobic Anxiety N = 827	0.62 (0.74)	0.44 (0.69)	7.861	<0.001	0.250
Paranoid Ideation N = 828	0.97 (0.78)	0.84 (0.78)	5.100	<0.001	0.167
Psychoticism N = 828	1.24 (0.90)	0.85 (0.85)	12.504	<0.001	0.465
BDI-II Score N = 690	26.06 (11.74)	16.35 (12.51)	18.209	<0.001	0.883

3.3. Comparison of Eating Disorder and General Psychopathology in Patients with Good and Poor Body Weight Outcomes

Patients with good body weight outcomes were not necessarily free from other symptoms of mental disorder. Table 3 lists the BMI and the EDI-2 scores separately for patients with good and poor body weight outcomes. With the exception of Interpersonal Distrust and Maturity Fears ($p > 0.05$), patients with good body weight outcomes reported more severe ED symptoms (EDI-2) at the beginning of treatment than patients with poor body weight outcomes ($p < 0.05$). At the end of treatment, patients in both outcome groups had converged to more similar and lower EDI-2 scores. Drive for Thinness, Body Dissatisfaction, Interoceptive Awareness, and Impulse Regulation still differed at the end of treatment between outcome groups, with more symptom severity in the good body weight outcome group. All effect sizes were small.

Table 4 compares the BSI and the BDI-II scores of patients with good and poor body weight outcomes. Essentially, the pattern described for EDI-2 scores was repeated for the BSI and BDI-II. Scores in the good body weight outcome group at the beginning of the treatment showed more severity in patients with good body weight outcomes compared to patients with poor body weight outcomes. Most of the severity scores still differed between outcome groups at the end of treatment, with higher scores in the good body weight outcome group. Again, all effect sizes were small.

3.4. Predictors of Good Body Weight Outcome

Results of the final logistic regression model are presented in Table 5. A higher BMI, later age at onset (15 years or higher), and higher BSI Somatization, BSI Anxiety, and EDI-2 Bulimia scores at admission to inpatient treatment increased the probability of reaching a BMI of at least 18.5 kg/m^2 at discharge from inpatient treatment. A total of 263 patients (27.3%) reached this good body weight outcome.

Table 3. Body mass index and Eating Disorder Inventory-2 scores in patients with poor and good body weight outcomes.

	Admission			Discharge		
	Poor Outcome Mean (SD)	**Good Outcome Mean (SD)**	**Mann–Whitney z-Value d**	**Poor Outcome Mean (SD)**	**Good Outcome Mean (SD)**	**Mann–Whitney z-Value d**
Body Mass Index kg/m^2 N = 699/263/699/263	14.66 (1.32)	15.65 (1.26)	10.156 $p < 0.001$ d = 0.756	16.89 (1.30)	19.25 (0.72)	23.931 $p < 0.001$ d = 2.018
Drive for Thinness N = 650/239/626/246	28.36 (10.08)	31.80 (9.03)	4.890 $p < 0.001$ d = 0.350	22.13 (9.92)	23.60 (9.66)	2.096 $p = 0.036$ d = 0.149
Bulimia N = 649/240/625/246	11.71 (6.29)	14.41 (7.96)	4.813 $p < 0.001$ d = 0.397	9.20 (3.76)	9.88 (4.12)	1.895 $p = 0.058$ d = 0.177
Body Dissatisfaction N = 644/239/616/246	38.12 (10.10)	41.04 (9.62)	3.705 $p < 0.001$ d = 0.293	35.27 (10.96)	35.70 (11.98)	0.766 $p = 0.044$ d = 0.038
Ineffectiveness N = 624/233/606/242	34.77 (10.49)	38.08 (10.18)	4.120 $p < 0.001$ d = 0.318	31.09 (10.69)	32.28 (11.01)	1.452 $p = 0.146$ d = 0.110
Perfectionism N = 651/239/623/245	20.16 (6.34)	21.19 (5.98)	2.163 $p = 0.031$ d = 0.164	19.10 (6.19)	19.92 (5.94)	1.820 $p = 0.069$ d = 0.134
Interpersonal Distrust N = 647/240/623/246	22.65 (6.55)	23.57 (6.24)	1.921 $p = 0.055$ d = 0.141	21.66 (6.57)	22.07 (6.65)	0.707 $p = 0.479$ d = 0.062
Interoceptive Awareness N = 650/236/622/246	33.03 (10.33)	37.09 (8.98)	5.378 $p < 0.001$ d = 0.406	28.25 (10.43)	30.37 (10.18)	2.979 $p = 0.003$ d = 0.205
Maturity Fears N = 637/237/619/245	28.45 (7.29)	29.37 (6.70)	1.894 $p = 0.058$ d = 0.130	26.40 (7.35)	26.87 (7.08)	1.044 $p = 0.297$ d = 0.064
Asceticism N = 629/241/611/240	24.06 (7.85)	26.19 (7.36)	3.732 $p < 0.001$ d = 0.276	20.90 (7.56)	21.68 (7.34)	1.622 $p = 0.105$ d = 0.104
Impulse Regulation N = 650/242/622/245	25.87 (8.08)	28.75 (8.20)	4.500 $p < 0.001$ d = 0.355	23.69 (8.16)	25.42 (8.71)	2.664 $p = 0.008$ d = 0.208
Social Insecurity N = 646/242/620/245	27.45 (7.09)	28.83 (6.49)	2.542 $p = 0.011$ d = 0.199	25.43 (7.33)	26.24 (7.49)	1.262 $p = 0.207$ d = 0.111

Table 4. Brief Symptom Inventory and Beck Depression-Inventory-II (BDI-II) scores in patients with poor and good body weight outcomes.

	Admission			Discharge		
	Poor Outcome Mean (SD)	**Good Outcome Mean (SD)**	**Mann–Whitney z-Value d**	**Poor Outcome Mean (SD)**	**Good Outcome Mean (SD)**	**Mann–Whitney z-Value d**
Somatization N = 662/246/632/241	0.92 (0.77)	1.20 (0.84)	4.635 $p < 0.001$ d = 0.347	0.54 (0.59)	0.65 (0.61)	2.872 $p = 0.004$ d = 0.188
Obsessive–Compulsive Symptoms N = 662/246/632/241	1.29 (0.89)	1.60 (0.92)	4.634 $p < 0.001$ d = 0.347	0.90 (0.79)	1.02 (0.83)	2.133 $p = 0.033$ d = 0.158
Interpersonal Sensitivity N = 662/246/631/241	1.55 (1.06)	1.87 (1.02)	4.304 $p < 0.001$ d = 0.312	1.23 (0.99)	1.39 (1.03)	2.217 $p = 0.027$ d = 0.164
Depression N = 662/246/632/241	1.46 (1.00)	1.78 (0.99)	4.309 $p < 0.001$ d = 0.321	1.01 (0.93)	1.18 (0.99)	2.376 $p = 0.018$ d = 0.181
Anxiety N = 662/246/632/241	1.04 (0.77)	1.31 (0.89)	4.050 $p < 0.001$ d = 0.336	0.80 (0.74)	0.89 (0.71)	2.071 $p = 0.038$ d = 0.113
Anger–Hostility N = 662/246/632/241	0.92 (0.67)	1.18 (0.80)	4.216 $p < 0.001$ d = 0.367	0.61 (0.62)	0.69 (0.71)	1.076 $p = 0.282$ d = 0.126
Phobic Anxiety N = 661/246/632/241	0.58 (0.73)	0.81 (0.80)	4.826 $p < 0.001$ d = 0.302	0.42 (0.69)	0.56 (0.74)	2.814 $p = 0.005$ d = 0.197
Paranoid Ideation N = 662/246/632/241	0.95 (0.78)	1.09 (0.79)	2.620 $p = 0.009$ d = 0.176	0.84 (0.79)	0.90 (0.77)	1.490 $p = 0.136$ d = 0.076
Psychoticism N = 662/246/632/241	1.22 (0.93)	1.42 (0.88)	3.376 $p < 0.001$ d = 0.221	0.84 (0.85)	0.91 (0.86)	1.178 $p = 0.239$ d = 0.082
BDI-II N = 606/226/560/223	25.13 (11.86)	29.58 (11.09)	4.741 $p < 0.001$ d = 0.382	15.36 (12.25)	17.90 (13.15)	2.525 $p = 0.012$ d = 0.203

Table 5. Predictors of good body weight outcome in adolescents treated for anorexia nervosa.

No.	Predictor	Odds Ratio	95% Confidence Interval	Wald-Statistics	*p*
1	Higher body mass index	1.828	1.566–2.134	58.346	<0.001
2	Age at onset at 15 years or higher	1.722	1.167–2.540	7.512	0.006
3	Higher BSI Somatization score	1.436	1.092–1.887	6.724	0.010
4	Higher BSI Anxiety score	1.320	1.016–1.714	4.319	0.038
5	Higher EDI-2 Bulimia score	1.029	1.003–1.056	4.830	0.028

R^2 = 0.23, N = 686. Note: All predictors were assessed at admission to inpatient treatment (df = 1). EDI-2 = Eating Disorder Inventory-2, BSI = Brief Symptom Inventory. Good body weight outcome was defined as the patient achieving a BMI at discharge from inpatient treatment of 18.5 or higher. An odds ratio above 1 means an increase in the probability of good body weight outcome.

4. Discussion

According to our knowledge, the present study includes, by far, the largest adolescent sample with inpatient treatment for AN. It reports treatment outcome and adds substantially to the evaluation of multimodal inpatient treatment, primarily based on CBT-E, in adolescents with AN, which also involved carers. Highest effect sizes were found for core ED symptoms with lower effect sizes for general psychopathology. ED symptoms were reduced significantly during treatment, with high effect sizes for weight increase and reduction in Drive for Thinness. Although improving during treatment, effect sizes for personality traits Perfectionism and Interpersonal Distrust were low, highlighting important topics to be addressed in subsequent outpatient psychotherapy. However, our questionnaires covered only the severity of these personality traits. We did not assess if and to what extent our therapy improved the ability to cope with consequences of these personality traits in everyday life outside the clinic. Sharing their life experience informally with other patients may also have contributed to better coping. This informal sharing of life experience between patients is a specific characteristic of inpatient treatment that merits further investigation.

Depression, anxiety, and other psychopathology also decreased significantly during treatment. Restoration to normal weight was predicted by a higher BMI at the beginning of treatment, a later age at AN onset of at least 15 years, and higher Somatization, Anxiety, and Bulimia scores at the beginning of treatment.

The duration of inpatient treatment in our adolescent sample was, on average, 96.69 days, or 13.81 weeks. Other German studies of adolescents with AN reported a somewhat longer mean inpatient stay of 14.6 weeks in a randomized controlled trial [14] and a longer median inpatient stay of 17 weeks in a multi-center adolescent AN registry study [20]. A study from Italy reported a similar length of stay of 13 weeks, with an additional 7 weeks of day hospital treatment [11]. Another study from France reported a longer inpatient treatment of 19 weeks [30], with a similar length of stay (20 weeks) reported in a sample from Scotland [16]. In a sample treated in England, length of stay averaged 15 weeks [31]. Considerably shorter inpatient stays were reported for adolescents with AN in Spain (30 days) [10], the United States of America, and Canada (11 to 50 days [32]; 11 days [33]; 26 days in a mixed adolescent/adult sample [34]; 38 days [35]). Similarly, median lengths of stay of 17 days for the year 2019 and 12 days for the year 2020 were reported by an Australian study [36]. Summarizing, the duration of inpatient treatment of our study was comparable to other European studies with the exception of Spain. Much shorter inpatient stays were reported for the North American continent and for Australia. These differences are mainly attributable to differences in the national health care systems. Striegel-Moore et al. [34] argue that short inpatient treatments are not sufficient for achieving weight restoration. This supports the usefulness of longer inpatient stays for the treatment of AN. On the other hand, the mean BMI at discharge from inpatient treatment in our study was about 17.50 kg/m^2. This means that a part of the patients remained below

this often-used threshold of 17.50 kg/m^2 for the diagnosis of AN and did not achieve weight restoration. However, the primary aim of inpatient treatment of AN is to give an impetus for improvement to very severe AN cases, and not weight restoration. Having improved in body weight and other medical factors, the indication for inpatient treatment is no longer present, and the patient has to be returned or newly referred to outpatient treatment. As a rule, health insurances will not bear the costs of inpatient treatment beyond what is absolutely necessary. A more recent proposal is home treatment following inpatient treatment. This recommendable treatment was shown to be suitable for maintaining or achieving target weight [37].

Concerning body weight, several studies reported results similar to our study. In these studies, the BMI at the beginning of inpatient treatment varied between 14.40 kg/m^2 and 15.50 kg/m^2 [10,14,19,20] which is near the admission BMI in our study (14.93 kg/m^2). In some studies, the BMI increased significantly during inpatient treatment, from 15.5 kg/m^2 to 18.4 kg/m^2 and 18.6 kg/m^2 [10,20], respectively, which is also similar to our findings, although the level of the values is higher than in our sample. This may indicate a more severe ED in our sample. In another study, an increase in BMI from 14.40 kg/m^2 to 17.01 kg/m^2 was reported [19]. These lower values may be attributable to the more severe BMI inclusion threshold of 17.50 kg/m^2 in this study. This study also reported an effect size of d = 2.01, higher than in our sample. Possibly, the lower BMI at the beginning of treatment allowed a steeper trajectory of increase in body weight.

Mairhofer et al. [19] reported changes of EDI-2 subscales during inpatient treatment. Although it is not stated explicitly in the publication, it seems that Mairhofer et al. applied a recoding procedure to the answer codes as proposed in the original publication of the Eating Disorder Inventory. This modification reduces the original 1–6 answer format to a 0–3 format, explaining the lower scores. Our study followed the instructions of the EDI-2 manual, building the scores from the format 1–6 without recoding [25]. Consequently, we will confine the comparison with our results to statistical significance and effect sizes. Both the present study and the study of Mairhofer et al. [19] reported significant improvement ($p < 0.05$) for EDI-2 subscales Drive for Thinness, Bulimia, Interpersonal Distrust, Interoceptive Awareness, Maturity Fears, Asceticism, Impulse Regulation and Social Insecurity. Improvement of EDI-2 subscales Body Dissatisfaction, Ineffectiveness, and Perfectionism was significant in the present study but not in the study of Mairhofer et al. [19]. Both studies point in the same direction and support the efficacy of multi-modal inpatient treatment for improving cognitive symptoms of AN in adolescents. The discrepancy regarding statistical significance may well reflect the increased statistical power of our larger sample of 962 vs. 126 inpatients in the sample of Mairhofer et al.

Efficacy of the inpatient CBT-E in our sample was also confirmed by the results of general psychopathology scores. The significant improvement for all assessments is supported by the findings of Dalle Grave et al. [11], which reported a significant decrease in the BSI-general symptomatic or severity index. This study also supports our finding of the efficacy and acceptance of inpatient CBT-E in adolescents treated for AN.

Dalle Grave et al. [11] also provided follow-up data for their sample of 26 inpatients after CBT-E treatment. In this study, weight gain and reduction in severity of ED and general psychopathology was maintained for over 12 months after treatment. Similarly, a 12-month follow-up in a small subgroup of our present sample showed a further increase in body weight and maintenance of the improved ED severity and depression one year after inpatient treatment [38]. Both our study and the study of Dalle Grave et al. [11] allow for the conclusion that CBT-E is a suitable inpatient treatment of adolescent AN, improving body weight, negative thoughts, body image, and other important areas. An additional study reported a BMI above 17.5 kg/m^2 in 80.4% of adolescents 7.5 years after inpatient treatment but a low quality of mental health [39].

Concerning the predictors of good body weight outcome, we did not confirm the findings of Schlegl et al. [22], although both studies shared part of the sample. One possible reason is the different approach to the outcome criterion (continuous variable of BMI change

versus a dichotomous BMI threshold). The earlier study considered any BMI change, while the present study defined a good body weight outcome threshold. Another possible reason is that Schlegl et al. [22] included the length of inpatient treatment in the predictive model. In a strict sense, this is not a predictor, as it is not precedent to treatment outcome. Including this variable limits the comparability of the results. In the present study, a higher BMI at the beginning of treatment increased the probability of good body weight outcome. This is in agreement with other studies, which reported a higher BMI at admission predicting good post-treatment weight maintenance [10], and a lower BMI predicting drop-out from inpatient treatment in a mixed sample of adolescent and adult patients [21].

Age at onset of AN at 15 years or higher also increased the probability of a good body weight outcome. This is still an early age at onset and, considering the age limit of our study of less than 18 years, this finding may reflect a shorter duration of AN, and thus a timelier intervention. Regrettably, in the hospital documentation, age at onset was only stored in categories, preventing the computation of the duration of AN in this sample. Another possibility is that these slightly older patients were more mature in their cognitive and mental development, and, thus, were able to gain more benefit from the therapy. The finding of lower age as a predictor of increase in BMI over treatment by Schlegl et al. [22] is contrary to our result. However, the approach to the prediction of outcome was different in these studies. Schlegl et al.'s outcome criterion was the change of BMI values in a multivariate linear regression analysis. This approach included negative and positive as well as small and large changes of BMI in a continuous outcome variable. The present study used a fixed BMI threshold as the outcome criterion and summarized negative and positive increases in BMI in the same category of poor outcome, as long as the BMI threshold of 18.5 kg/m^2 was not reached, ignoring the absolute value and sign of BMI change. Considering the known influence of sample and predictor selection on the results of regression analyses, the inclusion of the length of inpatient stay by Schlegl et al. may have also impacted the correlation between predictors. In the study of Herpertz-Dahlmann et al. [39], patients below age 12 did not have a worse outcome than older adolescent patients. This also contradicts the findings of Schlegl et al. [22] that lower age is correlated to increase in body weight.

Higher Anxiety and Somatization scores at admission also increased the probability of very good body weight outcome. In addition to these significant predictors, all EDI-2 and BSI scores were higher in patients with good body weight outcomes compared to patients with poor body weight outcomes in our adolescent sample, but the effect sizes were small. Fichter et al. [40] compared EDI-2 and BSI scores between the good and poor outcome groups in a predominantly adult sample and found only EDI-2 Perfectionism and EDI-2 Maturity Fears scores to differ between groups. Some scores at the beginning of treatment were also higher in the long-term good outcome group [40]. A possible explanation of these findings is an enhanced motivation to change and increased responsiveness to interventional measures in more anxious adolescents. This points to the usefulness of early intervention before a learning process of successful maintenance of negative cognitions about one's body sets in, which could lead to chronification and an enduring course of AN.

The final predictor of good body weight outcome was a higher Bulimia score. As one of the more tangible behavioral symptoms of AN, this symptom may well offer a good starting point for intervention suitable for establishing at least a preliminary working alliance of patient and therapist. Results from a study on predominantly adult female inpatients with AN, however, show contrary results. In a 2-year follow-up, neither binging nor purging behaviors were predictors of outcome, and, in a 6-year follow-up, binging behavior was a predictor of poor outcome, but purging behavior was no predictor [41]. In a similar study, the EDI-2 Bulimia score was no predictor of outcome in a 10-year follow-up [40].

Several limitations have to be considered in interpreting the results: (1) As in most studies on AN, nearly all patients included in the present study were females, and our results may not apply to male adolescent inpatients. However, our intention was to present a "natural" sample as it occurs in the practice of a specialized clinic. The percentage of boys

in our sample (2.7%) was very similar to the percentage of adolescent boys in the sample collected in a patient registry by Jaite et al. (2.3%) [20]; (2) Patients were from one clinic only and it is not known if the results apply to patients in other clinics; (3) Excluding the BMI, assessments were made by self-report questionnaires. However, as the focus of our research was on change of symptoms, the same assessments were used at the beginning and at the end of treatment; (4) Very little is known on predictors of outcome in adolescents with AN. Consequently, our interpretation of predictors is partially speculative and needs further support from other studies; (5) Our outcome definition focused on body weight restoration. While this is a central symptom with possible severe impact on the physical condition of the patient, this definition ignores other important symptoms of AN like the cognitive focus on body weight and shape, slimness ideal, and fear of gaining weight, as well as emotional conditions like depressive symptoms. Additional areas not covered by our outcome definition are the social and occupational functioning of the patients. From the data in the hospital documentation, we could not derive measures like, for example, the Morgan Russell Outcome Assessment Schedule [42], which is suitable for describing outcome in much more detail; (6) Patients improved while being in the clinic, but we have no data on how persistently this improvement could be maintained after returning to everyday life. However, results from a follow-up in a small subgroup of our sample showed a longer-lasting effect of CBT-E after the end of treatment [38]; (7) We could not extract detailed data on comorbidity, excessive exercise, and medication, limiting our set of potential predictors of outcome. This is an important future research question.

These limitations are offset by a number of strengths of our study: (1) The sample size is extraordinarily large, resulting in reliable estimates of symptom change; (2) Only variables assessed before the outcome were included in the search for real predictors of outcome; (3) Good body weight outcome was defined to reflect a normal body weight at the end of treatment.

5. Conclusions

Concluding, inpatient multi-modal CBT-E is effective in the treatment of severe AN. While weight restoration is important in AN, focusing on ED symptoms is not sufficient, and still more specific psychotherapy for personality traits like Perfectionism and Interpersonal Distrust, as well as comorbid symptoms of depression, anxiety, etc., is needed. Further research should address which elements of multi-modal CBT-E are the most important contributors to treatment success. The contributions of the family and carers to the improvement of AN also needs additional research.

Author Contributions: Conceptualization, U.V. and N.Q.; methodology, N.Q.; formal analysis, N.Q.; investigation, U.V., S.N., S.S. and T.B.; resources, U.V.; data curation, N.Q. and S.S.; writing—original draft preparation, N.Q.; writing—review and editing, all authors; project administration, U.V. and N.Q. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki. Ethical review and approval were waived for this study. The present study used only retrospective data in anonymized form. According to the guidelines by the institutional review board of the LMU Munich, retrospective studies conducted on already available, anonymized data are exempt from requiring ethics approval.

Informed Consent Statement: Patient consent was waived because all data used for the study were collected retrospectively and anonymously.

Data Availability Statement: In accordance with the data security guidelines of our facility, the Schön Klinik Roseneck, data relating to patients must not be publicly accessible.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Herpertz-Dahlmann, B.; Wille, N.; Hölling, H.; Vloet, T.D.; Ravens-Sieberer, U.; BELLA Study Group. Disordered eating behavior and attitudes, associated psychopathology and health-related quality of life: Results of the BELLA study. *Eur. Child Adolesc. Psychiatry* **2008**, *17* (Suppl. S1), 82–91. [CrossRef] [PubMed]
2. Herpertz-Dahlmann, B.; Dempfle, A.; Konrad, K.; Klasen, F.; Ravens-Sieberer, U.; BELLA Study Group. Eating disorder symptoms do not just disappear: The implications of adolescent eating-disordered behavior for body weight and mental health in young adulthood. *Eur. Child Adolesc. Psychiatry* **2015**, *24*, 675–684. [CrossRef] [PubMed]
3. Halvorsen, I.; Rø, Ø.; Heyerdahl, S. Nine-year follow-up of girls with anorexia nervosa and their siblings: Retrospective perceptions of parental bonding and the influence of illness on their everyday life. *Eur. Eat. Disord. Rev.* **2013**, *21*, 20–27. [CrossRef] [PubMed]
4. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*, 5th ed.; American Psychiatric Publishing: Washington, DC, USA, 2013.
5. Steinhausen, H.-C.; Jensen, C.M. Time trends in lifetime incidence rates of first-time diagnosed anorexia nervosa and bulimia nervosa across 16 years in a danish nationwide psychiatric registry study. *Int. J. Eat. Disord.* **2015**, *48*, 845–850. [CrossRef] [PubMed]
6. Klump, K. Puberty as a critical risk period for eating disorders: A review of human and animal studies. *Horm. Behav.* **2013**, *64*, 399–410. [CrossRef]
7. Herpertz, S.; Fichter, M.; Herpertz-Dahlmann, B.; Hilbert, A.; Tuschen-Caffier, B.; Vocks, S.; Zeeck, A. (Eds.) S3-Leitlinie Diagnostik und Behandlung der Essstörungen. 2018. Available online: https://www.awmf.org/leitlinien/detail/ll/051-026.html (accessed on 7 July 2023).
8. Boege, I.; Schepker, R.; Herpertz-Dahlmann, B.; Vloet, T.D. Hometreatment. Eine effektive Alternative zu konventionellen Behandlungsformen? *Z. Für Kinder Und Jugendpsychiatrie Und Psychother.* **2015**, *43*, 411–423. [CrossRef]
9. Herpertz-Dahlmann, B. Intensive treatments in adolescent anorexia nervosa. *Nutrients* **2021**, *13*, 1265. [CrossRef]
10. Castro-Fornieles, J.; Casula, V.; Saura, B.; Martinez, E.; Lazaro, L.; Vila, M.; Plana, M.T.; Toro, J. Predictors of weight maintenance after hospital discharge in adolescent anorexia nervosa. *Int. J. Eat. Disord.* **2007**, *40*, 129–135. [CrossRef]
11. Dalle Grave, R.; Calugi, S.; El Ghoch, M.; Conti, M.; Fairburn, C.G. Inpatient cognitive behavior therapy for adolescents with anorexia nervosa: Immediate and longer-term effects. *Front. Psychiatry* **2014**, *5*, 14. [CrossRef]
12. Godart, N.T.; Berthoz, S.; Curt, F.; Perdereau, F.; Rein, Z.; Wallier, J.; Horreard, A.-S.; Kaganski, I.; Lucet, R.; Atger, F.; et al. A randomized controlled trial of adjunctive family therapy and treatment as usual following inpatient treatment for anorexia nervosa adolescents. *PLoS ONE* **2012**, *7*, e28249. [CrossRef]
13. Goddard, E.; Hibbs, R.; Raenker, S.; Salerno, L.; Arcelus, J.; Boughton, N.; Connan, F.; Goss, K.; Laszlo, B.; Morgan, J.; et al. A multi-centre cohort study of short term outcomes of hospital treatment for anorexia nervosa in the UK. *BMC Psychiatry* **2013**, *13*, 287. [CrossRef] [PubMed]
14. Herpertz-Dahlmann, B.; Schwarte, R.; Krei, M.; Egberts, K.; Warnke, A.; Wewetzer, C.; Pfeiffer, E.; Fleischhaker, C.; Scherag, A.; Holtkamp, K.; et al. Day-patient treatment after short inpatient care versus continued inpatient treatment in adolescents with anorexia nervosa (ANDI): A multicentre, randomised, open-label, non-inferiority trial. *Lancet* **2014**, *383*, 1222–1229. [CrossRef] [PubMed]
15. Lock, J.; Litt, I. What predicts maintenance of weight for adolescents medically hospitalized for anorexia nervosa? *Eat. Disord.* **2003**, *11*, 1–7. [CrossRef] [PubMed]
16. Morris, J.; Simpson, A.V.; Voy, S.J. Length of stay of inpatients with eating disorders. *Clin. Psychol. Psychother.* **2015**, *22*, 45–53. [CrossRef] [PubMed]
17. Salbach, H.; Klinkowski, N.; Pfeiffer, E.; Lehmkuhl, U.; Korte, A. Dialectical behavior therapy for adolescents with anorexia and bulimia nervosa (DBT-AN/BN)—A pilot study. *Prax. Der Kinderpsychol. Und Kinderpsychiatr.* **2007**, *56*, 91–108.
18. Steinhausen, H.-C.; Seidel, R. Outcome in adolescent eating disorders. *Int. J. Eat. Disord.* **1993**, *14*, 487–496. [CrossRef]
19. Mairhofer, D.; Zeiler, M.; Philipp, J.; Truttmann, S.; Wittek, T.; Skala, K.; Mitterer, M.; Schöfbeck, G.; Laczkovics, C.; Schwarzenberg, J.; et al. Short-Term Outcome of Inpatient Treatment for Adolescents with Anorexia Nervosa Using DSM-5 Remission Criteria. *J. Clin. Med.* **2021**, *10*, 3190. [CrossRef]
20. Jaite, C.; Bühren, K.; Dahmen, B.; Dempfle, A.; Becker, K.; Correll, C.U.; Egberts, K.M.; Ehrlich, S.; Fleischhaker, C.; von Gontard, A.; et al. Clinical characteristics of inpatients with childhood vs. adolescent anorexia nervosa. *Nutrients* **2019**, *28*, 2593. [CrossRef]
21. Hubert, T.; Pioggiosi, P.; Huas, C.; Wallier, J.; Maria, A.-S.; Apfel, A.; Curt, F.; Falissard, B.; Godart, N. Drop-out from adolescent and young adult inpatient treatment for anorexia nervosa. *Psychiatry Res.* **2013**, *209*, 632–637. [CrossRef]
22. Schlegl, S.; Diedrich, A.; Neumayr, C.; Fumi, M.; Naab, S.; Voderholzer, U. Inpatient treatment for adolescents with anorexia nervosa: Clinical significance and predictors of treatment outcome. *Eur. Eat. Disord. Rev.* **2016**, *24*, 214–222. [CrossRef]
23. Naab, S.; Schlegl, S.; Korte, A.; Heuser, J.; Fumi, M.; Fichter, M.; Cuntz, U.; Voderholzer, U. Effectiveness of a multimodal inpatient treatment for adolescents with anorexia nervosa in comparison with adults: An analysis of a specialized inpatient setting. *Eat. Weight. Disord.* **2013**, *18*, 167–173. [CrossRef]
24. Garner, D.M. *Eating Disorder Inventory-2 Manual*; Psychological Assessment Ressources: Odessa, FL, USA, 1991.
25. Paul, T.; Thiel, A. *Eating Disorder Inventory 2, German Version*; Hogrefe: Göttingen, Germany, 2004.

26. Derogatis, L.R.; Melisaratos, N. The Brief Symptom Inventory: An introductory report. *Psychol. Med.* **1983**, *13*, 595–605. [CrossRef]
27. Franke, G.H. *BSI—Brief Symptom Inventory von Derogatis (Kurzform der SCL-90-R)—Deutsche Version*; Hogrefe: Göttingen, Germany, 2000.
28. Beck, A.T.; Steer, R.A.; Brown, G.K. *Beck Depression Inventory*, 2nd ed.; Manual; The Psychological Corporation: San Antonio, TX, USA, 1996.
29. Cohen, J. *Statistical Power Analysis for the Behavioral Sciences*, 2nd ed.; Lawrence Erlbaum Associates: Hillsdale, Australia, 1988.
30. Strik Lievers, L.; Curt, F.; Wallier, J.; Perdereau, F.; Rein, Z.; Jeammet, P.; Godart, N. Predictive fac-tors of length of inpatient treatment in anorexia nervosa. *Eur. Child Adolesc. Psychiatry* **2009**, *18*, 75–84. [CrossRef] [PubMed]
31. Gowers, S.G.; Clark, A.; Roberts, C.; Griffiths, A.; Edwards, V.; Bryan, C.; Smethurst, N.; Byford, S.; Barrett, B. Clinical effectiveness of treatments for anorexia nervosa in adolescents. Randomised controlled trial. *Br. J. Psychiatry* **2007**, *191*, 427–435. [CrossRef] [PubMed]
32. Kalisvaart, J.L.; Hergenroeder, A.C. Hospitalization of patients with eating disorders on adolescent medical units is threatened by current reimbursement systems. *Int. J. Adolesc. Med. Health* **2007**, *19*, 155–165. [CrossRef] [PubMed]
33. Schwartz, B.I.; Mansbach, J.M.; Marion, J.G.; Katzman, D.K.; Forman, S.F. Variations in admission practices for adolescents with anorexia nervosa: A North American sampie. *J. Adolesc. Health* **2008**, *43*, 425–431. [CrossRef]
34. Striegel-Moore, R.H.; Leslie, D.; Petrill, S.A.; Garvin, V.; Rosenheck, R.A. One-year use and cost of inpatient and outpatient services among female and male patients with an eating disorder: Evidence from a national database of health insurance claims. *Int. J. Eat. Disord.* **2000**, *27*, 381–389. [CrossRef]
35. Toulany, A.; Wong, M.; Katzman, D.K.; Akseer, N.; Steinegger, C.; Hancock-Howard, R.L.; Coyte, P.C. Cost analysis of inpatient treatment of anorexia nervosa in adolescents: Hospital and caregiver perspectives. *CMAJ Open* **2015**, *3*, E192–E197. [CrossRef]
36. Wong, J.W.S.; Skeldon, S.; Gill, E.; Taylor, E.; Billingham, W.; Stevenson, P.G.; Shipton, N.; Ferguson, G.; Collins, R.; Newton, R.; et al. The increase in medical admissions with anorexia nervosa during the COVID-19 pandemic in Western Australia. *Int. J. Eat. Disord.* **2023**, *56*, 1661–1666. [CrossRef]
37. Herpertz-Dahlmann, B.; Borzikowsky, C.; Altdorf, S.; Heider, K.; Dempfle, A.; Dahmen, B. 'Therapists in action'—Home treatment in adolescent anorexia nervosa: A stepped care approach to shorten inpatient treatment. *Eur. Eat. Disord. Rev.* **2021**, *29*, 427–442. [CrossRef]
38. Meule, A.; Schrambke, D.; Furst Loredo, A.; Schlegl, S.; Naab, S.; Voderholzer, U. Inpatient treatment of anorexia nervosa in adolescents: A 1-year follow-up study. *Eur. Eat. Disord. Rev.* **2021**, *29*, 165–177. [CrossRef] [PubMed]
39. Herpertz-Dahlmann, B.; Dempfle, A.; Egberts, K.M.; Kappel, V.; Konrad, K.; Vloet, J.A.; Bühren, K. Outcome of childhood anorexia nervosa-The results of a five- to ten-year follow-up study. *Int. J. Eat. Disord.* **2018**, *51*, 295–304. [CrossRef] [PubMed]
40. Fichter, M.M.; Quadflieg, N.; Crosby, R.D.; Koch, S. Long-term outcome of anorexia nervosa—Results from a large clinical longitudinal study. *Int. J. Eat. Disord.* **2017**, *50*, 1018–1030. [CrossRef]
41. Fichter, M.M.; Quadflieg, N. Six-year course and outcome of anorexia nervosa. *Int. J. Eat. Disord.* **1999**, *26*, 359–385. [CrossRef]
42. Morgan, H.G.; Hayward, A.E. Clinical assessment of anorexia nervosa-the Morgan-Russell outcome assessment schedule. *Br. J. Psychiatry* **1988**, *152*, 367–371. [CrossRef] [PubMed]

8. Publikation II

Thieme

Impact of Antipsychotic Medications on Weight Gain and Eating Disorder-Related Psychopathology in Adult Inpatients with Anorexia Nervosa

Authors
Tabea Bauman[1], David R. Kolar[2, 3], Christoph U. Correll[4, 5, 6, 7], Verena Haas[4], Ulrich Voderholzer[1, 3, 8]

Affiliations
1 Schoen Clinic Roseneck, Prien am Chiemsee, Germany
2 Clinical Child and Adolescent Psychology and Psychotherapy, Department of Psychology, University of Regensburg, Regensburg, Germany
3 Department of Psychiatry and Psychotherapy, Ludwig-Maximilians-University Munich, Munich, Germany
4 Department of Child and Adolescent Psychiatry, Charité-Universitätsmedizin Berlin, Berlin, Germany
5 Department of Psychiatry and Molecular Medicine, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Hempstead, New York, USA
6 Department of Psychiatry, Zucker Hillside Hospital, Glen Oaks, New York, USA
7 Center for Psychiatric Neuroscience, Feinstein Institute for Medical Research, Manhasset, New York, USA
8 Department of Psychiatry and Psychotherapy, University Hospital of Freiburg, Freiburg, Germany

Keywords
anorexia nervosa, adults, inpatients, weight gain, antipsychotics

received 23.05.2024
revised 29.08.2024
accepted 25.09.2024
published online 2024

Bibliography
Pharmacopsychiatry
DOI 10.1055/a-2436-9552
ISSN 0176-3679

Georg Thieme Verlag KG, Rüdigerstraße 14,
70469 Stuttgart, Germany

Correspondence
Tabea Bauman
Schön Klinik Roseneck
Psychosomatic Medicine
Am Roseneck 6
83209 Prien am Chiemsee
Germany
tbauman@schoen-klinik.de

ABSTRACT

Introduction The impact of antipsychotic use on weight gain and eating disorder-related psychopathology in adult inpatients with anorexia nervosa (AN) is unclear.

Methods Consecutively hospitalized adults with AN were retrospectively analyzed. Co-primary outcomes were body mass index (BMI) and weekly weight change. Secondary outcomes were Eating Disorder Inventory-2 (EDI-2) subscale scores 'drive for thinness' and 'body dissatisfaction'. Admission-to-discharge changes were compared in patients continuing pre-admission antipsychotics (APcont), starting antipsychotics (APnew) and patients without psychopharmacotherapy (noMed) using linear mixed models. Sensitivity analyses were conducted in subgroups matched for age, length of stay, baseline BMI and baseline EDI-2 scores. Subgroups were also compared regarding BMI trajectories, using non-linear growth curve models. Within-group analyses compared weight gain before vs. after the median antipsychotic onset week.

Results Of 775 adult inpatients (mean length of stay = 103.5 ± 48.0 days), 21.7 % received antipsychotics (APcont = 7.7 %; APnew = 13.9 %), i. e., olanzapine (n = 127, dose = 5.5 ± 3.1 mg/day) or quetiapine (n = 41, dose = 100.0 ± 97.7 mg/day), while 78.3 % did not receive any medication. Comparing all three groups, a significant time × group interaction was found for noMed and APnew vs. APcont ($p = 0.011$), but this effect disappeared when comparing matched subgroups. However, in matched subgroups (n = 54 each) APnew showed steeper weight gain vs. APcont both overall ($p = 0.011$) and after median antipsychotic initiation (5.8 ± 5.0 weeks) ($p \leq 0.001$). No significant group differences emerged in EDI-2 subscale scores.

Discussion In this naturalistic study, 22 % of adult inpatients received antipsychotics. However, neither weight gain nor AN-related psychopathology changed differently in patients treated with vs. without antipsychotics. Newly initiated antipsychotic treatment vs. continuation from pre-admission had better weight gain outcomes.

Introduction

Anorexia nervosa (AN) is a severe eating disorder with a median onset of illness of 15.5 years [1]. It is characterized by pathological underweight that is associated with an intense fear of gaining weight [2]. AN is also not infrequently associated with an urge for physical activity and physical hyperactivity [3, 4]. According to a recent meta-analysis [5], less than half the number of affected individuals (45 %) recover from AN, and 23 % have a chronic course. With 5.8/1000 patient-years, the associated mortality is very high [5], leading to > 16 years of potential life lost, second only to substance use disorders [6]. Due to these frequent problematic outcomes, optimization of treatment options for individuals with AN is highly desired.

The treatment of patients with AN includes realimentation to a healthy body weight through two aspects, including high-caloric realimentation [7, 8] and engaging in eating disorder-specific psychotherapy, which also further addresses disease-maintaining psychological aspects of the disorder [9]. To date no psychopharmacological treatment for AN has been recommended by national and international guidelines [10–13]. In clinical practice, it is not uncommon for second-generation antipsychotics, especially olanzapine and quetiapine, to be used off-label to benefit from their appetite/weight-increasing as well as sedative effects in case of extreme obsessive thoughts or physical hyperactivity. However, based on the current evidence, the potential value and risk-benefit ratio of antipsychotics in the treatment of patients with AN remains unclear.

Although almost all antipsychotics in other psychiatric disorders are known to have weight gain effects [14], prior studies and meta-analyses have shown mixed results for mainly adult patients with AN [15–25]. Over the past years, potential significant benefits of olanzapine regarding weight gain and improvement in psychological symptoms of AN were reported in two placebo-controlled, randomized clinical trials (RCTs) of adult patients with AN, including 34 day-hospital patients and 23 outpatients [15, 16], while two further RCTs found no significant benefits of olanzapine compared with placebo in 30 adult outpatients and 20 adolescents participating in a comprehensive eating disorders treatment program [17, 18]. Additionally, an outpatient-based RCT involving 21 participants found that quetiapine had no significant positive effects regarding weight gain and psychological symptoms of AN [19]. However, the latest and so far largest placebo-controlled RCT, including 152 adult outpatients with AN, found a statistically significantly greater increase in body mass index (BMI) for olanzapine vs. placebo (0.165 kg/m^2 per month), but no significant benefit on the improvement of psychological symptoms [20]. Moreover, while previous meta-analyses did not indicate that antipsychotics are effective in patients with AN [21–24], the most recent meta-analysis focusing only on studies with olanzapine reported a significantly greater increase in BMI for olanzapine vs. placebo in the four studies involving 239 adults (0.68 kg/m^2), but not in the three studies involving 65 adolescents with AN (0.66 kg/m^2) [25]. Furthermore, patients enrolled in RCTs are likely not fully representative of real-world patients. Previous open-label naturalistic studies about the effects of antipsychotics during inpatient treatment of 17 adults with AN have reported a significant increase in weight and a significant reduction in eating disorder symptoms, depression and anxiety for olanzapine [26] as well as significant differences in BMI and core psychopathology in eight severely ill inpatients with AN for quetiapine [27].

Due to the severity and frequent chronicity of AN and the lack of clarity about the role of antipsychotics in the management of individuals with AN, the aim of this study was to evaluate the impact of adjunctive antipsychotic medication (olanzapine or quetiapine) on weight gain and AN-related psychopathology in a large naturalistic sample of adult inpatients with AN. Based on the results of the largest RCT and most recent meta-analysis on this topic, we hypothesized a beneficial effect of antipsychotic augmentation, in particular on weight change.

Methods

Clinical records of consecutively admitted adults with AN were analyzed after receiving approval from the ethics committee of the Medical Faculty of the Ludwig-Maximilians-University Munich, Germany. For retrospective data analysis in this study, informed consent requirements were waived. Patients were treated naturalistically at the Schoen Clinic Roseneck (Prien am Chiemsee, Germany), a self-standing specialty clinic for patients with eating disorders, between 2014 and 2021. In line with the German S3-guideline for the treatment of AN [28], patients received a multimodal inpatient treatment program based on cognitive-behavioural therapy in group psychotherapy (100 min per session, up to three sessions per week) and individual psychotherapy (50 min per session, up to two sessions per week). In addition to general group psychotherapy, manualized eating disorder-specific group therapy was offered (nine 100 min sessions). The main elements included psychoeducation, behavioural and functional analysis, dealing with emotions and needs, body acceptance and relapse prevention. Additional therapy elements included supervised meals starting with 2000 kcal/d and increasing the daily calorie intake as needed to achieve a weight gain of 700–1000 g/week, body image exposure, social skills training, art therapy and weight-adapted exercise therapy. Nurses weighed patients up to twice a week in the morning under fasting conditions and dressed only in underwear. If patients failed to gain the targeted weight, further steps were taken, such as an increase in food intake and reduction in exercise, administration of high caloric supplements, or, in rare cases, temporary nasogastric tube feeding. Re-nutrition was accompanied by medical monitoring with internal medicine and neurological examinations, blood sampling (blood count, haematocrit, glucose, electrolytes, including phosphate, creatine kinase, creatinine, liver enzymes and thyroid hormones), electrocardiogram, cardiac ultrasound and bioelectrical impedance body weight analysis. Intervals for follow-up examinations were defined depending on the initial findings and the severity of the symptoms (underweight, bradycardia, orthostasis, purging behavior, etc.). For extremely underweight and malnourished patients with AN (BMI < 13 kg/m²) Koerner et al. [7] and Haas et al. [8] provided detailed information about the medical management and algorithm at the Schoen Clinic Roseneck.

Patient characteristics

Inclusion criteria were: (1) female patients ≥ 18 years, (2) meeting the International Classification of Diseases, 10th revision (ICD-10) criteria of AN (restricting or binge-purge type) and (3) received

inpatient treatment at the Schoen Clinic Roseneck between 2014 and 2021. Exclusion criteria for patients who received antipsychotic treatment were: (1) any other antipsychotic medication than olanzapine or quetiapine and (2) mirtazapine. Compared to selective serotonin reuptake inhibitors (SSRIs), mirtazapine was excluded due to its significant effect on weight gain [29, 30]. Exclusion criteria for patients who did not receive antipsychotics were: (1) any other psychopharmacotherapy. Patients were grouped into three categories: patients who were admitted with antipsychotic medication and continued to take olanzapine or quetiapine during inpatient treatment (antipsychotics continued group, APcont), patients who did not receive antipsychotic medication at baseline and started olanzapine or quetiapine during the course of inpatient treatment (antipsychotics new group, APnew) and patients who did not receive psychopharmacological treatment during inpatient treatment (no medication group, noMed).

Outcome measures

The co-primary outcome measures were BMI change (kg/m²) and average weekly weight change (kg/week). Height and weight were measured at admission as well as at discharge and were used to calculate BMI. Additionally, weight data were examined twice weekly (or more if needed) between admission and discharge. We averaged body weight data for each week to account for differences in weighing schedules.

Secondary outcome measures were AN-related psychopathology assessed using the German version of the Eating Disorder Inventory-2 (EDI-2) [31, 32]. The EDI-2 has 91 items that are answered on a six-point scale (1 = never to 6 = always) and 11 subscales. However, only two subscales assess AN-specific symptoms (drive for thinness and body dissatisfaction); thus, only these two subscales were used in the current analyses. Higher subscale sum scores indicate a stronger drive for thinness and body dissatisfaction, respectively.

Data analyses

All analyses were carried out using R 4.0.3 [33]. Groups were compared regarding baseline age, length of stay, BMI, drive for thinness and body dissatisfaction with analysis of variance. Changes in BMI, drive for thinness and body dissatisfaction from admission to discharge as a function of treatment groups were tested with linear mixed models using the *nlme* package [34]. Linear mixed models, as implemented in this study, can be understood as an extension to the analysis of variance for repeated measures that allows for missing values using maximum likelihood estimation. For all analyses, p-values < 0.05 were considered statistically significant without adjustment for multiplicity. Significant main effects were followed by Tukey-corrected Welch's t-tests.

As the naturalistically derived treatment groups naturally differed in several variables, we also examined changes in BMI, drive for thinness and body dissatisfaction from admission to discharge in groups that were matched to be similar in age, length of stay, baseline BMI and baseline EDI-2 subscale scores. Specifically, groups were matched pairwise based on a propensity score probit model with the nearest neighbours method using the *MatchIt* package [35]. For matched groups, all analyses were similar to previous analyses, except that comparisons were made pairwise.

Further, we explored BMI trajectories based on body weight between admission and discharge in the matched APcont vs. APnew groups as well as in the matched noMed vs. APnew groups. Due to large differences in antipsychotic treatment duration in our sample, we only report on the first 16 treatment weeks in our analyses, which was the median treatment duration and which was only coincidentally similar to the trial by Attia et al. [20]. Changes in BMI across treatment weeks were analyzed with growth curve analyses [36] using the *lme4* package [37]. Both linear and non-linear growth was modelled using orthogonal polynomials of time as fixed and random effects, respectively. We further added fixed effects of group as well as group × time interactions for linear and non-linear time terms. Then, we compared weight gain before and after antipsychotic medication onset within the APnew group and weight gain after the median week of onset in the APnew group compared to weight gain after the same time in the other two groups. We did this by pooling weight gain per week before and after the exact onset week on a patient-per-patient level for the within-group comparison. Then, we calculated the median onset week across all patients in the APnew group and compared weight gain prior to and after the median onset week across groups. Additionally, to identify moderators of the effect of antipsychotic medication on changes in BMI, we added age, BMI at admission, any psychiatric comorbidity, specific antipsychotic medication and other psychotropic medications as further variables to analyse timepoint × groups × moderators interactions.

Results

Patient and Treatment Characteristics

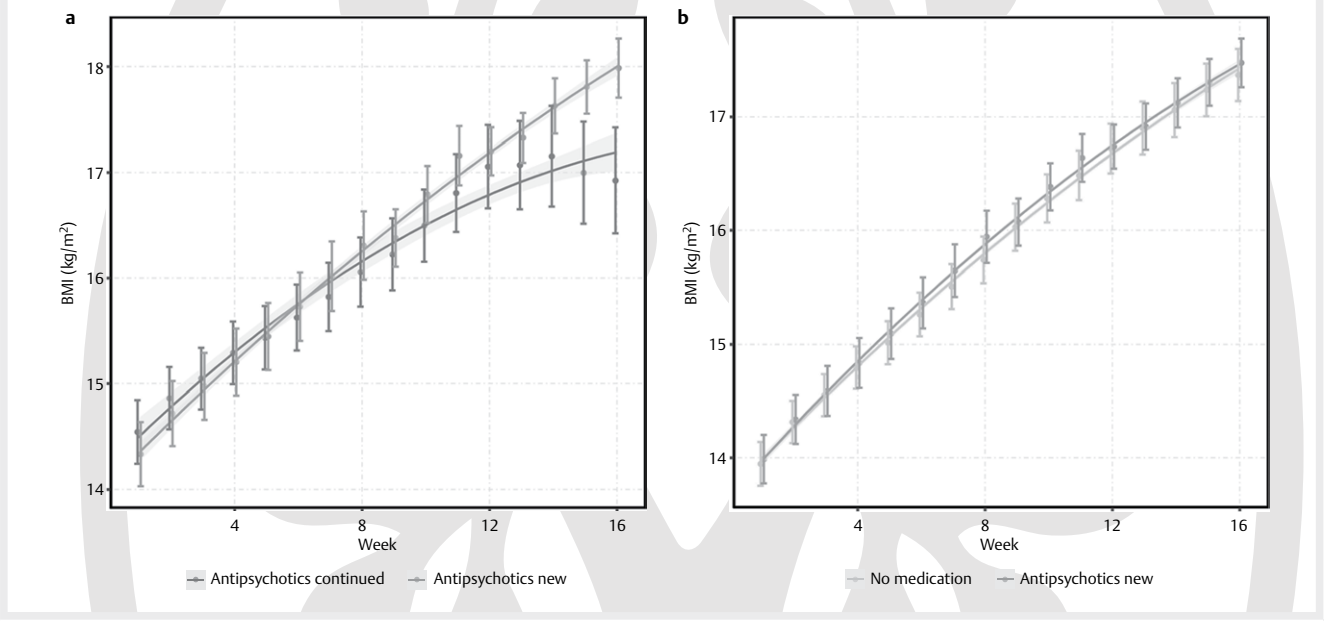
Data from 775 adult female inpatients were analyzed. At the time of admission, patients were, on average, 26.2 years (SD = 10.0 years) old, their mean BMI was 14.4 kg/m² (SD = 2.0 kg/m²) and their EDI-2 mean scores were 28.8 (SD = 8.7) for 'drive for thinness' and 37.2 (SD = 9.4) for 'body dissatisfaction' (▶ **Table 1**). The overall mean length of inpatient stay was 103.5 days (SD = 48.0 days) (▶ **Table 1**). Altogether, 60 (7.74 %) patients received antipsychotics prior to and during inpatient treatment, 108 (13.94 %) patients started antipsychotics during inpatient treatment and 607 (78.32 %) patients did not receive any adjunctive psychopharmacotherapy (▶ **Table 1**). The three groups differed significantly regarding baseline age (youngest in the APnew group, oldest in the APcont group), length of stay (longest in the APnew group), BMI (lowest in the APnew group, highest in the noMed group), EDI-2 subscale score drive for thinness (lowest in the noMed group, highest in the APcont group) and EDI-2 subscale score body dissatisfaction (lowest in the noMed group, highest in the APcont group) (▶ **Table 1**).

In the antipsychotic groups, olanzapine (n = 127, 75.60 %; dose: range = 1.25–15 mg, mean = 5.5 mg, SD = 3.1 mg; mg/kg body-weight: range = 0.03–0.5 mg, mean = 0.2 mg, SD = 0.1 mg) or quetiapine (n = 41, 24.40 %; dose: range = 12.5–500 mg, mean = 100.0 mg, SD = 97.7 mg; mg/kg body-weight: range = 0.3–10.2 mg, mean = 2.4 mg, SD = 2.2 mg) were included. In the APnew group, the mean time to antipsychotic onset was 5.8 weeks (range = 1–26 weeks, SD = 5.0 weeks). Other psychotropic medications in the antipsychotic groups included SSRIs (n = 79, 47.02 %).

▶ **Table 1** Demographic and illness characteristics of the full sample.

Variables	Total (*N* = 775)		No medication (*N* = 607)		Antipsychotics continued (*N* = 60)		Antipsychotics new (*N* = 108)		*p-value*	η_p^2
	n	*Mean (SD)*	*n*	*Mean (SD)*	*n*	*Mean (SD)*	*n*	*Mean (SD)*		
Age (years)	775	26.2 (10.0)	607	26.2 (10.1)[a]	60	29.6 (11.4)[a,b]	108	24.3 (8.0)[b]	.005	0.01
Length of stay (days)	775	103.5 (48.0)	607	101.0 (46.7)[a]	60	101.0 (50.1)[b]	108	119.4 (51.1)[a,b]	.001	0.02
Body mass index (kg/m²)	775	14.4 (2.0)	607	14.5 (1.9)[a]	60	14.3 (2.2)	108	13.9 (2.0)[a]	.020	0.01
Drive for thinness (EDI-2)	659	28.8 (8.7)	584	27.9 (8.7)[a,b]	54	33.0 (6.7)[a]	103	31.8 (8.8)[b]	<.001	0.04
Body dissatisfaction (EDI–2)	659	37.2 (9.4)	584	36.0 (9.1)[a,b]	54	42.0 (9.8)[a]	103	41.3 (8.8)[b]	<.001	0.06

Notes. EDI-2 = Eating Disorder Inventory-2; SD = standard deviation. Superscripts reflect Tukey-corrected significant differences between unmatched groups.



▶ **Fig. 1** **a** BMI trajectories across treatment weeks in the matched antipsychotic continuation vs. new antipsychotic initiation group. Error bars represent the standard error of the mean. BMI: body mass index. **b** BMI trajectories across treatment weeks in the matched no psychotropic medication vs. new antipsychotic initiation group. Error bars represent the standard error of the mean. BMI: body mass index.

The three subsamples matched on age, length of stay, baseline BMI and baseline EDI-2 subscale scores resulted in the following groups: noMed (n = 54) vs. APcont (n = 54), noMed (n = 96) vs. APnew (n = 96) and APcont (n = 54) vs. APnew (n = 54).

Primary Outcome Measures

Changes in body mass index from admission to discharge

In the entire sample, a significant time × group interaction was observed ($F_{(2,772)} = 4.53$, $p = 0.011$). The noMed group and the APnew group had a larger BMI increase from admission to discharge than the APcont group (noMed vs. APcont: $t_{(772)} = -2.14$, $p = 0.033$; APnew vs. APcont: $t_{(772)} = 3.00$, $p = 0.003$), without differences between noMed and APnew groups ($t_{(772)} = 1.85$, $p = 0.065$). When matched noMed vs. APcont groups and APnew vs. APcont groups were compared, there was no significant interaction ($F_{(1,106)} = 0.51$, $p = 0.477$; $F_{(1,106)} = 3.85$, $p = 0.052$) as well as for comparing matched noMed vs. APnew groups ($F_{(1,190)} = 0.01$, $p = 0.932$).

Body mass index trajectories across treatment weeks

To explore whether the onset of antipsychotic medication during inpatient treatment resulted in changes in BMI trajectories, we analyzed weekly BMI data. We compared matched APnew with APcont and noMed groups separately to identify differences in weight trajectories between groups. When comparing the APnew and APcont groups, both followed a nonlinear BMI trajectory (main week² effect: $F_{(1,72.03)} = 10.47$, $p = 0.002$; ▶ **Fig. 1a**), which continued more steeply after around week 12 for the APnew compared to the APcont group (week × group interaction: $F_{(1,86.10)} = 6.74$, $p = 0.011$). When comparing the matched APnew and noMed groups, both groups followed a slightly nonlinear trajectory (week²: $F_{(1,150.78)} = 16.06$, $p < 0.001$), which did not differ statistically significantly (all group main effects and week × group interactions $p = 0.153$; ▶ **Fig. 1b**).

▲ **Table 2** Mean weight gain in kg prior to and after median antipsychotic onset week* during hospitalization.

Treatment Group	Pre median onset week				Post median onset week				Within group comparison	APnew vs. APcont	APnew vs. noMed	APcont vs. noMed
	mean weight gain (kg)	SE	df	95 % CI	mean weight gain (kg)	SE	df	95 % CI	*p*-value	*p*-value	*p*-value	*p*-value
No medication (noMed)	0.76	0.00	774	0.76, 0.77	1.01	0.00	748	1.01, 1.02	$p < 0.001$	$p \leq 0.001$	$p \leq 0.001$	$p = 0.835$
Antipsychotics continued (APcont)	0.76	0.01	772	0.74, 0.78	1.01	0.01	748	0.99, 1.03				
Antipsychotics new (APnew)	0.64	0.00	772	0.63, 0.66	1.01	0.00	748	1.00, 1.03				

*Median week calculation was based on the new antipsychotic initiation group: 5.8 ± 5.0 weeks; APnew: antipsychotics newly initiated during inpatient treatment; APcont: pre-admission antipsychotics continued; noMed: no medication.

Mean weekly weight gain before and after the median antipsychotic onset week

To further explore weight change trajectories between groups, we calculated the median antipsychotic onset week in the APnew group (week 5.8 ± 5.0 weeks; i. e., at week 6, 50 % of the APnew sample were taking antipsychotic medications). We then calculated the patients' individual mean weight gains prior to and after the median onset week within each group for comparison. A significant interaction effect was found ($F_{(2,748)} = 43.14$, $p < 0.001$), indicating that groups differed in their weekly weight gain before and after week 6 (▶ **Table 2**). Follow-up tests revealed that compared to APcont, APnew showed a greater increase in weight from before to after week 6 than APcont ($t_{(748)} = 5.82$, $p \leq 0.001$) and noMed ($t_{(748)} = 9.25$, $p \leq 0.001$) groups, whereas the APcont and noMed groups did not differ from each other ($t_{(748)} = 0.21$, $p = 0.835$; ▶ **Fig. 2**).

Moderators of the effect of antipsychotic medication on changes in body mass index

Moderator analyses revealed no moderation of the effect of antipsychotic treatment on BMI change, neither by age, BMI at admission or any comorbidity in the full sample (three-way interactions of timepoint × groups × moderator, all $F_{(2,769)} \leq 1.71$, $p \geq 0.181$) nor antipsychotic type and other psychotropic medication in the APnew group specifically (timepoint × moderator; both $F_{(1,106)} \leq 0.69$, $p \geq 0.339$).

Secondary Outcome Measures

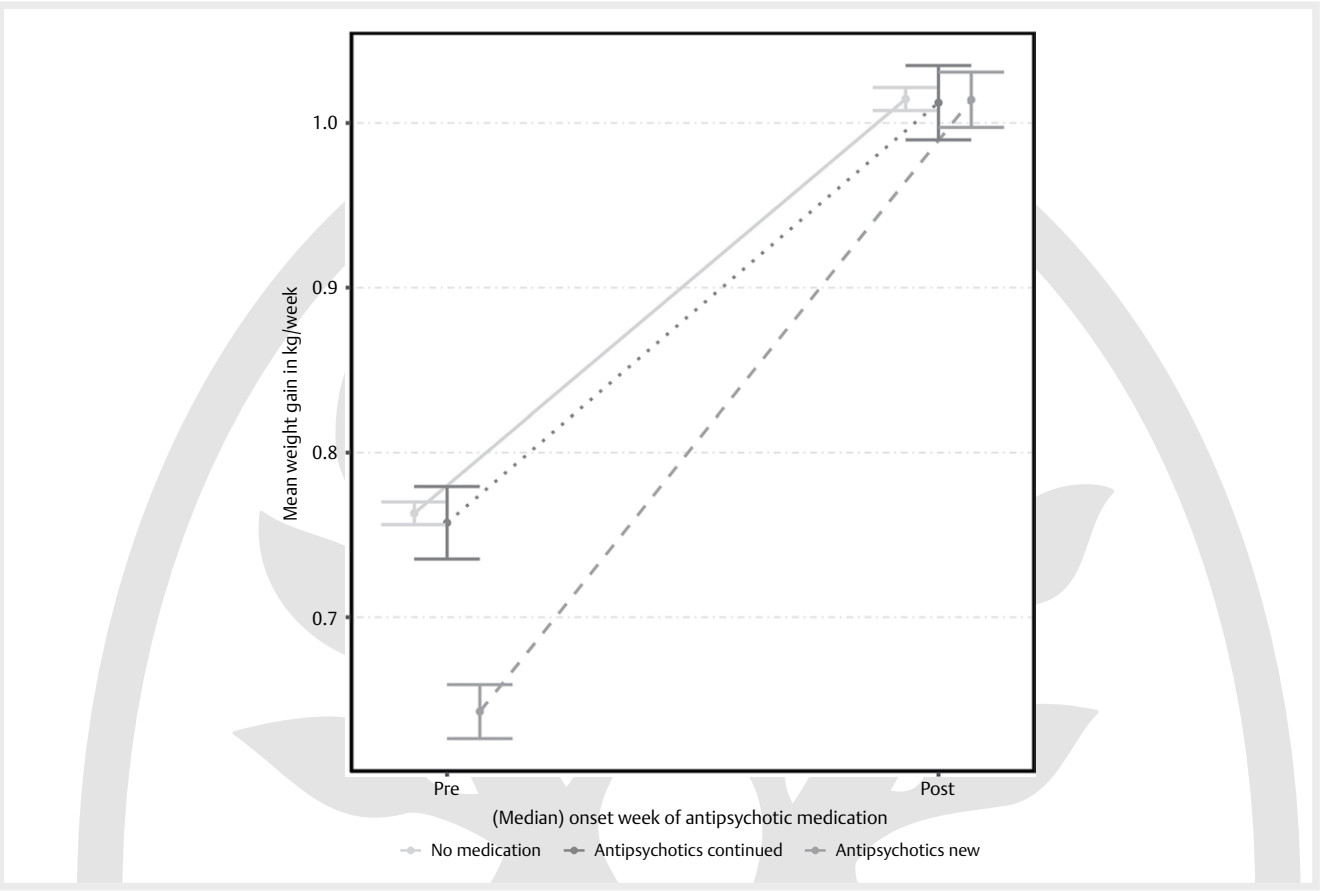
Changes in Eating Disorder Inventory-2 subscale scores from admission to discharge

In the full sample, no effect of antipsychotic medication on change in drive for thinness from admission to discharge was observed ($F_{(2,686)} = 2.13$, $p = 0.120$). However, when comparing matched noMed vs. APcont groups, the noMed group had a larger decrease in drive for thinness than the APcont group ($F_{(1,98)} = 6.52$, $p = 0.012$), but effects remained statistically non-significant for both other matched comparisons (matched noMed vs. APnew: $F_{(1,171)} = 1.88$, $p = 0.172$; matched APcont vs. APnew: $F_{(1,91)} = 2.69$, $p = 0.104$).

Likewise, no statistically significant difference in the change in body dissatisfaction from admission to discharge was found when analysing the complete sample ($F_{(2,686)} = 2.07$, $p = 0.127$). When comparing the matched noMed vs. APcont groups, again the noMed group had a larger decrease in body dissatisfaction over time than the APcont group ($F_{(1,98)} = 6.95$, $p = 0.010$), but no statistically significant effects emerged in the other comparisons (matched noMed vs. APnew: $F_{(1,171)} = 0.96$, $p = 0.328$; matched APcont vs. APnew: $F_{(1,91)} = 2.22$, $p = 0.140$).

Discussion

Under the naturalistic conditions of this study, almost 22 % of adult female inpatients with AN received antipsychotics (olanzapine or quetiapine) with overall no greater increase in weight or substantially better improvement in core AN-related psychopathology than psychopharmacologically untreated inpatients. Nevertheless, a slightly higher weight gain was seen after the onset of either olanzapine or quetiapine during the course of inpatient treatment com-



▶ **Fig. 2** A full sample comparison of the mean weekly weight gain before and after the median antipsychotic onset week in the new antipsychotic initiation group. Error bars represent the standard error of the mean. The median week of onset of antipsychotic medication use was calculated in the group newly initiating antipsychotics (5.8 ± 5.0 weeks) and, for comparison, applied to the continued antipsychotic and no medication groups.

pared to the group of patients who continued pre-admission antipsychotic treatment.

When comparing the two groups with antipsychotic treatment to those without any medication, those treated with antipsychotics had significantly lower BMI and significantly higher psychopathology scores at admission, indicating that antipsychotics were administered to patients with more severe AN, as seen before in a naturalistic adolescent inpatient sample [38]. Therefore, we hypothesize that the lack of differences in treatment outcomes may be partially explained by baseline differences in disorder severity and that antipsychotics may have helped to achieve comparable treatment outcomes. We further hypothesize that this effect seemed to be achieved in the initial phase after the onset of antipsychotics but diminished after a certain period, as in further comparison of the antipsychotic-treated groups a greater increase in weight was seen in patients who started an antipsychotic medication during the course of inpatient treatment than in patients continuing antipsychotic medication.

Based on previous findings [21–25] and the results of this naturalistic study, antipsychotics seem to have rather small effects on weight and AN-related psychopathology trajectories in inpatients with AN. This result can be attributed to various factors. First, medication effects might be more difficult to detect in a highly controlled inpatient treatment program for AN, whereas effects might be more clearly detectable in a less supervised outpatient treatment setting. In the randomized controlled study by Attia et al. [20] a modest therapeutic effect of olanzapine on weight was observed in adult outpatients with AN. Second, the differences between patients with AN and patients with other psychiatric disorders, who generally gain weight during antipsychotic treatment, especially on olanzapine and quetiapine [39], could be that one of the core behaviours of patients with AN is to successfully control hunger and restricting food intake and therefore not to gain weight despite possible appetite-stimulating effects of antipsychotics [30, 40]. Third, there might be other and still underresearched moderating factors for the effects of antipsychotic medications. De Young et al. [41] reported that there is a subgroup of patients with AN who suffer from delusional thinking with respect to their eating disorder cognitions. Future studies could examine the degree of delusional-like thinking of patients at baseline and compare antipsychotic effects between patients with and without delusional thinking. Other moderating variables could include different levels of physical activity [3, 4] that affect weight gain, and that could be a treatment target for antipsychotics in patients with AN and insufficient weight gain.

The results of this study need to be interpreted within the framework of its strengths and limitations. Strengths include the large

sample size and examining patients in a usual-care setting, which further helps to clarify if and in whom adjunctive antipsychotics might be useful in treating patients with AN. In RCTs, the problem is usually recruitment, as patients with AN have a fear of weight gain and are not interested or not willing to take medications with the potential of weight gain effects. Additionally, inclusion and exclusion criteria are quite strict to get at a better signal-to-noise separation but also because of the potential harm of medications in this vulnerable population. For example, in the previous randomized controlled study by Attia et al. [16], 603 patients had to be contacted to include 23 in the study. In that sense, our naturalistic treatment study is likely more generalizable to usual care settings and populations. Nevertheless, limitations include first the fact that this study was not a randomized-controlled trial but a naturalistic study. Second, this was a retrospective study, relying on data collected as part of usual care. Third, the AN diagnosis was made clinically, albeit based on ICD-10 criteria and by teams specialized in the treatment of AN. Fourth, although AN-related psychopathology via the EDI-2 was part of the usual care data collection, several important variables were missing, including AN subtype, specific psychiatric comorbidity, severity of comorbidities, duration and weight/AN-related psychopathology effect of pre-admission antipsychotic treatment. Fifth, this sample was exclusively female, so we cannot comment on antipsychotic effects on males with AN. Sixth, as routine data were retrospectively analyzed, there was insufficient information to report about safety, tolerability, as well as adherence to olanzapine or quetiapine. Especially, analyses of serum levels of the substances were obtained occasionally during routine treatment, but not in a standardized manner, so no sufficient data set was available that could have been meaningfully evaluated. Seventh, the dosing of olanzapine and quetiapine might have been too low to reach significant effects. Eighth, we cannot comment on the effects of other antipsychotics, especially aripiprazole and risperidone, that have also been used in patients with AN [42–45], although results are unlikely to be largely different, as all currently available antipsychotics share a similar mechanism of action. Ninth, this study was conducted in an inpatient setting specialized for the treatment of patients with eating disorders. Since the AN-specific non-pharmacologic milieu, behavioural and psychological treatment effects may have created a ceiling effect, we cannot exclude the efficacy of antipsychotics in less specialized settings. Finally, we cannot comment on the effects of antipsychotics initiated in patients with AN treated in outpatient settings or long-term outcomes post-hospital discharge. Nevertheless, despite these limitations, this is a large naturalistic study that assessed not only body weight but also AN-related psychopathology during inpatient treatment with vs. without augmentation of olanzapine or quetiapine, casting doubt on the effectiveness of antipsychotics beyond at least specialized inpatient care for AN.

In conclusion, our study underlines that antipsychotics are frequently prescribed during inpatient treatment for patients with AN, indicating the need for additional care options in patients with suboptimal treatment results. However, at least based on these data, there is no clear benefit of antipsychotic medication on weight and AN-related psychopathology treatment outcomes in adult female inpatients with AN in a naturalistic setting. Newly initiated antipsychotic treatment had better weight gain trajectories only compared to continuation of pre-admission antipsychotic treatment in whom the initial weight gain effect was not known. More studies, both randomized and conducted in naturalistic inpatient and outpatient settings, are needed to determine the potential benefits and adverse effects of antipsychotic use in patients with AN, both overall as well as in specific subgroups of patients that may be particularly responsive to antipsychotic treatment.

Acknowledgment

The authors would like to thank Adrian Meule for his efforts in data analysis.

Funding

The authors received no financial support for this study.

Conflict of Interest

The authors TB, DK, VH and UV declare that they have no competing interests. CUC has been a consultant and/or advisor to or has received honoraria from: AbbVie, Acadia, Adcock Ingram, Alkermes, Allergan, Angelini, Aristo, Biogen, Boehringer-Ingelheim, Bristol-Meyers Squibb, Cardio Diagnostics, Cerevel, CNX Therapeutics, Compass Pathways, Darnitsa, Delpor, Denovo, Gedeon Richter, Hikma, Holmusk, IntraCellular Therapies, Jamjoom Pharma, Janssen/J&J, Karuna, LB Pharma, Lundbeck, MedAvante-ProPhase, MedInCell, Merck, Mindpax, Mitsubishi Tanabe Pharma, Mylan, Neurocrine, Neurelis, Newron, Noven, Novo Nordisk, Otsuka, Pharmabrain, PPD Biotech, Recordati, Relmada, Reviva, Rovi, Sage, Seqirus, SK Life Science, Sumitomo Pharma America, Sunovion, Sun Pharma, Supernus, Tabuk, Takeda, Teva, Tolmar, Vertex and Viatris. He provided expert testimony for Janssen and Otsuka. He served on a Data Safety Monitoring Board for Compass Pathways, Denovo, Lundbeck, Relmada, Reviva, Rovi, Supernus and Teva. He has received grant support from Janssen and Takeda. He received royalties from UpToDate and is also a stock option holder of Cardio Diagnostics, Kuleon Biosciences, LB Pharma, Mindpax and Quantic.

References

[1] Solmi M, Radua J, Olivola M et al. Age at onset of mental disorders worldwide: Large-scale meta-analysis of 192 epidemiological studies. Mol Psychiatry 2022; 27: 281–295

[2] Treasure J, Zipfel S, Micali N et al. Anorexia nervosa. Nat Rev Dis Primers 2015; 1: 15074

[3] Grosser J, Hofmann T, Stengel A et al. Psychological and nutritional correlates of objectively assessed physical activity in patients with anorexia nervosa. Eur Eat Disord Rev 2020; 28: 559–570

[4] Lehmann CS, Hofmann T, Elbelt U et al. The role of objectively measured, altered physical activity patterns for body mass index change during inpatient treatment in female patients with anorexia nervosa. J Clin Med 2018; 7: 289

[5] Solmi M, Monaco F, Højlund M et al. Outcomes in people with eating disorders: A transdiagnostic and disorder-specific systematic review, meta-analysis and multivariable meta-regression analysis. World Psychiatry 2024; 23: 124–138

[6] Chan JKN, Correll CU, Wong CSM et al. Life expectancy and years of potential life lost in people with mental disorders: A systematic review and meta-analysis. eClinicalMedicine 2023; 65: 102294

[7] Koerner T, Haas V, Heese J et al. Outcomes of an accelerated inpatient refeeding protocol in 103 extremely underweight adults with anorexia nervosa at a specialized clinic in Prien, Germany. J Clin Med 2020; 9: 1535

[8] Haas V, Kohn M, Körner T et al. Practice-based evidence and clinical guidance to support accelerated re-nutrition of patients with anorexia nervosa. J Am Acad Child Adolesc Psychiatry 2021; 60: 555–561

[9] Monteleone AM, Pellegrino F, Croatto G et al. Treatment of eating disorders: A systematic meta-review of meta-analyzes and network meta-analyzes. Neurosci Biobehav Rev 2022; 142: 104857

[10] Herpertz S, Fichter M, Herpertz-Dahlmann B et al. Gemeinsame S3-Leitlinie "Diagnostik und therapie der essstörungen" [Joint German Guideline "Diagnosis and treatment of eating disorders"]. Berlin: Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften e.V. (AWMF); 2018

[11] National Guideline Alliance (UK). Eating disorders: Recognition and treatment. London: National Institute for Health and Care Excellence (NICE); 2017 updated 2020

[12] Crone C, Fochtmann LJ, Attia E et al. The American Psychiatric Association Practice Guideline for the treatment of patients with eating disorders. Am J Psychiatry 2023; 180: 167–171

[13] Himmerich H, Lewis YD, Conti C et al. World Federation of Societies of Biological Psychiatry (WFSBP) guidelines update 2023 on the pharmacological treatment of eating disorders. World J Biol Psychiatry 2023; 24: 1–64

[14] Bak M, Fransen A, Janssen J et al. Almost all antipsychotics result in weight gain: A meta-analysis. PLoS One 2014; 9: e94112

[15] Bissada H, Tasca GA, Barber AM et al. Olanzapine in the treatment of low body weight and obsessive thinking in women with anorexia nervosa: A randomized, double-blind, placebo-controlled trial. Am J Psychiatry 2008; 165: 1281–1288

[16] Attia E, Kaplan AS, Walsh BT et al. Olanzapine versus placebo for out-patients with anorexia nervosa. Psychol Med 2011; 41: 2177–2182

[17] Brambilla F, Garcia CS, Fassino S et al. Olanzapine therapy in anorexia nervosa: Psychobiological effects. Int Clin Psychopharmacol 2007; 22: 197–204

[18] Kafantaris V, Leigh E, Hertz S et al. A placebo-controlled pilot study of adjunctive olanzapine for adolescents with anorexia nervosa. J Child Adolesc Psychopharmacol 2011; 21: 207–212

[19] Powers PS, Klabunde M, Kaye W. Double-blind placebo-controlled trial of quetiapine in anorexia nervosa. Eur Eat Disord Rev 2012; 20: 331–334

[20] Attia E, Steinglass JE, Walsh BT et al. Olanzapine versus placebo in adult outpatients with anorexia nervosa: A randomized clinical trial. Am J Psychiatry 2019; 176: 449–456

[21] Kishi T, Kafantaris V, Sunday S et al. Are antipsychotics effective for the treatment of anorexia nervosa? Results from a systematic review and meta-analysis. J Clin Psychiatry 2012; 73: e757–e766

[22] Lebow J, Sim LA, Erwin PJ et al. The effect of atypical antipsychotic medications in individuals with anorexia nervosa: A systematic review and meta-analysis. Int J Eat Disord 2013; 46: 332–339

[23] de Vos J, Houtzager L, Katsaragaki G et al. Meta-analysis on the efficacy of pharmacotherapy versus placebo on anorexia nervosa. J Eat Disord 2014; 2: 27

[24] Dold M, Aigner M, Klabunde M et al. Second-generation antipsychotic drugs in anorexia nervosa: A meta-analysis of randomized controlled trials. Psychother Psychosom 2015; 84: 110–116

[25] Han R, Bian Q, Chen H. Effectiveness of olanzapine in the treatment of anorexia nervosa: A systematic review and meta-analysis. Brain Behav 2022; 12: e2498

[26] Barbarich NC, McConaha CW, Gaskill J et al. An open trial of olanzapine in anorexia nervosa. J Clin Psychiatry 2004; 65: 1480–1482

[27] Bosanac P, Kurlender S, Norman T et al. An open-label study of quetiapine in anorexia nervosa. Hum Psychopharmacol 2007; 22: 223–230

[28] Resmark G, Herpertz S, Herpertz-Dahlmann B et al. Treatment of anorexia nervosa-new evidence-based guidelines. J Clin Med 2019; 8: 153

[29] Watanabe N, Omori IM, Nakagawa A et al. Safety reporting and adverse-event profile of mirtazapine described in randomized controlled trials in comparison with other classes of antidepressants in the acute-phase treatment of adults with depression: Systematic review and meta-analysis. CNS Drugs 2010; 24: 35–53

[30] Pillinger T, Howes OD, Correll CU et al. Antidepressant and antipsychotic side-effects and personalised prescribing: A systematic review and digital tool development. Lancet Psychiatry 2023; 10: 860–876

[31] Garner DM. Eating Disorder Inventory-2: Professional Manual. Psychological Assessment Resources; 1991

[32] Paul T, Thiel A. Eating Disorder Inventory-2: Deutsche Version. Hogrefe Verlag; 2005

[33] R Core Team. R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing; 2021

[34] Pinheiro J, Bates D, DebRoy S et al. nlme: Linear and Nonlinear Mixed Effects Models. R package version 3.1–153

[35] Ho D, Imai K, King G et al. MatchIt: Nonparametric preprocessing for parametric causal inference. J Stat Softw 2011; 42: 1–28

[36] Mirman D. Growth Curve Analysis and Visualization Using R. Chapman and Hall; 2014

[37] Bates D, Mächler M, Bolker B et al. Fitting linear mixed-effects models using lme4. J Stat Softw 2015; 67: 1–48

[38] Frank B, Arnold S, Jaite C et al. Antipsychotic effects on anthropometric outcomes in anorexia nervosa: A retrospective chart review of hospitalized children and adolescents. J Eat Disord 2023; 11: 151

[39] Solmi M, Murru A, Pacchiarotti I et al. Safety, tolerability, and risks associated with first- and second-generation antipsychotics: A state-of-the-art clinical review. Ther Clin Risk Manag 2017; 13: 757–777

[40] Correll CU, Lencz T, Malhotra AK. Antipsychotic drugs and obesity. Trends Mol Med 2011; 17: 97–107

[41] De Young K, Bottera A, Kambanis E et al. Delusional intensity as a prognostic indicator among individuals with severe to extreme anorexia nervosa hospitalized at an acute medical stabilization program. Int J Eat Disord 2022; 55: 215–222

[42] Pruccoli J, Bergonzini L, Pettenuzzo I et al. The role of risperidone in the treatment of children and adolescents with anorexia nervosa. J Psychopharmacol 2023; 37: 545–553

[43] Hagman J, Gralla J, Sigel E et al. A double-blind, placebo-controlled study of risperidone for the treatment of adolescents and young adults with anorexia nervosa: A pilot study. J Am Acad Child Adolesc Psychiatry 2011; 50: 915–924

[44] Tahıllıoğlu A, Özcan T, Yüksel G et al. Is aripiprazole a key to unlock anorexia nervosa?: A case series. Clin Case Rep 2020; 8: 2827–2834

[45] Frank GK, Shott ME, Hagman JO et al. The partial dopamine D2 receptor agonist aripiprazole is associated with weight gain in adolescent anorexia nervosa. Int J Eat Disord 2017; 50: 447–450

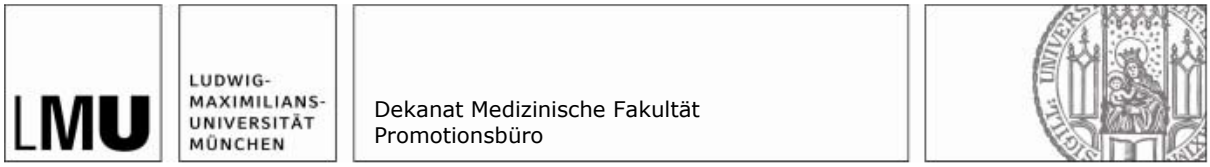
Danksagung

Mein Dank gilt Frau Professor Dr. med. Rebecca Schennach und Herrn Professor Dr. med. Ulrich Voderholzer für die Ermöglichung und Betreuung dieser Dissertation.

Besonderer Dank gilt Herrn Dr. rer. biol. hum. Dipl.-Psych. Norbert Quadflieg und Herrn Professor Dr. rer. nat. David Kolar für die umfangreiche statistische Arbeit.

Ich möchte mich außerdem bei den beiden Arbeitsgruppen bedanken, die zu den erfolgreichen Publikationen und damit dem Gelingen dieser Dissertation unterstützend und wohlwollend beigetragen haben.

Eidesstattliche Versicherung



Eidesstattliche Versicherung

Bauman, Tabea

Name, Vorname

Ich erkläre hiermit an Eides statt, dass ich die vorliegende Dissertation mit dem Titel

Einflussfaktoren auf die Wirksamkeit einer stationären Behandlung der Anorexia nervosa

selbständig verfasst, mich außer der angegebenen keiner weiteren Hilfsmittel bedient und alle Erkenntnisse, die aus dem Schrifttum ganz oder annähernd übernommen sind, als solche kenntlich gemacht und nach ihrer Herkunft unter Bezeichnung der Fundstelle einzeln nachgewiesen habe.

Ich erkläre des Weiteren, dass die hier vorgelegte Dissertation nicht in gleicher oder in ähnlicher Form bei einer anderen Stelle zur Erlangung eines akademischen Grades eingereicht wurde.

München, 29.01.2026 — Tabea Bauman

Ort, Datum — Unterschrift

Erklärung der Übereinstimmung

LMU LUDWIG-MAXIMILIANS-UNIVERSITÄT MÜNCHEN

Dekanat Medizinische Fakultät
Promotionsbüro

Erklärung zur Übereinstimmung der gebundenen Ausgabe der Dissertation mit der elektronischen Fassung

Bauman, Tabea

Name, Vorname

Hiermit erkläre ich, dass die elektronische Version der eingereichten Dissertation mit dem Titel:

Einflussfaktoren auf die Wirksamkeit einer stationären Behandlung der Anorexia nervosa

in Inhalt und Formatierung mit den gedruckten und gebundenen Exemplaren übereinstimmt.

München, 29.01.2026 — Tabea Bauman

Ort, Datum — Unterschrift